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UPDATE ON ENT

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ENT CONDITIONS

Goh Lee Gan

In this issue, several ENT conditions are revisited, namely, sinus diseases, snoring and obstructive sleep apnoea (OSA), tonsillectomy and adenoidectomy and hearing loss. Neck lumps may also have an ENT etiology and some understanding of what not to do is important.

"Sinus"

The term "sinus" is loosely used. The patient could mean it to be any of the following conditions: allergic / vasomotor rhinitis, viral sinusitis, bacterial sinusitis, nasal polyps, a deviated nasal septum, turbinate hypertrophy, adenoid hypertrophy, nasal neuralgia, tumours, a foreign body, anxiety or obstructive sleep apnoea and snoring. These conditions are differentiated in this issue.

OSA

Snoring is a common condition. It is estimated that at least 45% of normal adults snore occasionally and 25% are habitual snorers. Heavy snorers should be evaluated for obstructive sleep apnoea. This is defined as cessation of breathing of 10 seconds or more at least 5 times per hour of sleep. Sleep apnoea is diagnosed based on results of a sleep study (polysomnogram).

Tonsillectomy and adenoidectomy

Tonsillectomy and adenoidectomy have gone through fashions of advocacy and resistance. Current definite indications are severe respiratory obstruction causing sleep apnoea, hypoventilation, dysphagia or cor pulmonade; malignant tumours of the tonsils.

Hearing loss

Hearing loss is a common problem. It is estimated that 6% of the population suffer from hearing loss. Strategies to deal with the problem focus on prevention and early detection, improvement of rehabilitative medical devices and ultimately, restoration of physiologic hearing.

Neck lump

A correct diagnosis of a neck lump is important to ensure correct treatment. A diagnosis of a neck lump can be made easier by noting its anatomical site. At the lateral neck along the sternomastoid muscle, the differentiated diagnosis includes a branchial cyst, neuroma and metastatic lymph node. At the location interior or anterior to the earlobe, a lump would suggest a parotid mass. At the anatomical site of the thyroid gland, a thyroid nodule needs to be considered. A vague neck lump which does not seem to be confined to any anatomical site would include a pharyngeal pouch or retropharyngeal abscess as a differential diagnosis. Presence of other clinical features will help in the diagnosis.

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Interpretation and Management of Sinus Diseases - A Guide for the Family Physician

Lau Chee Chong

SUMMARY

In this paper, I have outlined a simple guide as to how to approach a patient with sinus disease in the context of a private family physician's practice. I have also set out some pointers that I believe are sometimes overlooked and that may help the family physician to diagnose and manage sinus diseases in the safest and most cost-effective ways possible.

KEYWORDS

Anterior ethmoidal nerve syndrome (nasal neuralgia)
Functional endoscopic sinus surgery (FESS)
Nasal neuralgia
Nasal polyps
Rhinitis - allergic/vasomotor
Sinus diseases
Sinus radiography
Sinusitis

INTRODUCTION

The term "sinus" has been used very loosely by many patients and doctors alike to denote a disease of the nose. Often, when a patient claims to have "sinus", it could mean any one of a range of diseases: allergic/vasomotor rhinitis, viral sinusitis, bacterial sinusitis, nasal polyps, a deviated nasal septum, turbinate hypertrophy, adenoid hypertrophy, nasal neuralgia, tumours, a foreign body, cancerophobia/ anxiety or obstructive sleep apnoea and snoring.

DIAGNOSIS OF SINUS DISEASES

Diagnosis of sinus diseases usually involves a precise and carefully-taken history, clinical evaluations and investigations.

History

A precise and carefully taken history can give us an accurate diagnosis in up to 90% of cases. A detailed and accurate history for sinus diseases should ideally include:

1. Stuffy nose
2. Rhinorrhoea
3. Post-nasal drip
4. Sneezing
5. Epistaxis
6. Smell
7. Paranasal pain/ headache
8. Family history
9. Cough
10. Allergy
11. Ear symptoms
12. Dental symptoms
13. Eye symptoms
14. Halitosis
15. Anxiety

Special note should be taken of the following:

Stuffy nose:

Stuffy nose can be objective or subjective. *Objective nasal obstruction* is when there is a real nasal blockage and the patient is not physically able to breath through the nostrils and must breathe through the month. *Subjective nasal obstruction* is when the patient believes that he or she is unable to breathe through the nose. This problem is aggravated by the patient's frustration. The patient's belief may stem from the nasal septum or collapse of the nasal alar when the patient breathes in rapidly. In a case of subjective nasal obstruction, the nasal passages are not actually completely blocked, there is usually adequate space for the passage of air and the patient does not need to breathe through the mouth.

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Cough:

Many patients who suffer from chronic cough and who are treated symptomatically by their family physicians or respiratory physicians find that their coughs do not clear with the medication. Such coughs are often due to post-nasal drip from chronic sinusitis. This sinusitis may be otherwise "silent" and the patient may not even suspect its existence.

Epistaxis:

Anterior epistaxis is common in children and can be caused by digital trauma, aggressive nose-blowing, sneezing, dry air or warm air. This type of epistaxis is usually self-limiting. Often all that is required is pinching of the soft part of the nasal alar against the Little's area (and not pinching of the bony part of the nose, as is often done).

Posterior or superior septal epistaxis often occurs in adulthood, particularly in hypertensive patients and patients on anti-coagulants. This type of epistaxis is often profuse and can be fatal.

Nasopharyngeal carcinoma bleeders usually experience blood-stained post-nasal drip. The epistaxis is usually from the post nasal space. Such a patient may often experience blood-stained sputum upon waking up in the morning. This blood-stained sputum is usually due to bleeding from the tumour from constant trauma caused by fluttering of the soft palate against the tumour during sleep, especially if the patient snores.

Dental problems:

Unilateral foul nasal discharge may be an indicator of maxillary sinusitis. The maxillary sinusitis is often due to apical root disease of the premolars or molars on the ipsilateral side. Such patients often need dental consult. Clearing up of the origin of the infection by the dental surgeon often clears up the maxillary sinusitis without nasal surgery. Failing to identify the diseased tooth often leads to unnecessary and unsuccessful nasal surgery.

Anxiety:

If a patient appears to be a very anxious person, it is often helpful to ask him if he has any friends or relatives who have recently been diagnosed with nasopharyngeal carcinoma or if he has recently read any media reports about nasopharyngeal carcinoma. Such patients often require only the reassurance of a nasopharyngoscopy and/or an EBV-serology.

Clinical evaluation in a family physician's setting

Clinical evaluation should include the ear, nose, throat, head and neck.

Clinical evaluation - ear

Look for evidence of eustachian tube dysfunction (secondary to nasal pathology), such as:

1. a retracted tympanic membrane;
2. attic refraction;
3. middle ear effusion;
4. discolouration of the tympanic membrane;
5. conductive hearing loss (Rinne's and Weber's tests - most effective with 512Hz tuning fork).

Clinical evaluation - nose

There are various types of clinical evaluation that can be conducted, including anterior rhinoscopy, posterior rhinoscopy, nasopharyngoscopy and rigid sinuscopy. Of these forms of clinical evaluation, it is possible for the family physician to obtain a lot of information from carefully conducted anterior rhinoscopy and posterior rhinoscopy in clinic.

Anterior rhinoscopy:

Anterior rhinoscopy can be conducted using a strong light source, such as a torch, halogen headlight, with a loupe or otoscope with a short speculum (so that the focal distance can reach deeper into the anterior nasal passage). It is ideal to examine the nose 10 minutes after applying decongestant or co-phenylcaine nasal spray or cocaine spray, as these cause the nasal mucosa

and turbinates to shrink. This enables the doctor to view the anterior nasal space very much more posteriorly and occasionally, the doctor may even be able to obtain a good view of the post-nasal space.

Posterior rhinoscopy:

Posterior rhinoscopy requires a halogen headlight with a post-nasal mirror. This is usually quite tricky and may require some practice. It may also be difficult if the patient is not co-operative.

Nasopharyngoscopy and rigid sinuscopy:

These usually require considerable practice, both in the insertion of the scope and in the interpretation of what is seen. The equipment required is probably not cost-effective for a family physician's practice unless the physician has a special interest in ENT practice or has done considerable posting in an ENT department.

Clinical evaluation - oropharynx

The oropharynx should be examined for evidence of post-nasal drip and hypertrophied lymphoid follicular band in the posterior wall of the oropharynx. Look for mucopus in the post-nasal space being squeezed inferiorly when the patient gags. I often make the patient gag gently at the end of the examination. When the patient gags, the soft palate contracts, squeezing the contents of the post-nasal space into the oropharynx. This often gives a good view of the contents of the post-nasal space, that may otherwise be hidden from view by the soft palate.

Clinical evaluation - neck

Examination should be made of the neck for cervical lymphadenopathy that may be an early sign of lymphatic metastasis.

Investigations

- Radiography
- EBV-serology

Radiography

Sinusitis - when to radiograph?

1. Radiography is not essential in the initial assessment for most cases of acute or subacute sinusitis, as a precise history and clinical evaluation often give a more accurate diagnosis than depending on shadows from radiography. In addition, the results of the radiography would not usually affect the plan of management (usually medical in the first instance).
2. Radiography is useful in cases of chronic sinusitis, where the sinusitis has failed to respond to an adequate course of medical treatment and where an ENT consultation or surgical intervention may be indicated.

Plain radiography

1. Generally, in diagnosing sinusitis cases, plain radiography should only be ordered for certain cases, as plain radiography fails to demonstrate details. The presence of mucus, pus, blood, tumour, oedema, polyps or cysts may be misleading as they all show up on the plain radiograph as opacity with similar density. In addition, radiography reports are often vague and subjective as the reporting radiologist does not usually have the benefit of the patient's full medical history or clinical findings. This makes reporting difficult and the radiologist may have to do some guesswork and generalisation, unless the referring doctor has indicated to the radiologist the specific pathology that is suspected.

2. Plain radiography may be useful to confirm suspected sinusitis, for a basic and preliminary assessment of larger sinuses, to determine the size of adenoids or to identify radio-opaque foreign bodies

CT-scan sinuses

CT-scan sinuses have become the mainstay for clearly identifying the bony structures, sinus ostia adequacy and intra-sinus abnormalities not seen

by nasopharyngoscopy or sinuscopy. It is often done when medical therapy has failed and when surgical intervention is being considered or planned or when an ENT consult is required. CT-scan sinuses allows the surgeon to have a "road map" during functional endoscopic sinus surgery.

Investigations - approximate cost of radiography of sinuses

Plain X-ray sinuses (3 films)	$45
*CT-scan sinuses (screening)	$200
CT-scan sinuses (limited)	$400
CT-scan sinuses (full)	$450

* For most purposes, *CT-scan sinuses (screening)* is probably the most cost-effective test for diagnosis and as a road map for functional endoscopic sinus surgery.

EBV-serology

EBV-serology is used as an indicator for underlying nasopharyngeal carcinoma. It can be used if there is a suspicion that the patient may have nasopharyngeal carcinoma. If the serology shows that the EBV-levels are elevated, a consultation with an ENT specialist would be mandatory. The more reliable tests are anti-EBV IgA VCA and anti-EBV IgA Ea.

NASAL NEURALGIA (ANTERIOR ETHMOIDAL NERVE SYNDROME)

Nasal neuralgia is certainly not a myth, but it is under-diagnosed and often misdiagnosed as migraine, tension headache or unilateral headache.

Characteristic pain of nasal neuralgia

Nasal neuralgia pain has the following characteristics:

- pain in the medial canthal region, radiating to the eye brow, forehead and top of the head;
- often unilateral (although it can be bilateral);
- often recurring at certain times of the day, such as during hot afternoons, early mornings or nights;
- sometimes recurring during temperature changes, exposure to dust or pre-menstrual period;
- often, but not necessarily, associated with nasal symptoms;
- patient often gets pain relief from nasal decongestants (a fact that patients often discover themselves, without knowing the reason why).

Nasal neuralgia - anatomy and cause

Anatomy: The first branch of the trigeminal nerve is sensory to the anterior and posterior ethmoidal nerves, the supra-trochlear nerve and the supra-orbital nerve. The supra-trochlear and supra-orbital nerves supply the forehead and vertex of the ipsilateral half of the head.

Cause: Anatomical abnormalities, such as:

a. superiorly deviated nasal septum;
b. bulbous septum or septal spur;
c. large middle turbinate;
d. concha bullosa

may cause the medial and lateral nasal walls to come into contact and compress the anterior or posterior ethmoidal nerve. This contact and compression of the anterior or posterior ethmoidal nerve (running along the nasal septum or the lateral nasal wall) causes the neuralgic pain and the referred pain to the supra-trochlear and supra-orbital nerves.

Nasal neuralgia - diagnosis

A simple *confirmatory test* can be performed to confirm nasal neuralgia. Nasal decongestant spray (oxymetazoline) directed onto the superior aspect of the ipsilateral nasal passage will often give a reduction in the severity of the pain within 15-20 minutes.

Long-term use of topical steroids may also reduce the frequency and severity of the pain. Decongestants such as pseudoephedrine and antihistamines would also reduce the pain, but may take longer than topical decongestant spray to be effective.

Diagnosis is based on the following significant factors:

1. a high index of suspicion;
2. a superiorly deviated nasal septum;

3. contact between the middle turbinate and septum;
4. the results of the above confirmatory test;
5. CT-scan finding of deviated nasal septum, bulbous septum, large middle turbinate or concha bullosa. In most cases, when the report is given for a CT-scan, such findings are not reported or are reported as "normal". We need to look ourselves for such anatomical abnormalities and at the proximity of the medial and lateral walls of the nasal passages.

If one were to identify all patients with unilateral headache and analyse them, one may well find that a large percentage of such patients do indeed have nasal neuralgia

Nasal neuralgia - treatment

The treatment will depend on the intensity of the nasal neuralgia.
If the nasal neuralgia is mild, the patient can be treated with decongestant spray (PRN), antihistamines (PRN) or decongestants (PRN) whenever the patient has pain or long term use of topical steroids if the pain is very frequent.
If the nasal neuralgia is severe, surgical intervention may be required to separate the contact between the medial and lateral nasal walls. The types of surgery would include submucous resection/septoplasty, trimming of inferior turbinates, trimming of middle turbinates and uncapping of concha bullosa. A simple surgery such as one of these listed usually gives the patient dramatic and permanent pain relief.

