

## PRACTICE POINTER

## Healthier ageing

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The authors explore the healthy behaviours we need to adopt for maintaining physical independence and social and mental wellbeing far into old age

Ageing is associated with a gradual decline in physical functioning with or without mental frailty. The ageing process is intrinsically complex, being driven by multiple causal mechanisms.<sup>1-2</sup> Genome instability, telomere damage, mitochondrial dysfunction, and inflammation are established mechanisms of ageing.<sup>w1 w2</sup> Age related changes in body composition include a relative increase in fat tissue and a gradual decline in muscle mass. Not everyone ages in the same way, however, and the term biological age is loosely used to indicate how well someone has aged in terms of the degree of decline in their physical functioning and their ability to meet physiological demands.<sup>3-4</sup>

Ageing is determined by complex interactions between biological, environmental, socioeconomic, and cultural factors,<sup>w3</sup> some of which are beyond the control of individuals. Factors that may contribute to the ageing process, such as poor nutrition,<sup>w4</sup> physical inactivity, smoking, and psychosocial characteristics (such as stress),<sup>w5</sup> may be modifiable. These factors are associated with the development of chronic diseases that are, in themselves, associated with physical and mental frailty and could be tackled at an individual level throughout life. Considerable geographic variation in the prevalence of major chronic diseases among older people suggests that chronic diseases are not an inevitable part of ageing.<sup>5</sup>

Although we acknowledge that there is an increasing need to recognise the long term care requirement of ageing populations, we consider that efforts should be made to promote healthier lifestyles as a way to age more healthily, given the large and increasing body of mainly observational evidence suggesting that healthier ageing is achievable through lifestyle modification.

**What is healthy ageing?**

Healthy ageing in older age could be considered to be “being free of any chronic disabling conditions and the prevalent conditions of older age; having the ability to be content or enjoy life; and being able to perform desired physical, men-

tal and social activities without any limitations.” Therefore, healthy ageing is largely commensurate with a quality of life that is related to good health.<sup>6</sup> The age related changes that occur with chronological age vary considerably,<sup>w6</sup> which suggests that it may be possible to attenuate the functional decline associated with rising chronological age by modifying biological age.<sup>6 w7</sup>

**How might healthier ageing be achieved?**

Healthier ageing is really aimed at the compression of morbidity in older age.<sup>7</sup> Therefore, the ideal goal should be to maintain physical independence and biological reserve and enjoy psychosocial wellbeing well into older age. Many healthy lifestyle behaviours are positively associated not only with better physical and mental functional health (indicators of biological ageing) but also with longevity, reduced risk of chronic diseases, and more quality adjusted life years.<sup>8-10 w8-w13</sup> For individuals, the aim of adopting healthy behaviours is to prevent chronic disease and preserve physical and mental function.

**Prevention of chronic disease**

Although ageing is not the sole cause of chronic disease, older age is strongly associated with many chronic diseases, such as arthritis, cardiovascular disease, and dementia. Because chronic diseases are associated with reduced physical function and poor quality of life, measures aimed at preventing chronic diseases (such as taking regular physical exercise, not smoking, and eating a healthy, balanced diet throughout life) are important basic steps towards healthier ageing.<sup>6</sup> Prospective epidemiological studies have shown that positive health behaviours are associated with reduced all cause mortality and cardiovascular disease, higher life expectancy, and greater health and wellbeing in older age.<sup>8-9 w1 w14 w15</sup>

Table 1 outlines the chronic health conditions common in older adults, the risk factors that have been shown to be associated with them, and lifestyle modifications for which evidence suggests that these conditions can be prevented.

