Malaria

GUIDELINES

Inpatient management of diabetic foot problems: summary of NICE guidance

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Foot problems that are related to diabetes ("diabetic foot" problems) affect a substantial number of people with diabetes, and 15% of people with diabetes will have a foot ulcer at some point in their lives. Diabetic foot ulcers precede more than 80% of amputations in people with diabetes and are the most common cause of non-traumatic limb amputation in the United Kingdom. Delays in diagnosis and management of diabetic foot problems increase morbidity and mortality, contribute to a higher amputation rate,[1] and seriously affect patients' quality of life—for example, by reducing mobility, leading to loss of employment, depression, and damage to or loss of limbs. Diabetic foot problems have a financial impact on the NHS through increased outpatient costs and bed occupancy and prolonged stays in hospital.

This article summarises the most recent recommendations in a short clinical guideline from the National Institute for Health and Clinical Excellence (NICE) on the management of diabetic foot problems in inpatients.[2]

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on bmj.com.

Multidisciplinary foot care team

- Each hospital should have a care pathway for patients with diabetic foot problems who need inpatient care. This care pathway is for people with diabetes who have *(a)* an ulcer, blister, or break in the skin of the foot; *(b)* inflammation or swelling of any part of the foot or any sign of infection; *(c)* unexplained pain in the foot; *(d)* fracture or dislocation in the foot, with no preceding history of substantial trauma; or *(e)* gangrene of all or part of the foot.[3] The multidisciplinary foot care team should consist of healthcare professionals with the specialist skills and competencies necessary to deliver inpatient care to such patients. The team should normally include a diabetologist, a surgeon with the relevant expertise in managing diabetic foot problems, a diabetes nurse specialist, a podiatrist, and a tissue viability nurse, with access to other specialist services necessary for delivering the care outlined in the guideline.

- The role of the multidisciplinary foot care team is to:
  - -Assess and treat the patient's diabetes, including interventions to minimise the patient's risk of cardiovascular events, and any interventions for pre-existing chronic kidney disease or anaemia (refer to the NICE guidance on chronic kidney disease[4] and on managing anaemia in people with chronic kidney disease[5])
  - -Assess, review, and evaluate the patient's response to initial medical, surgical, and diabetes management
  - -Assess the foot and determine the need for specialist wound care, debridement, pressure off-loading, and/or other surgical interventions
  - -Assess the patient's pain and determine the need for treatment and access to specialist pain services
  - -Perform a vascular assessment to determine the need for further interventions
  - -Review the treatment of any infection
  - -Determine the need for interventions to prevent the deterioration and development of Achilles tendon contractures and other foot deformities
  - -Perform an orthotic assessment and treat to prevent recurrent disease of the foot
  - -Refer patients for physiotherapy where appropriate
  - -Arrange discharge planning, which should include arranging for the patient to be assessed and managed in primary and/or community care and followed up by specialist teams (refer to the NICE guidance on preventing and managing foot problems in type 2 diabetes[6]).

Information and support for patients

- The patient should have a named contact—who

This is one of a series of *BMJ* summaries of new guidelines based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists. Further information about the guidance, a list of members of the guideline development group, and the supporting evidence statements are in the full version on bmj.com.

may be a member of the multidisciplinary foot care team or someone with a specific role as an inpatient pathway coordinator—who will follow the inpatient care pathway and be responsible for:
-Offering patients information about their diagnosis, treatment, and the care and support they can expect
-Communicating relevant clinical information, including documentation before discharge, within and among hospitals and to primary and/or community care.

Initial examination and assessment

- Remove the patient's shoes, socks, bandages and dressings and examine their feet for evidence of the following and document any identified new and existing diabetic foot problems:
-Deformity
-Ulceration
-Inflammation and/or infection
-Ischaemia
-Neuropathy
-Charcot arthropathy.

- Obtain urgent advice from an appropriate specialist if any of the following are present:
-Fever or any other signs or symptoms of systemic sepsis
-Clinical concern about possible deep seated infection (for example, palpable gas)
-Limb ischaemia.

Initial care (within 24 hours)

- For a patient with diabetic foot problems being admitted to hospital or already in hospital but with newly detected diabetic foot problems, refer to the multidisciplinary foot care team within 24 hours of the initial examination of the patient's feet. Transfer the responsibility of care to a consultant member of the multidisciplinary foot care team if a diabetic foot problem is the dominant clinical factor for inpatient care.

