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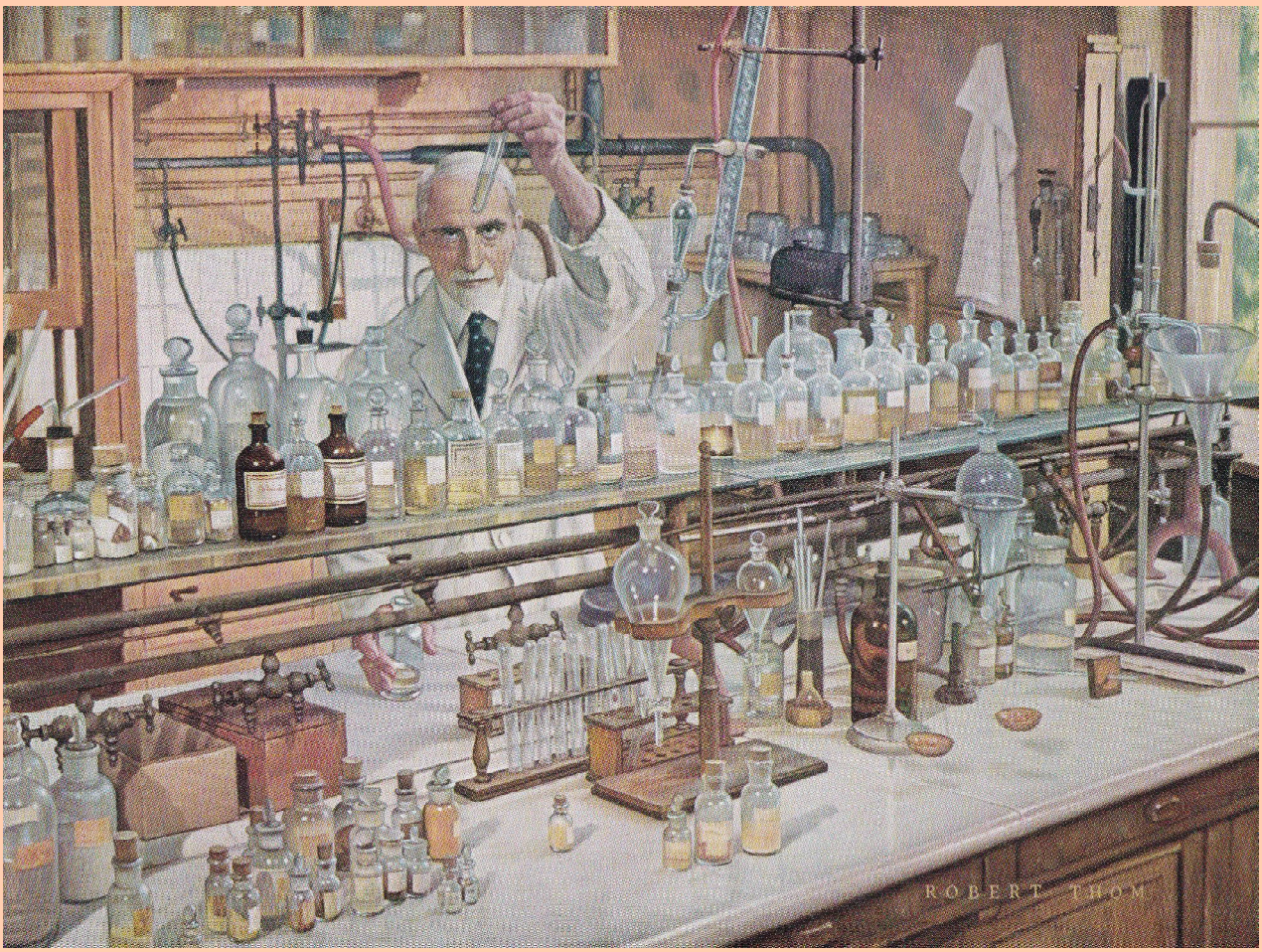

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Cover picture

THE DEVELOPMENT OF CHEMOTHERAPY

French pharmacist Ernest F. A. Fourneau, who headed laboratories in the Institut Pasteur, Paris, developed many chemical compounds to fight disease. His work stimulated intensive worldwide research for new medicinally active chemicals.

