education

FROM THE JOURNALS Edited highlights of weekly research reviews on https://bit.ly/2PLtil8

Laparoscopic surgery for gastric cancer in China

This non-inferiority, open label, randomised trial of 1056 people in China with locally advanced gastric cancer looked at whether laparoscopic or open distal gastrectomy resulted in better survival rates. Laparoscopic surgery is known to be more effective in early stage cancer, with similar outcomes and fewer complications, than open surgery. But once the disease is locally advanced, is it better to open the abdomen to allow dissection of D2 lymph nodes? The authors report that 94.6% of participants completed the study. Three year, disease-free survival rates were similar for laparoscopic and open resection (83.1% *v* 85.2%), as were recurrence rates over the three years (18.8% *v* 16.5%). Laparoscopy will be preferred by most patients, as outcomes seem to be no worse than with open surgery, and hospital stay and recovery times are shorter. An important caveat to generalising from these findings is that about a quarter of patients' tumours were down-staged from an initial clinical diagnosis of locally advanced cancer to early stage cancer. In centres where initial staging is more detailed, the same conclusions may not apply.

JAMA doi:10.1001/jama.2019.5359

Chronic lymphocytic leukaemia: two drugs better than one

Two oral drugs have been approved for chronic lymphocytic leukaemia: ibrutinib, an inhibitor of Bruton's tyrosine kinase, and venetoclax, an inhibitor of B cell lymphoma 2 protein. This small, phase II study of 80 participants (partly funded by AbbVie, which makes venetoclax) found that a combination of the two drugs seems to be effective for previously untreated, high risk patients over the age of 65 years with chronic lymphocytic leukaemia. Most patients had only a partial response after three cycles of ibrutinib, but 88% achieved complete remission after 12 cycles of combined therapy. Adverse events were similar to those reported in other studies with monotherapy (60% had toxic effects of grade 3 or higher, mostly neutropenia). Patients over 65 years old didn't fare worse than younger patients. Whether people who achieve complete remission after 24 cycles will need any further treatment is still not known. This study wasn't designed to compare outcomes with watchful waiting; but if I had chronic lymphocytic leukaemia, that is the question I'd want answered.

N Engl J Med doi:10.1056/NEJMoa1900574

Fast tracked cancer drugs don't live up to expectations

Oncologist Bishal Gyawali and colleagues ask a fascinating question—when a cancer drug gets accelerated approval from the US Food and Drug Administration (FDA) on the basis of a claim that there is "verified clinical benefit in a confirmatory trial," what exactly is meant by "verification of benefit"? The question resonates in the UK too, where there is often pressure to fast track new cancer treatments. This review of subsequent trials of 93 cancer drugs that received accelerated FDA approval from 1992 to 2017 showed that most drugs failed to live up to their pre-approval promise; just 20% showed improved overall survival. In a second article, Chen and colleagues investigated 85 FDA approvals of 59 cancer drugs and found that many were approved on the basis of low response rates. In an invited commentary, Richard Lehman and Cary Gross write: "These articles serve as a reminder that the accelerated approval pathway is a permissive process that tolerates nonrandomised trial methods and a variety of outcome measures that bear an uncertain relationship to patient benefit."

JAMA Intern Med doi:10.1001/jamainternmed.2019.0462
JAMA Intern Med doi:10.1001/jamainternmed.2019.0583
JAMA Intern Med doi:10.1001/jamainternmed.2019.0458

Blood treatment before cardiac surgery

This study found that giving a top-up of blood boosting products on the day before cardiac surgery reduced the need for postoperative blood transfusions in people who were anaemic or low in iron before their surgery. Time is often tight, as a lot of elective cardiac surgery is scheduled within days of an acute cardiac event. Evidence suggests that correcting isolated iron deficiency and anaemia preoperatively improves postoperative outcomes. This large scale, randomised controlled trial compared the need for red blood cell transfusions in the seven days after operation in patients with low haemoglobin concentration or isolated low ferritin, half of whom were given a combination of intravenous iron, subcutaneous erythropoietin alpha, vitamin B_{12}, and oral folic acid, and half of whom were given placebo. A larger study would be needed to show that the subgroup with iron deficiency benefit from the quick fix top-up.

Lancet doi:10.1016/S0140-6736(18)32555-8

Ann Robinson is an NHS GP and health writer and broadcaster

How should GPs respond to patients with symptoms?

For England and Wales, the National Institute for Health and Care Excellence (NICE) provides guidance on the criteria that warrant urgent action.[15] For example, referral is recommended for unexplained haemoptysis in people aged over 40 years, and urgent chest x ray is recommended in smokers with appetite loss or with thrombocytosis. However, the presentation of symptoms is often complex, as many people will have comorbidities,[16] and there is often no clear symptom signature.[17]

Only half of patients will have an isolated first symptom and, although haemoptysis is the most predictive symptom, it occurs in only 20% of patients.[18] Many patients present with non-respiratory symptoms. Hence prompt recognition of patients who do not fulfil NICE criteria depends on clinicians having a low threshold for requesting a chest x ray, and a low threshold for repeating or requesting further lung imaging if patients have a normal chest x ray and ongoing symptoms. Some national guidelines suggest computed tomography in the case of persistent symptoms despite a normal chest x ray.[19] Several risk prediction tools have been developed for use in primary care, but there is insufficient evidence to recommend their use.[20]

The prospect of biomarkers to identify people with early disease is of considerable interest. This includes novel technologies to detect volatile organic compounds in the breath and blood biomarkers.