Investigation of suspected diabetic foot infection

- If osteomyelitis is suspected and initial radiography does not confirm the presence of osteomyelitis, use magnetic resonance imaging (if this is contraindicated, consider white blood cell scanning instead).

Management of diabetic foot infection

- Each hospital should have antibiotic guidelines for management of diabetic foot infection.

Management of diabetic foot ulcers

- When choosing wound dressings, the multidisciplinary foot care team should take into account their clinical assessment of the wound, the patient's preference, and the clinical circumstances, and they should use wound dressings with the lowest acquisition cost.
- Do not routinely use negative pressure wound therapy, but consider this in the context of a clinical trial or as rescue therapy (when the only other option is amputation).

- Do not offer the following treatments for inpatient management, unless as part of a clinical trial:
-Dermal or skin substitutes
-Electrical stimulation therapy, autologous platelet-rich plasma gel, regenerative wound matrices, and deltaparin
-Growth factors (granulocyte colony stimulating factor, platelet derived growth factor, epidermal growth factor, and transforming growth factor β)
-Hyperbaric oxygen therapy.

Overcoming barriers

No agreed treatment pathways or service models exist for management of diabetic foot problems in inpatients. Current practice is thought to vary considerably, owing to a range of factors, including differences in the organisation of care from the time of acute care admission to discharge. However, prompt identification of diabetic foot problems, with appropriate treatment and referral, can reduce associated morbidity (including rates of amputation) and mortality.[1]

The NICE recommendations should facilitate the provision of timely and coordinated care for people with diabetic foot problems who are admitted to hospital (either for the primary diabetic foot problem or for other reasons but who also have a diabetic foot problems). They outline what care should be provided and how this should be organised, specifying key functions and members of the multidisciplinary team.

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Previous articles in this series

- Diagnosis, assessment, and management of harmful drinking and alcohol dependence (*BMJ* 2011;342:d700)
- Diagnosis and assessment of food allergy in children and young people (*BMJ* 2011;342:d747)
- Management of generalised anxiety disorder in adults (*BMJ* 2011;342:c7460)
- Sedation for diagnostic and therapeutic procedures in children and young people (*BMJ* 2010;341:c6819)
- Management of bedwetting in children and young people (*BMJ* 2010;341:c5399)

LESSON OF THE WEEK

Pituitary infarction: a potentially fatal cause of postoperative hyponatraemia and ocular palsy

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EDITORIAL by Kerr and Wierman

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Postsurgical hyponatraemia with ocular palsy suggests hypopituitarism from haemorrhagic infarction of an unsuspected pituitary adenoma

Hyponatraemia is the most common electrolyte disturbance in hospital inpatients. Accurate assessment of the cause and appropriate treatment are crucial.[1] Hyponatraemia after orthopaedic surgery is often caused by hypotonic fluids and factors that increase secretion of antidiuretic hormone, and it resolves with fluid restriction.[2 3] But this is not always the case, and other causes should be considered. We describe a patient with haemorrhagic infarction of a pituitary adenoma and symptoms of blurred vision from oculoparesis who presented shortly after hip replacement, in whom hyponatraemia was caused by cortisol deficiency.

Case report

A 58 year old man presented with a drooping right eyelid and diplopia nine days after a right total hip replacement. He had previously been fit and well requiring no regular drugs other than analgesia.

Surgery was performed under spinal anaesthesia. Blood pressure before surgery was 139/91 mm Hg. Within 30 minutes of anaesthetic induction his systolic blood pressure dropped to 90 mm Hg and was about 70 mm Hg for most of the procedure. He received 3 L of crystalloid in theatre and his blood pressure was 90/60 mm Hg at the end of surgery, rising to 152/95 mm Hg two hours later. He received prophylactic aspirin (150 mg daily) but no low molecular weight heparin.

About 10 hours after surgery he developed a severe headache, nausea, and vomiting. He was treated symptomatically and three days later the symptoms had largely resolved. On the day of discharge (postoperative day 6), his wife noticed drooping of his right eyelid and the patient mentioned that his vision had been blurred since surgery. A doctor was consulted by telephone and advised that no action was needed.