RHINITIS

Rhinitis is an inflammation of the lining of the nose, with one or more of the following symptoms:

- nasal congestion
- rhinorrhoea
- sneezing
- itching

Other related symptoms of rhinitis

- Post-nasal drip
- Hyposmia/anosmia
- Epistaxis
- Mouth-breathing
- Nasal voice
- Sleep disorder and obstructive sleep apnoea
- Eustachian tube dysfunction, otitis media
- Itchy and watery eyes
- Cough

Classifications of rhinitis

Infective rhinitis:
(a) Bacterial
(b) Viral

Allergic rhinitis:
(a) Seasonal ("hayfever") - peaks during spring and summer.
(b) Perennial - the symptoms are experienced all year round.

Vasomotor rhinitis ("hypersensitive nose" or "non- allergic rhinitis"):
(a) Idiopathic
(b) Non-allergic rhinitis with eosinophilia syndrome (NARES)
(c) Occupational
(d) Drug-induced
(e) Emotional
(f) Atrophic

The autonomic nervous system plays a vital role in the control of the state of the nose. Sympathetic tone causes vasoconstriction and reduces secretomotor function. Parasympathetic tone causes vasodilation and increases secretomotor function. This delicately balanced autonomic nervous system can be easily upset by various factors such as infective, allergic, environmental, hormonal or emotional factors.

In most rhinitis cases, the patient has a combination of allergic and vasomotor rhinitis. If these two forms of rhinitis persist long enough, some elements of infective rhinitis may be present

due to stasis and obstruction of the nasal passages and sinuses.

Rhinitis - examination of the nasal passages

On anterior rhinoscopy, the following tips may be useful to determine which aetiology is more predominant:

Infective rhinitis:

(a) there is hyperaemia of septum, floor of nose and turbinates;
(b) after application of decongestant spray, the mucosa turns slightly less hyperaemic;
(c) the oropharynx is inflamed;
(d) there is coloured mucopus (in bacterial rhinitis);
(e) there is scant and stringy mucopus (in viral rhinitis).

Allergic rhinitis:

(a) the mucous is clear;
(b) turbinates are pale, oedematous and "soggy" looking;
(c) after application of decongestant spray, the turbinates shrink slightly, but the colour remains the same or becomes more pale;
(d) the septum is usually slightly pale.

Vasomotor rhinitis:

(a) the mucous is clear;
(b) the turbinates are congested and engorged;
(c) after application of decongestant spray, the turbinates shrink remarkably and turn pale;
(d) the septum is usually slightly congested.

Treatment of allergic and vasomotor rhinitis

1. Reassure anxious patient or parents (many patients simply want to exclude a sinister pathology).
2. Most patients suffer from combination of allergic and vasomotor rhinitis.
3. Treatments should be tailored to patient's individual complaints.
4. Important to ask patient whether symptoms are bad enough to want medical or surgical treatment.
5. Inform patient that medical treatment is usually temporary and not curative.
6. Surgery (if indicated) is good for improving nasal passages and reducing nasal secretion. Submucous diathermy usually gives temporary relief for up to 6-18 months. Trimming of the inferior turbinates usually gives permanent relief from nasal obstruction and also in reducing watery rhinorrhoea (the inferior turbinates contain the major amount of mucous-secreting and serous-secreting glands of the entire nasal mucosa).
7. Allergy testing and immunotherapy in treatment of allergic rhinitis may be useful for certain patients in whom definite allergens have been identified and who have not responded to other forms of treatment.

If the rhinitis is *mild or moderate:*

- avoidance of allergens;
- regular aerobic exercise;
- antihistamines (PRN);
- decongestants (PRN);
- topical steroids if antihistamines or decongestants have to be taken too frequently;
- cromoglycate.

If the rhinitis is *severe:*

- avoidance of allergens;
- regular aerobic exercise;
- **topical steroids;**
- antihistamines (PRN);
- decongestants (PRN);
- systemic steroids (PRN);
- **surgery;**
- cromoglycate;
- allergy tests → kiv immunotherapy.

Surgical treatment of allergic and vasomotor rhinitis:

Surgery is indicated if the patient has:

1. excessive secretions;
2. anatomical obstruction due to deviated nasal septum or hypertrophied turbinates.

The aim of surgery is to improve symptoms by reducing the size of turbinates, resulting in enlarged nasal airways and a reduced number of secreting glands

Types of surgery for allergic and vasomotor rhinitis are:

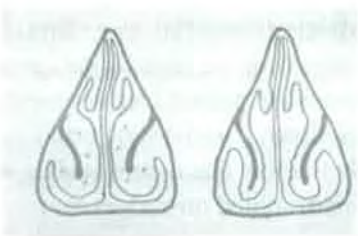
- Trimming of the turbinates;
- Submucous diathermy (SMD);
- Submucous resection/ septoplasty;
- Vidian neurectomy (this surgery is not popular, as the results are unpredictable and have not proven to be effective).

Trimming of inferior turbinates

Trimming of inferior turbinates gives excellent results for improvement of the airway and reduction of watery rhinorrhoea. The amount of turbinate to be excised can be tailored according to the size and configuration of the nasal passages. Removal of part of the lower border of the turbinate would permanently improve the nasal airway and reduce mucous secretion.

It is crucial that just the right amount of the inferior turbinate is removed. Too much removed may lead to loss of filtration function and excessive drying of the nasal passages. There has been some concern that trimming of the turbinates may lead to over-drying of the nose (atrophic rhinitis), but this fear has not really eventuated in our local context. It may be a more significant concern in countries with low humidity or when there has been an over-zealous resection of the turbinates.

Submucous diathermy



Submucous diathermy involves the cauterisation of the vasculature of the turbinates and destruction of the mucous-secreting glands. The bony part of the turbinate remains. This surgery gives considerable relief for a period of time. Unfortunately, the vasculature and mucous-secreting glands usually re-grow within 6-18 months, so submucous diathermy is often not effective in the long-term and there is a high incidence of patient dissatisfaction.

NASAL POLYPS

- Nasal polyps originate in the mucosa of the ethmoid sinuses or middle turbinates & protrude into the nasal cavity.
- They are composed of benign oedematous mucosa.
- The pathophysiology of polyp formation is believed to involve and inflammatory reaction in the respiratory mucosa in the middle meatal and ethmoidal mucosa. This leads to increased permeability of the blood vessels, plasma exudation and oedema, and, in turn, to epithelial rupture, prolapse of the lamina propria and the gradual enlargement of the resulting polypoid tissue.

Nasal polys - treatment

1. If the patient is totally asymptomatic, no treatment is required.
2. There is increasing evidence that the first-line treatment should be medical.
3. Surgery removes existing polyps but does not stop the original cause of the polyps.
4. Surgery is also indicated if malignancy is suspected or if medical therapy fails to control the symptoms.

Nasal polyps - medical treatment:

- topical nasal steroids;
- antihistamines;
- avoid aggravating factors and allergens;
- regular aerobic exercise;
- systemic steroids (PRN);
- cromoglycate;
- allergy testing → kiv immunotherapy.

Note that medical therapy is used to control symptoms, but it does not cure or eliminate the polyps. Medical therapy may need to be used for as long as the patient is symptomatic, the dose to be tailed down gradually (depending on the symptoms).

Nasal polyps - surgery:

Surgery is indicated if:
- medical treatment fails to control symptoms
- suspected malignancy

The aims of surgery are as follows:
- to improve airway
- to provide drainage of paranasal sinuses
- to remove ethmoidal air cell where the polyps originate
- to treat concomitant chronic sinusitis

Post-operative topical or systemic steroids may be required to prevent recurrence of polyps.

If medical and surgical treatment are unsuccessful, immunotherapy can be considered for patients for whom definite allergens have been identified.

SINUSITIS

Treatment of sinusitis

Acute sinusitis (< 4 weeks):

- Symptomatic treatment (decongestants, antihistamines and mucolytics)
- No antibiotics for mild sinusitis or suspected viral sinusitis
- Antibiotics for sinusitis in severe cases, cases with associated complications, cases that exceed 1 week or cases with escalating symptoms. First-line antibiotics should be tried first.

Subacute sinusitis (4 to 12 weeks):
- Antibiotics - 2nd or 3rd line antibiotics
- Non-sedating decongestants and antihistamines during the daytime
- Sedating antihistamines at night
- Mucolytics
- Steroids - 30mg prednisolone (om) on a reducing dose over 1-2 weeks

Chronic sinusitis (>12 weeks):
- Try longer course of medical therapy
- CT-scan to rule out structural obstructions, such as a deviated nasal septum, structural abnormalities or nasal polyps
- ENT consultation Æ kiv surgery

Recurrent sinusitis:
- Exceeding 3-4 episodes of sinusitis a year
- Consider long-term topical steroid to maintain good sinus ventilation and drainage and, in so doing, hope to prevent sinusitis
- Consider functional endoscopic sinus surgery if the sinusitis recurs too frequently.

FUNCTIONAL ENDOSCOPIC SINUS SURGERY (FESS)

This is basically an approach to the sinuses that utilises an endoscope and various other instruments to achieve good sinus drainage and aeration and removal of disease in the nasal passages and sinuses, while preserving as much of the function of the nose as possible. It is very effective in cases of sinusitis caused by bony and structural obstruction of sinus drainage.

However, FESS is less effective for nasal polyps (particularly allergic nasal polyps) because of the tendency of the polyps to recur. Sinusitis from allergic nasal polyps are best treated firstly with a trial of medical therapy (with antihistamines, topical steroids and intermittent doses of antibiotics and intermittent doses of systemic steroids). FESS is indicated in cases of large polyps or if the symptoms fail to respond to medical therapy.

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Snoring and Obstructive Sleep Apnoea - CPAP or Surgery

Ronald ***Brett***

INTRODUCTION

Snoring is a common condition. It is estimated at least 45% of normal adults snore occasionally and 25% are habitual snorers.

Snoring is caused by the vibration of the soft tissues of the throat (soft palate and uvula) during sleep. Narrowing and partial obstruction of the upper airway causes turbulent airflow while breathing resulting in this vibration.

CAUSES OF SNORING

Research shows that snoring often has more than one cause.

Poor muscle tone in the tongue and throat is one factor. This relaxed muscle tone can be caused be alcohol and drugs. The flabby muscles then allow the tongue to fall backwards and the throat muscles to drawn into the airway. Retrognathia also narrows the posterior airway space as the tongue falls back easily. Excessive bulkiness of the tissues of the throat also cause snoring e.g. large tonsils/adenoids, overweight people who have bulking necks. 40% of men with a collar size of ≥ 16.5 are snorers. The tissues in the throat can also be floppy from a long soft palate and uvula. This narrows the nasopharyngeal airway and vibrates during breathing.

An obstructed nasal passage is another factor e.g. from allergic rhinitis or a deviated nasal septum. This causes narrowing of the airway and creates air turbulence when breathing.

IS SNORING SERIOUS?

Snoring can be socially disruptive to family life. It is usually only a mild annoyance for occasional snorers but for habitual ones, it can cause serious social and marital discord. The snorer can be made an object of ridicule or become unwelcome roommates on vacations and business trips. Habitual snoring can cause sleep fragmentation and excessive daytime sleepiness for both the snorer and their loved ones. This leads to fatigue, and changes in mood and concentration.

Currently, habitual snoring is thought to be an early sign/precursor of upper airway resistance syndrome (UARS) obstructive sleep apnoea (OSA). Snoring may be the most obvious sign or clue to the more significant problem of OSA.

CAN SNORING BE CURED?

A large majority of snorers can be helped. For the mild and occasional snorers, self-help measures should be tried first. They should exercise to develop good muscle tone and lose weight. Avoid alcohol and heavy meals 3 hours before bedtime. Avoid getting overtired and to stop sleeping pills or antihistamines before sleep. Establish regular sleeping patterns. Try to sleep sideways. Lastly, to allow the non-snorer to sleep first.

Many other non-surgical measures have tried over the years ranging from throat lubricants to snoring activated alarms. Most do not work.

Dental appliances appear to offer the most help for both snoring and in some cases of apnoea. The dental device brings the lower jaw forward with the tongue and opens up the air passage behind.

RECOGNISING OBSTRUCTIVE SLEEP APNOEA

Obstructive sleep apnoea is the most exaggerated form of snoring. The snoring usually is broken up by episodes of totally obstructed breathing. OSA is defined as cessation of breathing of 10 seconds or more at least 5 times per hour of sleep. (See table 1)

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Table 1

Key terms in OSA
• Defined as the cessation of breathing during sleep • Apnoeic episode – cessation of breathing lasting 10 secs or more • Mild < 5 episodes per hour • Moderate 5 – 15 episodes per hour • Severe > 15 episodes per hour

When breathing is completely obstructed, the body reacts by waking itself up enough to start breathing again. These arousal may occur hundreds of times a night but may not fully awakens the patients. The patient may be unaware of the loud snoring, choking and gasping for air which can be frightening for the bed partner.

OSA affects 3.0% of men and 1.2% of women in Singapore. These are ethnic differences (1.6% Chinese, 3.7% Malay and 4.5% Indians). Symptoms of OSA are listed in table 2.

Table 2

Symptoms of sleep apnoea
• Excessive daytime sleepiness (EDS) • Loud, irregular snoring • Morning headaches • Irritability or moodiness • Poor concentration • Obesity • Hypertension • Frequent nocturnal urination

OSA is associated with many medical problems like hypertension, it increases the risk of acute myocardial infarction, strokes and sudden death.

Sleep Apnoea is diagnosed based on results of a Sleep Study (polysomnogram). This test involves overnight monitoring of the patient during sleep. The sleep study measures the number of apnoeas and decrease in oxygen saturation. It is also used to determine to correct pressures should continuous airway pressure therapy (CPAP) be required.

Patients who may have any of the symptoms listed in table 3 would benefit from OSA screening.

Table 3

When to refer for OSA screening
• When bed partners note that pattern or snoring is accompanied by silence • Silence is broken by gasps and loud snoring • Excessive daytime sleepiness/fatigue • Unrefreshing sleep • Body movements

TREATMENT FOR SNORING

For the habitual snorers where by simple self-help measures have failed, it is necessary to exclude OSA first before proceeding to any surgical measures. This is discussed later on.

A thorough ear, nose and throat examination of the snorer is done. Surgical treatment would depend on the diagnosis and site of obstruction. At times, the treatment can be as simple as managing the nasal allergy, straightening the septum or a Tonsillectomy.

Early on, the favoured surgical management of snoring was to do a Uvulopalatopharyngoplasty (UPPP) for removal of flabby tissue of the palate and open up the air passages. This was followed in the early 90's by a less aggressive procedure called the laser-assisted uvulopalatoplasty (LAUP). This involved more conservative removal of tissue from the throat using a laser. UPPP alone has been shown to have a 50% recurrence on snoring affer three years. UPPP is now generally limited to selected cases only.

