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Laryngitis

John M Wood,¹ Theodore Athanasiadis,² Jacqui Allen³

¹Otolaryngology, Head Neck Surgery, Princess Margaret Hospital for Children, Subiaco, WA, Australia
²Adelaide Voice Specialists, Adelaide, SA 5000, Australia

³North Shore Hospital, Auckland, New Zealand

Correspondence to: T Athanasiadis
theoathans@gmail.com

Cite this as: *BMJ* 2014;349:g5827
doi: 10.1136/bmj.g5827

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Laryngitis describes inflammation of the larynx, and a variety of causes result in the presentation of common symptoms. Laryngitis may be acute or chronic, infective or inflammatory, an isolated disorder, or part of systemic disease, and often includes symptoms such as hoarseness. Commonly, laryngitis is related to an upper respiratory tract infection and can have a major impact on physical health, quality of life, and even psychological wellbeing and occupation if symptoms persist.¹ Overall, laryngitis incorporates a cluster of non-specific laryngeal signs and symptoms that can also be caused by other diseases. Consequently diagnosis can be difficult and requires correlation of history, examination, and, if necessary, specialised assessment, including visualisation of the larynx and stroboscopy. Acute laryngitis is typically diagnosed and managed at the primary care level. In at risk populations, or those with persisting symptoms, referral to a specialist otolaryngologist should be considered. The aim of this review is to assist non-specialists in assessing and managing people with laryngitis and to identify the cohort that requires specialist input.

What is laryngitis?

The larynx is a complex organ that is important for airway protection and maintaining safe swallowing and positive pressure in the pulmonary system. It is integral to cough, straining, and swallowing, and has immunological² and even hormonal³ functions. Disease related changes in the larynx can impair some or all of these functions. The term laryngitis is descriptive and refers to inflammation of the larynx. It is typically used to describe acute infective laryngitis, one of the most common diseases of the larynx.⁴ However, a multitude of other causes of laryngeal inflammation present with similar signs and symptoms. Typically, laryngitis includes dysphonia, air wasting (excessive loss of air through the incompletely closed glottis resulting in a breathy voice), and pain or discomfort in the anterior neck, and it may include other symptoms such as cough, throat clearing,

SUMMARY POINTS

The cause of laryngitis is varied and determines appropriate treatment

Acute laryngitis is common and generally self limiting

Clinicians should re-visit the diagnosis and ensure endoscopic examination has been performed if symptoms persist or red flag symptoms develop

Initial assessment must consider airway patency and rule out malignancy

Patients with compromised immunity may be at increased risk of infectious causes

The impact of laryngopharyngeal reflux is becoming widely recognised, with research focused on improving diagnosis and treatment

SOURCES AND SELECTION CRITERIA

We searched Medline, PubMed, and the Cochrane Database of Systematic Reviews, using the search terms "laryngitis", "laryngeal inflammation", and "dysphonia". In addition we searched for specific conditions: "laryngopharyngeal reflux", "sarcoidosis", "pemphigoid", and "tuberculosis". Studies were limited to adult populations and where possible included systematic reviews and randomised controlled trials; we also included case reports to emphasise important problems.

globus pharyngeus (feeling of a lump in the throat), fever, myalgia, and dysphagia.

How common is it?

The prevalence of laryngitis is difficult to estimate. A review conducted by the Royal College of General Practitioners in the United Kingdom in 2010 reported an average incidence of 6.6 cases of laryngitis and tracheitis per 100 000 patients (all ages) per week.⁵

How is it assessed?

Laryngeal symptoms may have many causes. They are usually driven by four broad disease processes: inflammation, neoplastic and structural abnormalities, imbalance in muscle tension, and neuromuscular dysfunction.⁶ Laryngeal symptoms arise from one or a combination of these processes. A careful history and examination is crucial in determining the primary factor and helping to identify other factors leading to persisting symptoms.

The first consideration in the initial assessment of patients with laryngeal symptoms should be airway patency. Patients with stridor or respiratory distress need urgent assessment in a setting where airway support can be provided quickly if needed.

