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Cover picture

America's first Apothecary General (1775-1783)

First American Apothecary General was Bostonian Andrew Craigie, commissioned in 1777. Previously he served Massachusetts' Committee of Safety as Apothecary; took part in the Battle of Bunker Hill. He served America throughout the War of Independence.

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

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

Management of glaucoma

Introduction

Glaucoma is a disease which causes characteristic optic neuropathy and a progressive visual field loss. It is a potentially blinding condition which can lead to a permanent visual disability. The most important risk factor is the raised intraocular pressure (IOP) secondary to reduced aqueous outflow through the filtration angle.

Classification

Glaucoma may be congenital or acquired. Glaucoma can be further subclassified into angle closure type and open angle type based on the mechanism by which aqueous outflow is impaired. Glaucoma may also be primary or secondary depending on the presence or absence of the associated factors (uveitis, steroid treatment, pseudoexfoliation) contributing to the pressure rise.

Clinical features

Symptoms and signs depend on the type of glaucoma.

Primary open angle glaucoma (POAG)

POAG is the most prevalent type, affecting approximately 1 in 100 of the general population over the age of 40 years. It is generally bilateral but not always symmetrical. It is an adult onset asymptomatic disease characterised by elevated intraocular pressures of >21 mmHg, open normal angle on gonioscopy, glaucomatous optic nerve damage, and visual field loss.

Angle closure glaucoma

In classical cases of acute angle closure glaucoma there is a rapidly progressive unilateral visual loss associated with periocular pain, redness, and nausea and vomiting. It commonly affects south east Asian women around the age of 60 years. Slit lamp examination shows severely elevated IOP (50 - 100 mmHg), ciliary flush, shallow anterior chamber with peripheral iridocorneal contact, corneal oedema, aqueous flare, and a fixed semi-dilated pupil. Intermittent angle closure occurs in predisposed eyes and the diagnosis is based on the characteristic history of recurrent attacks of transient blurring of vision with haloes around the lights, ocular discomfort and frontal headache.

Normal tension glaucoma

It is an asymptomatic disease characterised by a mean IOP of <21 mmHg with glaucomatous optic nerve damage and visual field loss. Gonioscopy shows open drainage angle with absence of secondary causes for glaucomatous optic nerve damage.

Panel 1. Risk factors and associations for primary open angle glaucoma

- Age – most cases present after the age of 60 years
- Race – common in blacks
- Family history – frequently inherited and a risk to siblings of 10% and to offspring of 4% has been suggested.
- Myopia
- Diabetes mellitus
- Reduction of perfusion pressure – visual field progression may occur despite a well controlled IOP if there is a nocturnal dip in blood pressure

Panel 2. Features of glaucomatous optic nerve damage

- Increased vertical cup disc ratio
- Notching of the neuroretinal rim
- Peripapillary atrophy
- Retinal nerve fibre dropouts
- Bearing of circumlinear blood vessels
- Disc margin haemorrhages

Examination and investigations

Examination requires appropriate equipment, sufficient training in examination techniques, and accurate reliable recording of findings. Although resources vary widely across the country, there is a minimum acceptable standard of equipment and training.

1 A slit lamp with indirect lens (70 to 90D) and/or direct ophthalmoscope

2 An automated perimeter

3 A goniolens that allows indentation gonioscopy

4 A Goldmann-style applanation tonometer

Central corneal thickness (CCT) measurement is important as thicker corneas are associated with artificially elevated IOP measurements, and thinner corneas with artificially depressed IOP measurements.

At baseline some form of imaging may be useful to provide a record of optic nerve head (ONH) appearance. Colour photography provides an image almost identical to that seen during clinical examination. If colour photos are not available, detailed manual drawing is recommended, even if it is difficult to draw a good picture of an ONH: the act of making a drawing however encourages a thorough clinical evaluation of ONH.

Visual field testing is a mandatory part of glaucoma management, for diagnosis and even more so in follow-up. The goal of glaucoma treatment is to prevent a loss of quality of life at an affordable cost. Loss of visual function is associated with loss of quality of life, and it is therefore necessary to know each patient's visual field loss. The large controlled, randomised glaucoma treatment trials have shown that disease progression is common even at normal levels of intraocular pressure. Hence tonometry alone is never sufficient in follow up of glaucoma patients. Regardless of IOP, visual fields must also be performed.