One of a series: *A History of Pharmacy in Pictures*, presented by Parke, Davis & Company.

George A. Bender, Director Robert A. Thom, Artist

Management approach in Graves' disease

Introduction

Graves' disease, named after Robert J. Graves, MD, in 1830s, is an autoimmune disease characterized by hyperthyroidism, diffuse thyroid enlargement and ophthalmopathy. Antibody formation against the thyroid-stimulating hormone (TSH) receptor on thyroid follicular cells has been implicated in the pathogenesis of the Graves' disease. TSH receptor antibodies (TSHRAb) are specific for Graves' disease. Atypical presentations occur and euthyroid Graves' and ophthalmic Graves' are examples where the clinician needs a high degree of suspicion for diagnosis. Diagnosis is based on the typical clinical features supported by biochemical confirmation. Uncontrolled disease can cause severe hyperthyroidism leading to arrhythmias, heart failure, metabolic derangements and visual impairment due to ophthalmopathy. The principal treatment goal is to diagnose the condition early, and to achieve clinical and biochemical remission as soon as possible. Remission needs to be maintained as early treatment cessation after euthyroidism is achieved may lead to relapse. Anti-thyroid drugs, radio-active iodine and surgery are the main treatment modalities available. Overtreatment with anti-thyroid medications, radio-active iodine and thyroidectomy may lead to hypothyroidism. Appropriate treatment should make the patient euthyroid and also preserve the patient's long-term metabolic health. This article focuses on the management of Graves' disease.

Clinical findings

When thyrotoxicosis coexists with a goitre, ocular signs and relevant symptoms, the diagnosis of Graves' disease is apparent. The clinical features of Graves' disease are shown in Table 1. However, 50% of patients with Graves' disease may not show clinically evident ophthalmopathy, making the diagnosis less apparent. Some manifestations of hyperthyroidism such as palpitations and tremor are caused by increased adrenergic tone and may suggest an anxiety disorder. Elderly patients often present with atypical features such as weight loss or isolated atrial fibrillation. A high degree of clinical suspicion is needed in the diagnosis of such cases. Graves' disease may be associated with other autoimmune diseases and hypokalaemic periodic paralysis.

Table 1. Clinical features of Graves' disease

Hyperthyroidism	
Symptoms	*Signs*
Weight loss	Tremor
Increase appetite	Tachycardia
Tremor	Atrial fibrillation
Irritability	Full pulse
Heat intolerance	Hyperkinesis
Frequent loose stools	Warm peripheries
Palpitations	Lid lag and "stare"
Itching	Goitre, bruit
Goitre	Palmar erythema
Loss of libido	Conjunctival oedema
Erectile dysfunction	Proximal myopathy
Oligomenorrhoea	Hyperactive reflexes
Amenorrhoea	Pretibial myxoedema
Ophthalmopathy	
Symptoms	*Signs*
Eye irritation	Lid lag and "stare"
Dry eye	Ophthalmoplegia
Diplopia	Periorbital oedema
Visual blurring	Exophthalmos
Periorbital oedema	Diffuse goitre, bruit
	Clubbing

Diagnosis

Ultrasensitive third generation TSH assay has the highest sensitivity and specificity and should be used as the initial screening test. All patients with Graves' disease show suppressed or low TSH with elevated free thyroxine (FT4) level, confirming hyperthyroidism. However, a minority of patients will have an increased total or free T3 level with a normal FT4 level and a suppressed TSH level, which is termed as "T3 thyrotoxicosis". This may represent the early stage of hyperthyroidism in Graves' disease. Subclinical hyperthyroidism is defined as a normal serum free T4 and free T3 levels, with a subnormal serum TSH level.

When characteristic signs of Graves' disease are present and biochemical investigations confirm hyperthyroidism, no further investigations are necessary for diagnosis. In a thyrotoxic patient with a smooth thyroid with no definite ophthalmopathy, measurement of TSHR-Ab is useful to distinguish Graves' disease from other causes of thyrotoxicosis. Measurement of levels of circulating TSHR-Ab has replaced the need for the radio-active iodine uptake (RAIU) scan for confirmation of the diagnosis. Two common two differential diagnoses are toxic adenoma and toxic multinodular goitre, both of which can be differentiated by RAIU scan.