Having assessed the airway, the history should cover the nature and chronology of voice symptoms, any exacerbating and relieving factors, and the patient's voice use and requirements. In addition to the description of vocal problems, it is important to ask about associated symptoms of dysphagia, odynophagia, otalgia, reflux, globus pharyngeus, weight loss, pulmonary health, and choking. Box 1 outlines the red flag symptoms that should prompt an urgent referral to exclude malignancy. Contributing medical conditions or the effects of treatment should be considered, as should lifestyle factors, including smoking, diet, and hydration. The impact on quality of life and psychosocial wellbeing should also be addressed.

Investigations include a general head and neck examination covering the oral cavity, oropharynx, and neck, and an assessment of the patient's voice. This can be done by way of a simple scale: grade 1 (subjectively normal voice), grade 2 (mild dysphonia), grade 3 (moderate dysphonia), grade 4 (severe dysphonia), and grade 5 (aphonic), with addi-

Box 1 | Red flag symptoms for early referral (adapted from Schwartz et al⁷)

- Stridor—emergency referral
- Recent surgery involving the neck or recurrent laryngeal nerve
- Recent endotracheal intubation
- Radiotherapy to the neck
- History of smoking
- Professional voice user (for example, singer, actor, teacher)
- Weight loss
- Dysphagia or odynophagia
- Otagia
- Serious underlying concern by clinician

tional qualifiers used as necessary—for example, breathy, strained. Alternatively, a widely used grading system is the GRBAS (grade, roughness, breathiness, asthenia, strain) scale. It is a simple and reproducible method to assess voice change and quality. This tool grades hoarseness, roughness, breathiness, asthenia (weakness), and strain on a scale of 0-3, with 0 representing normal, 1 mild degree, 2 moderate degree, and 3 high degree.⁸ Either scale may be used by practitioners to track changes in voice over time and also allows other practitioners to understand the degree of voice dysfunction from notation.

What are the causes of acute laryngitis?

Acute laryngitis is commonly caused by infection (viral, bacterial, or fungal) or trauma.⁹ Inflammation and oedema of the larynx impairs vibration of the vocal folds, with resulting symptoms.⁹ Inflammation may involve any area within the larynx, including the supraglottis (epiglottis, arytenoids, and false vocal folds), the glottis (true vocal folds), and subglottic regions. The larynx may be affected directly by inhaled material or by haematogenous spread, infective secretions, or as a consequence of irritation from contact trauma—for example, coughing. Symptoms may persist but are usually self limiting, with a duration of less than two weeks. In general practice, treatment is generally supportive, with voice rest, adequate hydration, and mucolytics.

Viral laryngitis

Viruses are the most common cause of acute laryngitis, most often rhinovirus, adenovirus, influenza, and parainfluenza. Other viruses should be considered, particularly in patients who are immunocompromised (for example, due to herpes species, human immunodeficiency virus, coxsackievirus). Rarely, severe infections such as herpes simplex can result in laryngeal erosion and necrosis.¹⁰

Bacterial laryngitis

Bacteria are also an important cause of acute laryngitis, and distinction between viral and bacterial infections can be difficult. The two may coexist, with viral illness allowing opportunistic bacterial superinfection to occur. Commonly identified bacteria include *Haemophilus influenzae B* (HiB), *Streptococcus pneumoniae*, *Staphylococcus aureus*, β haemolytic streptococci, *Moraxella catarrhalis*, and *Klebsiella pneumoniae*.^{4 11} Production of pseudomembrane or serous casts, purulence, marked erythema, and co-involved dis-

tant sites (for example, lung, tonsils) are often suggestive of bacterial disease. Historically, diphtheria was associated with a pathognomonic grey membranous cast that could actually cause airway obstruction. With vaccination this is rarely seen nowadays. Viral illness may manifest blisters, particularly herpes zoster, and can be associated with nerve paresis involving the lower cranial nerves. Equally, erythema and pain disproportionate to the mucosal appearances can be representative of viral disease. Fever may be present in both, as can systemic symptoms. Reaction to antibiotics can indicate viral disease in retrospect—for example, production of rash when amoxicillin is given in the presence of Epstein Barr virus infection.