The GDx is a scanning laser polarimeter and quantifies the nerve fibre layer (NFL) thickness by providing a map of the retardation of polarized light in the parapapillary retina.

Optical coherence tomography (OCT) is available as (a) time-domain and (b) spectral-domain. Both techniques provide a quantitative estimate of the retinal nerve fibre layer (RNFL) thickness.

Management

Glaucoma is a progressive optic neuropathy; if left untreated, the patient may go blind.

The aim is to preserve visual function. IOP is the only known causal risk factor, that can be manipulated effectively. Target pressure is a useful concept in the practical management of glaucoma patients. Target IOP is the pressure estimated to slow or halt disease progression. When the target is achieved, the patient needs continued monitoring for structural and functional changes. Target IOP needs to be individualised within a risk category. The least quantity of medication and thus of side effects to achieve the desired therapeutic response should be the consistent goal. Most patients with OAG are treated initially with topical medication. Laser trabeculoplasty is an effective initial option. Surgery may be considered in some circumstances, eg. if there is severe glaucoma, very high IOP, and concerns about compliance.

Panel 3. Target IOP depends on

1. IOP level before treatment
   - The lower the untreated IOP levels, the lower the target IOP should be.
2. Stage of glaucoma
   - The greater the pre-existing glaucoma damage, the lower the target IOP should be.
3. Rate of progression during follow-up
4. Age and life expectancy
   - Younger age requires lower target IOP.
5. Presence of other risk factors, eg. exfoliation syndrome.

Medical treatment

Medical treatment is effective for the majority of patients and generally widely available and acceptable. Choose the most appropriate medication with greatest chance of reaching the target IOP, with best safety profiles and minimal inconvenience. Start low and slow with minimum concentration and minimum frequency, as this is life long treatment.

Table 1. Meta-analysis of randomized controlled trials on IOP lowering effect of topical medication

	% IOP difference from baseline	
	Peak	*Trough*
Bimatoprost	-33	-28
Travoprost	-31	-29
Latanoprost	-31	-28
Timolol	-27	-26
Brimonidine	-25	-18
Betaxolol	-23	-20
Brinzolamide	-20	-17
Dorzolamide	-20	-17

Laser treatment

Argon laser trabeculoplasty involves application of discrete laser burns to the trabecular meshwork. It enhances aqueous outflow and lowers the intraocular pressure. It is performed in open angle glaucoma usually as an adjunct to medical treatment. YAG laser iridotomy is performed in angle closure glaucoma to create an opening in the peripheral iris to break the pupillary block.

Table 2. Efficacy, safety and dosing frequency of various drug classes

Drug class	*Daily dosage*	*Efficacy*	*Side effects*	
			Local	*Systemic*
PGAs	1x	+ + + +	+ to + +	0
β-blockers	1x to 2x	+ + +	+	+ to + + +
a_2-Agonists	2x to 3x	+ + to + +	+ +	+ to + +
CAIs				
Topical	2x to 3x	+ +	+ +	0 to + +
Systemic	2x to 4x	+ + + +	0	+ + to + + + +
Cholinergics	3x to 4x	+ + +	+ + + +	0 to + +
Hyperosmotic agents	Stat dose(S)	+ + + + +	0	+ + to + + + +
Proprietary fixed combinations				
β-blockers + CAI	2x	+ + + to + + + +	+ +	+ to + + +
β-blockers + PGA	1x	+ + + + to + + + + + +	+ to + +	+ to + + +
β-blockers + pilocarpine	2x	+ + + +	+ + + +	+ to + + +
β-blockers + a_2-agonist	2x	+ + + to + + + +	+ to + +	+ to + + +

Surgery

Trabeculectomy is the gold standard and lowers the IOP by creating a fistula, which allows aqueous outflow from the anterior chamber to subtenon space. This procedure is usually performed when medical therapy has failed to achieve adequate control of IOP.