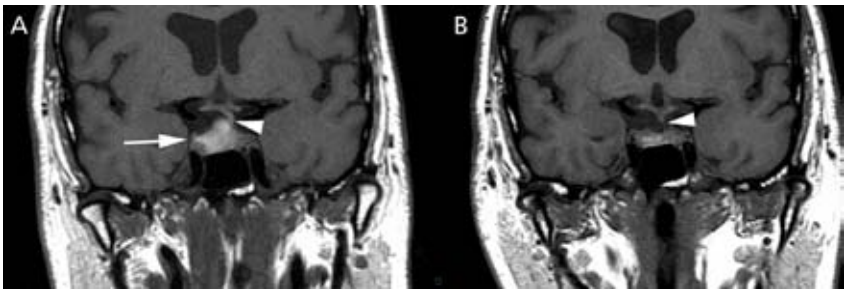

Fig 1 | (A) Magnetic resonance (T1 coronal) imaging of the head 11 days after surgery showing a bilobed haemorrhagic intrasellar mass measuring 14×13×12 mm extending into the right cavernous sinus where it impinges on the region of the oculomotor nerve (arrow). (B) Magnetic resonance imaging (T1 coronal) of the pituitary 10 weeks after surgery showing that the high density pituitary lesion had reduced in size to 12×4.5 mm. The pituitary stalk is deviated to the left (arrowheads in parts A and B)

The patient presented to his general practitioner nine days after surgery with his right eye completely closed and a mild intermittent headache. On examination he was clinically normovolaemic and had no features of hypopituitarism. He had right sided ptosis and a sluggishly reactive and slightly dilated right pupil. He had normal abduction but moderate restriction of right eye movements in all other directions, consistent with an isolated partial right oculomotor nerve palsy. His visual acuity and visual fields were normal. He was admitted under neurosurgery and a diagnosis of posterior communicating artery aneurysm was considered.

He was hyponatraemic, with a sodium value of 128 mmol/L (reference range 136-146), and fluids were immediately restricted to 1 L per 24 hours. Magnetic resonance imaging and magnetic resonance angiography of the head incidentally showed an enlarged pituitary gland, with diffuse high T1 signal consistent with a subacute pituitary haemorrhage. He showed no evidence of a posterior communicating artery aneurysm. Pituitary magnetic resonance imaging two days later (fig 1A) showed a bilobed haemorrhagic intrasellar/suprasellar mass measuring 14×13×12 mm, consistent with haemorrhage into a pituitary macroadenoma. The mass extended into the roof of the right cavernous sinus, where it abutted the right oculomotor nerve at its peripheral aspect.

Despite fluid restriction, the next day (postoperative day 10) plasma sodium was 129 mmol/L, urine sodium was 55 mmol/L, and urine osmolality was inappropriately high (626 mmol/kg). Plasma cortisol at 9 am was low (51 nmol/L; 250-800), free thyroxine was also low (7 pmol/L; 10-24), and thyroid stimulating hormone was normal (0.49 mIU/L; 0.4-4.0), consistent with secondary hypoadrenalism and hypothyroidism. The cortisol result was not available until a day later (postoperative day 11), and at that stage intravenous (50 mg eight hourly) and later oral hydrocortisone supplementation was started, after which the hyponatraemia promptly resolved (fig 2). He was maintained on oral hydrocortisone (15 mg at 8 am, 5 mg at 3 pm) and daily thyroxine (50 µg).

Further pituitary function tests showed luteinising hormone and follicle stimulating hormone values of 0.4 IU/L (2-8) and 1.9 IU/L (2-14), respectively, and total testosterone was also low at 1.1 nmol/L (9-38), confirming secondary hypogonadism. Prolactin and insulin-like growth factor 1 were within normal limits. Two days after the markedly low cortisol measurement, plasma adrenocorticotrophin was normal at 9.2 pmol/L (1-12). During admission his right eye symptoms gradually resolved and he was discharged 14 days after surgery.

The initial non-suppressed plasma adrenocorticotrophin concentration raised the possibility of recovery of pituitary function and prompted repeat measurement of morning cortisol and adrenocorticotrophin on postoperative day 20

(after omitting hydrocortisone for 24 hours). Plasma adrenocorticotrophin was in the reference range at 10 pmol/L (1-12) and cortisol was 515 nmol/L (250-800), confirming recovery of the pituitary-adrenal axis. Total thyroxine was 58 nmol/L (55-140) and thyroid stimulating hormone was 0.43 mIU/L (0.4-4.0). Treatment with hydrocortisone and thyroxine was then stopped.