Unusual causes of bacterial laryngitis in developed nations include mycobacterial and syphilitic disease, although these are still seen in developing countries or areas with large immigrant populations.¹² Diagnosis can be difficult, as lesions may appear ulcerative, mimic neoplasia or candidiasis, or have a non-specific inflammatory appearance. Ultimately tissue diagnosis is essential to assess for tumour, which is considerably common, or to identify acid-fast bacilli on microscopy. Suspicion should be high in patients from developing countries with high rates of tuberculosis and those who are immunocompromised.¹³

Supraglottitis and epiglottitis—Owing to the rapid progression of airway compromise, especially in children, much of the literature on acute bacterial laryngitis concerns supraglottitis and epiglottitis, particularly in the context of *H influenzae*.¹⁴ Patients present with rapidly progressing odynophagia, dysphagia, hoarseness, drooling, and stridor. This constellation of symptoms indicates a high risk of impending airway compromise and requires emergency assessment and airway management. Treatment for less severe cases includes humidification through nebulised normal saline, or constant humidified oxygen, corticosteroids, intravenous antibiotics, and nebulised adrenaline. HiB vaccination has altered the epidemiology and incidence of supraglottitis and epiglottitis, most notably in the paediatric population, with a substantial decrease in presentations.¹⁴

Fungal laryngitis

Laryngeal candidiasis is a common yet under-diagnosed disease, presenting in both immunocompromised and immunocompetent patients and accounting for up to 10% of presentations.¹⁵ Risk factors include recent use of antibiotics and use of inhaled corticosteroids.¹⁶ Laryngeal examination usually demonstrates whitish speckling of the supraglottis or glottis. At times, diffuse laryngeal erythema and oedema may be seen without these plaques. Candidiasis may mimic other disorders, particularly hyperkeratosis, leucoplakia, and malignancy, and these must be ruled out by biopsy or imaging. Although such infections most often occur in immunocompromised patients, they can occur in patients with normal immunity when there are alterations to the mucosal barrier,¹⁶ such as after chemoradiotherapy, prolonged use of inhalers, or laryngopharyngeal reflux. Biopsy can be difficult to obtain and culture may take several weeks, although fungal elements may be detected more rapidly on Gram stains. Consequently some experts have recommended the diagnosis is implied from a combination of strong clini-

cal suspicion with adequate treatment response to oral antifungal tablets and antifungal solution.

Phonotrauma

Laryngeal inflammation can arise from collision forces of the vocal folds. Such injury can occur with excessive voice use or misuse during phonation.¹⁷ Yelling, screaming, forceful singing, and strained voicing may result in diffuse inflammation and erythema within the larynx.¹⁸ Consequently those in professions with high vocal demands, such as professional singers, actors, and teachers are at much greater risk of developing voice disorders.¹⁸⁻¹⁹ Although injury is most often limited to the superficial layers of the vocal fold, and endoscopic findings may be minimal, wound healing after repeated episodes can lead to long term changes and persistent symptoms. The larynx may be traumatised in other ways, including blunt or penetrating trauma, chronic coughing, or habitual throat clearing.¹⁸ These may be acute or may persist, with development of chronic laryngitis.

How is acute laryngitis treated?

Management of laryngitis varies depending on the severity. Patients with acute airway compromise or presumed epiglottitis should be referred for urgent management. Most cases of acute laryngitis are self limiting and typically resolve within two weeks. Management options include vocal hygiene and antibiotics.