Panel 4. Management of acute angle closure glaucoma

- Intravenous osmotic agents (mannitol)
- Oral acetazolamide 500 mg
- Topical timolol, pilocarpine and steroids
- Analgesia
- Laser iridotomy to break the pupillary block-timing varies with severity of the attack and the corneal clarity

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Management of rickettsial infections (typhus fever)

Introduction

Rickettsiae, are Gram-negative, obligatory intracellular cocobacilli that primarily infects endothelial cells, and cause acute, potentially lethal disease with systemic multi-organ involvement. The currently known pathogenic rickettsia species have been genetically and antigenically classified into two main groups, as the spotted fever group and the typhus group. A general characteristic of rickettsiae is that mammals and arthropods are natural hosts. Rickettsioses are usually transmitted to humans by arthropods. The spotted fever group includes about 20 species of rickettsiae mostly transmitted by ticks, whereas the typhus group is mainly vectored by lice, fleas and ticks. In addition, there are unclassified rickettsias which infect ticks, insects, leeches, and even amoebae. Scrub typhus is caused by *Orientia tsutsugamushi* and the agent of murine typhus is *Rickettsia typhi*. In Sri Lanka, prevalence of spotted fever, scrub typhus and murine typhus has been established, and the clinical data have been described. The spotted fever is the most prevalent and widely distributed rickettsial infection in Sri Lanka, with the highest incidence occuring in the western slope of the upcountry.

The severity of rickettsial infections varies from self-limited mild illnesses to fulminating life-threatening infection. Rickettsiae exert their pathologic effects by adhering to and invading the endothelial lining of the vasculature of various organs. Once inside, the organisms either multiply or accumulate in large numbers before lysing the host cell (typhus group), or

they escape from the cell, damaging its membrane and causing the influx of water (spotted fever group). The most important pathophysiologic effects are increased vascular permeability with consequent oedema, loss of blood volume, hypoalbuminaemia, decreased plasma osmotic pressure, and hypotension. The clinical features of rickettsial diseases correspond to the damaged tissues and endothelial cells characterised by focal or disseminated vasculitis and perivasculitis, particularly involving lungs, liver, spleen and central nervous system. Clinically, this produces a classic maculopapular rash with variable severity especially involving palms and soles.

Clinical features

Early clinical features are non-specific and may mimic benign viral fever. Onset of the disease may be gradual or abrupt, beginning about 1-2 weeks following a bite of an infected vector. As many of the patients are unaware of the vector bite, they are unable to recall the exposure history.

The typical rash is maculopapular and distributed all over the body, predominantly involving limbs, palms and soles. The rash is generally erythematous at the beginning, but it becomes murky with time. In severe cases of spotted fever the rash becomes necrotic assuming a fern leaf appearance. Other manifestations include nausea or vomiting, headache, myalgia, arthralgia, arthritis, abdominal pain, diarrhoea, conjunctival injection, lymphadenopathy, peripheral oedema, periorbital oedema, hepatomegaly and splenomegaly. Deafness has been reported in scrub typhus.

In untreated cases the disease becomes very severe causing multiple organ dysfunctions. Non-cardiogenic pulmonary oedema, adult respiratory distress syndrome, interstitial pneumonia, acute renal failure, haemorrhagic rash, peripheral oedema and hypovolemic hypotension are some of them. The central nervous system manifestations include delirium, cranial nerve palsies, ataxia, aphasia, hemiplegia, spasticity, seizures, altered mental status, photophobia and coma.

Diagnosis

Diagnosis of rickettsioses is often made clinically as the specific serological tests are not frequently available. The clinical diagnosis is based on the presence of fever with an erythematous discrete maculopapular rash with or without an exposure history. Furthermore, a rapid defervescence with specific antibiotic therapy is an important feature in the diagnosis.

Investigations

No rapid laboratory tests are available to diagnose rickettsial diseases early in the course of illness. The specific diagnosis is done with serological and molecular biological studies. Serologic assays that demonstrate antibodies to rickettsial antigens (indirect immuno-fluorescence, complement fixation, indirect haemag-glutination etc.) are preferable over the widely available non-specific Weil-Felix serological test for diagnosis of rickettsioses. The value of testing 2 sequential serum or plasma samples together to show a rising antibody level is more important in confirming acute infection with rickettsial agents, because antibody titres may persist in some patients for years after the original exposure. Molecular biological tests based on polymerase chain reaction is a useful technique for early diagnosis before seroconversion. The routine investigations such as full blood counts, urine full report, ESR, liver enzymes help the clinical diagnosis and detecting complications.

Management

The mainstay of the management is the specific antibiotic therapy initiated early in the illness. The fever usually subsides within 24-72 hours after starting antibiotic therapy, which should be continued for 5-7 days. Doxycycline is the drug of choice and is preferred over other tetracyclines. The dose of doxycycline is 200 mg/day preferably given 100 mg b.d orally for adults and children with body weight more than 45 kg. For those with body weight less than 45 kg, the dose is adjusted as 5 mg/kg/day, not exceeding 200 mg/day. Tetracyclines are not approved for children less than 8 years. However, doxycycline carries a low risk of dental staining at the recommended dose and duration.