How can we improve diagnosis and treatment?

The NHS in England has recently implemented a timed lung cancer diagnostic pathway aiming to streamline investigations for suspected lung cancer, allowing earlier treatment alongside a more rapid "all clear" for patients found not to have cancer.[21]

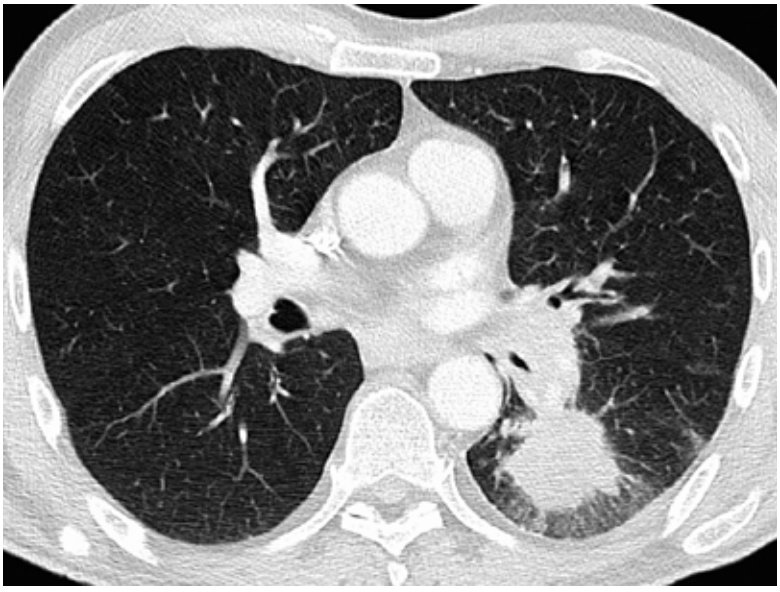
The variations seen between treating centres are thought to contribute to poorer UK outcomes. An estimated 500 deaths could be prevented annually if the proportions of patients treated with surgery and radical radiotherapy matched those in centres in the highest quintile of treatment rates.[22] Similarly, there is known variation between general practitioners in their propensity to investigate patients equally.[23]

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Comments by a patient peer reviewer have been incorporated to help capture the patient perspective.

EDUCATION INTO PRACTICE

- Do you consider a chest x ray when a current or former smoker attends with non-specific symptoms?
- Consider your last patient with lung cancer. Were there opportunities for earlier investigation and diagnosis?
- Do you discuss early palliative care with all eligible patients?
- Do you offer smoking cessation interventions to patients who continue to smoke after diagnosis?



PR MICHEL BRAUNER, ISM/SPL

Fig 2 | Computed tomography (CT) scan of the chest of a male patient with adenocarcinoma in the lower left lung (at right)

What should be undertaken?

The starting point is contrast enhanced computed tomography (CT) of the thorax including neck and upper abdomen (fig 2). If initial CT demonstrates distant metastases or involvement of the supraclavicular or cervical lymph nodes, sampling allows staging and pathological subtyping (immunohistochemical and molecular analysis) in one procedure. If the disease seems suitable for radical treatment (either surgical or oncological), positron emission tomography-computed tomography (PET-CT) is indicated due to its high sensitivity for distant metastases. PET-CT has lower specificity for mediastinal disease, so systematic nodal sampling is preferred when imaging has indicated possible nodal spread. This is usually performed by sampling under endoscopic ultrasound guidance (usually endobronchial ultrasound guided transbronchial needle aspiration) which is more sensitive and cost effective than surgical staging alone.[24]

The requirements for pathological and genetic analysis of tumour biopsies have become more complex alongside the substantial increase in treatment options for advanced disease. The historical distinction between small cell and non-small cell lung carcinoma has evolved into more precise immunohistochemical subtyping between squamous and non-squamous non-small cell lung carcinoma, alongside assays that predict response to immunotherapy and genotyping to assess suitability for targeted therapies.

What are the latest management options?

Early stage disease Surgical lobectomy remains the preferred treatment for medically fit patients with operable early stage lung cancer, with radical radiotherapy a lower morbidity alternative for patients with limited physiological reserve. Recent developments include the roles of minimally invasive surgery and newer radiotherapy techniques.

Over recent years, practice has shifted from open lobectomy towards video assisted thoracoscopic surgery. These two approaches showed similar outcomes in a large propensity matched analysis from the US.[25] To date there has been no randomised comparison, but a UK trial has recently completed recruitment and will report shortly.[26]

Radical oncological treatment of early stage lung cancer has been revolutionised by the development of stereotactic ablative radiotherapy (SABR) for peripheral tumours. This delivers a higher dose than conventional radical radiotherapy and has better overall survival.[27] Several studies attempting to randomise between surgery and SABR have failed to recruit, although one study is ongoing in North America (https://clinicaltrials.gov/ct2/show/NCT02984761).