In patients with unilateral ophthalmopathy or who are euthyroid, CT or MRI scanning of the orbits is required. These scans will show the characteristic swelling of the extraocular muscles and increased retro-orbital fat associated with Graves' disease. Comprehensive ophthalmic assessment, electrocardiogram and 2D echocardiogram may be required in patients with complicated disease.

Management

The goals of treatment of Graves' disease are to control symptoms and to achieve and maintain remission. Anti-thyroid drugs, vadio-active iodine and thyroidectomy are the treatment options available to restore euthyroid status but all three have potentially serious side-effects. It is important for the patient to be well informed about all three treatment options and their potential side-effects. Ideally a patient who is suspected to have Graves' disease needs to be evaluated by a specialist physician or an endocrinologist, before starting specific therapy. With complicated disease, a multidisciplinary approach involving a cardiologist, an ophthalmologist and a radiologist may be required.

Symptomatic therapy

β-blockers such as propranolol are used for symptom control until specific therapy normalises peripheral thyroid hormone levels. Calcium channel blockers such as verapamil and diltiazem, are effective alternatives in patients who do not tolerate or are not suitable for β-adrenergic blocking agents. Non-selective β-blockers such as propranolol and long-acting selective β-blockers such as atenolol or metoprolol are recommended for symptomatic treatment. The starting dose of propranolol is 20-40 mg 3-4 times daily and it is the preferred agent during pregnancy and breast-feeding. Atenolol can be started at a dose of 25-50 mg daily but can be increased up to 100 mg as required. β-blockade alone is not recommended as the sole therapy. Occasionally, higher doses of β-blockers are required for symptom control and reducing the heart rate to an acceptable level.

Specific therapy

Antithyroid drugs

Anti-thyroid drugs act mainly by inhibiting iodide organification and coupling, thereby reducing synthesis of thyroid hormones. They include carbimazole, methimazole, and propylthiouracil (PTU). Carbimazole is rapidly converted to methimazole in the serum (10mg of carbimazole is transformed to approximately 6mg of methimazole). PTU also inhibits peripheral conversion of T4 to T3. This may be beneficial in the first few weeks of therapy in severe hyperthyroidism.

Unless hyperthyroidism is mild, anti-thyroid drugs are usually administered initially at a higher dose and titrated to a lower maintenance dose depending on the biochemical response. The "block and replacement regimen", in which thyroxine therapy is added to anti-thyroid drugs when euthyroidism is attained, is not generally recommended, because it has been shown to result in a higher rate of anti-thyroid drug related side-effects. Anti-thyroid drugs may rarely lead to serious side-effects. Skin rash develops in 7% to 12% of patients and agranulocytosis in 0.1% to 0.5%. All patients taking antithyroid drugs should be educated and warned about the early symptoms of agranulocytosis, and advised to stop taking the medication and seek urgent medical attention if symptoms develop. Hepatitis and vasculitis also occur, more commonly with PTU. If anti-thyroid drugs are discontinued because of side-effects or relapse occurs after a course of therapy, patients are treated with radio-active iodine therapy or in selected cases, surgical thyroidectomy.

Carbimazole is initiated at a dose of 15 mg two or three times daily based on symptom severity. Most patients achieve euthyroidism at a dose of 15mg-30mg. PTU has a shorter duration of action and is usually administered two or three times daily, starting with 50-150mg three times daily. PTU has caused fulminant hepatic necrosis requiring liver transplantation, and children are more susceptible to hepatotoxic reactions from PTU than adults. So