The latest technique in the management of snoring by using low level radio-frequency application with a small electrode to the soft palate. This causes shrinkage and stiffening of the redundant soft palatee The procedure is performed under local anesthesia or mild sedation. Most patients can return to work the next day and only require 1-2 days of mild analgesia. They may require 2-3 applications at 8 week interval for a good result.

MANAGEMENT OF OSA

CPAP or Bipap are the principle treatment for OSA.

If patients do well on this, no surgical intervention is required. Surgery is reserved for patients who have failed other non-invasive methods and are unable to tolerate CPAP. Surgery is directed at the site of obstruction. After the patients are evaluated with a cephalometric Xray for anthrometric measurements and doing the mueller manouvre with the fibreoptic nasoendoscope.

Surgery can range from a UPPP procedure to more elaborate tongue or hyoid suspension procedure. These procedures are directed at opening up the airway.

Lately, radio-frequency application to the base of tongue and palate has been found to be useful and less invasive in the treatment OSA where the obstruction is limited to a flabby soft palate and base of tongue. Table 4 provides a guideline to evaluate snoring.

CONCLUSION

Habitual snoring can be an early sign of sleep apnoea. Heavy snorers should be evaluated to exclude sleep apnoea.

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Table 4

Guidelines for evaluation

Snoring Patient
↓
history from bed partner
↓
check nose and throat / exclude OSA
↓
starting advising diet / weight loss
↓
encourage exercise
↓
try nasal decongestants
↓
stop smoking
↓
avoid alcohol / drugs
↓
sleep positioning

OSA suspicion	**Simple snorers**
↓	↓
Refer for Sleep Study + CPAP	failed treatment
↓	Refer for surgical Mx.
Surgery	i.e. somnoplasty LAUP

The Singapore Family Physician

Tonsillectomy & Adenoidectomy - Controversies

K A Abraham

SUMMARY

This paper was presented at an E.N.T. Seminar organized for General Practitioners on Sunday 27th August 2000. It attempts to review the status of tonsillectomy and adenoidectomy and the controversies that exists surrounding its practice. Reference is made especially to a relevant study conducted at the Children's Hospital of Pittsburgh. Acceptable indications are suggested for both these surgical procedures separately.

Tonsillectomy & Adenoidectomy - Controversies

INTRODUCTION

Perhaps no surgery, especially in children, in the 20th Century, has caused more controversy among doctors, than tonsillectomy and adenoidectomy. Today it would appear that some of this controversy is being clarified.

It is worthwhile looking briefly at the history of this conflict. Tonsillectomy was first described by Celsus as early as *50* A.D. while adonoidectomy, records show, was undertaken in the latter half of the 19th century (W. Meyer in Copenhagen) The two operations (T's & A's) were done together, increasingly in the early 2Oth century, based on the "focus of infection" theory. Even many systemic diseases like Rheumatism, mental retardation and anorexia was attributed to diseases of the tonsils and adenoids.

In the 1930-40's, doubts began to be raised on this, as epidemiological studies showed a natural decline of upper respiratory infections in children as they grew older. Also information spread that tonsillectomized persons were at increased risk of contracting Polio. Also about this time antibiotics became available.

In the 1950's, strong resistance began to appear especially among Paediatricians, who felt that children were being subjected to unnecessary surgery.

However, support remained among some doctors based on personal experiences. Also more recent trials support its efficacy in certain life threatening airway obstruction and among orthodontists, who felt it assisted jaw development.

WHAT IS THE CONTROVERSY?

The first and most importance is its indication and following it, it's efficacy. The second is it's possible, long term, harmful effects. Finally whether financial incentives influence surgical decisions.

WHY THE CONTROVERSY?

It lies in the lack of convincing evidence, until recently, of reliable evidence that T's & A's is more effective then conservative treatment. Most of the studies had one flaw or another, making results inconclusive or inadequate. One of the major drawbacks was the exclusion of severely affected children, on ethical grounds, and the inclusion of mildly affected ones, in whom the benefits may have been very slight. To avoid many of the flaws of previous studies the Children's Hospital of Pittsburgh, supported by the U.S. National Institute of Health, conducted a study, with strict criteria, between 1974 and 1994. It was prospective, randomized and controlled. It focused on 1: The efficacy of T's in reducing the frequency of sorethroats and pharyngitis. 2: The efficacy of A's in reducing the frequency and severerity of otitis media. 3: The efficacy of A's in reducing nasal obstruction due to large adenoids 4: The cost/ benefit ratio of the surgery. The latter being a very involved subject, it will not be discussed in this article.

The characteristics of the study were:

1: a dedicated team, comprising Paediatricians, E.N.T. suegeons, Internists, audiologists, and radiologists.

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2: stringent entry criteria for separate trials for T's and A's
3: standardized Systems for rating clinical findings
4: screening allergy skin tests/ serum Ig levels
5: interobserver reliability tests
6: middle ear function by auroscopy and impedance studies
7: cephalometric X'ray studies
8: monitoring of subjects

It is not possible to discuss here, all these in detail but we could look at the criteria for entering in this first controlled trial of tonsillectomy on the basis of recurrent sorethroats.

They were :
1: 3 episodes in each of 3 years
5 episodes in each of 2 years
7 episodes in one year
2: Each episode had to be characterized by one or more of the following:
a. Temperature 101 degrees F.(38.3 degrees C) or higher
b. Enlarged (>2cm.) or tender anterior cervical glands
c. Tonsillar exudates
d. Positive culture for Gp. A beta Hem. Strep. Infection
3: Adequate antibiotic treatment for proven or suspected Strep infection
4: Each episode confirmed by examination and documentation Children were divided, both randomly and by parents choice, for surgical or conservative treatment.

FINDINGS OF THE STUDY

1. The limitations of undocumented history of recurrent throat infections. (It immediately points to the important role the Family Physician and G.P. plays when referring patients)
2. The efficacy of T's in reducing recurring throat infections:

Up to 3 years; about 90% in the surgical group had no throat infections while about 35% in the non surgical group had no throat infections However, follow up of the non surgical group, also showed a drop in the number of throat infections. They concluded that treatment should be individualized, based on parents/child's preference, anxiety and tolerence levels of the illness, school performance and availability of adequate surgical and anaesthetic facilities.

3. The efficacy of A' s in reducing otitis media

The study involved children who had myringotomy and tube insertion, but continued to have middle ear infection, after extrusion of the tubes.

Up to 2 years follow up, favoured the surgical group again, but many in the adenoidectomy group also continued to have otitis media. The researchers concluded that adenoidectomy was justified on an individual basis, like in the tonsillectomy study.

A second study was done on children with secretory otitis media, who had not undergone myringotomy. The benefits of adding adenoidectomy and tonsillectomy on these children was assessed. The preliminary data did not justify the benefits of including these operations as an initial procedure.

4. The efficacy of A's in reducing nasal obstruction

The results of this study showed that, up to at least 2 years good results were achieved. The full results are yet to be reported. In the non surgical group some spontaneous improvement occurred but complete resolution was rare.

Other beneficial effects of A's like improvement of abnormal facies remain to be evaluated.

Two other trials by Maw and his co- workers and Gates et al favoured A's as an initial procedure in reducing recurrent otitis media. However, the statistical significance could be questioned.

CURRENT ACCEPTABLE INDICATIONS OF T'S & A'S

Definite Indications

1. Severe Respiratory Obstruction Causing sleep apnoea, Hypoventilation, dysphagia or cor pulmonae
2. Malignant tumours of the tonsils

Reasonable Indications

1. Recurrent tonsillitis
2. Chronic tonsillitis
   - attacks not responding to antibiotics
   - crypt obstruction causing halitosis
   - complications of tonsillitis e.g. Quinsy
3. Adenoidectomy
   - Obstructive Adenoid Hypertrophy
   - Recurrent otitis media, after rejection of ventilating tubes

"Grey Areas" would be

1) whether adenoidectomy should be considered as an initial operation when doing myringotomies. I would personally favour it only if nasal obstruction is also a problem.

2) whether tonsillectomy should be routinely done when adenoidectomy is being done. Most of us would consider indications for T's & A's separately.

ADVERSE EFFECTS OF T'S & A'S

1. Surgical and Anaesthetic Risks:
   The surgeon should be fully aware of the possible serious risks, however small, of these operations. All necessary precautions must be taken.
   Complications should be preventable under today's modem conditions
2. Decrease in Immunity:
   Many observers have noted a drop in the level of IgG but not IgA or M, following these procedures. It is important to note that it does not drop below normal levels. Also no subsequent increase in throat infections was noted in these studies. It appears that no serious immunological risks accompany the removal of tonsils and adenoids. Admittedly, a very remote, still unknown, risk may be present and hence the operation should only be conducted for sound indications.

3 The earlier fears of an increased risk of Polio in tonsillectomized persons is today no more valid with the universal immunization against Polio

4 Vianna et al published a paper suggesting a link between tonsillectomy and increased risk of Hodgekin's disease. This has been largely been dispelled by later studies.

CONCLUSION

Two important points need to be stressed. The first is the important role the General Practitioner/ Family Physician plays in making the properly documented diagnosis. This will go a long way in helping the E.N.T. surgeon in his assessment. The second is the stringent criteria the surgeon must exercise in recommending surgery.

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The Singapore Family Physician

Neck Lumps - What Not To Do?

Loh Leong Eam

SUMMARY

This article gives a brief description of the diagnosis and management of neck lumps which are commonly encountered in family as well as specialist practice.

Key words:
Branchial cyst, Neuroma, Pharyngeal pouch, Retropharyngeal abscess, Thyroid nodule, Parotid mass, Metastatic lymph node.

INTRODUCTION

The diagnosis of neck lump can be made easier by noting its anatomical site. At the lateral neck along the Sternomastoid Muscle, differential diagnosis includes Branchial Cyst, Neuroma and metastatic lymphnode. At classical anatomical site such as inferior or anterior to the earlobe, a parotid mass needs to be considered. Vague neck lump which does not seem to be confined to any anatomical site would include Pharyngeal Pouch and retropharyngeal abscess.

BRANCHIAL CYST

Branchial Cyst forms as a result of anomaly in the development of branchial cleft during fetal development. It usually appears at the anterior border of the Sternomastoid Muscle and appears as a result of infection. C T scanning confirms its cystic nature and treatment is excision to prevent recurrence.

NEUROMA

Neuroma or neurilemmoma is a benign growth of the Schwann cells of the nerve fibre. The commonest nerve in the neck to grow a neuroma is the Vagus Nerve. MRI shows a signal intensity consistent with neuroma. Management is by excision. Sometimes by slitting the capsule and removing the neuroma and saving the nerve axon, paralysis of the verve may be avoided.

PHARYNGEAL POUCH

Pharyngeal Pouch is a herniation of the pharyngeal mucosa through weakness in the pharyngeal constrictor muscle. The symptoms consist of dysphagia, halithosis and cough due to regurgitation of the food collected in the pouch. When filled up with food, there may be vague swelling in the neck. Barium Swallow will reveal the pouch when it is filled up with barium. Management is excision. The pouch is packed with gauze through oesophagoscopy. This facilitates identification of the pouch during surgery.

RETROPHARYNGEAL ABSCESS

Swallowed fishbone which becomes impacted in the oesophagus is very common in our population. Failure to remove the bone will result in complications such as retropharyngeal abscess or perforation of the oesophagus by the bone. When abscess form, the patient will be dysphagic and feverish. Depending on the size of the abscess, a vague swelling of the neck or bull neck forms. The abscess needs to be drained and the bone removed.

PAROTID MASS

The classical site for a parotid mass is anterior or just below the ear lobe. CT scanning helps to confirm that the mass is in the parotid gland and to assess whether the deep lobe is involved. Fine needle aspiration cytology may help to decide whether the mass is benign or malignant. When the mass is in the superficial lobe, superficial parotidectomy excises the mass as well as gives the histological diagnosis. If at frozen section, the mass is malignant, the deep lobe of the parotid is removed as well, completing total parotidectomy.

THYROID NODULE

Thyroid nodule poses little difficulty in diagnosis. Clinically it moves with swallowing. Ultrasound

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helps to confirm diagnosis and to detect any other clinically nonpalpable nodule. In non-toxic nodule as confirmed by thyroid function test, fine needle aspiration is done. If the cytology is non carcinoma, try thyroxine suppression test for six months. If these is complete resolution of the nodule, monitor the patient. If there is incomplete resolution, proceed to surgery. The surgery that is done for carcinoma of the thyroid is total thyroidectomy. If there is metastatic lymphnode, Functional Neck Dissection is done; removing only the lymphnodes and sparing the Internal Jugular Vein, Sternomastoid Muscle and Accessory Nerve.

METASTATIC LYMPHNODES

Nasopharyngeal Carcinoma commonly metastasises to the upper lateral cervical lymphnode. Other common symptoms are epistasis and blocked ear. The postnasal space can be easily examined with a nasendoscope and biopsied. Treatment for Nasopharyngeal Carcinoma and the metastatic lymphnode is radiotherapy.

Carcinoma of the larynx metastasises to the mid-lateral cervical lymphnode. In advanced cases, Total laryngectomy with Radical Neck Dissection is done.

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The Singapore Family Physician

Hearing Loss: State-of-the-art Management

Low Wong Kein

INTRODUCTION

Hearing loss is a common problem in Singapore as well as the rest of the world. It is estimated that 6 % of the population sutters from hearing loss. Therefore, given a population of 4 million, Singapore should have nearly a quarter million people with hearing loss. It is a disability that has significant impact on one's life. It adversely affects the adult socially and at work. In children, various aspects of development, including speech and psycho-social, are affected. One can experiment plugging both ears (which give about 40-50 dB loss) for a day, to appreciate the significant disability resulting from hearing loss. With modern technology, overcoming the disability of hearing loss has progressed tremendously in recent years. Better technology has allowed hearing loss to be accurately recorded, even in young children. Better understanding of patho-physiology of hearing loss, has resulted in improvement of the preventive and treatment aspects of this condition. Modern technology has led to the development of devices that can overcome deafness by using different mechanisms. Therefore, state-of the-art management strategies, have led to minimizing the ill effects of hearing loss.