Ten weeks after discharge his third cranial nerve palsy had fully resolved and pituitary function was normal. The patient gave no history to suggest a pituitary adenoma before the haemorrhagic infarction. Repeat magnetic resonance imaging of the pituitary showed that the mass lesion to the right of the midline had greatly reduced in size to 12×4.5 mm (fig 1B).

Discussion

The history, clinical features, and radiological features in this case are consistent with haemorrhagic infarction (pituitary apoplexy) of a presumed pre-existing non-functioning pituitary adenoma causing reversible anterior hypopituitarism and a transient right third cranial nerve palsy.

Pituitary apoplexy is a potentially life threatening condition, originally described in 1898 by Bailey.[4] Risk factors include surgery (particularly coronary artery surgery), coagulopathy, and pituitary stimulation tests. However, most patients have no obvious precipitating cause and no history of pituitary adenoma.[5 6] We found two other case reports of pituitary apoplexy after routine total hip replacement.[2 7] Although the pathogenesis of pituitary apoplexy is unclear, hypotension and fluctuations in blood pressure have been suggested to increase risk in people undergoing surgery.[6] This may be relevant to our patient who had prolonged intraoperative hypotension. Immediate management is with hormone replacement and correction of fluid and electrolyte abnormalities. Patients may then be managed conservatively or surgically.[8]

Untreated cortisol deficiency can be fatal, so the condition must be recognised and treated immediately.[8] Headache is the most common presenting symptom. Other symptoms and signs include nausea and vomiting, diplopia or visual field deficit, ophthalmoplegia, meningism, and reduced consciousness.[8 9] Although our patient had headache, nausea, and vomiting, these symptoms are commonly seen postoperatively and their importance was not recognised. Instead he was treated symptomatically, and the diagnosis might have been missed if he had not presented later with a third nerve palsy.

On readmission he was hyponatraemic, and a diagnosis of syndrome of inappropriate antidiuretic hormone secretion was made, leading to the initiation of fluid restriction. However such a diagnosis requires exclusion of cortisol deficiency, either primary or secondary. Patients with adrenocorticotrophin deficiency causing secondary cortisol deficiency typically have increased plasma concentrations of antidiuretic hormone, a reflection of the normal tonic inhibitory action of cortisol on the release of this hormone. The high circulating concentration of antidiuretic hormone limits the ability to excrete a water load, which places these patients at risk of hyponatraemia, particularly if secretion of antidiuretic hormone is further stimulated in the postoperative setting and hypotonic fluids are given.[1 10] In our patient the diagnosis of hyponatraemia secondary to adrenocorticotrophin deficiency was confirmed by the morning cortisol of only 51 nmol/L and supported by the response of the hyponatraemia to hydrocortisone replacement (fig 2).

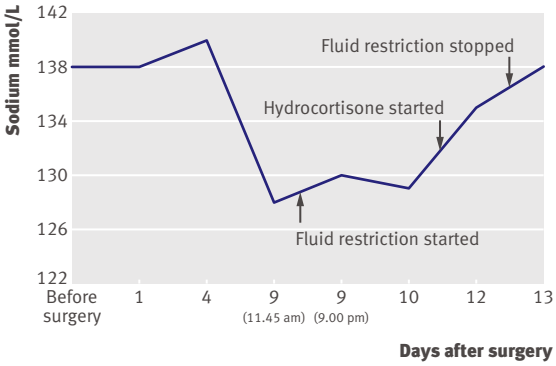

Fig 2 | Plasma sodium concentrations and response to interventions

In conclusion, our case highlights the difficulty of diagnosing pituitary apoplexy in a patient with an undiagnosed pituitary adenoma after surgery because many of the symptoms are non-specific. Because surgery is a risk factor for pituitary apoplexy and pituitary adenomas are not uncommon (overall prevalence of 17%, 0.2% macroadenomas),[11] maintain a high index of suspicion in patients presenting with headache, nausea, and vomiting in association with hyponatraemia postoperatively. Do not assume that the low sodium value is caused by the syndrome of inappropriate antidiuretic hormone secretion and give hydrocortisone promptly to those with possible adrenocorticotrophin deficiency. Arrange ongoing follow-up so that pituitary function can be monitored to check for further pituitary dysfunction or, as in this case, possible resolution of hypopituitarism.

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Patient consent obtained.