**Stopping smoking**

Smoking is an established risk factor for many chronic conditions, including ischaemic heart disease, stroke, chronic obstructive pulmonary disease, and dementia, and avoidance of smoking is associated with a low incidence of these conditions.<sup>w16 w17</sup> Smoking cessation has been associated with reduced mortality even after a major event such as a stroke.<sup>w18</sup>

**Ensuring a healthy diet**

Because chronic diseases including diabetes, cardiovascular disease, cancer, osteoporosis,<sup>w19-w22</sup> and obesity are associated with dietary factors, a balanced diet is advisable (table 2). Although a balanced diet is achievable for most people, surveys of the UK population show that recommendations

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**SUMMARY POINTS**

Ageing affects people in different ways, with a wide variation in age related physical and mental functioning

Healthier ageing is achievable through modifying some lifestyle factors—such as stopping smoking, being more physically active, and eating a balanced diet

For healthier ageing, eat mainly nutrient dense foods that are rich in vitamins and minerals and low in fats and sugar

Balancing energy intake and expenditure is important for maintaining healthy weight

Preventing chronic diseases may promote healthier ageing through better physical and mental health

**Table 1 | Preventable and avoidable major chronic conditions, their main risk factors, and the action needed to reduce these risk factors**

Chronic conditions	Modifiable risk factors and behaviours	How best to reduce risk factor
<b>Preventable</b>		
Ischaemic heart disease	Hypercholesterolaemia, obesity, low grade systemic inflammation	Adopt a balanced diet, be physically active, avoid smoking
Hypertension	High salt intake	Reduce salt intake
Chronic obstructive pulmonary disease	Smoking	Avoid smoking
Type 2 diabetes	Obesity (especially visceral obesity)	Be physically active, adopt a balanced diet
Peripheral vascular disease	Smoking	Avoid smoking
Osteoporosis	Lack of vitamin D	Get more exposure to sun
	Inactive lifestyle	Be physically active
	Smoking	Avoid smoking
Stroke	Hypertension	Reduce salt intake
	Inactive lifestyle	Be physically active
<b>May be preventable</b>		
Arthritis (osteoarthritis)	Obesity	Adopt a balanced diet, be physically active
Depression	Lack of social engagement, isolation	Adopt a social life, take physical activity
Vascular dementia	Cerebrovascular disease, hypertension, smoking, obesity	Adopt a balanced diet, be physically active, avoid smoking

for food and nutrient consumption are largely not met for fruit and vegetables, oily fish, red and processed meat, sugars, saturated fat, fibre, salt, alcohol, and some vitamins and minerals<sup>w20</sup>; only those for percentage total fat and energy intake are met. Therefore, there is still a great need to encourage people to eat a balanced, healthy diet.

The current UK, American, and international dietary recommendations for eating a healthy balanced diet (table 2)<sup>11 12 w20 w21 w23-w25</sup> represent current knowledge and consensus opinion. These guidelines can be met by following the “eatwell plate” model of healthy eating<sup>13</sup> and by eating different food types in the correct proportions (figure). People who do not eat fish or fish oils should be encouraged to consume rich sources of the plant based n-3 polyunsaturated fatty acid  $\alpha$ -linolenic acid (walnuts, flaxseeds, hempseeds, and their oils, plus rapeseed (canola) oil

because the evidence suggests potential benefits in people who do not eat fish.<sup>14 w26</sup>

### Maintaining regular physical activity

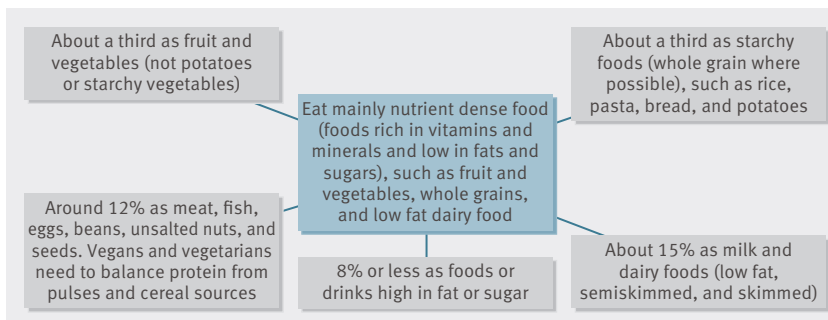
A low level of physical activity is associated with higher incidence of chronic diseases and chronic disabling conditions.<sup>w13 w27 w28</sup> Exercise seems to modify the gene-environment interactions for intermediate risk factors such as obesity, as having a physically active lifestyle seems to reduce the likelihood of obesity in those with a genetic predisposition to obesity.<sup>w29 w30</sup> Physical activity has also been associated with better bone density and greater muscle mass and confers positive effects on mental health and wellbeing.<sup>w29</sup>