TYPES OF DEAFNESS

a) Conductive deafness affects the sound conducting mechanism from external to the inner ear. Lesions of the external ear, tympanic membrane and middle ear can result in conductive hearing loss. In the external ear, there may be wax, foreign bodies, polyps or canal stenosis. The eardrum may be perforated or thickened such as in tympanosclerosis. The middle ear cleft may be filled with effusion fluid (serous otitis media), blood (haemotympanum), pus (acute otitis media) or cerebro-spinal fluid. The ossicular chain in the middle ear may be disrupted after trauma or infection; or its mobility could be impaired eg in otosclerosis. In general, conductive hearing loss can be rectified surgically, with modern surgical techniques and tools. The advent of the ENT operating microscope (first used in Singapore in 1958) has made a great difference in achieving good results. More recently, the introduction of the otoscope has made minimally invasive ear surgery feasible. Surgical tools such as high-powered drills and lasers have made surgery faster and safer. Biomedical advances like better biodegradable materials, and ossicular prosthesis which are more effective and inert, have made surgery more acceptable. Modern sterilization techniques have enabled various allograft materials to be used with minimal risk of disease transmission.

b) In sensori-neural deafness, the defect is at the cochlea (inner ear) or retro-cochlear levels (cochlear nerve and central pathways). Certain sensori-neural hearing loss may improve with medical therapy eg some cases of syphilitic otitis and Meniere's disease; or by surgery eg in perilymph fistula. However, the majority of sensori-neural deafness such as in presbycusis, noise-induced deafness and ototoxicity, do not improve. Therefore, prevention, early detection and effective rehabilitation of hearing loss are important.

PREVENTION

This has great relevance in noise-induced deafness. Loud noise of 85dB for more for 8 hours per day over prolonged periods of time, can result in noise-induced deafness. In Singapore, legislative procedures are in place to require cases of noise-induced deafness to be notified to Ministry of Manpower. Employers are required to take the necessary preventive measures and workers are compensated for noise-induced deafness. Preventive measures include limiting where possible, industrial noise generated as well as enforcing the use of ear protection in noisy environments. Sound conditioning is currently being explored as a possibility of preventing noise-induced deafness (McFadden & Henderson, 1999). This concept is based on observations that

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guinea pigs that have been pre-exposed to moderate levels of acoustic stimulus, incurred less damage from high levels of exposure, than animals that had not been similarly conditioned. Research is currently aimed at defining the limits of the conditioning effect and elucidating the effect's underlying mechanisms.

EARLY DETECTION

It has been estimated that 1 in 1,000 newborns have significant hearing loss. It is well established that newborn hearing screening programmes which are confined only to high risk groups such as premature babies and neonatal jaundice, detects only about 50% of all born with hearing loss. This is because about 50% of newborn with significant hearing loss have no identifiable risk factors and often no outward signs. The Task Force on Infant and Newborn Hearing and Joint Committee on Infant Hearing have recommended that all infants with hearing loss should be identified by 3 months of age and should receive intervention by 6 months of age (McMurray, 2000). Otherwise, speech and language developments are likely to be significantly affected. With current behavioural hearing screening tests, the average age of detection of congenital deafness is two and a half years of age; as it is often difficult to recognize children with hearing loss. Therefore, there are many states of the US and countries in Europe which have legislative procedures in place for universal newborn hearing screening programmes, using objective screening tools. In Singapore, the ministry of Health is currently studying the feasibility of a universal newborn hearing programme. Even with a successful newborn hearing screening programme, it is important to be mindful that a child can develop hearing loss at a later stage. It is therefore, important that primary health physicians always maintain a high index of suspicion of hearing loss in children, who often present with only very subtle symptoms.

DIAGNOSIS

Audiometric tests are broadly divided into behavioural and electro-physiological tests. These tests have come a long way from their rudimentary beginnings, in terms of accuracy and usefulness. For example, evoked response audiometry not only objectively records hearing thresholds, it is able to differentiate between damage to cochlear or retro-cochlear levels. In recent years, the advent of steady state evoked potential technology enables objective thresholds to be recorded for individual frequencies, as opposed to evoked response audiometry, which is not frequency specific. Otoacoustic emission technology has proven to be an extremely useful screening tool in detecting hearing loss in newborns. It is based on the concept that healthy cochlear hair cells contract in response to external sounds; and in the process of contraction, emit a sound which can be objectively measured. Current day audiologic equipment can even measure inner ear pressures and cerebro-spinal fluid pressure.

HEARING AIDS

Hearing aid technology has improved tremendously in recent years (Sweetow & Bingea, 2000). Conventional hearing aids provide mono-aural amplification for louder hearing; and binaural hearing for better localization and directional hearing. Digital amplification available today has enabled added features and processing schemes that were not possible before, making hearing amplification even better and more comfortable. It is still a challenge however, to develop hearing aids capable of truly enhancing signal-to-noise ratio, enabling patients to understand speech in noisy environments. Besides better functioning, the trend for hearing aid technology is for increasing miniaturization, which has progressed from body worn aids, to behind the ear, in the canal and in the ear hearing aids. There are now hearing aids which are implantable into the middle ear, either partially or fully. The potential advantages of implantable hearing aids are elimination of feedback, no occlusion effect, improved fidelity and cosmetics. Bone anchored hearing aids are suitable for a selected patients, such as those with chronic external ear infections or discharging mastoid cavities. This technology involves implanting a titanium screw into skull behind the ear, which bio-integrates with bone. The hearing aid is in

turn, fitted onto the top of the screw. Amplified sounds can then be conducted into the inner ear, without the need to wear any device in the ear canal itself.

COCHLEAR IMPLANTS

Some patients have cochlear hair cell damage so severe that conventional hearing aids are of inadequate benefit. Such patients may benefit from a cochlear implant, which when implanted into the inner ear, by-passes the damaged hair-cells of the cochlear and to directly stimulate the auditory nerve. The fact that electrical stimulation of the auditory nerve could be translated into sound was realized as early as 1800, when Volta experimented on himself by applying electricity into his own ear with a metal rod. Today, sophisticated multi-channel cochlear implants potentially capable of restoring hearing in patients with profound hearing loss, are available. This is now an established practice world-wide, with more than 20,000 patients implanted. In Singapore, a comprehensive cochlear implant programme was started at the Singapore General Hospital in 1996. Since then more than 70 patients, both children and adults, have been implanted in the programme with generally excellent results (Low et al, 1999).

ADVANCES IN CELL/MOLECULAR BIOLOGY

Regeneration /repair and protection of auditory hair cells and auditory neurons is an exciting rapidly evolving field. It has generally been accepted that hearing loss resulting from hair cell damage is irreversible because human ear has been considered to be incapable of regenerating or repairing these sensory elements following severe injury. But recent studies have shown that certain growth factors such as TGF-alpha, neurotropin type 3 and brain-delivered neurotropic factor are capable of promoting auditory cell/neuron repair/regeneration (Feghali et al, 1998). Administration of growth factors to the inner ears of animals is now possible, with the use of implanted catheters and miniature infusion pumps. Gene therapy has also been shown to be an effective method of providing long-term support to auditory hair cells. These advances suggest that it is possible in future to prevent /repair auditory hair cell damage in humans.

CONCLUSION

Hearing loss is a significant problem in Singapore, both in children and adults. In adults, it affects quality of life and productivity. In children, it leads to developmental delays, notably speech and language. With today's technology, it is possible to effectively overcome this disability in most cases. Future strategies will focus on prevention and early detection, improvement of rehabilitative medical devices and ultimately, restoration of physiologic hearing.

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The Singapore Family Physician

Treatment of Osteoporosis

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INTRODUCTION

Osteoporosis is defined as a progressive systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. It is a frequent problem of the post-menopausal women and is clinically important because of the morbidity and mortality associated with fractures commonly of the vertebrae, hips and distal radius. It is estimated that 40% of all women above the age of 50 years will suffer from an osteoporotic fracture at some point in time. The prevalence of the disease will rise with an increasingly aging population and the impact of this is one of the reasons why the World Health Organisation has dedicated this decade (2000-2010) The Bone and Joint Decade.

MEASUREMENT OF BONE MINERAL DENSITY

The diagnosis of osteoporosis can be made based on the measurement of bone mineral density (BMD) under the WHO criteria (Table 1). The value of BMD that is two and a half standard deviations or more below the young adult mean value (ie. T-score < or = -2.5) defines osteoporosis, even in the absence of a osteoporotic fracture. A T-score of between -1 to -2.5 is considered to indicate low bone mass or osteopenia, and a value greater than -1 is normal. The BMD is often measured at the lumbar spine and hip, and the use of Dual-energy X'ray Absorptiometry (DEXA) is widely regarded as the method of choice for the measurement. The use of BMD measurement allows the identification of those at risk of osteoporosis and the initiation of preventive therapy before the occurrence of fractures.

RISK FACTORS FOR OSTEOPOROSIS

The bone mineral density of a person is generally influenced by the peak bone mass, which is achieved usually by the age of 30 years, and the rate of bone loss thereafter. Although the peak bone mass is mostly determined by genetic factors, other factors such as nutritional status and calcium intake during growth; hormonal and environmental factors may play a role as well. The rate of bone loss is enhanced in the post-menopausal woman due to the decline in sex hormones. The factors that contribute to osteoporosis are listed in Table 2.

PREVENTION OF OSTEOPOROSIS AND FRACTURES

Due attention to the modifiable risk factors will help in the prevention of osteoporosis. Adequate daily calcium and vitamin D intake should be maintained whether by dietary means or with

Table 1

WHO criteria for osteoporosis in women

Category	T-score	Definition
1) Normal	> -1	BMD</= 1 SD below the mean of young healthy Women
2) Low bone mass (osteopenia)	-1 to -2.5	BMD between 1 to 2.5 SD below the mean of young healthy women
3) Osteoporosis	< -2.5	BMD > 2.5 SD below the main of young healthy women
4) Severe osteoporosis	< -2.5	BMD > 2.5 SD below the mean of young healthy women and the presence of one or more fragility fractures

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Table 2

Factors contributing to osteoporosis	
1) Genetic or constitutional eg.	- White or Asian - Family history (maternal history of fractures) - small body frame - premature menopause (<45 years) - late menarche
2) Lifestyle and nutritional eg.	- nulliparity, prolonged amenorrhoea - smoking - excessive alcohol intake - inactivity, prolonged immobilisation - low body weight
3) Medical conditions eg.	- anorexia nervosa, malabsorption - endocrine disorders (hyperparathyroidism, thyrotoxicosisk hypogonadism, hypercortisolism - osteogenesis imperfecta - rheumatoid arthritis - chronic disorders (renal failure, obstructive lung disease, neurological disorders)
4) Drug eg.	- corticosteroid therapy (> 7.5mg/day for > 6 months) - anticoagulants - anticonvulsants - excessive thyroid therapy - chronic phosphate-binding antacid use

supplements. In our Asian population, the recommended daily calcium requirement is 1000mg for young males (11 - 18 years), 800mg for young females (11 - 18 years) and 700mg for all adults (19 years and above). Daily vitamin D requirements are 400 IU for less than 65 years and 800 IU for those above 65 years. Regular weight-bearing exercises such as brisk walking are beneficial to skeletal health, however excessive vigorous exercises can lead to secondary amenorrhoea and predispose to osteoporosis. For those at risk of fractures, the prevention of falls is important and this include modifying the home environment (eg. ensuring non-slippery floors, adequate lighting) if necessary. In the elderly, exercises that strengthen muscles and improve balance, and minimising the use of sedatives are measures that can reduce risk of falls.

DRUG THERAPY FOR OSTEOPOROSIS

Under the guidelines drawn by the Osteoporosis Society (Singapore), drug treatment should be considered for all those who had an osteoporotic fracture or whose BMD is less than -2.5 SD (T-score) below the mean of young healthy women. For those whose BMD lies in the "osteopenic" range (T-score between -1 to -2.5), treatment with hormone replacement therapy could be considered in the post-menopausal women as it has other benefits besides the prevention of bone loss. The use of other therapeutic agents in this group of patients will depend on the patient's acceptability of the benefit / risk ratio of drug treatment, including the cost of long term therapy. If no treatment is initiated for those with bone osteopepenia, the BMD could be repeated in a year's time to re-evaluate the bone mass. A rate of bone loss of more than 4 % would be indication for starting drug therapy.

The agents used in the treatment and prevention of osteoporosis act by inhibiting bone turnover (eg oestrogens, bisphosphonates), stimulate bone formation (eg. fluoride) or by other heterogneous effect (eg Vitamin D and derivatives).

a) Hormone replacement therapy (HRT)

In the absence of any contra-indication, HRT should be considered early in the management of post-menopausal women. Estrogen therapy has been shown to prevent further bone loss in menopause and reduce the risk of both vertebral and non-vertebral fractures. In the Study of Osteoporotic Fractures, post-menopausal women who were currently taking estrogen had a relative risk of 0.66 of sustaining a non-vertebral fracture compared with those not taking estrogen. The beneficial effect on bone loss occurred irrespective of the age at which estrogen therapy was started but is greater in those who took it within five years after menopause. HRT has other advantages which include relief of menopausal symptoms, prevention of dementia and its cardioprottective effects, although the recent Heart and Oestrogen-Progesterone Replacement Study (HERS) has cast some doubt on the latter effect.

b) Selective Estrogen Receptor Modulators (SERMS)

The advantage of selective estrogen receptor modulators over estrogen therapy is its lack of association with breast and uterine cancers. The SERMS have a favourable effect on lipid metabolism but do not relief menopausal symptoms. The skeletal effect of this group of drug was demonstrated in the MORE (Multiple Outcomes of Raloxifene Evaluation) trial using Raloxifene, which showed a 30-50% reduction in vertebral fractures but no significant reduction in no-vertebral fractures compared to placebo. The MORE trial also showed an increase risk of venous thromboembolus in those receiving Raloxifene and patients who have a history of such events should avoid taking it.

c) Bisphosphonates

The bisphosphonates are analogues of pyrophosphate that reduce bone resorption. The two bisphosphonates commonly used for treating post-menopausal osteoporosis are etidronate and alendronate. Etidronate has to be given in a cyclical fashion (ie. 400mg daily for two weeks followed by supplemental calcium daily for 11 weeks) because continuous daily dosing may impair none mineralization. Alendonate is taken daily and studies have shown that is increases bone mineral density and reduces spinal and hip fractures by about 50%. The bisphophonates are poorly absorbed from the gut and should be taken on an empty stomach. Food intake must be avoided at least two hours before and after taking etidronate, and half an hour after taking alendronate.

d) Calcitonin

In addition to its bone resorption properties, calcitonin which is a peptide normally produce by the thyroid C cells, has analgesic effect and is particularly useful for managing acute vertebral fractures. It can be given parentally (subcutaneous or intra-muscularly) with doses varying from 50 to 100 IU daily, or intra-nasally (200 IU daily). Nausea is the most frequent side effect encountered when calcitonin is given parentally and is dose dependent. Local nasal irritation occurs in some patients using nasal spray and this mode of administration may not be acceptable for those patients with nasal conditions.

e) Vitamin D metabolite and analogues

Calcitriol (1,25 dihydroxyvitamin D3) and its synthetic analogue, alfacalcidol (1 alpha-hydroxyvitamin D) enhances calcium absorption and reduce the effects of parathyroid hormone induced bone resorption. These agents have been shown, in some studies, to decrease vertebral fracture risk and prevent corticosteroid-induced osteoporosis. A major concern with the use of Vitamin D derivatives is the occurrence of hypercalcaemia and hypercalciuria which may

induce nephrocalcinosis. Patients on these drugs should monitor the calcium levels periodically and avoid taking calcium supplements.

f) Others

Few agents can stimulate bone formation and these include flouride salts and parathyroid hormone. These drugs may increase bone mineral density but their effect on reducing fracture rates is still not proven. Stanozolol and nandrolone are anabolic steroid most commonly used to treat osteoporosis but they are associated with various side effects including raised hepatic transaminases, virilisation, and atherogenic lipid profile. Testosterone replacement therapy is useful for male osteoporosis due to hypogonadism.