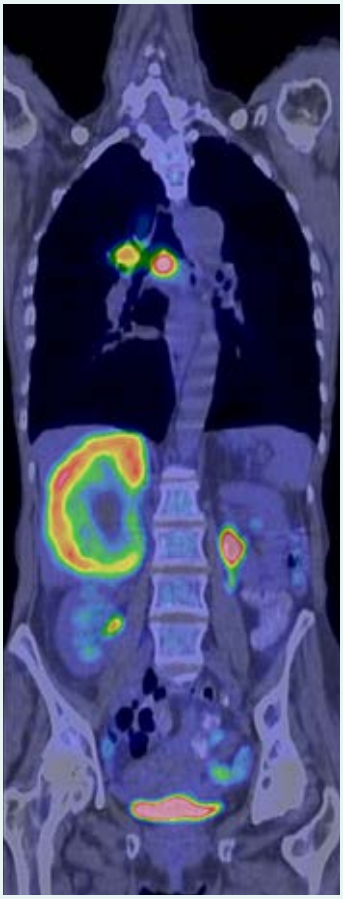
Locally advanced disease Treatment options for patients with locally advanced lung cancer (involving hilar or mediastinal lymph nodes) now recommended by NICE[28] include surgery with adjuvant (postoperative) chemotherapy or chemotherapy and radiotherapy given in combination. The updated NICE guidance also recommends consideration of chemoradiotherapy followed by surgery for some patients, although this is rare in practice.[28] The recommendation is based on a new meta-analysis showing improved progression-free survival with this approach.[29] There is evidence that immunotherapy after chemoradiotherapy is beneficial.[30] Management of localised small cell lung carcinoma is with chemoradiotherapy[31]; prophylactic cranial irradiation reduces brain metastases and improves survival.

Metastatic disease There have been considerable recent changes in the management of metastatic non-small cell lung carcinoma. For patients whose tumours harbour epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) mutations, tyrosine kinase inhibitors are the treatment of choice, with second line agents (third generation tyrosine kinase inhibitors or cytotoxic chemotherapy) reserved for those who progress or develop resistance. Increasingly, other molecular targets are being exploited.

The management of patients without such mutations has been transformed by the advent of immune checkpoint inhibitors (immunotherapy). Precise indications for immunotherapy (monotherapy versus combination treatment with chemotherapy, and first line versus second line treatment) depend on the extent to which the tumour expresses programmed death ligand 1 (PD-L1), and the patient's performance status (only licensed for use in relatively fit patients), with practice evolving at a rapid rate. For those patients ineligible for or not responding to immunotherapy, palliative chemotherapy remains the standard of care.

Metastatic small cell lung carcinoma is primarily managed with chemotherapy, and consolidation chest radiotherapy is beneficial for patients who respond to chemotherapy.[32]

A small proportion of people with symptoms relating to airway occlusion by tumour may benefit from local treatment with stenting, argon plasma coagulation, or photodynamic therapy.



CENTRE JEAN PERRIN/ISM/SPL

Coloured PET-CT scan of a patient with liver cancer spread from metastatic cancer in right lung

INFORMATION RESOURCES FOR PATIENTS

- Patient.info. Lung cancer. 2017. https://patient.info/health/lung-cancer-leaflet
- Cancer Research UK. Lung cancer. 2017. https://www.cancerresearchuk.org/about-cancer/lung-cancer
- British Lung Foundation. Lung cancer. https://blf.org.uk/support-for-you/lung-cancer
- Roy Castle Lung Cancer Foundation. Lung cancer information. https://www.roycastle.org/how-we-help/lung-cancer-information
- Macmillan Cancer Support. Information and support: Lung cancer. https://www.macmillan.org.uk/information-and-support/lung-cancer

ADDITIONAL EDUCATIONAL RESOURCES

- National Institute for Health and Care Excellence. Clinical Knowledge Summary: Symptoms suggestive of lung and pleural cancers. https://cks.nice.org.uk/lung-and-pleural-cancers-recognition-and-referral#!diagnosisSub
- National Institute for Health and Care Excellence. Suspected cancer: recognition and referral (NICE guideline NG12). Section 1.1 Lung and pleural cancers. 2017. https://www.nice.org.uk/guidance/ng12/chapter/1-Recommendations-organised-by-site-of-cancer#lung-and-pleural-cancers
- Patient.info. Professional articles: Lung cancer. 2017. https://patient.info/doctor/lung-cancer-pro

What interventions should be offered for people living with and beyond lung cancer?

Many patients with lung cancer and their families will need psychological support to help cope with the consequences of their diagnosis and treatment. Many patients continue to smoke after diagnosis, placing them at higher risk of treatment toxicity, cancer recurrence, second primaries, and poorer survival.[33] Quitting smoking after a diagnosis can improve prognosis regardless of cancer stage.[34] All patients who continue to smoke must be offered interventions to help them quit. Discussions should be conducted in a manner that minimises stigma and blaming.

The only randomised study of follow-up imaging found no survival benefit from regular computed tomography after surgical resection.[35] In patients with metastatic disease, palliative radiotherapy is effective in the management of symptoms such as pain and haemoptysis. Early input from palliative care should be considered for patients with advanced disease, including those receiving active treatment, although access may vary internationally. Early palliative care improves outcomes, including survival.[36]

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EASILY MISSED?