carbimazole (and methimazole) have become the first-line anti-thyroid drug therapy for Graves' disease, except during the first trimester of pregnancy, in the treatment of thyroid storm, or when reactions occur with carbimazole therapy, where PTU is preferred. Free T4 and freeT3 levels should be monitored monthly and the dose adjusted until a maintenance dose of carbimazole at 5-10 mg/d is achieved. The level of TSH may remain low for weeks to months after anti-thyroid drugs are initiated and are unsuitable for monitoring therapy early in the course of treatment. Once euthyroid levels are achieved with the minimal dose of medication, clinical and laboratory monitoring of therapy can be arranged every 2-3 months. Prospective studies show that 18 months of treatment with anti-thyroid drugs are associated with a higher rate of remission than after 6 months of therapy. No further benefits have been shown in patients receiving 42 months of therapy. Recent reviews indicate that the remission rate following anti-thyroid drugs is around 30%-40%. A suppressed TSH level after a course of anti-thyroid drugs is invariably associated with relapse, and alternative therapy should be considered. Routine white blood cell counts and complete blood counts and differential counts should be obtained if relevant symptoms are present. Routine monitoring of liver function tests are unnecessary but indicated only if clinical features suggestive of liver dysfunction are present. When anti-thyroid drugs in sufficient doses fail to achieve euthyroidism, poor adherence should be considered before switching to alternative therapy.

Radio-active iodine

Radio-active iodine (RAI) therapy is a safe, cost-effective and well tolerated treatment option in Graves' disease. The major sequel is permanent hypo-thyroidism requiring lifelong thyroxine replacement therapy. RAI can induce a short-term increase in thyroid hormone level. To prevent this, pretreatment with anti-thyroid drugs are used, especially in severe hyperthyroidism, the elderly, and individuals with substantial co-morbidity. Anti-thyroid drugs should be discontinued 2-3 days before the administration of RAI. In patients with risk of worsening of hyper-thyroidism, resuming carbimazole 3-7 days after RAI administration should be considered. RAI is contra-indicated in pregnancy and during lactation, and it is prudent to obtain a pregnancy test 48 hours before treatment in any woman with childbearing potential. Aggravation of ophthalmopathy may occur in 15% of patients after RAI therapy. This may be prevented by concomitant corticosteroid therapy. The usual approach is a short course of prednisolone tapered over 2-3 months. Following RAI therapy thyroid function tests should be monitored at suitable intervals to detect cases of failure of RAI or development of hypothyroidism. RAI is the most commonly used treatment for Graves' disease in the USA, and anti-thyroid drugs are more popular in Europe.

Surgery

Surgery may be preferred for women planning a pregnancy in less than 6 months, with normal thyroid hormone levels, pressure symptoms, large goitres or when thyroid malignancy is suspected. Surgery may be considered also in patients with moderate to severe active Graves' disease when other modalities are ineffective or contra-indicated. Before surgery, patients are treated with anti-thyroid drugs until euthyroidism is achieved. Patients are treated 7 to 10 days before surgery with pharmacological doses of iodine to reduce vascularity of the thyroid gland. Iodine is contra-indicated in pregnancy as it may inhibit fetal thyroid function significantly. In Graves' disease total or near-total thyroidectomy is preferred over subtotal thyroidectomy as there is a greater chance of recurrence with the latter. If the patient is euthyroid at the time of surgery, thyroxine is started immediately postoperatively. The most common complications following near total or total thyroidectomy are hypocalcaemia due to hypoparathyroidism, left recurrent laryngeal nerve injury, and postoperative bleeding. Surgery should only be performed by surgeons with experience.

Management of extrathyroidal manifestations

Patients with a mild degree of Graves' ophthalmopathy are often diagnosed late. It is important to assess its activity and severity. Active disease is best treated with immunosuppressive drugs, whereas inactive disease is best treated with rehabilitative surgery based on the severity. Patients with mildly active ophthalmopathy can be managed with lubricant eye drops and ointments, sunglasses for surface symptoms, and prisms for diplopia. For patients with active moderate to severe and sight-threatening ophthalmopathy, first-line treatment is intravenous corticosteroid (eg. methylprednisolone) pulse therapy. Orbital irradiation with or without corticosteroids may be used for moderate to severe cases. Rehabilitative surgery has an important role in moderate to severe and sight-threatening orbitopathy

even when the disease is inactive. Optic neuropathy should be treated urgently with high doses of intravenous corticosteroids. Patients who smoke should be asked to quit smoking. Dermopathy is best treated with topical corticosteroids. Currently there are no effective treatments for acropachy.