CONCLUSION

The aim of treating osteoporosis is to prevent fragility fractures. Osteoporotic fractures are associated with increased mortality, significant morbidity, high socio-economic cost and severe fracture pain that are sometimes refractory to treatment. There are currently effective treatment that can reduce the risk of osteoporotic fractures. Identification of those at risk with early diagnosis and treatment of osteoporosis will help to reduce fractures resulting from this treatable condition.

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The Singapore Family Physician

Treatment and Prevention of Pneumococcal Infections in the Adult

Ling Moi Lin

SUMMARY

The development of drug resistant *Streptococcus pneumoniae* (DRSP) in the last decade world-wide has posed interesting challenges to the management of pneumococcal infections. New antimicrobials like the newer fluoroquinolones, Synercid or Linezolid are promising agents for penicillin- or macrolide- resistant pneumococci. However, the role of the pneumococcal vaccine needs attention as it can serve as an adjunct measure in our strategy against the increasing incidences of DRSP in our country.

Keywords: *Streptococcus pneumoniae, resistance, vaccine, prevention, treatment*

INTRODUCTION

Pneumococcal disease is a leading cause of serious illness in children and adults world-wide caused by *Streptococcus pneumoniae.* It is a common pathogen for many community-acquired infections, namely acute otitis media, upper and lower respiratory tract infections. In the United States, it is estimated that approximately 3,000 cases of meningitis, 50,000 cases of bacteraemia, 500,000 cases of pneumonia, and more than 40,000 deaths are due to *S pneumoniae.*[1] In 1984, the case fatality ratios were reported as 5% for pneumonia, 20% for bacteraemia, and 30% for meningitis.[2] Our local data showed an overall case fatality rate of 29.5% in patients with pneumococcal bacteraemia, with higher rates seen in the extreme age groups (39.5% in <1 year old and 50% in those >60 years old).[3] Serious pneumococcal infection is most prevalent in the extremes of age. In the United Sates, the case fatality rates in the elderly for pneumococcal pneumonia is estimated to be higher than the 5-7% estimated for the general population; and a figure of as high as 80% has been estimated for meningitis in the elderly versus 30% in the general population.[4]

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DRUG RESISTANT *STREPTOCOCCUS PNEUMONIAE* (DRSP)

Pneumococci with intermediate resistance (MIC 0.1-1.0 μg/ml) or high level resistance (MIC ≥ 2 μg/ml) to penicillin have become increasingly common in many countries. The Alexander Project, a world-wide study on the comparative activity of various antimicrobial, conducted in 1995 revealed astounding results (see Table 1).

Table1 Epidemiology of penicillin resistant Streptococcus pneumoniae (PRSP)

Country	% resistance to penicillin
Britain	10.7
France	58.1
Hong Kong	66.8
Indonesia	52.8
Malaysia	10.5
Pakistan	28.1
Philippines	1.5
Singapore	25.4
Spain	54.2
Switzerland	10.0
Thailand	69.2
USA	19.8

In 1998, the Alexander Project reported an overall 64.8% susceptibility to penicillin, 13.2% intermediate and 22% resistance in the 4,017 isolates collected worldwide. Highest prevalence was reported for Hong Kong (1.5% penicillin intermediate, 60.7% penicillin resistant) and lowest prevalence in the Netherlands (3.2% penicillin intermediate, 0% penicillin resistant).[5] The changing epidemiology of PRSP in Singapore is shown in Fig.1

Overall macrolide resistance has been noted to be significant high at 16.5% in 1996 from the Alexander project, in contrast to 10.4% penicillin

Fig 1 Penicillin resistance in *Streptococcus pneumoniae*

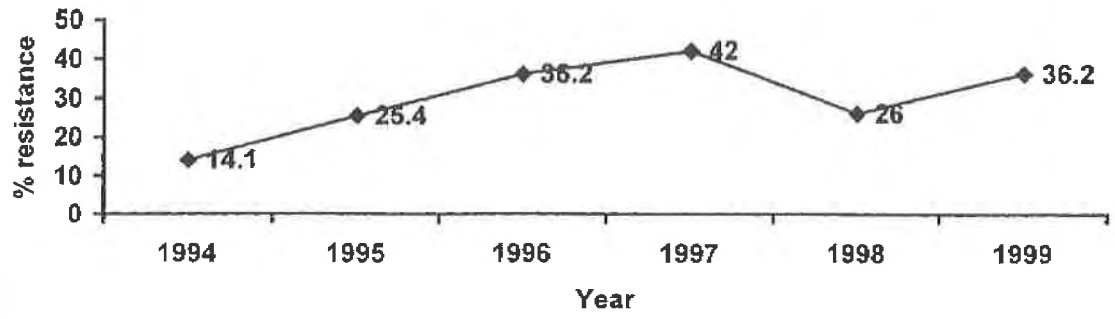
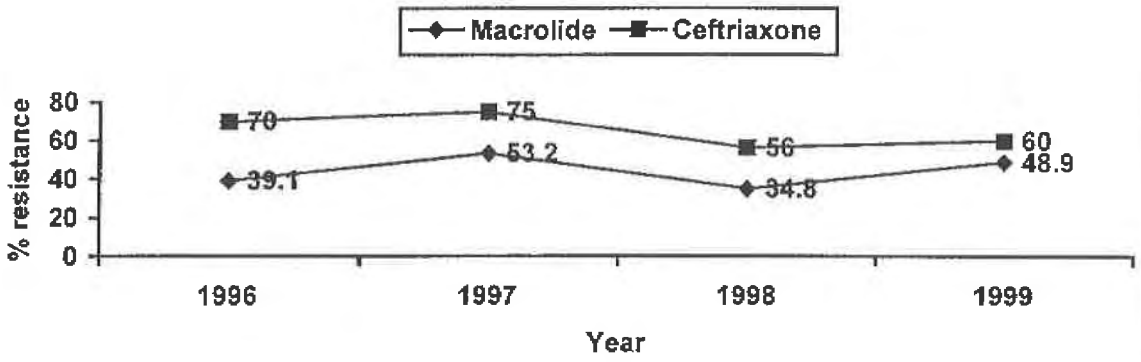


Fig 2 Macrolide and ceftriaxone resistance in *Streptococus pneumoniae*



resistance. This has increased to 28.2% in 1998 and Fig 2 shows our local data with respect to this. Cross-resistance is also seen with the newer macrolides, clarithromycin and azithromycin.

In essence, we have a problem of DRSP at our hands, which complicated the management of pneumococcal infections and make choosing empiric antimicrobial therapy for suspected cases of meningitis, pneumonia and otitis media increasingly difficult.

TREATMENT

In general, penicillin remains the mainstay of therapy for pneumococcal infections caused by susceptible strains. Oral ß-lactams (amoxicillin, cefuroxime, cefpodoxime) are adequate for mild to moderate infections caused by susceptible strains. Other oral cephalosporins are less active.

For severe pneumococcal infections, high dose intravenous penicillin G (16-24 million units daily for susceptible strains) should be used, or a 3rd generation cephalosporin (cefotaxime or cefriaxone). For severe pneumococcal infections caused by intermediate or high grade resistant strains, cefotaxime or ceftriaxone should be used. However, for meningitis caused by cephalosporin resistant pneumococci, ceftriaxone should be combined with vancomycin. Macrolides are appropriate for susceptible strains of pneumococci but where prevalence of macrolide resistance is high, alternative agents should be considered for empirical treatment of severe pneumococcal infections. Clindamycin may be an option. New antimicrobials like the newer fluoroquinolones, quinuprisitin-dalfoprisitn (Synercid) or linezolid (Zyvox) are promising agents for penicillin- or macrolide- resistant pneumococci.

Questions have been raised with regards to the clinical impact of DRSP. Length of stay of a bacteraemic patient with DRSP is 15.8 compared to 12 days for a patient with a penicillin susceptible S *pneumoniae*. Moreover, there is no documented increased mortality or treatment failure seen in patients with DRSP, especially in those with respiratory diseases. Arising from this, the DRSP Therapeutic Working Group 2000 has recommended that MIC breakpoints be changed for respiratory isolates from ≤0.06 μg/ml to MIC≤1 μg/ml for penicillin susceptible strains, MIC=2 μg/ml for penicillin intermediate and MIC≥4 μg/ml for penicillin resistance.[6] These increased breakpoints will result in a marked reduction in our incidence of PRSP since most of our isolates are of MIC ≤4 μg/ml. Moreover, the use of the newer quinolones have been recommended to be reserved for those where first line therapy failed, patients who are allergic to penicillin or in those with documented infection with DRSP i.e. MIC≥4 μg/ml. The rationale for this is the observation that there is already increased incidence of ofloxacin or ciprofloxacin resistance in the DRSP strains and the possible development of cross-resistance to the gram negative bacteria.

PREVENTION

The currently available vaccine, Pneumovax^{R}, is a 23-valent vaccine incorporating the common serotypes of *Streptococcus pneumoniae*. An epidemiological study done form 1977-1986 in Singapore confirmed that the common serotypes implicated in invasive pneumococcal infections are covered by the vaccine.[3] Another study done in 1995 demonstrated that the vaccine covers 91.3% of the invasive isolates.[7]

The vaccine is both effective and protective against invasive pneumococcal infections. The Advisory Committee on Immunization Practices (ACIP)[1], the American Academy of Paediatrics, the American College of Physicians and the American Academy of Family Physicians has recommended its use.[8]

Patients recommended for immunization include[1]:

- Patients > 65 years old
- Patients with chronic cardiovascular disease (including congestive cardiac failure and cardiomyopathy
- Patients with chronic pulmonary disease (including chronic obstructive lung disease and emphysema)
- Patients with diabetes mellitus
- Patients with asplenia (including those with sickle cell disease and splenectomy)

Pneumococcal vaccine is effective in preventing pneumococcal disease, and its cost-effectiveness is comparable to that of similar preventive medical interventions in elderly and high-risk patients. In a US retrospective cohort study (1986-1988) involving 762 vaccinated and 1,161 randomly selected non-vaccinated individuals, the projected cost of pneumococcal pneumonia is more than 3 times the costs associated with vaccination plus treatment costs for vaccinated subjects who contracted pneumonia.[9] This amounts to a cost saving of US$141,098/1,000 people vaccinated. In a study by Sisk et al, vaccination of those ≥65 years saved approximately US$8 (1993 US$) in net medical costs and gained 1.21 days of healthy life.[10]

In making the prevention of pneumococcal diseases a reality, it is recommended that patients be evaluated for immunization at each office visit, prior to hospital discharge and also upon admission to chronic and long-term facilities. As noted by the American College of Physicians, "... comprehensive adult immunization requires an organized approach to ensure that indicated vaccines are offered to all patients. If this is done, the extraordinary potential of immunization to prevent disease can become a reality in clinical practice."[11]

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The Singapore Family Physician

Proctalgia Fugax - A Disease Long Forgotten?

Yim Heng Boon

SUMMARY

I present a case report on a middle-aged lady who complained of paroxysmal, sharp anal pain for the past one week. Clinical examination was unremarkable and sigmoidoscopy revealed no abnormality. She was treated for a presumptive diagnosis of proctalgia fugax and apparently responded well to lorazepam as well as nifedipine. This article aims to increase the awareness among the physicians of this benign, functional condition.

Keywords

Paroxysmal, anal pain, Proctalgia fugax.

CASE REPORT

A 38 year old assistant nurse presented to the gastroenterology specialist clinic with the problem of paroxysmal, sharp episodic anal pain for the past one week. Each episode of pain lasted only a few seconds and was not associated with change in bowel habits. There were also no fever, bleeding per rectum, mucus in stools nor any loss of weight. She did occasionally have tenesmus sensation but these were mild and not bothering her much. There was no family history of colon cancer though one of her children unfortunately passed away at age one from some neurological problem. Her only other significant medical history was that of a tiny right renal calculus which was treated conservatively.

Clinical examination revealed a rather excitable lady with sable vital signs. Perianal examination revealed no anal fissure nor any adjacent abscess or fistula opening. There was also no external prolapsed haemorrhoids seen. Per rectal examination revealed no mass and stool colour was brown. A sigmoidoscopy was performed and this revealed no abnormality up to the splenic flexure.

The impression then was proctalgia fugax and she was reassured and initially prescribed with chlordiazepoxide. The medication was later converted to lorazepam and a low dose nifedipine and she apparently responded dramatically well to this with no more recurrence of the paroxysmal anal pain.

DISCUSSION

Proctalgia fugax is a relatively common but little known cause of anorectal pain. It is a form of functional anorectal pain. According to the guidelines set by the Committee on Functional Anorectal Disorders, Multinational Working Teams to Develop Diagnostic Criteria for Functional Gastrointestinal Disorders (Rome II) [1], there are two forms of functional anorectal pain; levator ani syndrome as well as proctalgia fugax. Both of these can be distinguished from each other on the basis of the symptom duration, frequency and character of pain.

Proctalgia fugax classically presents as paroxysmal severe anorectal pain which lasts only a few seconds to minutes. It then suddenly resolves spontaneously. There is no associated change in bowel habit. The attacks are infrequent. The diagnosis of proctalgia fugax is based on symptoms and after excluding other pathology. Tables 1 and 2 show the diagnostic criteria of proctalgia fugax and that of levator ani syndrome for comparison. There are several studies which suggest that smooth muscle spasm may be the cause of proctalgia fugax. [2,3] There is also some suggestion of increased association of perfectionistic, anxious or hypochondriac personality with this problem.