Pituitary adenomas

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A 58 year old man describes increasing fatigue and loss of motivation over a year. Routine blood tests are normal. He is going through a divorce and he and his GP agree that the symptoms are likely related to stress. On a routine eye check he is found to have a bitemporal hemianopia. Pituitary magnetic resonance imaging (MRI) reveals a 2.5 cm pituitary macroadenoma elevating and compressing the optic chiasm. On further questioning, the patient describes a four year history of erectile dysfunction.

Pituitary adenomas are often clinically silent or manifest with non-specific symptoms, which can lead to a delayed diagnosis. This article provides a summary of clinical features and investigations to help non-specialists and primary care doctors to recognise and diagnose pituitary adenoma.

What is a pituitary adenoma?

Pituitary adenomas are benign tumours arising from hormone expressing cells in the anterior pituitary gland. They account for 10-25% of intracranial neoplasms[1] and occur sporadically in most cases. They are broadly categorised as "functioning" (hormone secreting) and "non-functioning" (non-secreting) adenomas. They can be further classified by cell type and size.

Functional adenomas are more common and tend to present earlier, in younger patients, with symptoms or signs of hormone excess (eg, hyperprolactinaemia) (table). By contrast, non-functioning adenomas are clinically silent until the lesion has become large enough (usually >1 cm) to have mass effect.

WHAT YOU NEED TO KNOW

- Check visual fields in patients presenting with headache coexisting with possible hypopituitary symptoms
- Consider the diagnosis in men with fatigue and ask about low libido or erectile dysfunction; check 9 am testosterone, prolactin, luteinising hormone (LH), and follicle stimulating hormone (FSH)
- Consider the diagnosis in women with oligo/amenorrhoea; check LH, FSH, oestradiol, and prolactin

CPD READING
0.5 HOURS

LEARNING MODULE

See http://learning.bmj.com for linked learning module

HOW COMMON ARE PITUITARY ADENOMAS?

- Pituitary adenomas are very common (up to 16% from autopsy and imaging studies) but only 0.1% progress to cause morbidity[21]
- Previous population studies of pituitary adenomas have probably underestimated true prevalence. A community study of more than 80 000 inhabitants showed that prevalence of pituitary adenomas per 100 000 was fourfold higher than previous estimates at approximately 1:1000.[22] Other population studies confirm this[23-25]

How do pituitary adenomas present?

Symptoms and signs relate to mass effect (visual defect, headache, ophthalmoplegia, hypopituitarism) or hormone hypersecretion, or a combination of both.

Common neurological symptoms

Visual field deficit—the visual field defect usually goes unnoticed by the patient until severe, and is typically a bitemporal hemianopia due to chiasmatic compression (figs 1 (below) and 2 (see bmj.com)).

Headaches are common in pituitary adenomas (37-70%) but are usually non-specific and often not the predominant presenting feature, unless in association with acromegaly or pituitary apoplexy.[2 3] In pituitary apoplexy, headache is sudden, severe, and often associated with visual disturbance or ocular palsy.

Common endocrine symptoms

Hypopituitarism—pituitary macroadenomas (adenomas >1 cm) can be associated with hormone hyposecretion due to progressive compression of the normal pituitary gland cells.[5] Growth hormone deficiency is most common and can cause a wide variety of non-specific symptoms including fatigue and weight gain (table).

Functioning adenomas—clinical manifestations of hormone excess are listed in the table. This hormone excess can be difficult to detect if clinically mild. Prolactinomas are the most common pituitary adenoma and cause amenorrhoea in women when prolactin levels are only mildly elevated, leading to earlier presentation in females.

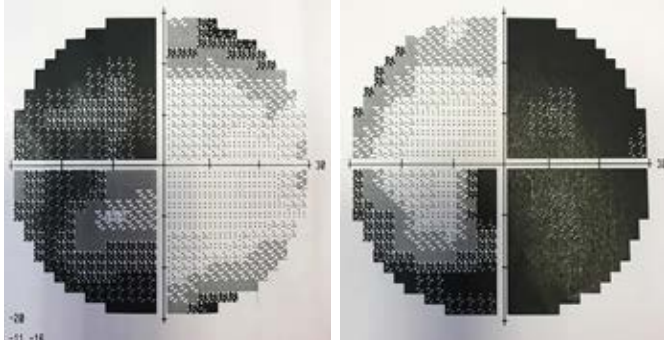

Fig 1 | Humphrey visual field perimetry showing a bitemporal hemianopia present prior to pituitary surgery