Vocal hygiene

Vocal hygiene refers to measures such as voice rest, hydration, humidification, and limiting caffeine intake. These measures are invaluable in the symptomatic treatment of laryngeal inflammation. Care of the voice should be recommended to all presenting with vocal difficulties as this provides symptomatic relief and is good practice to carry forward, even as laryngitis resolves. Periods of voice rest may be as short as 48 hours or as long as a week, and a simple rule of thumb can be to recommend voice rest until patients find it comfortable to hum. Then modest speech can be resumed. Hydration is vital, particularly in those who snore or mouth-breathe at night. Hydration may be achieved just by chewing sugar-free gum, or increasing total fluid intake during waking hours (250 mL per waking hour). Caffeine is dehydrating and increases reflux and therefore exacerbates both snoring and pharyngolaryngeal irritation. Fewer than two standard espressos a day is recommended. Many sodas and “smart drinks” also contain high levels of caffeine.

Vocal difficulties can result from hyperfunctional vocal behaviours, which in professional voice users can limit or even end their career. High risk groups include singers, performers, and teachers. Holistic voice hygiene programmes encompass a multifactorial approach. Most programmes focus on four main tenets: dealing with the amount and type of voice use, reducing phonotraumatic behaviours, improving hydration, and enhancing lifestyle to improve vocal health, such as reducing caffeine and alcohol intake, smoking cessation, and managing medical conditions. The role of local lubrication, systemic hydration, control of laryngopharyngeal reflux, and allergies are often addressed.²⁰ A study of teachers found such programmes demonstrated a reduction in vocal misuse and resulting voice symptoms.²¹ However, reviews

conducted on the benefit of vocal hygiene found limited data for either therapeutic or preventive techniques.²⁰

Antibiotics

Treatment of acute laryngitis with antibiotics is widely debated, with frequent reports of inappropriate prescribing of antibiotics for upper respiratory tract infections.²² A Cochrane systematic review of two trials involving a total of 206 adults found no benefit in treating acute laryngitis with antibiotics, as measured by differences in objective voice scores at one and two weeks' follow-up.⁴ The first included study compared a five day course of penicillin V with placebo and reported no difference in patient reported symptoms at 2-6 months' follow-up. The second study compared erythromycin with placebo and found a subjective reduction in voice disturbance at one week and a reduction in cough at two weeks in the erythromycin group. Signs and symptoms such as persistent fever (>48 hours), purulent sputum, membrane formation, or associated distant disease should prompt consideration of antibiotic treatment.

When should people with laryngitis be referred?

Patients with acute airway compromise or suspected epiglottitis or supraglottitis should be assessed in hospital as an emergency. Acute laryngitis is often self limiting and typically resolves within two weeks. The persistence of laryngeal symptoms beyond three weeks is defined as chronic laryngitis. It can indicate additional laryngeal disease and warrants examination. Acute laryngitis may become chronic, with a shift in the underlying pathophysiology. It may be a direct consequence of the initial acute laryngitis episode or have a completely different or concomitant or superimposed cause. A recent retrospective study found that three quarters of patients referred to an otolaryngologist with an initial diagnosis of acute laryngitis had a different final laryngeal diagnosis.²³ Importantly, nearly half the patients with laryngeal cancer had an initial diagnosis by their primary care doctor of either acute laryngitis or non-specific dysphonia. This highlights the need for adequate laryngeal examination by an otolaryngologist in all patients with persisting symptoms, or in those who generate a high degree of suspicion, such as heavy smokers.

There is debate as to how long dysphonia may be present before warranting laryngoscopy. Many otolaryngologists would recommend laryngoscopy if dysphonia is present for more than three weeks without an obvious cause, such as acute illness or intubation. Interestingly, guidelines from the American Academy currently state that direct laryngeal examination is warranted for dysphonia that is present for up to three months, or sooner if there are concerns.⁷ This recommendation is based on a cohort study, which found that a delay in diagnosis of laryngeal cancer greater than three months led to poorer survival outcomes.⁷ The statement is also qualified by highlighting certain groups that require more urgent review, particularly if the cause may be life threatening or reduce professional viability or voice related quality of life⁷; these groups include people with red flag symptoms and those who rely on their voice for their occupation (box 1). If symptoms persist for longer than three weeks, we recommend that patients should be referred to an otolaryngologist to exclude malignancy.