The health departments of each constituent country of the United Kingdom recommend that all adults, including adults aged 65 years or older, should take a minimum of

**Table 2 | Summary of guidelines for achieving a healthy, balanced diet in adults, based on current UK, American, and international dietary recommendations<sup>11 12 w20 w21 w23-w25</sup>**

Foods and nutrients	How best to do it	Reason
Calorie (energy) intake	Control calorie intake to maintain appropriate energy balance and BMI. Aim to maintain a BMI of <25 by eating “low energy dense foods”	Too much energy intake compared with expenditure leads to obesity
Protein and red meat	Eat protein rich foods from different vegetable and animal sources (lean meat, fish, eggs, beans, soya products, unsalted nuts, and seeds). Ensure adequate protein intake (0.75 per kg a day) if aged >50 years. Balance protein foods with fruit and vegetables at meals. If you are consuming more than 90 g red and processed meat a day, consider reducing consumption	Adequate protein intake may slow loss of muscle mass and prevent onset of sarcopenia. Red and processed meat is associated with probable increased risk of colorectal cancer
Calcium rich foods	Eat low fat dairy products, nuts and seeds, dark green vegetables, tofu, and tinned fish	To maintain bone density and reduce risk of osteoporosis
Fruit and vegetables a day	Eat at least five portions a day. Eat a variety of fruits and (non-starchy) vegetables covering a range of colours (fresh, frozen, and tinned can be used)	To reduce risk of cardiovascular disease and probable decrease in risk of certain cancers
Fibre and whole grain foods	Try to eat more whole grains and foods containing fibre, and limit refined grains (whole grains with the outer fibre layer removed). For starchy foods (eg rice, pasta, and bread) eat whole grain varieties when you can. Aim for 18 g fibre a day	To maintain bowel function and prevent constipation
Salt	Limit salt intake to 6 g a day. Limit consumption of salty foods. Do not add salt at table. Read food labels	A high salt intake is a risk factor for hypertension, heart disease, and stroke
Fish	Eat at least one portion of oily fish a week	To reduce the risk of cardiovascular disease
Fat and sugar	Consume minimal amounts of foods containing saturated fats and sugars, and limit added sugars (fizzy drinks, confectionery, cakes, pies, biscuits, table sugar). Aim for $\leq 35\%$ energy from fat and $<11\%$ energy from added sugars	To reduce the risk of cardiovascular disease and the likelihood of eating a high calorie diet
Saturated and trans fats	Limit foods that contain saturated fats and trans fats by avoiding foods that contain partially hydrogenated oils, and limit solid fat intake, high fat meats, and high fat dairy products	To reduce the risk of cardiovascular disease
Vitamin B <sub>12</sub>	Eat foods containing vitamin B <sub>12</sub> (such as meats, yeast extracts, or those that are fortified, such as fortified breakfast cereals)	To prevent vitamin B <sub>12</sub> deficiency anaemia
Alcoholic drinks	Consume alcohol in moderate amounts and within or lower than the government guidelines (that is, no more than 3-4 units a day for men and no more than 2-3 units a day for women)	To reduce the risk of liver disease and certain cancers. Alcohol provides additional calories that contribute to obesity

BMI= body mass index (weight (kg)/ height (m)<sup>2</sup>).



Proportions of food types to eat to achieve a balanced diet

30 minutes moderate activity at least five times a week or in those who are regularly active at moderate intensity a minimum of 75 minutes of moderate to vigorous intensity activity spread across the week.<sup>15</sup> The box outlines suggestions for how older adults might meet these recommended levels of exercise.<sup>16</sup>

### Multiple lifestyle interventions

Comparatively few intervention studies have examined the effects of lifestyle interventions on multiple risk factors; most have looked at outcomes related to the prevention of cardiovascular disease, and only a few were primary prevention studies.<sup>17 w31 w32</sup> Nevertheless, owing to the complex interaction between lifestyle behaviours, the ageing process, and age related diseases, intervention-level evidence on healthy ageing is limited.