Chloramphenicol is equally effective and has the advantage of availability in intravenous form for use in severe cases. Chloramphenicol inhibits bacterial growth by inhibiting protein synthesis. The dose regimen

of chloramphenicol for adults is 50 mg/kg/day, six-hourly and should not exceed 4 g/day. For children the dose should be adjusted as 100 mg/kg/day, divided six-hourly, not exceeding 4 g/day.

Complications such as thrombocytopaenia, hypoalbuminaemia, hypotension, and coagulation defects require supportive management. In complicated cases, adjunctive therapy with steroids is indicated. The steroids help to minimise immune mediated damage caused by vasculitis.

The management of rickettsial infections in pregnancy is a contentious issue as tetracyclines and chloramphenicol are contraindicated during pregnancy. Tetracyclines are known to cause malformation of teeth and bones in the fetus, and hepatotoxicity and pancreatitis in the mother. Chloramphenicol given during the third trimester of pregnancy carries the risks of the grey baby syndrome. So far the safest effective drug is azithromycin given as 500 mg/day for 3 days. Ceftriaxone is an alternative that can be used in pregnancy by the intravenous route. However, both azithromycin and ceftriaxone are comparatively less potent than chloramphenicol in their anti-rickettsial effects.

Prevention

Avoidance of vector exposure remains an important part of protection against rickettsial infections, by proper clothing and use of repellants. In case of bites, prompt removal of ticks might prove beneficial in prevention. Attempting to control the tick reservoir is not usually feasible and careful body inspection for ticks after being in a tick habitat would be beneficial. Use of antibiotics following tick exposure is not indicated to prevent rickettsial infection. Education plays an important role in prevention.

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Management of common cardiac problems in children

Common cardiac problems in children can be classified in to congenital and acquired disorders. The former are commoner (6-8 per 1000 live births) than acquired problems, and contribute significantly to childhood morbidity and mortality.

Common congenital heart problems

Congenital heart lesions can be broadly divided into shunt lesions, obstructive lesions and cyanotic lesions. However, this is only for explanatory purposes and there is overlap between categories when there is combination of defects and in complex lesions.

Shunt lesions

A shunt lesion is one where there is shunting of blood from left to right at chamber level or great artery level. Three common shunt lesions are atrial septal defect (ASD), ventricular septal defect (VSD) and patent ductus arteriosus (PDA). Not all shunt lesions should be corrected as some of them are haemodynamically insignificant. A haemodynamically significant shunt is generally associated with symptoms and cardiomegaly in the chest xray.

Atrial septal defect (ASD)

ASD is one of the most common shunt lesions. There are three types of defects depending on their location in the interatrial septum (IAS). Ostium secundum defect (OS ASD), which is the most common of the three, is located in the central part of the IAS. Sinus venosus defect is located close to either superior or inferior vena cava, and ostium primum defect close to the atrio-ventricular valve.

Management of ASD depends on the type of defect and its anatomical features. Small secundum ASDs are likely to close spontaneously. Most of the OS ASDs can be closed using a device in the cardiac catheterisation laboratory (transcatheter closure). The closure is done when the child is about four years of age as there is no added advantage in closing it before. These patients usually remain asymptomatic and rarely need medication.

Ventricular septal defect

Management of ventricular septal defect depends on the size and its location in the interventricular septum. Most of the children with moderate to large VSDs are symptomatic and need heart failure treatment until they go for closure of the defect. Definitive treatment is surgical closure. Very few patients with multiple muscular VSDs or very large VSDs will need pulmonary artery banding as a palliative procedure. Transcatheter closure of perimembranous VSD is associated with complete heart block in about 5% of patients. Hence the procedure cannot be recommended in children, especially those weighing less than 10 kg.

Perimembranous and muscular VSDs may close spontaneously, so it is necessary to observe the child who is relatively asymptomatic. Subpulmonic VSDs and inlet VSDs are unlikely to close spontaneously. They need surgical closure if the child is symptomatic or if there is evidence of volume overload of the left atrium and left ventricle.

Patent ductus arteriosus

PDA is the most serious of the three shunts as the left to right shunt continues during the whole cardiac cycle. These children are symptomatic and develop pulmonary hypertension early. Majority of PDAs are suitable for transcatheter closure with either a coil or a device.