Prevalence and features of pituitary adenoma by tumour subtype

Symptoms (There may be no symptoms or signs and biochemistry can be normal)	Signs	Biochemistry*	Cell type of pituitary adenoma	Hormone secreted	Prevalence per 100 000 population[2-4]
Fatigue; erectile dysfunction/low libido in men Amenorrhoea in women Visual disturbance; headache	Unilateral or bitemporal hemianopia. Loss of body hair and gynaecomastia in men	Low 9 am testosterone with low or inappropriately normal FSH/LH; normal or raised prolactin; low TSH and low FT4; low 9 am cortisol	Gonadotroph (non-functioning)	Usually FSH and LH secretion is so low that these tumours are basically non-functioning	41
Erectile dysfunction in men Oligo/amenorrhoea in women	Galactorrhoea. Unilateral or bitemporal hemianopia	High prolactin	Lactotroph (prolactinoma)	Prolactin	54
Headache, sweating, increasing hand and foot size	Coarse facies, frontal bossing, enlarged nose, prognathism, interdental separation, macroglossia, enlarged hands and feet, carpal tunnel syndrome	High insulin-like growth factor-1(IGF-1)	Somatotroph (acromegaly)	Growth hormone	14
Mood disturbance, truncal weight gain, fatigue and muscle weakness (eg, walking upstairs)	Round plethoric facies, proximal myopathy, purple striae, thin skin, easy bruising, truncal obesity	9 am cortisol does not suppress <50 nmol/l after 1 mg overnight dexamethasone suppression test. High 24 h urinary free cortisol; elevated late night salivary or serum cortisol	Corticotroph (Cushing's disease)	Adrenocorticotrophic hormone	6
Thyrotoxicity (although mild in comparison with Graves' disease) Palpitation, weight loss, anxiety, insomnia, menstrual disturbance in women	Tachycardia, tremor, visual field deficit	Inappropriately raised or normal TSH with elevated FT4 and FT3	Thyrotroph (TSHoma)	TSH	0.28

*Most laboratories use well validated assays with limited biological variability. 9 am cortisols are the exception in that a large range of "normal" results exist; generally GPs should follow local laboratory guidance as to what may constitute an ambiguous result and need further assessment with short synacthen test.

Why is it missed?

Clinical practice shows that both functioning and non-functioning pituitary adenomas are likely missed initially due to non-specific symptoms such as tiredness, weight gain, problems with periods, libido, and erectile dysfunction (table). Underlying endocrine problems are a relatively rare cause of such symptoms in primary care, therefore the relevant initial examinations for pituitary adenoma (visual fields and blood tests) may not be considered.

Functioning pituitary adenomas

Most functioning pituitary adenomas present with signs or symptoms of hormone excess (eg, hyperprolactinaemia, growth hormone excess, or hypercortisolism) (table). Diagnosis may be missed due to a gradual manifestation of hormone hypersecretion over the course of years, with non-specific symptoms and subclinical disease at first. On average, diagnosis is delayed by 6-7 years from first symptom onset in acromegaly[6 7] and 3-4 years for Cushing's disease,[8] largely because of this insidious symptom onset.

Non-functioning pituitary adenomas

Diagnosis of non-functioning pituitary adenomas is also often delayed and mean time to diagnosis from symptom onset is estimated to be 1.96 ±2.9 years.[12]

Patients often present due to neurological symptoms arising from mass effect of the pituitary adenoma, such as headache or visual field defects. Earlier, subtle symptoms of hypopituitarism are also non-specific (eg, fatigue, loss of libido) and often attributed to those of ageing, or other more common conditions.

Symptoms can improve, if not be reversed, with timely treatment

Why does it matter?

Timely diagnosis matters because pituitary adenomas are a reversible cause of blindness, debilitating symptoms affecting quality of life, increased risk of comorbidities, and increased mortality. Some pituitary adenomas can be imminently life threatening if not treated, for example, in the case of adenocorticotropic hormone (ACTH) deficiency. The low libido, erectile dysfunction, menstrual disturbance, and infertility associated with some pituitary adenomas can have a huge impact upon an individual and their relationships.[13]

Importantly these symptoms can improve, if not be reversed, with timely treatment.[13] For example, debilitating fatigue caused by TSH and/or ACTH deficiency will improve with thyroxine and hydrocortisone replacement. Low libido can improve with testosterone and oestrogen therapy. Prolactinomas are an easily treatable cause of infertility and menstrual disturbance, and once treated, patients are able to conceive normally.

Blindness can occur due to pressure effects of a large pituitary adenoma on the optic chiasm and tracts. Timely intervention can result in improvement in vision within hours of waking from trans-sphenoidal surgery such that patients are able to read and drive where previously limited. A meta-analysis of visual outcomes after pituitary surgery found that complete recovery was probably less likely if the pre-operative visual defect was severe and of longer duration,[14] with one study finding worse outcomes if the visual field deficit had been present for more than a year.[15] Visual field defects caused by a macroprolactinoma can also improve rapidly with dopamine agonist therapy.[16 17]

How is it diagnosed?

Clinical features

History

If patients present with any of the possible symptoms of a pituitary adenoma (table), ask about the other associated symptoms to distinguish between a functioning pituitary adenoma or hypopituitarism and to guide appropriate examinations and blood tests.

Physical examination

Examine for signs (table) to distinguish between a functioning pituitary adenoma or hypopituitarism and guide appropriate blood tests.

- Offer all patients with a headache a visual field to confrontation test (see bmj.com)—a simple screening examination that helps identify large pituitary macroadenomas.
- In suspected Cushing's and acromegaly it can be useful to ask patients for old photographs of themselves to help identify change.

Investigations

Offer pituitary screen blood tests to patients with symptoms of hypopituitarism (fatigue, low libido, erectile dysfunction, oligo- or amenorrhoea), including FSH, LH, 9 am testosterone (in men), oestrogen (in women), 9 am cortisol, TSH, and Free T4.

If hormone excess is suspected, offer the relevant test (table).

Blood tests may be requested based on the predominant symptoms.

Fatigue has many causes but we would suggest test for 9 am cortisol, free T4, and TSH to help exclude a pituitary cause.