### Ways to stave off frailty and functional decline

#### Sarcopenia and falls

Sarcopenia is age related loss of muscle mass and strength that is thought to be a fundamental component of frailty<sup>18</sup> and is associated with falls among older adults. Lean muscle mass is lost at a rate of about 1% a year after age 50 years, with mechanisms being unclear.<sup>19</sup> Suggested mechanisms include the greater rate of breakdown than synthesis of muscle proteins, neurodegenerative processes, reduced production of anabolic and sex hormones, dysregulation of cytokine secretion, and the blunting of the positive effects of exercise in older age.<sup>18 w33</sup> Because inadequate nutrition and a sedentary lifestyle have been associated with sarcopenia, a physically active lifestyle and a balanced diet are important in avoiding falls in later life.<sup>18 w34</sup>

#### Preventing cognitive decline and mental frailty

Evidence from UK surveys shows that the trajectory for functional mental health (unlike for physical health) improves from a young age to middle and early older age but then starts to decline (in those aged over 75 years).<sup>6 20</sup> However, the extent of the decline varies with the individual. Furthermore, the prevalence of dementia increases sharply from about 2% of those aged 65–69 years to about 25% of those older than 85 years in Western populations.<sup>w35</sup> Established risk factors for dementia include current smoking, physical inactivity, and chronic medical conditions.<sup>w36</sup> Therefore, the recommended lifestyle interventions to prevent dementia include regular physical activity and avoidance of smoking.<sup>w37</sup> Physical activity is also effective in preventing and treating depression in older adults.<sup>21</sup>

### Are vitamin supplements needed?

Adopting a diet high in nutrient dense foods and low in fat and sugar is the best way to achieve a healthy intake of vitamins and minerals; supplements are not routinely necessary. However, some population groups, including those not able to eat a full range of foods, may need vitamin supplements. As many as 15% of individuals in the UK are estimated to have low serum concentrations of 25-hydroxyvitamin D and 80% have concentrations considered to be suboptimal.<sup>w38</sup> Adequate levels of vitamin D are essential for good bone health, and low serum concentration of 25-hydroxyvitamin D has been associated with osteomalacia and osteoporosis; falls in adults; and more recently with higher rates of other chronic diseases.<sup>w39</sup> Vitamin D supplementation is associated with a reduced risk of falls.<sup>22</sup> Dietary sources of vitamin D are limited mainly to animal products such as oily fish and to fortified margarine. Although exposure to sunlight is the major source of vitamin D, many adults avoid sun exposure as it has been associated with an increased risk of skin cancer.<sup>w38</sup> Recent consensus recommendations from cancer, heart, diabetes, osteoporosis, and dermatological societies recommend about 10 minutes of sun exposure once or twice a day (depending on skin type), without sunscreen and taking care not to burn.<sup>23</sup> In the UK effective production of vitamin D from skin occurs between May and September. Vitamin D supplementation may be needed where neither diet nor sunlight exposure is adequate.<sup>w20</sup>

### Which is more important for healthier ageing—physical activity or healthy diet?

Because basal metabolic rate declines with age, even in physically active people,<sup>24</sup> maintaining a balance between energy intake and expenditure is important throughout life especially as the potential for physical activity to potentiate weight loss reduces with age. Furthermore, the amount of physical activity to achieve weight loss is considerable without taking into account energy intake. What the ideal range of body mass index is for older adults, is not clear, especially for the oldest old people. Whereas being underweight in older age is known to be associated with poor health outcomes,<sup>25</sup> the associations with overweight and obesity in older age are less clear. On the basis of the available evidence, both physical activity and a healthy diet seem to be needed for healthier ageing.