Heart failure in shunt lesions

Diagnosis and management of heart failure is important in shunt lesions. Tachycardia, tachypnoea and hepatomegaly are features of heart failure, but all three may be seen in a child with respiratory tract infection or bronchiolitis (apparent hepatomegaly due to liver being pushed down). A chest xray will show

cardiomegaly if there is a shunt lesion or hyperexpanded lung fields if there is bronchiolitis. Heart failure in a shunt lesion should be managed using diuretics alone (frusemide with spironolactone), or a diuretic with an afterload reducing agent (captopril).

Obstructive lesions

Obstructive lesions can be divided into left-sided obstructions and right-sided obstructions. Critical left-sided obstructions will compromise systemic perfusion and similar right-sided obstructions will compromise pulmonary blood flow. Common obstructive lesions are pulmonary stenosis or atresia, aortic stenosis, and coarctation of aorta. If the obstruction is severe, distal perfusion is usually maintained through the PDA which is called duct dependent systemic or pulmonary circulation, depending on the compromised system. In these children maintaining the patency of the ductus arteriosus is important for survival. If the PDA closes in a patient with duct dependent pulmonary circulation the patient will become severely cyanosed and eventually acidotic due to hypoxia. If it is a duct dependent systemic circulation the patient will maintain saturation, but will eventually become acidotic due to poor perfusion. Heart failure in obstructive lesions is rare and is associated with critical stenosis. It is a medical emergency and the patient should be immediately subjected to either transcatheter or surgical correction after initial stabilisation.

Aortic stenosis

Aortic stenosis is commonly associated with bicuspid aortic valve and the treatment of choice is balloon dilation. However, the procedure is done only if the child is symptomatic or if there is significant left ventricular hypertrophy as there is approximately 20% chance of developing aortic regurgitation.

Coarctation of aorta

This is one of the congenital heart diseases which can be confidently diagnosed during neonatal examination. Absent or low volume femoral pulse compared to brachial pulse should raise the suspicion. Treatment of choice is surgical correction as there is a significant incidence of re-coarctation after balloon dilation. However, balloon dilatation can be used as a bridging therapy in those who have left ventricular failure or those who have other risk factors for surgery.

Pulmonary stenosis

Isolated valvar pulmonary stenosis, which is the commonest right sided obstructive lesion, is usually dealt with by transcatheter balloon dilation. The procedure is done only when the obstruction is moderate to severe. Patients with subvalvar or supravalvar obstructions need surgical correction of the lesion.

Cyanotic lesions

Common cyanotic lesions are tetralogy of Fallot, transposition of great arteries, tricuspid atresia and total anomalous pulmonary venous drainage. There are numerous more complex lesions that can present with cyanosis.

Tetralogy of Fallot

This is the commonest cyanotic heart disease and management depends on the degree of cyanosis, which in turn is determined by the degree of right ventricular outflow tract obstruction. When the obstruction is severe the child becomes more cyanosed due to shunting of deoxygenated blood from right to left through the VSD. If they have well developed branch pulmonary arteries total correction is done around one year of age. If the branch pulmonary arteries are smaller in size or if they have significant cyanosis or hypercyanotic spells a shunt is created from innominate artery to pulmonary artery (Blalock Taussig shunt) to augment growth of pulmonary arteries and to improve oxygen saturation. Patients with tetralogy of Fallot do not develop heart failure (except in rare variants), and their major issue is hypercyanotic spells.

Management of a hypercyanotic spell

What really causes a hypercyanotic spell is poorly understood and there are many theories proposed including infundibular spasm. However, the popular infundibular theory fails to explain why it occurs even in pulmonary atresia. Hypercyanotic spells are not limited to tetralogy of Fallot and can occur in any condition where there is a large VSD or common chamber pumping into both systemic and pulmonary

circulations in combination with restricted pulmonary blood flow. It may occur in univentricular heart with pulmonary stenosis, any condition with pulmonary atresia with duct dependent pulmonary circulation, and even in tricuspid atresia with pulmonary stenosis.

Hypercyanotic spells should be managed as a medical emergency and the main aim of management is to increase pulmonary blood flow. This can be achieved by keeping them in the knee-chest position, and giving a fluid bolus of 10-20 ml/kg. 100% oxygen should be administered and morphine 0.1-0.2 mg/kg iv/im can be used to reduce distress and hyperpnoea. Propranolol can be given intravenously, 0.05-0.1 mg/kg as a slow bolus over 10 min, but the patient should be closely monitored for bradycardia. Acidosis can be corrected with sodium bicarbonate. If the child continues to have spells he may need general anaesthesia and ventilation or an emergency surgical intervention.