Management of Graves' disease in pregnancy

Anti-thyroid drugs cross the placenta, and may cause fetal hypothyroidism. Because of minimal placental transfer with PTU, and possible association of aplasia cutis and choanal atresia with carbimazole (and methimazole), PTU is the preferred therapeutic option during the first trimester of pregnancy. The lowest dose of PTU to maintain FT4 level at or just above the upper limit of normal range should be used, monitoring therapy every 2-4 weeks after initiation and 4-6 weekly once target level is achieved. Using FT3 or TSH level to monitor may be misleading as TSH may remain suppressed throughout the pregnancy and attempts to nomalise FT3 levels may lead to an elevated TSH level. Due to the concern of fulminant liver failure with PTU, switching to carbimazole after the first trimester of pregnancy must be considered. The natural course of Graves' disease in pregnancy is gradual improvement in the second and third trimesters, and treatment should be adjusted accordingly. TSHR-Ab may cross the placenta, causing neonatal hyperthyroidism in 1% of pregnancies of women with Graves' disease. An elevated fetal heart rate (> 160 beats/min) may be an early clue. Measurement of TSHR-Ab level in the third trimester may predict neonatal hyperthyroidism.

Sub-clinical hyperthyroidism

Treatment of sub-clinical hyperthyroidism should be individualized and based on the patient's age, symptoms and co-morbidities. In patients with sub-clinical hyperthyroidism who are over 65 years, or those with established cardiovascular disease or osteoporosis, treatment with anti-thyroid drugs is justified. Other patients should be monitored by measuring thyroid function tests every 6 months.

Summary

Graves' disease is a complex autoimmune disease affecting multiple organ systems. A high level of suspicion is required for prompt diagnosis. Early diagnosis is important to prevent serious visual, cardiac and metabolic complications. Because all available treatments have significant side-effects, extensive discussion with the patient about available therapeutic options is key to good management.

Competing interests: None declared.

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Antibiotic prophylaxis for dental procedures

Summary

Patients at risk of developing infective endocarditis or infection of a prosthetic joint may require antibiotic prophylaxis during dental treatment.

Current guidelines recommend prophylaxis less often than in the past. This is because of concerns about antimicrobial resistance and an increased understanding about the daily incidence of bacteraemia.

There is international variation in the recommendations for preventing infective endocarditis so Australian health professionals should consult Australian guidelines. Conditions for which prophylaxis is still recommended include prosthetic heart valves and rheumatic heart disease in patients at high risk of endocarditis.

Most experts no longer recommend antibiotic prophylaxis for dental procedures in patients with prosthetic joints.

Keywords: antibiotic prophylaxis, dentistry, endocarditis, joint prosthesis

*(Aust Prescr 2017; **40**: 184-8)*

Introduction

Antibiotic prophylaxis has been used in dentistry for patients at risk of infective endocarditis or prosthetic joint infection. The scientific rationale for prophylaxis was to eliminate or reduce transient bacteraemia caused by invasive dental procedures. Despite a long history of use and multiple guidelines for prophylaxis, there remains uncertainty about its effectiveness. In the last 10 years, there have been significant changes to the guidelines for antibiotic prophylaxis. These changes have been driven partly by global concerns about antimicrobial resistance[1] and subsequent recommendations that any prescription of antibiotics should be appropriate and judicious.[2]

Another factor that has driven the changes has been the recognition that the incidence of transient bacteraemia caused by oral hygiene procedures is often the same as the incidence caused by many dental treatments for which prophylaxis has traditionally been given. Regular toothbrushing and flossing pose a greater risk in relation to both infective endocarditis[3] and prosthetic joint infection[4] than episodic dental treatment.

Toothbrushing,[5] flossing,[6] pulsating water irrigators[7] and interdental woodsticks[8] can all produce bacteraemia. Gingival inflammation has been significantly associated with an increased incidence of bacteraemia caused by toothbrushing.[9] However, the incidence of bacteraemia with flossing does not differ significantly between people with or without periodontal disease.[10] The incidence and magnitude of bacteraemia caused by flossing are the same as that caused by deep scaling/root planing within the same patients,[11] yet deep scaling/root planing is considered an 'invasive dental procedure' that has traditionally required antibiotic prophylaxis.