Box 2 | Common causes of chronic laryngitis

Inflammatory

Allergic

Unclear whether symptoms related to allergic rhinitis or asthma, or primarily from larynx^{24 25}

Diagnosis can be difficult: non-specific findings, hard to differentiate from laryngopharyngeal reflux

Laryngopharyngeal reflux

Non-specific cluster of laryngeal manifestations

Evidence of different pathophysiology to gastro-oesophageal reflux disease

Autoimmune

Autoimmune disorders

Chronic laryngitis may be a manifestation of systemic disease such as rheumatoid arthritis, pemphigoid, systemic lupus erythematosus, and amyloidosis

High degree of suspicion is needed in the setting of other systemic symptoms, such as arthritis, cutaneous changes, and mucous membrane lesions

Rheumatoid arthritis

The prevalence of laryngeal symptoms in people with rheumatoid arthritis is reported to be between 30% and 75%²⁶

Includes cricoarytenoid joint fixation, recurrent laryngeal nerve neuropathy, myositis, and laryngeal nodules

Mucous membrane pemphigoid

Rare chronic autoimmune vesiculobullous disease
Manifests as blisters or bullae of the ocular and oral mucous membranes, with involvement of aerodigestive tract
Laryngeal involvement is a rare but life threatening complication, affecting 12% of patients²⁷

Managed with cyclophosphamide and prednisolone; role of surgery unclear

Granulomatous

Sarcoidosis

Laryngeal sarcoidosis is present in 0.5-5% of patients with sarcoidosis²⁸

Commonly presents with non-specific laryngeal symptoms²⁹

Dysphonia may be present due to recurrent laryngeal nerve palsy from mediastinal lymphadenopathy

Examination may reveal oedematous laryngeal mucosa, with supraglottis being the most commonly involved site. The vocal folds are rarely involved

Biopsy is required to confirm the diagnosis

Treated with systemic corticosteroids; or more rarely intralesional injections or laser resection²⁸

ADDITIONAL EDUCATIONAL RESOURCES

Resources for healthcare professionals

Revez L, Cardona AF. Antibiotics for acute laryngitis in adults. *Cochrane Database Syst Rev* 2013;3:CD004783—highest level evidence suggests that antibiotics are not useful for acute laryngitis

Resources for patients

Egton Medical Information Systems. Laryngitis (www.patient.co.uk/health/laryngitis-leaflet)—well written leaflet for patients, summarising laryngitis

American Accreditation HealthCare Commission. Laryngitis (www.ncbi.nlm.nih.gov/pubmedhealth/PMH0002361/)—bullet points on laryngitis, which provide useful patient information

What are the causes of chronic laryngitis?

Chronic laryngitis is defined as laryngitis that persists beyond three weeks. It can be due to a range of different disease processes, ranging from inflammatory processes, such as allergic laryngitis and laryngopharyngeal reflux, to autoimmune disorders such as rheumatoid arthritis, and granulomatous disease such as sarcoidosis. Chronic laryngitis is less prevalent in primary practice but is the primary indication for referral. By definition, chronic laryngitis implies persistent laryngeal problems, and the glottis should be directly visualised in this situation. While a detailed description of each cause of chronic laryngitis is outside the scope of this review, box 2 summarises the features of the common causes of chronic laryngitis.

Laryngopharyngeal reflux/extraoesophageal reflux

Over the past 30 years it has been increasingly recognised that extraoesophageal manifestations of gastro-oesophageal reflux disease (GORD) may include laryngitis. Large population based studies have reported that patients with GORD are at increased risk for associated laryngeal or pulmonary complications.³⁰ Symptoms of laryngopharyngeal reflux include non-specific laryngeal manifestations, such as hoarseness, dysphagia, odynophagia, globus pharyngeus, chronic cough, and throat clearing. Furthermore, laryngopharyngeal reflux has been associated with other conditions, such as vocal cord nodules, both premalignant and malignant changes in the larynx, and even sinusitis and otitis media.³¹ There is increasing evidence that the pathophysiology of laryngopharyngeal reflux differs from that of GORD, with patients affected by laryngopharyngeal reflux experiencing more daytime (upright) reflux without oesophagitis.³¹