Hypogonadism—LH, FSH, oestradiol, and prolactin are the minimum required investigations for diagnosis of persistent amenorrhoea. These tests identify hyperprolactinaemia or gonadotrophin deficiency, and are also relevant to more common causes such as polycystic ovarian syndrome or ovarian failure. Erectile dysfunction, low libido, and hypogonadal symptoms (which can include fatigue) should be assessed with 9 am testosterone, LH, FSH, and prolactin.

Referral

Refer patients with sudden onset headache and visual symptoms urgently to the emergency department.

If blood results show pituitary dysfunction coexisting with neurological symptoms (headache, visual field deficit, or visual disturbance), make an urgent referral to endocrinology for urgent pituitary magnetic resonance imaging (MRI) (fig 3 (below) and 4 (see bmj.com)) and formal visual field perimetry.

If the patient has headache and visual field disturbance without evidence of pituitary dysfunction it may be more appropriate to refer urgently to ophthalmology for formal perimetry +/– urgent MRI as indicated.

If biochemical features of pituitary dysfunction are present (low testosterone/oestrogen with low or normal FSH/LH, low FT4, and inappropriately normal TSH, low 9 am cortisol, evidence of excess hormone secretion) without neurological symptoms, refer to endocrinology for further assessment.

Ultimately, a pituitary adenoma can only be completely excluded with normal MRI, but if a patient has normal pituitary biochemistry (on screening for hypo- or hypersecretion if suspected) and normal visual fields, then it is unlikely that a pituitary adenoma is significantly contributing to symptoms and an MRI is not required.

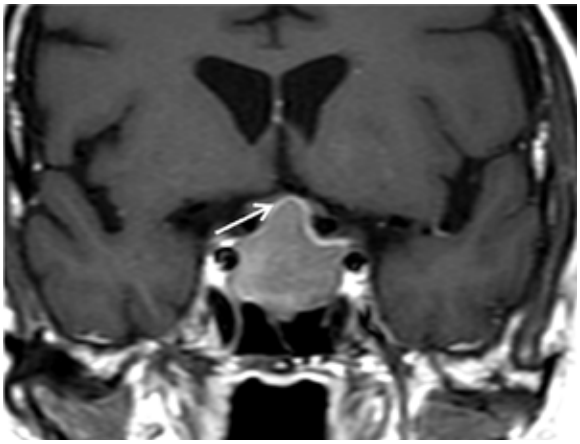

Fig 3 | Contrast MRI pituitary showing compression of the optic chiasm by a pituitary macroadenoma prior to surgery

How is it managed?

Patients may fear that they have a "brain tumour" and worry that it is malignant. Reassure them that pituitary adenomas are benign and usually treatable either with surveillance or with surgery and adjunctive radiotherapy +/– medical therapy if required. This is managed by endocrinologists, usually in a multidisciplinary setting. Surgery is the mainstay of treatment apart from prolactinomas where dopamine agonist therapy is first line. Hormone deficiencies are replaced with hydrocortisone, levothyroxine, testosterone, oestrogen, and growth hormone as necessary. In patients with significant comorbidity, decision for surgery is a balance between preserving vision and avoiding the risks of surgery and general anaesthetic.

Pituitary apoplexy is treated with urgent replacement of acute hormone deficiencies and trans-sphenoidal decompression as indicated.

Pituitary adenomas are increasingly diagnosed incidentally when the brain is imaged for an unrelated problem. Most of these cases will be reviewed by endocrinology and if the pituitary adenoma is non-functioning, clear of the optic chiasm, and not causing hypopituitarism, they are simply kept under surveillance in case of future growth and effects.[19 20]

Competing interests: None declared.

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EDUCATION INTO PRACTICE

- Are you aware of the different ways that pituitary adenoma can present and which initial tests can help with diagnosis?
- Do you routinely ask about libido and sexual function in people presenting with fatigue?
- How will your practice change as a result of reading this article?

HOW WERE PATIENTS INVOLVED IN THE CREATION OF THIS MANUSCRIPT?

The manuscript was read by a patient when in draft version. The content was amended to incorporate his feedback, which included his concerns about having a 'brain tumour,' which we address in the Management section.

WHAT YOUR PATIENT IS THINKING

Let's talk about the notion of being cured

Amy Robertson

describes how language around cure has shaped her understanding of wellness in chronic conditions

ROSE LLOYD

I first encountered the notion of cure as a little girl. I received a diagnosis of arthritis at the age of 2 and remission was a central part of conversations about my condition. Although I cannot recite the specifics, I distinctly remember the energy of those conversations. There was so much hopefulness that hinged on my going into remission, so much relief when it seemed that I had, and such deep sadness when my arthritis "came back." I took all of it in: the hope and the despair, the powerful notion that remission was the key to my wellness, and ultimately the sense that I was fundamentally broken and unwell.

Cure as an experience

Cure has been communicated to me across my lifetime in two salient ways.

"Cure" and "normal" have projected impossible standards on to my body

Health professionals often communicate to me a "best case scenario" in which I will heal from each of my chronic medical conditions. The "next best thing" is that I would have as few symptoms, or get as close to normal, as possible. Cure, as an experience, is about hoping to become normal, and it is achieved through medical intervention.