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Previous articles in this series

- Hypothyroidism in a patient with non-alcoholic fatty liver disease (*BMJ* 2011;342:c7199)
- Acute liver failure after administration of paracetamol at the maximum recommended daily dose in adults (*BMJ* 2010;341:c6764)
- Proton pump inhibitors and acute interstitial nephritis (*BMJ* 2010;341:c4412)
- Opioid induced hypogonadism (*BMJ* 2010;341:c4462)

10-MINUTE CONSULTATION

Malaria prevention

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This is part of a series of occasional articles on common problems in primary care. The *BMJ* welcomes contributions from GPs.

A 30 year old pregnant woman going home on holiday to Nigeria attends the clinic to get a prescription for malaria prevention tablets for herself and her two children

What you should cover

Malaria is a potentially life threatening but preventable infectious tropical disease, caused by the *Plasmodium* parasite and transmitted by the *Anopheles* mosquito.

- Ask what type and duration of holiday they plan—Sub-Saharan Africa is endemic for the most severe form of malaria, caused by *Plasmodium falciparum*. Risk increases in rural regions, with high humidity (such as during monsoon season), and with length of stay in the endemic region.
- Explore health beliefs about immunity to malaria—People who have survived childhood in malaria endemic regions usually have developed immunity. However, patients who migrate to non-endemic areas often believe that they are still immune although this type of immunity declines in the absence of regular exposure.
- Advise on the complications of malaria in pregnant women and in children—*P falciparum* malaria in pregnant women can cause severe complications such as miscarriage and prematurity, and can increase maternal morbidity and mortality. Children are at risk of serious complications such as hypoglycaemia and cerebral malaria. No prophylactic regimen provides complete protection, and the patient should consider if travel is essential.

What you should do

Advise on the avoidance and prevention of mosquito bites—Emphasise the importance of wearing trousers, socks, and long sleeved shirts when outside between dusk and dawn (when the *Anopheles* mosquito bites). Insect repellents should be applied to exposed skin using formulations of between 30-50% diethyltoluamide (DEET), and may be used during pregnancy and on children aged over two months. A mosquito bed net impregnated with insecticide should be used, tucked in under the mattress, and re-impregnated with pyrethroids (such as permethrin) every six months.[1]

Malaria chemoprophylactic agents and their main side effects

- Chloroquine/proguanil: gastrointestinal disturbances (both drugs), and mouth ulcers (proguanil)
- Mefloquine: neuropsychiatric disturbances
- Doxycycline: photosensitivity (rare) and oesophagitis
- Malarone (atovaquone/proguanil): gastrointestinal disturbances and headache

USEFUL READING

Information for clinicians

National Travel Health Network and Centre travel health information sheet—www.nathnac.org/pro/factsheets/malariaproph.htm; and advice line for health professionals: +44 0845 602 6712

Health Protection Agency Advisory Committee on Malaria Prevention in UK Travellers guidelines—www.hpa.org.uk/infections/topics_az/malaria/guidelines.htm

Health Protection Agency Malaria Reference Laboratory—www.malaria-reference.co.uk

Centers for Disease Control and Prevention—http://cdc.gov/malaria/travelers/index.html

Information for patients

Patient UK malaria prevention—www.patient.co.uk/health/Malaria-Prevention.htm

Identify which chemoprophylactic agents are effective in the region travelled to—Drugs used for malaria chemoprophylaxis are chloroquine and proguanil in combination, atovaquone and proguanil in combination (Malarone), mefloquine, or doxycycline. However, the falciparum malaria endemic to all of sub-Saharan Africa and to some parts of South East Asia and South America is now resistant to chloroquine and use is no longer recommended in these areas. Either Malarone, mefloquine, or doxycycline must be used instead.[1] Country specific information can be found at the Centers for Disease Control and Prevention website.

Choose malaria prophylactic drugs appropriate for pregnant women (if travel cannot be postponed) or children—Chloroquine can be used in children and in all trimesters of pregnancy, but is often ineffective owing to resistance.[1] Doxycycline is contraindicated in pregnant women, breastfeeding women, and in children under 12 years because it can cause staining in growing bones and teeth. Malarone can be used for children, but is contraindicated in pregnancy. Mefloquine can be used for children and in the last two trimesters of pregnancy. If travel cannot be postponed, mefloquine may be prescribed in the first trimester after taking expert advice (for example, by consulting a local travel health specialist, or by calling the National Travel Health Network and Centre advice line for health professionals, in the UK—see Useful reading).