The prevalence of laryngopharyngeal reflux is difficult to determine, particularly as typical heartburn is absent in 57-94% of patients.³² However, it has been estimated to be present in 10% of patients presenting to an otolaryngologist³³ and over half the patients referred with voice disorders.³⁴ The diagnosis of laryngopharyngeal reflux is controversial as no ideal test is available. The results of dual probe pH monitoring have varied,³² with some studies showing, particularly in chronic cough, that the pH of refluxate is not important.³⁵ Recent studies have considered the utility of pH-metry with intraluminal impedance testing and symptom association probability scores. Impedance allows consideration of non-acid and mixed reflux episodes in relation to symptom generation. This improves temporal association of symptoms with reflux episodes of any pH, which may be relevant in atypical symptoms of reflux such as cough or globus pharyngeus. New diagnostic tools including the lateral flow pepsin assay or Peptest (RDBiomed, Hull, United Kingdom), and the Restech pharyngeal probe (Respiratory Technology Core, San Diego, CA) are currently in validation studies and may prove to be of clinical use in future.³⁶ Several studies have identified pepsin as one of the injurious agents in laryngopharyngeal reflux, with injury compounded in the presence of an acidic environment.³⁷ Pepsin can be endocytosed by hypopharyngeal cells and may be reactivated later. Furthermore, it is not inactivated until the pH is greater than 8 and retains around 20% activity at a pH of 6.8, the average pH of the laryngopharynx.

Despite acknowledgment that reflux laryngitis is not merely an acid phenomenon, management still centres on

QUESTIONS FOR FUTURE RESEARCH

What is the role of targeted antireflux treatments such as pepsin inhibitors and the Linx system? (Linx is a cirlet of magnets inserted at the lower oesophageal sphincter in a laparoscopic procedure designed to augment closing pressures).

What role does neural dysfunction play in chronic laryngitis or dysphonia?

high dose use of proton pump inhibitors (PPIs), both as a therapeutic and as a diagnostic technique. A significant percentage of patients with laryngopharyngeal symptoms fail to improve with use of PPIs and may require physical reflux barriers such as Gaviscon liquid (Reckitt Benckiser, Hull, United Kingdom). In addition, the duration of treatment with PPIs is uncertain. A recent systematic review, including eight randomised controlled trials, found only two studies where PPIs were significantly more effective than placebo. The studies concluded that the current body of literature is insufficient to make reliable conclusions about the benefits of PPIs in laryngopharyngeal reflux. Antisecretory drugs also present an important side effect profile, including bloating, epigastric discomfort, inhibition of calcium and magnesium absorption, atrophic gastritis, and drug induced acid hypersecretion. PPIs should only be prescribed for a defined period and then symptoms reviewed. Where symptoms remain, further investigation should be considered, including pH-metry, impedance, laryngoscopy, gastroscopy, manometry, and videofluoroscopic swallowing study, depending on the cluster of symptoms. Hyperacidity, association of symptoms with or after meals should prompt pH study with impedance. Where there is associated solid food dysphagia, gagging, or choking a videofluoroscopic assessment of swallowing is recommended. If symptoms are dyspeptic in nature (bloating, belching, food triggered) then gastroscopy may help.