Table 1: Diagnostic criteria of proctalgia fugax

1. Recurrent episodes of pain localised to the anus or lower rectum; and
2. Episodes last from seconds to minutes; and
3. There is no anorectal pain between episodes.

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Table 2: Diagnostic criteria for levator ani syndrome

At least 12 weeks, which need not be consecutive, in the preceding 12 months of:

1. Chronic or recurrent rectal pain or aching;
2. Episodes last 20 minutes or longer; and
3. Other causes of rectal pain such as ischaemia, inflammatory bowel disease, cryptitis, intramuscular abscess, fissure, haemorrhoids, prostatitis, and solitary rectal ulcer have been excluded.

Most patients have only transient, infrequent episodes of pain and should be reassured. However, for those with frequent episodes of pain, several papers have been published regarding the various medications prescribed empirically for this problem. Eckardt VF et al [4] conducted a randomised, double-blind, placebo-controlled, cross-over study utilising inhaled salbutamol for the treatment of proctalgia fugax in 18 patients. He concluded that inhalation of salbutamol could shorten attacks of severe pain in patients with proctalgia fugax though the mechanism of action was unknown. Babb RR [5] advocated using nifedipine for the treatment of proctalgia fugax. Swain R [6], who himself had proctalgia fugax, self prescribed oral clonidine 150 micrograms twice a day and dramatically responded to it with complete resolution of symptoms within 3 days. Lowenstein B et al [7] described a single case which responded to topical nitroglycerin. The last two reports were anecdotal papers and future controlled, randomised trial involving an adequate sample size should be conducted to verify the efficacy of both clonidine and topical nitroglycerin. Finally, non-medical treatment modality include warm bath has been advocated.

CONCLUSION

This paper aims to educate and remind the physicians regarding this relatively common and yet unknown functional disease. The diagnosis is based on classical symptoms and many expensive investigation modalities can be avoided if one has ample knowledge of this disease. Various treatments have been advocated for those with significant severity, though none has been well established. Hopefully, in the near future, randomised controlled studies involving an adequately large sample size would be carried out to establish treatment for this intriguing problem.

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The Singapore Family Physician

Influenza - Role of Drugs & Vaccine

Chan Kwai Peng

INTRODUCTION

Influenza is one of the most significant acute respiratory infections, contributing to significant morbidity and mortality worldwide. There have been influenza pandemics for centuries and in the 20th century, 3 pandemics have taken place, in 1918, 1957 and 1968. The most devastating was the one in 1918, in which over 20 million people died. This exceeded the number who perished in the First World War itself. The United States Centers for Disease Control and Prevention have indicated that another pandemic is highly likely (1) and should that happen, the CDC has estimated, using death rates, hospitalization data and outpatient visits, that there would possibly be 89,000 to 207,000 deaths, 314,000 to 734,000 hospitalizations, 18 to 42 million outpatient visits, and 20 to 47 million additional illnesses in the United States. The estimated economic impact would be US$71.3 to $166.5 billion, not including disruptions to trade and society (2).

CLINICAL FEATURES OF INFLUENZA

There is a tendency for doctors and patients to label all respiratory ailments as "flu" or "gastric flu" depending on whether gastrointestinal symptoms are present or not. In reality, influenza is a respiratory tract infection caused by influenza A and B viruses. The infection is characterised by abrupt onset of fever, sore throat, non-productive cough, myalgia, headache, severe malaise and rhinitis, non-specific symptoms which could be caused by a variety of respiratory viruses. The looseness with which the clinical diagnosis is made would not matter if management had remained mainly symptomatic but with specific treatment now available, we ought to be stricter with the usage of "flu".

The incubation period for influenza is 1–4 days, with an average of 2 days. If uncomplicated, the syndrome is over in 3- 7 days, but cough and malaise can persist for 2 or more weeks(3,4).

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The risks for complications, hospitalizations and deaths are higher among persons aged 65 years and above, very young children and persons of any age with some underlying health conditions. Young children may develop croup, pneumonia or otitis media as complications. In some others, influenza can exacerbate underlying pulmonary or cardiac disease or lead to bacterial or viral pneumonia. Severe illness may be associated with encephalopathy or postinfectious encephalitis.

VIROLOGY OF INFLUENZA

Influenza A and B are the two types of influenza viruses that cause epidemic human disease. There are subtypes of influenza A viruses based on 2 surface glycoproteins: haemagglutinin (H) and neuraminidase (N). Influenza B viruses are not classified into subtypes. Both influenza A and B viruses are further divided into strains or variants depending on their antigenic characteristics. New variants arise as a result of frequent point mutations in the H and N antigens during viral replication. Since 1977, the two influenza A subtypes, H1N1 and H3N2, have been co-circulating with influenza B worldwide.

If a person has immunity to the surface antigens, especially haemagglutinin, the likelihood of infection and severity of disease if infection occurs is reduced. However, antibody against one influenza virus type or subtype provides little, if any, protection against another type or subtype. In addition, antibody to one antigenic variant might not protect against a new variant even if it belongs to the same type or subtype. Because variants develop so frequently, seasonal epidemics occur and this is the reason for incorporating one or more new strains of the virus in the vaccine each year.

EPIDEMIOLOGY

Influenza viruses cause outbreaks globally. In temperate countries, the influenza season occurs in winter. In Singapore, influenza is present

throughout the year although increased activity is usually seen from April to June and November to January.

ROLE OF LABORATORY DIAGNOSIS

The appropriate treatment of patients with respiratory illness depends on accurate and timely diagnosis. To confirm the clinical diagnosis of influenza, laboratory investigations are necessary. The virus can be cultured from respiratory specimens such as throat washing, nasal wash or nasopharyngeal aspirate. This method is important because only cultured viruses can provide specific information on the antigenic characteristics of the circulating influenza subtypes and strains. Virus culture and strain characterisation are the bases of worldwide influenza surveillance as set up by the WHO. These surveillance data are needed to compare current circulating influenza strains with vaccine strains, to aid decisions about influenza treatment and prophylaxis and to guide the WHO in making recommendations for the composition of the influenza vaccine each year, in February for the Northern Hemisphere and in September for the Southern Hemisphere.

Laboratory confirmation can also be achieved by direct detection of viral antigen or nucleic acid from respiratory specimens or by serology through the demonstration of a rising antibody titre.

OPTIONS FOR CONTROLLING INFLUENZA

The main option for controlling influenza is vaccination. An important adjunct to vaccine is the use of influenza-specific antiviral drugs for chemoprophylaxis or treatment.

Vaccines

Immunity to influenza is primarily mediated by secretory IgA and serum IgG antibodies directed against haemagglutinin and neuraminidase. Since

Registered Influenza Vaccines in Singapore

Product	Composition (as Aug 2000)	Distributor	Manufacturer	Cost to pharmacy
Fluvax	A/Sydney/5/97 (H3N2) A/New Caledonia/20/99 (H1N1) B/Yamanashi/166/98 (B/Beijing/184/93-like)	United Italian Trading	Commonwealth Serum Laboratories, Australia	$28 + $25 (freight charges)
Fluarix	A/Sydney/5/97 (H3N2) A/New Caledonia/20/99 (H1N1) B/Yamanashi/166/98 (B/Beijing/184/93-like) [will be changed to A/Moscow/10/99(H3N2)-like; actual strain A/Panama/2007/99]	SmithKline Beecham	Sachsisches Serumwerk Dresden, Germany	$11.50
Vaxigrip	A/Sydney/5/97 (H3N2) A/Beijing/262/95 (H1N1)-like B/Yamanashi/166/98 (B/Beijing/184/93-like) [will be changed to A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like]	Aventis	Pasteur Merieux Serums & Vaccins, France	$12

haemagglutinin attaches viruses to cells and neuraminidase is involved in the release of virus from infected cells, antibodies directed against these proteins disrupt the two key processes in viral infection and replication.

Composition

The influenza vaccine contains three viruses: influenza A H1N1, influenza A H3N2 and influenza B. The vaccine for the 2000-2001 influenza season in the Northern Hemisphere comprises A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Beijing/184/93-like antigens. When vaccine and epidemic strains are well matched, the risk for outbreaks can be reduced if there is a high vaccination rate among persons living in closed settings, such as nursing homes and other chronic care facilities, and among staff.

Types

Three general types of inactivated influenza vaccine are being manufactured – whole-virus vaccine, split-virus vaccine (inactivated virus solubilized into subunits) and purified-surface-antigen vaccine (purified surface glycoproteins). Each of these vaccines may be used in adults but split-virus or purified-surface-antigen preparations must be used in children because this group may develop significant febrile reactions to the whole-virus vaccine.

Efficacy

The efficacy of the vaccine is about 70% - 90% among healthy persons under 65 years old. The efficacy may be lower in the elderly and in those with certain chronic diseases. However, among such persons, the vaccine can prevent secondary complications and reduce hospitalization and death (3). The vaccine is 30%-70% effective in preventing hospitalization for pneumonia and influenza among the elderly living outside of chronic care facilities. Among those in nursing homes, the vaccine is 50%-60% effective in preventing hospitalization or pneumonia and 80% effective in preventing death, although its effectiveness in preventing influenza is lower, often ranging from 30%-40%(3).

Recommendations for use

Vaccination is recommended for persons who are at increased risk for complications and for those who can transmit influenza to those at high risk (3). Thus in the first group, it should be offered to the elderly, to residents of chronic care facilities, to those who have underlying medical conditions such as heart and lung diseases, diabetes mellitus, renal dysfunction, haemoglobinopathies or immunosuppression, as well as children and teenagers on long-term aspirin therapy and therefore may be at risk for Reye syndrome after influenza infection. Health-care workers, employees of chronic care facilities who have contact with patients or residents and household members of persons in high-risk groups should be vaccinated.

Contraindications

Since the vaccine viruses are grown in hens' eggs and may contain residual egg protein, it should not be administered to those with known anaphylactic hypersensitivity to eggs. Amantadine or rimantadine may be considered as alternatives for preventing influenza A in these people. Persons with fever should not be vaccinated until their symptoms have abated.

Dosage

The vaccine is given as two doses at least 1 month apart to children above 6 months of age if they have not been previously vaccinated. Among adults, it is given as a single dose. The vaccine is administered intramuscularly, into the deltoid in adults and older children and into the anterolateral aspect of the thigh in the case of infants and young children. It takes about 2 weeks for protective antibody levels to develop in the healthy adult. The antibody titre falls with time such that it is usually low a year after vaccination. This factor, together with the frequent antigenic changes of the circulating influenza strains, dictate the necessity for annual vaccination.

Side effects and adverse reactions

It should be emphasized that inactivated influenza vaccine contains noninfectious killed viruses and cannot cause influenza and that coincidental respiratory disease not related to influenza vaccination can occur after vaccination.
Most people tolerate the vaccine well. The most common side effect is soreness at the vaccination site, which is generally mild, and affects 10%-64% of patients (3). Fever, malaise, myalgia, and other systemic symptoms most often affect persons who have had no exposure to the influenza virus antigens in the vaccine e.g. young children. These reactions begin 6-12 hours after vaccination, persisting for 1-2 days.

There are the immediate, presumably allergic, reactions (hives, angioedema, allergic asthma, systemic anaphylaxis). These are rare and are probably due to hypersensitivity to some vaccine component, including egg protein, as alluded to before.

Simultaneous administration of other vaccines

The target groups for influenza and pneumococcal vaccination overlap considerably. Both vaccines can be administered at the same time at different sites without increasing side effects. Children can receive influenza vaccine at the same time they receive other routine vaccinations (3).

Antiviral agents for influenza

Drug	Regostered in Singapore	Route of administration	Indication	Dosage	Cost to pharmacy
Amantadine	Yes	Oral	Treatment & prophylaxis of influenza A	*1-9 yrs*: 5 mg/kg/ day up to 150 mg in 2 divided doses *10-64 yrs*: 100 mg bd ≥ *65 yrs*: ≤100 mg/day	$1.79/100 mg capsule Treatment: 5 days Prophylaxis: duration of outbreak
Rimantadine	No	Oral	Treatment (adults only) & prophylaxis of influenza A	*1-9 yrs* (prophylaxis): 5 mg/kg/day up to 150 mg in 2 divided doses *10-13 yrs* (prophylaxis): 100 mg bd *14-64 yrs*: 100 mg bd ≥ *65 yrs*: 100 or 200 mg/day	NA
Zanamivir	Yes	Oral inhalation	Treatment of influenza A & B	≥ *12 yrs*: 10 mg bd x 5 days	$38 per course
Oseltamivir	No	Oral	Treatment of influenza A & B	≥ *18 yrs*: 75 mg bd x 5 days	NA

Both tables are adapted from: T Y Ti and A E Ling. What you need to know about influenza. Drug Information Newsletter 2000; 19(1). With permission from T Y Ti.

Antiviral drugs

There are not many drugs effective against the influenza virus. The older drugs, amantadine and rimantadine, are effective only against influenza A and are approved for its treatment and prophylaxis. The two newer drugs, zanamivir and oseltamivir, have activity against both influenza A and B viruses and have been approved for treatment of uncomplicated influenza infections (zanamivir: ≥ 12 years, oseltamivir: ≥ 18 years), but not yet for prophylaxis. Although an important adjunct to influenza vaccine for the control and prevention of influenza, these drugs are not a substitute for vaccination.

Amantadine and Rimantadine

Action

Amantadine and rimantadine act by inhibiting the uncoating of the influenza A viruses, an initial stage in viral replication. They are **not** effective against influenza B and other respiratory viruses.

Treatment

When used within 2 days of illness onset by otherwise healthy adults, amantadine and rimantadine can reduce the severity and duration of uncomplicated influenza A illness by about 1 day. They have not been shown to be effective in preventing serious influenza-related complications.

Prophylaxis

Both amantadine and rimantadine are indicated for the prophylaxis of influenza A and are about 70%-90% effective. Chemoprophylaxis may be offered to these groups of people: 1) those at high risk for complications of influenza but are vaccinated after an influenza outbreak has begun in a community to protect them during the time from vaccination until immunity has developed; 2) all residents in institutions that house persons at high risk when influenza outbreaks occur in the institutions; 3) unvaccinated persons who have frequent contact with persons at high risk; 4) those at high risk who are expected to have an inadequate antibody response to influenza vaccine; 5) those at high risk who should not be vaccinated.