Prescribe appropriately for the travel date and duration—Mefloquine should be started at least a week before travel, but starting two to three weeks before travel has the advantage of allowing tolerability to be assessed (particularly in those who have not tried it before). Doxycycline and Malarone can be started the day before travel. Chloroquine/proguanil should be started a week before

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- Hypoglycaemia (*BMJ* 2011;342:d567)
- Gout (*BMJ* 2010;341:c6155)
- Macromastia (large breasts): request for breast reduction (*BMJ* 2010;341:c5408)
- Hallux valgus (*BMJ* 2010;341:c5130)
- Chalazion (*BMJ* 2010;341:c4044)

travel. Malarone is not licensed for use for more than one month in a malarious area, whereas the other drugs can be used for longer periods. All the drugs apart from Malarone should be continued for four weeks after returning (Malarone should be continued for seven days).

Address issues of compliance, side effects, and follow-up—The main side effects of malaria prophylactic drugs are summarised in the box. Patients may prefer chloroquine (which is often ineffective) to Malarone because chloroquine is much cheaper and is often more familiar to patients (as it is much more widely used in sub-Saharan Africa). Counsel the patient about specific side effects particular to the drug chosen. Mefloquine can cause neuropsychiatric side effects[1] and should be avoided in patients with psychiatric illnesses or epilepsy. Instruct the patient to seek immediate medical attention if they develop a fever from one week after arrival at their destination to 12 months after return. If a patient receives antimalarial treatment while on holiday, this should be communicated to their GP on their return.

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

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ANSWERS TO ENDGAMES, p 715. For long answers go to the Education channel on bmj.com

CASE REPORT

A 42 year old man with bilateral exophthalmos and weight loss

1 The presence of symptoms and signs of thyrotoxicosis in a patient with bilateral exophthalmos and a diffusely enlarged thyroid gland indicate a diagnosis of hyperthyroidism caused by Graves' disease.
2 Serum thyroid stimulating hormone, free thyroxine, and free triiodothyronine concentrations should be measured to establish the presence and assess the degree of hyperthyroidism. In addition, computed tomography or magnetic resonance imaging of the orbits is indicated in this patient.
3 A β blocker should be started to provide initial control of the symptoms of thyrotoxicosis. Thionamides (such as carbimazole or methimazole) should also be prescribed to block the synthesis of thyroid hormones.
4 The patient should be advised to give up smoking and use eye lubricants, and should be referred to a specialist centre for assessment and management of his Graves' ophthalmopathy. Administration of intravenous glucocorticoids is indicated.

CASE REPORT

A man with hypophosphataemia

1 **The patient has tumour induced osteomalacia, with coexisting vitamin D insufficiency.**
2 **The biochemical hallmarks of tumour induced osteomalacia are hypophosphataemia, phosphaturia as a result of renal phosphate wasting, and a low or inappropriately normal concentration of serum calcitriol. Tumours are usually small, benign, slow growing, mesenchymal, and difficult to locate, mostly occurring in the extremities and craniofacial area. Tumours are localised using computed tomography or magnetic resonance imaging, but positron emission tomography-computed tomography and octreotide scanning may be used if neither of these tests is successful. Normalisation of biochemical markers after tumour resection confirms the diagnosis.**
3 **The basic pathophysiological defect in tumour induced osteomalacia is renal phosphate wasting. The tumour produces circulating factors called phosphatonins, such as fibroblast growth factor 23 (FGF-23). This factor inhibits sodium dependent phosphate reabsorption in the proximal renal tubules and downregulates 25-hydroxyvitamin D-1α-hydroxylase, resulting in hypophosphataemia and osteomalacia.**
4 **The definitive treatment is complete tumour resection. Medical treatment comprises replacement of calcitriol, alone or combined with phosphate.**

STATISTICAL QUESTION

Observational study design I

Answer *c* is true.

ON EXAMINATION QUIZ

Risk factors for stroke

Answer B is correct.

ANATOMY QUIZ

Heart segments on short axis computed tomography section

A: Mid-inferoseptal—right coronary artery
B: Mid-anteroseptal—left anterior descending artery
C: Mid-anterior—left anterior descending artery
D: Mid-anterolateral—left circumflex artery
E: Mid-inferolateral—left circumflex artery