### When to start taking steps for achieving healthier ageing

Ageing could be said to begin at the very beginning of life and to accelerate after age 30. Many chronic diseases are asymptomatic in their early stages, and the biological underpinnings of functional decline may begin before older age. Therefore, acting on the principle that it is “never too early to start,” minimising risk factors throughout one’s life is prudent. As shown by large prospective population based studies, adherence to a healthy lifestyle in middle age reduces the risk of mortality and cardiovascular events,<sup>8 w15</sup> which suggests that it is also “never too late to start.”

### Conclusion

Future research into ageing should ideally focus on establishing causal links between lifestyle factors and

### TIPS FOR OLDER ADULTS ON HOW TO ACHIEVE A PHYSICALLY ACTIVE LIFESTYLE

- The recommended levels of activity can be achieved either by doing all the daily activity in one session or through shorter bouts of 10 minutes or more<sup>16</sup>
- Activity can be activities of everyday life (such as climbing stairs or brisk walking) or participation in more structured exercise or sport<sup>16</sup>
- Taking part in varying types of physical activity is probably best because although most types of physical activity have beneficial effects on health, these health effects differ
- Older people (65 years and over) should take particular care to keep moving and retain their mobility
- Specific activities that promote improved strength, coordination, and balance are beneficial for older people<sup>16</sup>

the ageing process through well conducted intervention studies and on how an individual can best maintain physiological reserve as he or she ages. Currently, healthier ageing seems achievable, at least in part, by adopting behaviours that have been associated with a reduced risk of developing chronic diseases and with better long term functional ability.

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## EASILY MISSED?

# Phaeochromocytoma

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This is one of a series of occasional articles highlighting conditions that may be more common than many doctors realise or may be missed at first presentation. The series advisers are Anthony Hamden, university lecturer in general practice, Department of Primary Health Care, University of Oxford, and Richard Lehman, general practitioner, Banbury. To suggest a topic for this series, please email us at [easilymissed@bmj.com](mailto:easilymissed@bmj.com).

A 51 year old woman presented with a few months' history of episodic anxiety associated with sweating, flushing, and palpitations. The symptoms were thought to be menopausal but they were not relieved by oestrogen hormone replacement therapy. She also had a history of hypertension that was increasingly difficult to control, despite treatment with three antihypertensive agents. Her general practitioner, concerned about a possible phaeochromocytoma, referred her to an endocrinologist. Further investigation showed markedly raised urine metanephrines and a right adrenal mass on computed tomography, consistent with a diagnosis of right adrenal phaeochromocytoma.

## What is a phaeochromocytoma?

A phaeochromocytoma is a catecholamine producing tumour arising from the chromaffin cells of the adrenal medulla (85% of cases) or extra-adrenal paraganglia.<sup>1</sup> Although it may be malignant, symptoms usually result from the excess secretion of catecholamines.

## Why is phaeochromocytoma missed?

Phaeochromocytomas are uncommon in secondary care and rare in primary care. The symptoms and signs of a phaeochromocytoma, which vary greatly, are often non-specific and similar to those of many common conditions, such as anxiety. The so called classic symptoms of a phaeochromocytoma, such as paroxysmal headache, palpitations, and sweating, are often absent. Hypertension may not be present in 10-20% of cases.<sup>1</sup> As a result, diagnosis is often delayed, with an average interval of three years between the initial symptoms and diagnosis, and many cases are diagnosed only at autopsy.<sup>2-4</sup>

## Why does this matter?

Although we estimate from prevalence data<sup>3</sup> that an average full time general practitioner will have only about a 50% chance of seeing a new case of phaeochromocytoma in their career, it is important not to miss the diagnosis. Unrecognised and untreated phaeochromocytoma has high morbidity and mortality through cardiovascular