To be most effective as prophylaxis, the drug must be taken each day for the duration of influenza activity in the community.

Dosage

The use of amantadine and rimantadine among children under 1 year of age has not been adequately evaluated and rimantadine is approved only for prophylaxis in children. For children aged 1-9 years, the dosage is 5 mg/kg/day, up to 150 mg in 2 divided doses. The approved dosage for persons 10 – 65 years old is 100 mg twice a day. However, for children weighing less than 40 kg, 5 mg/kg/day, regardless of age, is advisable. For those older than 65 years old, the dosage is 100 mg/day or less for amantadine but 100 or 200 mg/d for rimantadine. In patients with impaired renal function, the dosage should be reduced. The dosage of rimantadine should be reduced to 100 mg/day in severe hepatic dysfunction (3) [75% of rimantadine is metabolized by the liver; apparent clearance is 50% lower in liver disease].

Duration

To reduce the emergence of antiviral drug-resistant viruses, the drugs should be discontinued generally after 3-5 days of treatment or within 1-2 days after the disappearance of signs and symptoms.

Side effects and adverse reactions

Both drugs can cause central nervous system side effects such as nervousness, anxiety, difficulty concentrating, delirium, hallucinations and seizures. These effects occur more frequently with amantadine, among the elderly and those who have renal insufficiency or seizure disorders. Their effects on pregnant women and their foetuses are not known, but in view of their teratogenicity and embryotoxicity in animals, they should be used in pregnancy only if the potential benefit justifies the potential risk to the embryo or foetus.

Drug interactions

There is a potential for amantadine to interact with drugs that affect the CNS and concomitant administration of antihistamine or anticholinergic drugs can increase the incidence of adverse CNS reactions. There are no known clinically significant interactions between rimantadine and other drugs.

Zanamivir and Oseltamivir

Action

Zanamivir and oseltamivir inhibit the neuraminidase enzyme of both influenza A and B viruses. Neuraminidase is an important surface protein which enables the release of influenza virus from infected cells, promotes spread of infection within the respiratory tract and also may reduce the ability of respiratory mucus to inactivate the virus (5).

Treatment

Both drugs shorten the duration of symptoms of uncomplicated influenza in febrile patients by about 1 day if treatment begins within 30 h of clinical onset (6). Like amantadine and rimantadine, zanamivir and oseltamivir have not been shown to prevent serious influenza-related complications and there are few studies of their efficacy for treatment in children.

Dosage

Zanamivir is not approved for use in children under 12 years of age. For persons above 12 year old, the recommended dosage is two 5-mg oral inhalations of the medicated powder twice daily i.e. 10 mg twice daily, using a plastic device, for 5 days. Patients will benefit from instruction and demonstration of the proper use of the device. Data on the safety and efficacy for patients with impaired renal function are limited.

Oseltamivir is approved for persons ≥ 18 years of age and 75 mg twice daily is administered by mouth. Reduced dosage is recommended for patients with renal impairment but the safety of the drug in patients with creatinine clearance less than 10 ml/min is not known.

Pharmacokinetics

Zanamivir has poor oral bioavailability. After an orally inhaled dose, 70%-87% is deposited in the oropharynx and 7%-21% in the lungs. About 4%-17% is systemically absorbed and is excreted unchanged in the urine. Unabsorbed drug is excreted in the faeces.

Oseltamivir, on the other hand is significantly absorbed systemically (80%) following oral administration. It is metabolized to oseltamivir carboxylate, the active neuraminidase inhibitor, in the liver. Both the metabolite and the parent drug are excreted in the urine.

Side effects and adverse reactions

Persons with asthma or chronic obstructive pulmonary disease when treated with zanamivir for influenza-like illness experience a >20% decline in FEV1 or peak expiratory flow rate. Bronchospasm, dyspnoea and allergic reactions such as oropharyngeal oedema and rash have been reported during postmarketing surveillance. If physicians decide to prescribe the drug to patients with underlying respiratory disease after carefully considering potential risks and benefits, there must be proper monitoring and supportive care and patients must be warned to have a fast acting inhaled bronchodilator available.

The most common adverse reactions encountered with oseltamivir are nausea and vomiting which might be less severe if the drug is taken with food.

Because their effects on pregnant women and their foetuses are not known, zanamivir and oseltamivir should be used in pregnancy only if the potential benefit justifies the potential risk to the embryo or foetus.

As these drugs are new, the full spectrum of adverse reactions associated with them will be better known with time and experience.

Drug interactions

Limited clinical data are available regarding drug interactions with zanamivir and oseltamivir.

Drug resistance

Viral resistance to zanamivir and oseltamivir has developed during treatment but whether this will occur less frequently than with amantadine and rimantadine is unknown.

CONCLUSION

Influenza is a significant respiratory ailment with risks for complications, hospitalizations and death to the elderly, very young children or those of any age who have respiratory or cardiac diseases or other chronic medical conditions. Vaccination against influenza is the most effective means of preventing and controlling influenza and its more severe complications.

Antiviral drugs like amantadine and rimantadine can be used for treatment and prophylaxis of influenza A, and newer drugs like zanamivir and oseltamivir, for treatment of both influenza A and B. These drugs are an adjunct to the control of influenza and have not been shown to be effective in preventing serious complications related to influenza. To be effective, the diagnosis must be accurate and treatment commenced within 48 h of clinical onset. The modest benefit of reducing the duration of symptoms by a day in otherwise healthy patients must be weighed against the cost of treatment, the low accuracy of clinical diagnosis of influenza and the adverse effects associated with the drugs.

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The Singapore Family Physician

A Personal Approach to Glycaemic Control in Type 2 Diabetes Mellitus

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SUMMARY

Treatment of Type 2 diabetes mellitus can be a difficult problem. Although initial treatment of diabetes of recent onset is often not difficult, diabetes is a progressive disease. Even patients who are on regular treatment find it increasingly difficult to maintain good glycaemic control over the course of their disease. When we encounter patients with diabetes we have to somehow find ways to improve and more importantly maintain good control of blood glucose. The drugs that are currently available for treatment of diabetes are many but none are truly ideal. Inspite of the plethora of drugs available many patients are difficult to control. I present a personal approach to the problem of glycaemic control of Type 2 diabetes.

Keywords:
Diabetes Mellitus, Treatment, Insulin, Oral Hypoglycaemic agents

INTRODUCTION

Type 2 diabetes is a common clinical problem The prevalence of diabetes has been increasing progressively in Singapore and has now reached 9% of the adult population. Of this the vast majority (more than 90%) belong to the group called type 2 diabetes, previously also known as Non-Insulin Dependent Diabetes Mellitus. The management of diabetes can be simple and yet difficult. The major difficulty is the maintenance of good glycaemic control over the long-term in order to prevent long-term complications of diabetes which are responsible for the high rates of mortality and morbidity in diabetic patients.

Glycaemic control is only one aspect of the management of diabetes although it is a prominent one. It must be said that other aspects can be just as important.

PATIENT FACTORS IN THE MANAGEMENT TYPE 2 DIABETES

It is often frustrating to think that such a common condition should have no truly revolutionary treatment inspite of many years of research. The three pillars of treatment remain diet, oral hypoglycaemic agents and insulin. Although some new oral agents have been added, none can solve the problem of hyperglycaemia perfectly. The perfect drug would lower the blood glucose to the desired level without causing hypoglycaemia and yet allow the patient to eat anything and any amount of food that they like. Patients often ask why there are no better drugs invented for diabetes. Doctors in turn often blame patients for not controlling themselves better.

Since it does not appear likely that a perfect drug for type 2 diabetes is going to be discovered in the near future, we have to do our best to make do with the present ones. I list here some of the patient factors that may hinder good glycaemic control and are worth considering:

Misconceptions about diet

There are probably more misconceptions about diet in diabetes than anything else connected to the treatment of diabetes. It does not help that there are a million opinions about diet and diabetes and that every Tom. Dick, Harry and others are all too ready to offer their own opinion to anyone who has diabetes. Almost all of these are inaccurate or misleading. Most patients ask the wrong questions and therefore have no answers. Most patients imagine food items to be divided into two distinct categories – Food that can be eaten and those that cannot. It is like having the concept that people have be easily divided into two distinctly separate groups – rich or poor. It is not that simple. It is far more important to understand the need to limit quantities of food. Even if you are able to finally convince the patient

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that quantity needs to be reduce (a task that may undoubtedly increase your risk of high blood pressure, heart attack, stroke and other major catastrophes) it is very difficult for the patient to appreciate that this quantity may be so small that they may not fell satisfied. The quantity of food that may be allowed to ensure good glycaemic control may be very small indeed. How do you convince patients that it may be healthier for them to feel a little hungry and have good glycaemic control?

The fear of taking medications on a long-term basis

This is a common fear and to my mind far more deeply rooted in our Asian community as compared to the Western one. Many patients are convinced, inspite of the lack of actual evidence, that long-term medications will ultimately harm the body, weaken it and lead to many illnesses. For such patients, proof is not required. To them it is perfectly logical that long-term medication cannot be good for a person. Many patients are reluctant to start on medications or to increase the dose of medications and many surreptitiously reduce the dose of medications prescribed. We need to work on helping patients overcome this fear.

Reluctance to accept insulin treatment

Insulin is not the ultimate answer to type 2 diabetes. However, in the absence of better solutions, it is still often necessary to exhibit insulin to somehow bring that blood glucose level down. It is not uncommon to encounter a situation where the fasting blood glucose level remains high inspite of good dietary control and oral agents raised to the dose whereby hypoglycaemia occurs at other times of the day and yet the fasting blood glucose remains high. This is due to inappropriate hepatic gluconeogenesis and often insulin is required (and even then sometimes it does not work). To my mind, glucose toxicity is the bigger enemy. If hyperglycaemia is not corrected, glucose toxicity leads to worsening beta cell function and this worsens the situation. Delay in control of glycaemia leads to ultimate loss of beta cell function. When the patient finally agrees to try insulin, even insulin may not work. Doctors need to be able to have some answers for some common excuses that patients have for not wanting insulin therapy. These excuses include inconvenience, frequent travels, poor eyesight, fear of needles, etc. There are now a number of implements like the insulin pen, auto-injecting devices, different ways of giving insulin (like bedtime insulin only) that can be used to counter the excuses put forward. Sometimes patients reluctantly accept insulin if their excuses find a reasonable answer. Once they accept insulin and find that it is not all that horrible, the first important hurdle has been overcome.

Reluctance to monitor blood glucose at home

Treating diabetes without home blood glucose monitoring is difficult. If the patient is on insulin it is almost impossible to try to adjust the regime of insulin properly without home blood glucose monitoring. It is like telling a person to drive within the speed limit when that person's car does not have a speedometer. Actually it is worse because there are no other cars around to guide him or for him to follow. Fortunately this reluctance is getting less in recent years and we live in hope of seeing machines capable of non-invasive methods of measuring blood glucose.

DOCTOR FACTORS - SOME POINTERS FROM UKPDS

The role of the doctor is to understand the requirements for good management of type 2 diabetes including what the realistic goals of treatment should be adopted, given the lack of perfect drugs for its treatment. The UKPDS (United Kingdom Prospective Diabetes Study) which took 21 years and 23 millions pounds to complete, provides a sound foundation for the principles of managing type 2 diabetes. Some useful pointers from the UKPDS include the following:

The value of good glucose control

It is clear from UKPDS that patients assigned to more intensive control of blood glucose with stricter targets for glucose levels had better

outcomes. This was consistent in terms of diabetic endpoints, microvascular complications, myocardial infarction and diabetes related deaths. All these were reduced by a more intensive policy of controlling blood glucose levels over the period of study. The price for getting better control was more episodes of hypoglycaemia and polypharmacy. One point worth noting is that in both the conventional and intensive groups, over time, there was a progressive rise of the HbA 1c levels. This suggests the progressive nature of the disease. Diabetes does get progressively more difficult to control. The best time to control it well (and to keep is well controlled) is at the beginning of the disease.

The choice of agents

In UKPDS, the two oral sulphonylureas, Chlorpropamide and Glibenclamide, were compared to insulin and there was in addition a sub group of obese patients treated with Metformin. From a practical point of view, without going into the details, the points worth remembering are that the different agents employed with an intensive policy were equally effective in controlling the blood glucose levels and reducing the undesirable end-points. The differences were in weight gain and hypoglycaemic episodes. Weight gain was least in the Metformin treated group but weight gain was a problem with the sulphonylureas and insulin.

Hypoglycaemic episodes were also more frequent in insulin treated as compared to sulphonylurea treated patients and least in Metformin treated patients. Although in this trial Metformin was the initiating agent only for obese subjects, the result is impressive and a case may be made for more use of Metformin especially in newly diagnosed diabetics where an episode of severe hypoglycaemia may discourage the patient from long-term drug treatment thereafter.

The value of blood pressure control

This was another important area addressed by the UKPDS. Apart from good glycaemic control strict blood pressure control, aiming for a target blood pressure below 140/80 mm Hg, resulted in very impressive reductions in all diabetes related endpoints. Given the great difficulty in controlling blood glucose levels over the long term, the value of blood pressure control is well worth noting. We know that inspite of all our efforts many patient cannot maintain good blood glucose control. Good blood pressure control depends largely on drugs and not as much on strict diet control or lifestyle changes and is more manageable for the patients. The cost is again polypharmacy but this is a reasonable price to pay given the impressive advantages of better blood pressure control.

PARMACOLOGICAL AGENTS IN TYPE 2 DIABETES

Oral agents

There are now many oral agents employed in the treatment of type 2 diabetes and more are on the way. There are also studies showing some positive results for the use of combinations of oral agents with insulin.

Sulphonylureas

This is the oldest group of oral agents used for treating type 2 diabetes. Its main mode of acting is to increase the secretion of insulin by binding to sulphonylurea receptors on the beta cells. By doing so its main drawback is the propensity to cause hypoglycaemia. Its use on the long term is also associated with weight gain.

There are now man sulphonylureas in the market. Older ones, called first-generation sulphonylureas, like Tolbutamide and Chlorpropamide are still available. First generation sulphonylureas are highly protein bound and may cause more drug interaction with other protein bound drugs. Tolbutamide is a mild agent and probably less effective in reducing more severe degrees of hyperglycaemia. However, this feature is also useful if it is used to treat mild cases of newly diagnosed diabetes. Chlorpropamide is still one of the most powerful sulphonylureas available. In the UKPDS, the extent of reduction of HbA 1c and blood glucose was comparable in the groups

treated with Glibenclamide and Chlorpropamide. Chlorpropamide can cause severe prolonged hypoglycaemia and this feature has made it unpopular. It should be avoided in the elderly patient (more than 65 years old).