Infective endocarditis

The annual incidence of infective endocarditis is approximately 3–10 per 100 000 people[12] but its mortality rate is around 20%.[13,14] About half of all cases occur in patients with no known cardiac risk factors.[14] Staphylococci cause the majority of cases in developed countries[12,13] with the highest incidence found in patients over 65 years old undergoing diagnostic or interventional procedures in hospitals.[14]

Viridans streptococci are found as commensal organisms in the mouth and in plaque. They account for approximately 20% of native valve and 25% of cases of late prosthetic valve infective endocarditis.[15] Studies show that viridans streptococcal bacteraemia occurs commonly with invasive dental treatments, especially tooth extraction.[16] Anaerobic oral bacteria seldom cause infective endocarditis.[17]

Evolution of prophylaxis guidelines

Since the 1950s there has been a progressive reduction in the use of antibiotics in the prevention of endocarditis following dental therapy (see Table). Different countries have made different recommendations. The changes in the USA in 2007 limited prophylaxis to patients with conditions including prosthetic cardiac valves or valves repaired with prosthetic material, previous infective endocarditis, unrepaired and repaired congenital cardiac defects and cardiac transplants with subsequent valvulopathy. Patients with mitral valve prolapse, even with severe regurgitation, no longer required prophylaxis.[18]

In 2008 the abolition of antibiotic prophylaxis for all patients in the UK was a radical change in practice.[19] It resulted in considerable controversy including claims from UK cardiologists that patient safety would be compromised.[20] There were allegations of making a cost-effectiveness judgment on the basis of insufficient evidence and for instituting a de facto population-wide clinical trial.[21]

Following these changes in the USA and UK, revised infective endocarditis prophylaxis guidelines were soon introduced in Australia,[22] New Zealand[23] and Europe.[24] These countries followed the USA and reduced the types of cardiac conditions requiring prophylaxis.

The reason for differing opinions on prophylaxis is the lack of evidence on which to base conclusions. A Cochrane review found no randomised controlled trials that had studied the efficacy of antibiotic prophylaxis for preventing infective endocarditis due to dental treatment.[25] This review identified only one case-control study[26] which found no significant effect of penicillin prophylaxis. The review therefore concluded that there was no evidence that antibiotic prophylaxis was effective or ineffective in preventing infective endocarditis in at-risk individuals undergoing invasive dental procedures.[25]

Outcome studies

As there is a lack of evidence about the efficacy of antibiotic prophylaxis, expert groups have assessed studies investigating associations between guideline changes and the incidence of infective endocarditis. While an increased incidence following a reduced use of antibiotics would suggest that there is a need for prophylaxis, methodological limitations in some studies mean that it is difficult to say that the cases of endocarditis were related to dental procedures.

Two retrospective studies in the USA[27,28] showed no changes in the rate of infective endocarditis due to viridans streptococci three years after the revision of the guidelines in 2007. A third study found a significant increase in streptococcal infective endocarditis, but

Table **Evolution of guidelines for endocarditis prophylaxis**

Year	Organisation	Recommendation for patients without penicillin hypersensitivity
1955	American Heart Association	Intramuscular benzylpenicillin for all patients at risk
1982	British Society for Antimicrobial Chemotherapy	Oral amoxicillin, 3 g one hour before treatment, 1.5 g six hours after treatment
1997	American Heart Association	Oral amoxicillin, 2 g one hour before treatment
2007	American Heart Association	Prophylaxis limited to high-risk patients
2008	National Institute for Health and Clinical Excellence (UK)	No antibiotic prophylaxis

it did not report the incidence of viridans streptococcal infective endocarditis, nor provide any data on dental treatment or antibiotic prophylaxis.[29] No firm conclusions can therefore be drawn about the impact of the change in the guidelines.

In France, a prospective study[30] found no increase in infective endocarditis following revision of the guidelines. However, the number of patients who had dental treatment in the preceding three months was low both before and after the revision. The study concluded that changes in the guidelines had not resulted in any increase in streptococcal infective endocarditis, but no specific conclusions were made regarding the efficacy of antibiotic prophylaxis for dental treatment.[30]

Two studies in England[31,32] have investigated the impact of the recommendation to cease prophylaxis. From 2000 to 2008, before the guidelines were changed, there had been a steady increase in cases of infective endocarditis as well as cases 'possibly' attributable to oral streptococci. The rate of increase in infective endocarditis did not alter significantly in the 25 months after introduction of the new guidelines.[31] However, despite a 78.6% reduction in prescriptions for antibiotic prophylaxis, there were still approximately 2000 prescriptions per month during that time. More than 90% were from dentists, suggesting that they were still prescribing prophylaxis to patients at high risk of infective endocarditis.