### HOW COMMON IS PHAECHROMOCYTOMA?

- The prevalence of phaeochromocytoma in hypertensive patients attending general medical outpatient clinics is 0.1–0.6%<sup>1</sup>
- Autopsy studies have shown a prevalence of 0.05%, but many of these cases had not been diagnosed in life<sup>3</sup>

complications of catecholamine excess and untreated malignancy.<sup>1–6</sup> A hypertensive crisis can be precipitated if a patient with unrecognised phaeochromocytoma is treated with  $\beta$  blocking medication (without  $\alpha$  blockade, leading to unopposed  $\alpha$  receptor mediated vasoconstriction) or undergoes surgery (which can trigger catecholamine release). Additionally, symptoms of phaeochromocytoma are often debilitating and lead to poor quality of life. The condition can be treated effectively with  $\alpha$  blocking medication followed by surgery. About 10% of phaeochromocytomas are malignant, and early diagnosis and treatment may reduce the risk of metastasis.<sup>2</sup> Furthermore, phaeochromocytoma can be associated with genetic disorders, such as multiple endocrine neoplasia type 2—familial phaeochromocytoma and medullary thyroid carcinoma with primary hyperparathyroidism (type 2a) or mucosal neuromas and Marfanoid habitus (type 2b). Therefore the diagnosis can also assist investigation and early identification of phaeochromocytoma and related conditions in family members.

### How is phaeochromocytoma diagnosed?

#### Clinical

The most common clinical features of phaeochromocytoma include hypertension (80–90% of cases), palpitations (60%), headaches (50%), sweating (50%), pallor (40%), and psychological symptoms such as anxiety or panic (35%).<sup>1–2</sup> The combination of episodic headache, sweating, and palpitations has been reported to have high specificity (>90%) for phaeochromocytoma.<sup>1</sup> Other less common features include weight loss, lethargy, tremors, nausea, dyspnoea, vertigo, flushing, orthostatic hypotension, and hyperglycaemia. Patients infrequently present with a hypertensive crisis, shock, or cardiovascular emergencies such as myocardial infarction or arrhythmia. Symptoms of phaeochromocytoma are episodic in about 65% of cases, typically lasting from minutes to an hour.<sup>2</sup> Hypertension is sustained in 50–60% of cases but may be episodic (30%) or absent, even on repeated testing (10–20%),<sup>1</sup> making diagnosis potentially difficult. The National Institute for Health and Clinical Excellence (NICE) in England and Wales currently recommends that general practitioners refer for investigation if they suspect a phaeochromocytoma in a patient with hypertension, and it suggests that labile or postural hypotension, headaches, palpitations, pallor, and excess sweating are possible symptoms.<sup>7</sup> Worsening of symptoms after introduction of a  $\beta$  blocker and labile blood pressure during surgery should also raise the suspicion of phaeochromocytoma. Screening of

asymptomatic patients with hypertension is not recommended owing to the high false positive rates of currently available tests.<sup>1</sup> On the other hand, consider investigations even in the absence of hypertension if symptoms suggest phaeochromocytoma.

About 25% cases of phaeochromocytoma are currently diagnosed in asymptomatic patients after the incidental finding of an adrenal mass on imaging performed for unrelated reasons (adrenal incidentaloma).<sup>1</sup> Undertake biochemical screening for phaeochromocytoma in all cases of adrenal incidentaloma.<sup>8</sup> Screening of asymptomatic patients with a genetic predisposition to phaeochromocytoma (such as multiple endocrine neoplasia type 2) is also indicated.

### Investigations

When phaeochromocytoma is clinically suspected, investigate further by confirming the presence of excess catecholamine secretion. Measurement of catecholamines in a 24 hour urine collection has traditionally been used; however, this method has largely been replaced by measurement of metanephrines (metabolites of catecholamines) either in a 24 hour urine collection or in plasma, both of which have better diagnostic sensitivity.<sup>9–10</sup> Although urine collection can often be performed in primary care (unlike plasma measurement, which requires sample refrigeration or rapid processing), most general practitioners would refer for specialist advice. We recommend referral of any patient where there is high suspicion of phaeochromocytoma.