A single episode of a definite hypercyanotic spell is an indication for early surgical repair; either total correction or Blalock Taussig shunt.

Complex cyanotic heart diseases

There is no definition for complex cyanotic heart disease, but generally there is a combination of shunts and obstructive lesions, and most of them are suitable only for univentricular repair. During univentricular repair systemic venous return is directly diverted into the pulmonary circulation, bypassing the heart, usually in two stages.

The first stage is called bidirectional Glenn shunt in which the SVC is anastomosed to the pulmonary artery when the child is between 6 months to 2 years of age. The second stage, which is done between 2-5 years of age, is called Fontan completion or total cavo-pulmonary communication in which the IVC blood is directed to the pulmonary artery.

Conclusions

Proper management of congenital heart diseases is important in bringing down associated morbidity and mortality. Even for simple lesions, decisions on whether to operate or not depend on anatomy, haemodynamics, presence of heart failure, risk of development of pulmonary hypertension, risk of endocarditis, risk of cerebral thromboembolism, failure to thrive, recurrent lower respiratory tract infections, recurrent hospitalisations, effect the family, and socio-economic factors. All these need to be weighed against morbidity and mortality, risk of intervention, or surgery. Timing of intervention or surgery is also important as this affects overall outcome. Medical management of symptoms of heart failure or cyanotic spells is only a bridging therapy until definitive intervention or surgery is done except for patients who are selected for conservative management.

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Mouthwashes

Summary

A mouthwash may be recommended as an antimicrobial, a topical anti-inflammatory agent, a topical analgesic, or for caries prevention. Many different mouthwashes are commercially available and patients and health professionals struggle to select the most appropriate product for a particular need. The selection needs to take into consideration factors such as the patient's oral condition, their disease risk and the efficacy and safety of the mouthwash. Mouthwashes are an adjunct to, not a substitute for, regular brushing and flossing.

Key words: dentistry, oral disease.

(Aust Prescr 2009;32:162-4)

Introduction

Plaque is the primary aetiologic agent in the development of dental caries, gingivitis and periodontal disease.[1] Mechanical removal of plaque through frequent and efficacious brushing and flossing is the principal means of preventing periodontal diseases and diminishing the risk of caries.[2] However, some individuals lack the dexterity, skill or motivation for mechanical plaque removal. Mouth-rinsing is easier to perform and may aid in controlling supragingival plaque and gingivitis[3], but it should always be used in conjunction with mechanical hygiene. Mouthwashes should only be used for short periods of time and should never be the sole means of oral hygiene.

A mouthwash may be recommended to treat infection, reduce inflammation, relieve pain, reduce halitosis or to deliver fluoride locally for caries prevention.[4] There is a multitude of mouthwashes available for these purposes. A consensus panel has recommended that an antiseptic mouthwash should be used as a daily adjunct to mechanical cleaning for prevention of oral disease.[5] However, this panel did not explore the long-term adverse effects of daily mouthwash use and it did not recommend a particular product or offer health practitioners guidelines for selecting an appropriate product. Recommending particular mouthwashes should take into consideration the patient's ability to perform good oral hygiene practices (tooth brushing and dental flossing), the condition of their teeth, gingivae and oral mucosa, their risk of oral disease (for example, presence of xerostomia), and the proven efficacy of the mouthwash and its potential adverse effects.

Chlorhexidine

Chlorhexidine gluconate is a cationic bis-guanide with broad spectrum antimicrobial activity. It is currently the most effective mouthwash for reducing plaque and gingivitis.[6] Use of chlorhexidine is not associated with development of resistant organisms. As chlorhexidine may interact with fluoride and sodium lauryl sulfate (a detergent found in toothpastes), it should be used after rinsing with water or 0.5-2 hours after using toothpaste.

Current recommendations are for twice-daily chlorhexidine to be used only as a short-term adjunct, or as an aid in disinfection of surgical sites, to improve wound healing, or as a short-term treatment of halitosis. It is not recommended for long-term use due to its numerous adverse effects. These include tooth and restoration staining, soft tissue staining, increased calculus deposition, unpleasant taste, taste alteration, burning sensation, desquamation and mucosal irritation. Chlorhexidine may also potentiate oral discomfort in patients with chemotherapy-induced mucositis, xerostomia or ulcerative oral mucosal conditions.