What I internalised from a lifetime of conversations like these is that my body is broken and I will likely never be well. "Cure" and "normal" have projected impossible standards on to my body. And the narratives of brokenness and unwellness that I internalised have had painful consequences for me: chronic anxiety about my health, a negative self image, and a lack of agency around my wellness.

Extraordinary bodies

Fortunately, I have been on a journey to heal my relationship with my body. Here, I invite you to be a part of this healing for patients like me, by asking you to consider the following re-framings: bodies with chronic medical conditions are extraordinary bodies, resilient bodies, bodies deeply committed to healing themselves again and again with support. Wellness is more about one's experience of life and investment in oneself than about external standards or sets of circumstances.

Health professionals can actualise these framings by using their expertise to help patients achieve their own wellness goals. They can ask patients to identify goals and work with them to identify care that meets their goals. They can narrate patients' bodies as resilient, help patients to remember and tap into their own healing potential, and avoid using language such as "normal" or "functional."

I recognise that I am asking you to do something that is in my experience counter-cultural. After all, not all bodies heal themselves, even with the support of medical technology. Indeed, this latter critique emerges from a vision of healing that centres around returning to a state of minimal symptoms and maximal functionality, as defined against an external norm. I am inviting you to participate in a different vision, in which healing is about thriving within one's life as it is, where medical professionals support that thriving with their expertise rather than define it for us.

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WHAT YOU NEED TO KNOW

- The notions of cure, normal, and functional narrate patients with chronic medical conditions as broken and unwell
- Framing patients' bodies as resilient can be empowering
- Identifying what wellness means for a patient can ensure you are both working towards the same goals

EDUCATION IN PRACTICE

- What does it mean to you for a patient to be healthy or well?
- How could you encourage patients to think about what wellness means to them?
- How could thinking of bodies with chronic conditions as resilient and extraordinary change the language you use with patients?

CASE REVIEW

A child with a congenital hand anomaly

A 5 month old infant attended a paediatric hand clinic with his parents. The presenting complaint was a duplicated thumb on his right hand. The anomaly was detected on a routine baby check by a paediatric junior doctor, who referred the infant to a paediatric hand surgeon.

The child's parents confirmed that the baby was born at term and was otherwise clinically well. There was no family history of congenital hand abnormalities.

On examination, the patient had two well formed thumbs on his right hand (fig 1); each with a nail plate. Both thumbs were reduced in size compared with the contralateral thumb and both had poorly defined interphalangeal joint creases, indicative of reduced mobility. The radial sided thumb was axially deviated (ulnarwards), whereas the ulnar sided thumb was well aligned.

The patient could be seen actively flexing and extending the metacarpophalangeal and carpometacarpal joints and was also capable of active and passive palmar abduction at this carpometacarpal joint.

A radiograph of the ulnar and radial parts of the patient's right thumb is shown in fig 2.

1 **What congenital anomaly does the radiograph show?**
2 **Why do children with this condition require referral to paediatric specialists?**
3 **How is this condition treated?**

Submitted by Jenny Wright, Mark Pickford, and Asit Khandwala

Parental consent obtained.

Cite this as: *BMJ* 2019;365:l1847

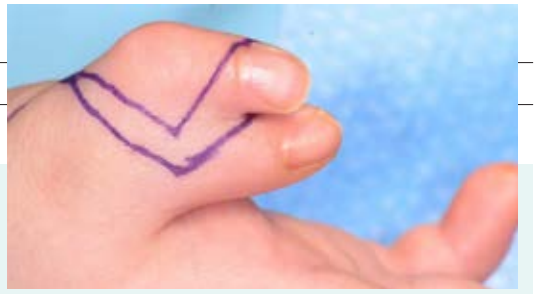


Fig 1 | Photograph of the patient's thumbs

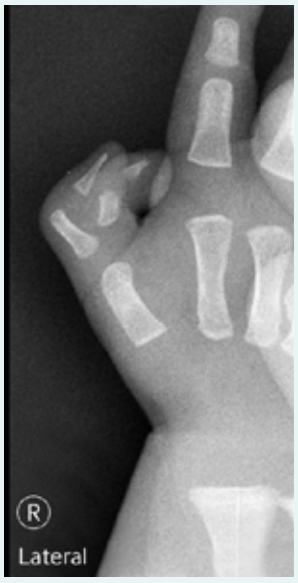


Fig 2 | Radiograph of the patient's thumbs

If you would like to write a Case Review or Spot Diagnosis for Endgames, please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

answers For extra material, including patient outcome, go to bmj.com/endgames

CASE REVIEW **A child with a congenital hand anomaly**

1 What congenital anomaly does the radiograph show?

Pre-axial (radial sided) polydactyly. The radiograph shows a duplication of the proximal and distal phalanges (fig 3).

The radial sided thumb is usually considered the duplicated part or accessory thumb because it is typically smaller and less functional in comparison to the ulnar sided thumb.

2 Why do children with this condition require referral to paediatric specialists?

The British Society for Surgery of the Hand recommends early paediatric assessment because around 20% of cases are associated with a genetic disorder, syndrome, or other congenital abnormality, including acrocephalopolysyndactyly syndrome, Fanconi anaemia, Down's syndrome, Holt-Oram syndrome, short ribs polydactyly syndrome, and VACTERL association (vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities).