This possibility was supported by a subsequent survey[33] four years after the guidelines changed. It found that 36% of dentists had provided antibiotic prophylaxis and one-third had treated patients who had taken prophylaxis prescribed by a medical practitioner. The survey also found that the majority of infectious diseases physicians and cardiologists and 25% of the dentists thought that patients with prosthetic heart valves should receive antibiotic prophylaxis for dental treatment despite the guidelines to the contrary.[33]

In contrast with the short-term English study,[31] the more recent study[32] found that five years after the guidelines changed, there had been a significant increase in the incidence of infective endocarditis. The investigators were unable to identify the number of cases caused by viridans streptococci and the results were confounded by residual prescribing of antibiotic prophylaxis, with an average of more than 1300 prescriptions per month in the last six months of the study.[32]

The earlier English study[31] had been interpreted as evidence that antibiotic prophylaxis was unnecessary for patients at risk of infective endocarditis undergoing invasive dental procedures. However, the more recent study[32] has been interpreted as evidence that antibiotic prophylaxis is necessary for at-risk patients.[34] Both studies have methodological deficiencies that make it impossible to arrive at a cause-and-effect conclusion in relation to antibiotic prophylaxis and infective endocarditis caused by dental procedures.

Current guidelines

Expert committees around the world have recently issued updated guidelines. In the UK, NICE concluded that there was insufficient evidence to change its existing guidelines and it continues to recommend no routine antibiotic prophylaxis for dental treatment for patients at risk of infective endocarditis.[35] In contrast, expert committees in Europe,[36] the USA[37] and Australia,[38] despite assessing the same evidence as NICE, continue to recommend antibiotic prophylaxis in selected patients (see Box).

The NICE guidelines have continued to attract opposition in the UK.[34,39] Concerns have been expressed that by following the NICE guidelines, rather than the European guidelines, an extra 419 cases of infective endocarditis could occur per year in the UK including a possible 66 extra deaths.[34] There have also been claims that NICE has incorrectly calculated the risk of deaths from anaphylaxis if antibiotic prophylaxis is given. No cases of fatal anaphylaxis with amoxicillin prophylaxis were reported in the UK during 1972–2007.[40] There were also no reported cases of fatal anaphylaxis in the USA.[18] In contrast, an investigation of the use of oral clindamycin for prophylaxis in England found a significant risk. There were 15 fatalities during 1969–2014, mostly due to *Clostridium difficile* infection.[41]

Box **Cardiac conditions for which antibiotic prophylaxis is recommended for dental treatment in Australia**

Prosthetic cardiac valve or prosthetic material used for cardiac valve repair

Previous infective endocarditis

Congenital heart disease *but only* if it involves:
- unrepaired cyanotic defects, including palliative shunts and conduits
- completely repaired defects with prosthetic material or devices, whether placed by surgery or catheter intervention, during the first six months after the procedure (after which the prosthetic material is likely to have been endothelialised)
- repaired defects with residual defects at or adjacent to the site of a prosthetic patch or device (which inhibits endothelialisation)

Rheumatic heart disease in patients at high risk of endocarditis (indigenous Australians and those at significant socioeconomic disadvantage)

Heart transplant patients (consult the patient's cardiologist for specific recommendations)

Source: Reference 38

No clinical trials have yet been published to validate whether antibiotic prophylaxis for invasive dental procedures, for example extractions, can provide significant protection against infective endocarditis in at-risk patients. Australian dentists and medical practitioners are therefore advised to follow the current guidelines published in Therapeutic Guidelines: Antibiotic[38] (see Box) which follow closely the guidelines recommended in the USA[37] and Europe.[36] These are to give amoxicillin, or ampicillin, before the procedure. Cefalexin is recommended for patients hypersensitive to penicillin, unless they have a history of immediate hypersensitivity in which case clindamycin is used.[38]