Benzydamine hydrochloride

Benzydamine hydrochloride is added to some chlorhexidine-containing mouthwashes for its analgesic, anti-inflammatory, antimicrobial and anaesthetic properties. Although the exact mechanism of action of benzydamine is unknown, it is thought to affect the

production of prostaglandin and thromboxane, reduce pro-inflammatory cytokine production by macrophages and stabilise cell membranes.[7]

Studies have shown that benzydamine can significantly reduce the severity, duration and incidence of radiation-induced mucositis and is well tolerated by patients. It is therefore recommended for radiation-induced oral mucositis and ulcerative mucosal conditions such as recurrent aphthous ulcerative disease.

Essential oils

Mouthwashes containing four phenol-related essential oils (thymol, eucalyptol, menthol and methyl salicylate in up to 26% alcohol) claim to penetrate the plaque biofilm and thus kill micro-organisms that cause gingivitis. These mouthwashes display broad spectrum antimicrobial activity, prevent bacterial aggregation, slow bacterial multiplication, retard plaque maturation and decrease plaque mass and pathogenicity.[8] Their mechanism of action is thought to involve bacterial cell destruction, bacterial enzyme inhibition and extraction of endotoxin from Gram-negative bacteria. They also have anti-inflammatory and prostaglandin synthetase inhibitory activity and act as antioxidants by scavenging free oxygen radicals. Clinical studies have concluded that essential oils are effective in reducing plaque, gingivitis and halitosis due to their bactericidal and plaque-permeating abilities.[9]

Mouthwashes containing essential oils have been recommended as an adjunct to mechanical oral hygiene, particularly in patients who have impaired oral hygiene and those who suffer from gingival inflammation despite regular brushing and flossing. These mouthwashes can help support gingival health around dental implants. They are not recommended for patients suffering from xerostomia, dental erosion due to a low oral pH, or oral mucosal disease due to possible ethanol-induced mucosal irritation and dryness. These mouthwashes are unsuitable for children due to the risk of accidental ingestion of high doses of ethanol.

Cetylpyridinium chloride, sodium benzoate and triclosan

Cetylpyridinium chloride is a quaternary ammonium compound with antiseptic and antimicrobial properties.[10] It is cationic and thus binds to bacterial surfaces causing disruption of the cell membrane, leakage of intracellular components and disruption of metabolism. Mouthwashes containing cetylpyridinium chloride inhibit and reduce plaque build-up. Those containing sodium benzoate as the active ingredient are thought to act by dispersing fatty, proteinaceous and carbohydrate substances. This weakens plaque attachment and aggregation making it easier to remove during tooth brushing. Triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether) is used to increase the ability of mouthwashes to bind to the oral mucosa and thus be available for longer periods of time.

Clinical studies have shown that mouthwashes with these ingredients significantly lower plaque weight and reduce gingival inflammation. However, other studies have yielded contradictory results showing that some of these products are no better than a placebo or water rinse in reducing plaque and gingivitis scores.[11]

A mouthwash has recently been released that is composed of a two-phase oil-water formula with the oil phase consisting of olive oil and other essential oils, and the aqueous phase containing cetylpyridinium chloride. This product is alcohol-free and has been shown to have a significant effect on halitosis when compared to alcohol-containing essential oil mouthwashes.[12]

Oxygenating agents

Hydrogen peroxide has been used to relieve minor gingivitis because of its oxygenating cleansing action. It is also used to relieve soreness caused by dentures, orthodontic appliances and following dental procedures. Hydrogen peroxide is a bleaching agent with strong oxidising properties and some products also contain ethanol as an antimicrobial, preservative and solvent. Other products are powders composed of sodium perborate monohydrate which undergoes hydrolysis when mixed with warm water to produce hydrogen peroxide and borate. All these products act by liberating oxygen to loosen debris, remove light stains and kill obligate anaerobes. They are also broad spectrum antimicrobials and have been shown to reduce gingivitis and staining.[13]

Oxygenating mouthwashes have been recommended for the treatment of acute ulcerative disease, to reduce

gingival inflammation before fixed prosthodontic treatment, and for patients with a physical or intellectual impairment that limits good oral hygiene. They can also be used for stain removal and as a soaking solution for dentures.