3 How is this condition treated?

Corrective surgery by a paediatric hand surgeon when the child is around a year old, when there are fewer risks from general anaesthesia. It commonly involves ablation of the radial-sided duplication and reconstructive techniques to optimise functionality, stability, and cosmesis of the retained thumb.

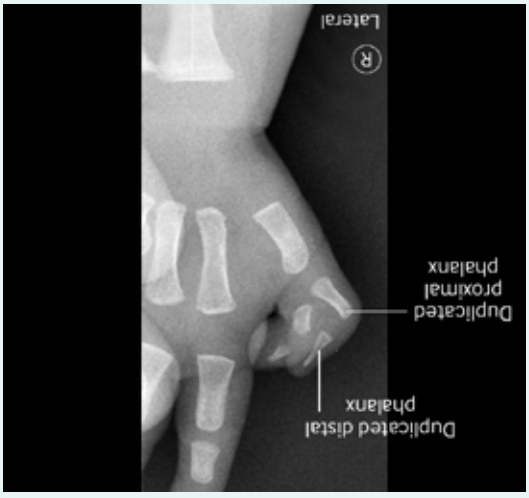


Fig 3 | Radiograph showing duplication of the distal and proximal phalanges of the right thumb

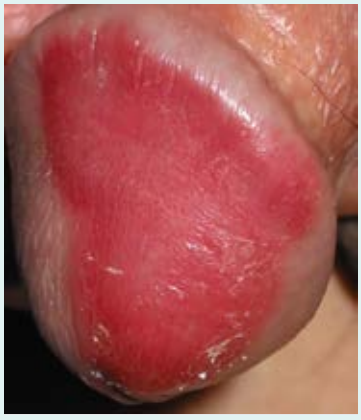
CPD READING
0.5 HOURS

You can record CPD points for reading any article. We suggest half an hour to read and reflect on each.

LEARNING MODULE

Articles with a "learning module" logo have a linked BMJ Learning module at http://learning.bmj.com.

Well demarcated erythema of the glans penis



A 47 year old man presented with a one year history of well circumscribed desquamation, erythema, and mild pruritus on his glans penis (figure). There were no lesions on his scalp, trunk, extremities, oral mucosa, or nails. Rapid plasma reagin, treponema pallidum particle assay, and human immunodeficiency virus serology were negative. Histology revealed marked hyperkeratosis, parakeratosis, and neutrophilic clusters in the stratum corneum, in keeping with psoriatic balanitis.

About 63% of patients with psoriasis vulgaris have genital involvement, but only 2-5% of patients have lesions limited to the genital area.

Uniformly distributed dotted vessels on a pale red background may be visible on dermatoscopy[3] but biopsy provides the definitive diagnosis.

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Patient consent obtained.

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Medication reviews

Because doctors find it easier to start a new drug than to stop an old one, many patients end up taking a long list of prescribed medicines. Medication reviews, especially if they involve patients and take account of their preferences, ought to help. However, a randomised trial in people over 70 who were taking more than six long term medications suggests that the benefit is disappointingly small (*PLoS Med*). Reviews decreased the number of prescribed drugs, improved health related quality of life according to one scale (although not according to another), but failed to reduce the overall number of health problems.

Familial hypercholesterolaemia

A registry study from the US finds that, although the risks of familial hypercholesterolemia are well known, many people with the condition are unrecognised and under-treated (*J Am Coll Cardiol*). Among nearly 2000 patients under the age of 50 who were diagnosed with acute myocardial infarction, nearly one in 10 met criteria for probable or definite familial hypercholesterolaemia. Many of them had not been taking a statin before the event. Worse, only two thirds were on high intensity statin treatment when they were discharged.

A purpose in life

A feeling of having a strong sense of purpose in life leads to better mental and physical health and a higher quality of life, according to a longitudinal study of middle-aged and older adults from the US (*JAMA Netw Open*). The benefit is surprisingly large. People in the highest of five categories of having a sense of purpose in life had half the mortality of people in the lowest category during four years of follow-up — even after adjustment for physical activity, body mass index, educational level, and chronic illness.

Complications of cardiopulmonary resuscitation

Adverse effects of cardiopulmonary resuscitation include rib fractures, haemopericardium, pneumothorax, and fat emboli, to list but a few. Obviously, these occur in the person receiving resuscitation rather than the person giving it. However, a case report of a doctor who performed a long stint of cardiac compressions during a night shift shows that clinicians can experience adverse effects too. Twelve hours after the incident, he developed pain and limitation of movement in his left shoulder. Magnetic resonance imaging revealed a tear in the long head of biceps (*BMJ Case Rep*).

Measles

In the year from April 2018 to March 2019, more than 11 000 incident cases of measles were reported in the 30 countries of the European Economic Area, with Italy, France, and Romania contributing the largest number (https://ecdc.europa.eu/sites/portal/files/documents/measles-monthly-report-may-2019.pdf). As a blog in the *London Review of Books* says, this is a scandal because measles should be extinct. There are no human or animal reservoirs of infection. The vaccine is cheap and effective. Achieving 95% immunisation rates worldwide, which would see the disease gone forever, doesn't await a technological breakthrough but only the right politics (https://www.lrb.co.uk/blog/2019/may/the-measles-scandal).

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