Prosthetic joint infection

Bacteraemia caused by dental procedures has been considered a surrogate measure of the risk of prosthetic joint infection.[42] As a consequence, there has been a long history of antibiotic prophylaxis for dental procedures despite a lack of evidence for oral *Streptococcus* species being significantly involved in prosthetic joint infection.[43] The overall infection rate for prosthetic joints is approximately 1.5% with the main infecting organism being the skin commensal staphylococci.[42]

Evolution of prophylaxis guidelines

Differing protocols have been published over the years regarding antibiotic prophylaxis for dental treatment of patients with prosthetic joints. The recommended intervals during which prophylaxis should be given have ranged from the first three months to the first two years after joint replacement.[43]

In Australia, guidelines published in 2005 by the Arthroplasty Group of the Australian Orthopaedic Association in conjunction with the Australian Dental Association recommended that prophylaxis was not required for dental treatment, including extraction, after three months in a patient with a normally functioning prosthetic joint.[44] For immunocompromised patients, consultation with the patient's treating physician was advised. However in 2010 Therapeutic Guidelines: Antibiotic stated that for patients with prosthetic joints: 'prophylaxis is not recommended as risks of adverse effects outweigh the benefits of prophylaxis'.[45] Despite these guidelines, some orthopaedic surgeons continued to require that patients with no significant medical history and a healthy, functioning prosthetic joint must receive lifetime antibiotic prophylaxis for all dental visits.

Current guidelines

In 2012, an expert committee of the American Academy of Orthopaedic Surgeons and the American Dental Association reviewed the available evidence on dental treatment and prosthetic joint infection.[42] Only one study satisfied the search criteria.[4] This case-control study found that dental procedures are not risk factors for subsequent prosthetic joint infection and that antibiotic prophylaxis does not reduce the risk of infection. A clinical practice guideline was published recommending that: 'The practitioner might consider discontinuing the practice of routinely prescribing prophylactic antibiotics for patients with hip and knee prosthetic joint implants undergoing dental procedures'.[42]

The wording of this recommendation created some confusion among dentists so an expert panel was therefore convened. It concluded that the evidence in relation to hip and knee prosthetic joints could be extrapolated to all joints on the basis of the morphological and physiological characteristics of the tissues involved.[46] The guideline was amended to read: 'In general, for patients with prosthetic joint implants, prophylactic antibiotics are not recommended prior to dental procedures to prevent prosthetic joint infection'.[46]

Currently, antibiotic prophylaxis for patients with prosthetic joints who are undergoing dental treatment is not routinely recommended in Australia,[38] the USA,[42] Canada,[47] the UK[48] or New Zealand.[49]

Choosing when to prescribe prophylaxis

In situations where a patient has a significant immunodeficiency or an already infected prosthetic joint, the dentist should discuss the situation not only with the orthopaedic surgeon, but also with the physician managing the patient to determine the need for appropriate prophylaxis.

What should a prescriber do if an orthopaedic surgeon insists that a healthy patient with a healthy prosthetic joint must receive antibiotic prophylaxis for dental treatment? The dentist should discuss the patient's medical status and plan dental treatment with the orthopaedic surgeon. If the orthopaedic surgeon recommends prophylaxis but the dentist considers that it is not recommended based on the guidelines, then the orthopaedic surgeon should be invited to prescribe antibiotic prophylaxis and thus be responsible for any adverse outcomes which might result from use of the antibiotic. The patient must be fully informed of the existing guidelines and a clear explanation given for the dentist's decision not to recommend antibiotic prophylaxis.

Conclusion

In Australia, expert opinion recommends antibiotic prophylaxis for dental treatment to prevent infective endocarditis in patients with specific cardiac risk factors receiving specific dental treatments. However, antibiotic prophylaxis is not recommended routinely for patients with prosthetic joints.

All guidelines for prophylaxis stress the importance of optimising dental health before the placement of cardiac or orthopaedic prostheses to ensure that no dental sepsis is present. Patients should then be encouraged and trained to practise good oral hygiene and be advised to have regular dental check-ups to maintain their dental health.

Conflict of interest: none declared

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