The sensitivity of metanephrine measurement to detect phaeochromocytoma is 97% for urinary levels and 99% for plasma levels compared with 86% for urinary catecholamines, among symptomatic patients, those with a previous or family history of phaeochromocytoma, or those with an incidental adrenal mass.<sup>10</sup> Likewise, the specificities for urinary and plasma metanephrines are 93% and 89%, respectively, compared with 88% for urinary catecholamines.<sup>10</sup> False positive results are common, owing to the relative infrequency of phaeochromocytoma in those tested and to the presence of other medical conditions (such as obstructive sleep apnoea) and medications (such as tricyclic antidepressants, phenoxybenzamine, clozapine, calcium channel blockers, and  $\beta$  blockers) that can cause elevation of metanephrines. Furthermore, severe physical and psychological stress (for example, major surgery, myocardial infarction, severe pain, panic attacks) could increase catecholamine secretion, leading to false positive results. Concentrations of metanephrines that are over four times normal levels are associated with very high probability of phaeochromocytoma; however, lower raised concentrations will require further biochemical assessment, which may include repeat testing after withdrawal of implicated medication. By contrast with the now infrequently used measurement of urine vanillyl mandelic acid, dietary restrictions are not needed when performing these investigations.

When a phaeochromocytoma has been confirmed biochemically, imaging methods such as computed tomography, magnetic resonance imaging, or meta-iodobenzylguanidine radioisotope scanning are used to locate the primary lesion and screen for metastases.

### KEY POINTS

Common symptoms of phaeochromocytoma include episodic palpitations, headaches, sweating, and psychological symptoms such as anxiety or panic

Hypertension is present in 80–90% of cases but may be episodic

Symptoms of phaeochromocytoma are variable and non-specific, leading to frequent long delays between onset and diagnosis

The recommended initial investigation for a suspected phaeochromocytoma is measurement of metanephrines (a metabolite of catecholamines) in 24 hour urine collection or in plasma

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- Femoral hernias (BMJ 2011;343:d7668)
- Coarctation of the aorta in the newborn (BMJ 2011;343:d6838)
- Appendicitis (BMJ 2011;343:d5976)

**How is pheochromocytoma managed?**

A pheochromocytoma is treated with  $\alpha$  receptor blocking medication followed by surgery. However, because the tumour can recur even after apparently successful surgery for benign disease, lifelong follow-up is needed.<sup>1</sup> Genetic testing should be considered, particularly in patients under the age of 50 years, in patients with multiple or malignant pheochromocytoma, and in those with a positive family history.<sup>9</sup>

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## ANSWERS TO ENDGAMES, p 48 For long answers go to the Education channel on bmj.com

### PICTURE QUIZ

#### A 34 year old man with bilateral anterior uveitis and a rash



Fig 3



Fig 4

- 1 The tattoo has a raised indurated appearance over the surface of the pigment (fig 3). The chest radiograph shows bilateral hilar lymphadenopathy (fig 4).
- 2 The combination of anterior uveitis, rash, and bilateral hilar lymphadenopathy can be caused by sarcoidosis, mycobacterial infection, or lymphoma, but the most likely diagnosis is sarcoidosis. The pathognomonic feature is the reaction within the patient's tattoos, which would not occur with the other differential diagnoses. It is caused by the accumulation of non-caseating granulomas—the pathophysiological end feature of sarcoidosis.
- 3 Sarcoidosis is unusual in that it can affect any organ. A common acute presentation (9-34%) is Löfgren's syndrome, which consists of erythema nodosum, arthralgia, and bilateral hilar lymphadenopathy. A similar proportion of patients present with respiratory symptoms (including wheeze) or incidental findings on chest radiography. Sarcoidosis should also be considered in patients with unexplained neurological and cardiac symptoms because it can potentially have a fatal outcome.
- 4 Because the remission rate is high, only patients with symptomatic or organ threatening sarcoidosis require treatment. Prednisolone is the recommended treatment, at a starting dose of 0.5 mg/kg/day for four weeks, but higher doses may be needed for cardiac sarcoidosis or neurosarcoidosis. It can be reduced to a maintenance dose and should be continued for several months before re-evaluation.

### ANATOMY QUIZ Branches of the abdominal aorta

- A Splenic artery, branch of coeliac axis
- B Coeliac axis
- C Superior mesenteric artery
- D Left renal artery
- E Inferior mesenteric artery

### STATISTICAL QUESTION

**Parametric v non-parametric statistical tests**  
Statements *a*, *b*, and *c* are true, whereas *d* is false.