Povidone-iodine containing mouthwashes

Povidone-iodine, an iodophore in which iodine is linked to povidone, displays an affinity for the cell membrane thereby delivering free iodine directly to the bacterial cell surface. It has a broad spectrum of activity against bacteria, fungi, protozoa and viruses. The mouthwash has been shown to be effective in reducing plaque and gingivitis and may be a useful adjunct to routine oral hygiene. It also reduces the incidence, severity and duration of radiation mucositis. Absorption of excess iodine has been postulated to result in metabolic complications, however this is not of concern in patients without pre-existing thyroid disease[14] and if the patient spits out the solution.

Antibacterial peroxidase mouthwashes

Mouthwashes that are directed against the bacterial peroxidase system contain four enzymes (lysozyme, lactoferrin, glucose oxidase and lactoperoxidase). They have been formulated to help restore the saliva's natural antimicrobial activity for the relief of xerostomia, gingivitis, minor gum irritations and halitosis. These mouthwashes do not contain alcohol or detergent, but they do have a low pH (5.15) which may pose a risk of dental erosion during long-term use.[15]

Fluoride-containing mouthwashes

Fluoride assists in the prevention of dental caries by promoting remineralisation with fluorapatite and fluoro-hydroxyapatite, thereby increasing enamel resistance to acid attack. Fluoride is available in different concentrations as either acidulated phosphate fluoride or sodium fluoride. Fluoride mouthwashes reduce dental caries[16] and they are recommended for patients at high risk of dental caries including those with xerostomia after irradiation and chemotherapy, those who have difficulty with oral hygiene procedures and those undergoing fixed orthodontic treatment. Fluoride mouthwashes are not indicated in children younger than six years of age as the risk of ingestion is high.

Sodium bicarbonate

A mouthwash can be prepared by dissolving one teaspoon of sodium bicarbonate in a glass of water.[17] It is recommended in patients suffering from xerostomia or erosion due to its ability to increase salivary pH and suppress the growth of aciduric micro-organisms such as *Streptococcus mutans*. Sodium bicarbonate can improve taste and it neutralises acids and thus prevents erosion. It is bland and will not irritate the oral mucosa in patients with xerostomia or oral ulcerative disease.

Alcohol in mouthwashes

Ethanol in mouthwashes is used as a solvent, preservative and antiseptic. It causes protein denaturation and lipid dissolution, so it has antimicrobial activity against most bacteria, fungi and viruses. Studies have shown that high concentrations of alcohol (above 20%) in mouthwashes may have detrimental oral effects such as epithelial detachment, keratosis, mucosa) ulceration, gingivitis, petechiae and pain.

There is increasing evidence that there may be a direct relationship between the alcohol content of mouthwashes and the development of oral cancer. The risk of acquiring cancer (oral cavity, pharynx, larynx) is increased by over nine times in smokers, over five times in those who also drink alcohol, and by almost five times in those who neither smoke nor drink alcohol. A recent review of the literature suggested that it would be inadvisable to recommend the long-term use of alcohol-containing mouthwashes.[18]

Conclusion

Patients and oral health practitioners are faced with a multitude of mouthwash products containing many different active and inactive ingredients. Making informed decisions as to the suitability of a particular product for a particular patient can be a complex task. Although many popular mouthwashes may help to control dental plaque and gingivitis, they should only be used for a short time and only as an adjunct to other oral hygiene measures such as brushing and flossing. Long-term use of ethanol-containing mouthwashes should be discouraged given recent evidence of a possible link with oral cancer. Fluoride mouthwashes should be encouraged in patients with a high risk of caries.

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Current information about drug registration

New chemical entities registered

Generic name	**Brand name**	**Dosage form**	**Manufacturer**	**Importer**	**Therapeutic class / use(s)**
Methylphenidate hydrochloride	Ritalin 10	Tablet, 10 mg	Novartis, Spain	Baurs	Attention deficit hyperactivity disorder (ADHD)
Sitagliptin	Januvia	Tablet, 100 mg	MSD, Italy	Mansel	Antidiabetic
Desmopressin	Minirin	Tablet, 0.1 mg 0.2 mg	Ferring, Switzerland	Swiss Biogenics	Vasopressin analogue / diabetes insipidus
Carboprost	Prostodin	Injection, 125 mcg 250 mcg	AstraZeneca, India	Hemas	Postpartum haemorrhage

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