Overall, the treatment of extraoesophageal reflux should include dietary and behaviour modification, with judicious use of antisecretory drugs. Liquid alginate preparations and H₂ receptor antagonists have been used in combination with PPIs in recalcitrant cases.³⁶ The role of laparoscopic fundoplication is well established in patients with GORD and typical symptoms. Some investigators recommend antireflux surgery

TIPS FOR NON-SPECIALISTS

- Dysphonia of duration more than three weeks requires direct laryngoscopy
- Dysphonia associated with otalgia, stridor, neck mass, or dysphagia should be considered related to malignancy until proved otherwise
- Failure to respond to proton pump inhibitor treatment does not exclude a diagnosis of reflux laryngitis
- Behavioural modification and hydration or humidification are invaluable in symptomatic treatment of inflammatory laryngitis

for patients with laryngeal symptoms.³⁸ However, a review of 893 consecutive patients who underwent a laparoscopic fundoplication identified 93 with throat symptoms. Those who experienced typical GORD symptoms in addition to “throat” symptoms improved similarly to those with only typical GORD symptoms of heartburn or regurgitation. Patients with objective evidence of GORD, dual channel pH monitoring and laryngeal examination suggesting laryngopharyngeal reflux, and only experiencing throat symptoms were less likely to benefit from surgery. Fewer than half in this group benefited from surgery, and patients should be counselled appropriately if this option is being considered.^{20 33} Failure to respond to optimal combined antireflux treatment should prompt consideration of alternative causes of laryngeal symptoms.

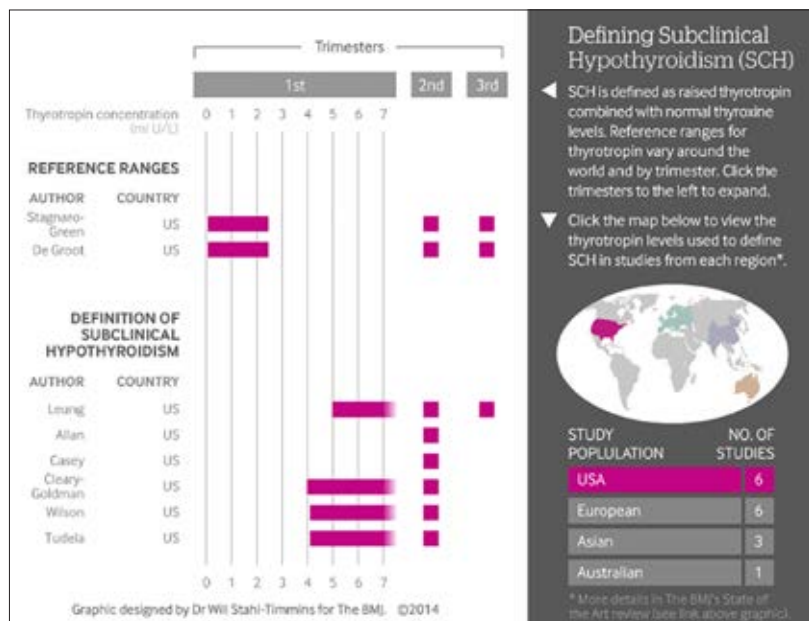
Contributors: JMW drafted and revised the manuscript. TA designed the article outline and critically revised and edited the manuscript. He is guarantor. JA drafted and reviewed the manuscript.

Competing interests: We have read and understood the BMJ policy on declaration of interests and declare the following: none.

Provenance and peer review: Commissioned; externally peer reviewed. References are in the version on thebmj.com.

State of the art reviews

Diagnosis and management of subclinical hypothyroidism in pregnancy



This week our State of the Art review is the diagnosis and management of subclinical hypothyroidism in pregnancy (<http://doi.org/10.1136/bmj.g4929>). Subclinical hypothyroidism is defined as raised thyrotropin combined with a normal serum free thyroxine level. The prevalence of undiagnosed subclinical hypothyroidism in pregnant women ranges from 3% to 15%.

Early diagnosis is essential as the condition is associated with multiple adverse outcomes in the mother and fetus including spontaneous abortion, pre-eclampsia, gestational hypertension, gestational diabetes, preterm delivery, and decreased IQ in the offspring.

The review summarises the effects of subclinical hypothyroidism on the mother and fetus, and the recommendations for diagnosis and treatment. It discusses how to measure and interpret thyroid function tests, and the pros and cons of universal screening for thyroid disease during pregnancy. It concludes with a description of prospective ongoing trials.

Use our interactive tool to explore the definitions of SCH in key studies.