The second generation sulphonylureas include several representatives now. Glibenclamide is still generally used as the benchmark for comparison. There is not that much to choose between the members of this group in terms of effectiveness in lowering blood glucose. Glibenclamide is probably slightly more prone to causing hypoglycaemia particularly prolonged hypoglycaemia. In this respect the used of Glibenclamide in elderly diabetic needs extra caution or should be avoided. Other agents like Glipizide and Glicazide are similar and can be used interchangeably. The newer agent, Glimeperide, is said to cause slightly less hypoglycaemia. Its effectiveness is similar to Glibenclamide. It remains to be seen if represents a significant improvement over the others.

Biguanides

This group has only one member, Metformin, which is widely used for treatment of diabetes. Another member, Phenformin, has a high propensity to cause lactic acidosis and is no longer used in most countries. We still occasionally encounter some patients who have managed to get phenformin from overseas from places like China.

Metformin reduces insulin resistance and does not increase insulin secretion. It does not cause hypoglycaemia and is not associated with weight gain. These are the two major advantages over sulphonylureas. In terms of the actual amount of glucose reduction that can be achieved, it is comparable to sulphonylureas. Its main drawback is the common occurrence of gastrointestinal side effect, in particular diarrhoea. To an extent this can be reduced by starting on a small once daily dose. Patients accept it better ifthey are warned beforehand to look out for gastrointestinal symptoms.

Metformin is often used in combination with sulphonylureas. It appears to increase the effect of lowering the blood glucose somewhat and in practice is often used when one agent alone is not enough to control the blood glucose level. There was a surprising result in the UKPDS which showed that the group using both sulphonylurea and Metformin appeared to have higher mortality for no known reasons. The authors did not think that this result warranted a recommendation to stop using this combination but could offer no good explanation for its occurrence. At present there remains no answer. It may be a small point for arguing in favour of switching to insulin rather than to use more and more oral agents.

Alpha glucosidases Inhibitors

This group of drugs act at the level of the gastrointestinal tract. It acts as a competitive inhibitor of oligosaccharide digestion. It has no significant systemic effect and does not cause hypoglycaemia. This is one of the major attractiveness of this drug. In terms of its ability to control hyperglycaemia its effect is modest. It reduces post-prandial hyperglycaemia but can reduce fasting hyperglycaemia as well probably as a result of reducing glucose toxicity (after reducing post prandial hyperglycaemia) Like Metformin it may be used in newly diagnosed diabetics especially if the problem is one of post-prandial hyperglycaemia rather than severe fasting hyperglycaemia.

It can be combined with sulphonylureas and Metformin producing modest further reduction in the blood glucose and HbA 1c levels. However, for severely hyperglycaemic patients, it is not clear whether combining so many oral agent really adds to the final impact or merely delays the inevitable – switching to insulin. There are a few studies showing additional benefit when added to insulin treated patients.

Its major drawback is the propensity to cause gastrointestinal side effects. The most notable is increased flatulence and this can be embarrassing for some patients. Others include diarrhoea and abdominal discomfort. Patients vary in their ability to tolerate this side effect and this also

depends on the type of diet adopted. It is worthwhile to start on a small dose and increase it gradually. All patients should be earned of the gastrointestinal effects so that they are psychologically prepared to it. Symptoms usually subside with time.

Repaglinide

This is a member of a new group of oral diabetic agents. They are different in chemical structure to the sulphonylureas but promote insulin secretion in a way similar to the sulphonylureas. They too act on the sulphonylurea receptors. They differ slightly in pharmacokinetics and pharmacodynamics from sulphonylureas but the propensity to cause hypoglycaemia is not different. They have a short duration of action and appear to help control post-prandial hyperglycaemia with a fairly rapid onset of action. HbA 1c reduction and reduction of fasting blood glucose levels are comparable to Glibeclamide.

The exact place of this agent is not that well defined yet as it is relatively new. There appears to be no advantage in adding this agent together with other sulphonylureas. Its place is probably to be used instead of other sulphonylureas.

Thiazolindienediones

This is a new group of drugs used to reduce insulin resistance without increasing the secretion of insulin. It is structurally different from the biguanides but in a practical sense, its effect is similar to Metformin. The actual mode of action is not clearly known but it is proven to improve glucose uptake in the muscles and reduce blood glucose to an extent comparable to Glibenclamide and Metformin. It does not cause significant hypoglycaemia.

The first member of this group to be approved for use in the USA was Troglitazone and this drug was included in the trial for Primary Prevention of Type 2 Diabetes (treating patients with Impaired Glucose Intolerance to see if progress to overt diabetes can be prevented). Unfortunately one patient developed liver failure and this drug was withdrawn from the trial. Subsequently Troglitazone was withdrawn completely from the US market in March 2000.

There are now other members of this group of drugs entering the market and these are said to be less likely to cause this particular idiosyncratic action on the liver. Rosiglitazone has just been introduced in Singapore.

Thiolinedinediones are still new but potentially useful and more studies will in the coming years will help to define their place in the management of type 2 diabetes. Liver function test needs to be monitored in patients treated with this group of drugs. This adds to the cost of using such agents.

Insulins

Insulin has often been seen as the last time of defense in the fight against type 2 diabetes. Patients and doctors alike see insulin as the last resort. Often it is used as a threat to get patients to comply with treatment. I think these views of insulin are not necessarily correct or helpful.

Insulin is one way of treating type 2 diabetes. When used for newly diagnosed type 2 diabetes its effectiveness is comparable to Chlorpropamide and Glibenclamide in the UKPDS. However, as diabetes is a progressive disease, many patients eventually fail to respond to oral agents and would require insulin for control. In this setting even when insulin is employed, not all patients manage to achieve satisfactory control with insulin. Are we perhaps introducing it too late (when the metabolic chaos has become too advanced)?

It is perhaps not helpful that today there are so many permutations in the use of insulin. One can use one or more of several types of insulin (of varying durations of action) and one can employ one, two or more injections daily. Worse still, there are now studies showing that insulin combined with sulphonylureas, metformin, acarbose and troglitazone all seem to offer additional benefit. What about insulin together with sulphonylurea and biguanide and alpha-glucosidase inhibitor all added together? I am sure these studies would soon appear to confound the issue further. Perhaps it is out of desparation that we are using "super-

polypharmacy" on these poor uncontrolled diabetics. In the short-term (as most of these studies are), perhaps it is not surprisingly that they have a modest positive effect and this effect may be lost if the same treatment is continued (when the enthusiasm or motivation of participating in a trial has subsided).

How can we try to sort out a practical way of using insulins in the treatment of type 2 diabetes? There are no easy ways. Each physician is probably biased in some ways depending on personal habit and preferences. To me it is a situation of ''By All Means Control Some". If it works for that patient, it is okay.

I will try to present here a few consideration that I use in my practice to help me decide on which permutation to use on which patient.

Types of insulin

I generally consider insulins as being in the following categories:

- Short-acting insulins. These insulins if used along would need to be given three times a day before each meal. More often they are used in combination with intermediate acting insulins and give ntwice a day.
- Intermediate-acting insulins. Thsese are usually given twice a day, either alone or in combination with short-acting insulins. A bedtime dose of intermediate acting insulin can also be used to reduce the fasting hyperglycaemia and the patient may use oral agents in the day.
- Long Acting Inuslins. Thsese are gnerally not very commonly used. They are given once daily but on it own it is seldom employed.It is more commonly used in combination with short-acting insulin (given thrice say before each meal).
- Pre-mixed insulins. These insulins are made up of combinations of short and intermediate acting insulins. They come in various ratios, like 30-70, 50-50 or 20-80. Their main advantage is that the patient does not have to purchse two bottles of insulin and do not have to bother with learning how to mix the insulins. The obvious disadvantage is the lack of flexibility unless one is prepared to use different pre-mixed insulin at different times of the day eg 30-70 in the morning and 50-50 in the evening.

At what times of the day does the patient have hyperglycaemia?

All diabetic patient have hyperglycaemia now or then or almost all the time. There are so many factors that determine the level of the blood glucose and these factors may change from day to day. It is not easy to generalise but we can try to broadly divide patients into two groups:

- Those whose main problem is fasting hyperglycaemia. Some patients start the day with a high fasting blood glucose and the rest of the day is high but not spectacularly so. These patients can benefit from just reducing the fasting levels. Some patients even have lower post-prandial levels than fasting levels. These patients may benefit from once daily insulin at bedtime just to bring down the fasting levels. They can continue oral agent in the day.
- Those who have hyperglycaemia all over the place or perhaps no particular pattern cab be discerned. This is the more common group. Often dietary indiscretion causes big fluctuations and no discernible pattern. This is the most difficult group. Often without a stricter dietary control, not much can be achieved. Most of these patients would need at least two injections a day (usually of mixed intermediate and short-acting insulins with one or two doses of intermediate-acting insulins or one dose of long-acting insulin to provide a baseline level of insulin throughout the day. I often persuade patient to try two injections a day first to get them to accept insulin in the first place and later change to three injections a day when it can be shown to them that two injections a day is still not ideal.

Starting on Insulin

The first step is to get the patient to accept insulin. Sometimes the patient determines the number of injections. If the patient is only prepared to accept one injection a day, that is at least a first hurdle overcome. In that case I usually use the bedtime regime with tablets in the day.

If the patient has severe hyperglycaemia and to my mind clearly cannot be controlled on once daily insulin, I try to use two injections a day (before breakfast and before dinner) I use either a pre-mixed insulin or (my own preference) to use a mixture of intermediate and shorting acting insulins. We generally need less shorting acting insulin for the first dose because most people take small breakfasts and a bigger proportion of shorting acting insulin because dinners are commonly the largest meal of the day. The weakness of this regime is the poor control of post-lunch hyperglycaemia and the frequent pre-lunch hypoglycaemia. This can be overcome if the patient accepts three injections of short-acting insulin before each meal.

Patients vary greatly in their degree of insulin sensitivity and resistance and the dose of insulin cab vary a lot from patient to patient. Generally we start with a conservative dose and once we know a bit more about the glucose reaction to the insulin given we can adjust accordingly. Home blood glucose monitoring helps in adjusting the insulin to the most optimal regime.

Insulin and Oral Agents

There are now many studies looking into the combination of insulin and the various classes of oral agents. Most of these studies give positive results suggesting that the addition of oral agents to insulin treated patients may bring forth better control. However, most of these studies are short-term studies and we must be mindful of the natural bias of positive papers in medical journals. Negative studies often do not get published. We must also ask whether the same degree of improvement can be achieved by further adjustment of the insulin regime. The third question is whether the improvement can be sustained over long periods of several years. These questions have no easy answers but what is clear is that the use of both insulin and oral agents clearly increases the cost to patients and subject patients to the disadvantages (and possible adverse effects) of both insulin and oral agents.

In practice the temptation to just add an oral agent rather than to attempt further increase of insulin or further adjustment of insulin is very strong. Patients also appear to accept this.

My own practice is firstly to decide if the patient may benefit from just once daily insulin at bedtime. Only patients with fairly good daytime blood glucose levels and a high fasting blood glucose are the most likely to benefit from this regime. In fact many fairly recent-onset diabetic patients belong to this category. This group of patients has good blood glucose control and may even get hypoglycaemia if the oral agents are increased further. However, the fasting blood glucose remains high inspite of diet, exercise and oral agents. It is often tempting to leave these patients alone because it is not all that bad. However, if once daily insulin is introduce at bedtime, the fasting hyperglycaemia can often improve and the HbA 1c can be brought down to normal.

If the patient clearly has very severe hyperglycaemia throughout various times of the day, often these patients need more than one dose of insulin. These are often patients who have a long history of diabetes (more than 10 years) Most of these patients do not respond well to oral agents any more. My practice is usually top change these patient completely to insulin (either twice daily or more often, if they are willing to accept it). I will stop oral agent completely. Thereafter I would adjust the regime of insulin to get optimal control. If after progressively increasing and adjusting the insulin dose, control remains poor, I may consider adding one oral agent. The total dose of insulin per day is a rough guide. Generally if we work our way up to 1 to 1.5 units of insulin per kg body weight per day (say 90 units for a 60 kg patient), further increase may not bring about better response. This is when I would consider adding either a sulphonylurea or Metformin. If there are no contraindications.

APPROACHES TO TYPE 2 DIABETES

I would like to discuss two common categories of patient that may see us in our clinic.

Newly diagnosed type 2 diabetes

My view is that this category of patients is the one that we need to manage as well as possible. The newly diagnosed patient is very receptive and this is the time to instill the right ideas and approaches to diabetes. They are also the patients who still have reasonable residual beta cell function. We must try to conserve this beta cell function and this can be achieve by maintaining very strict glycaemic control.

Aim for normal blood glucose levels and normal HbA 1c levels

We must not be guilty of setting targets that are too low. Diabetes is a progressively disease and when overt diabetes is diagnosed there is already considerable metabolic disturbance of the body. Diet alone is seldom enough for control except initially. I favour earlier exhibition of oral agents to get normalisation of blood glucose levels. We are on the brink of introducing oral agents for patients wit Impaired Glucose Tolerance if the prevention studies are positive. Why then are we still suing diet alone for overt diabetes?

Avoid Hypoglycaemia

Strict glycaemic control is initially not difficult to achieve as patients are very motivated. Often the patient's blood glucose levels improve and insulin resistance improves (due to reduced glucose toxicity). Many patients who may initially have very high blood glucose levels can achieve normal levels and even are prone to hypoglycaemia. One important rule is to try to avoid the patient having a severe episode of hypoglycaemia. This can be frightening and patients are likely to think that oral agents are bad for them and be resistant to subsequent introduction of oral agents. In this respect, I find that Glibenclamide is often prone to causing hypoglycaemia. If the hyperglycaemia is mild, Metformin is a good choice. Acarbose can also be sued and would not cause hypoglycaemia. Although we have always reserved Metformin for obese patients, I do not think that this does not always need to be the case.

Have a sense of urgency

Beta cells are at stake. We should treat aggressively and if good control is bot achieved in a matter of months consider more aggressive forms of treatment including insulin. This is not a irreversible step because often insulin resistance can improve and patients may go back to oral agents.

Long-standing poorly controlled type 2 diabetes

This is a difficult category but is perhaps the most common clinical problem we face. Patients come with a host or previous misconceptions or misunderstanding and possible bad experience with hypoglycaemia. Still we are expected to do something. Some may already have advanced complications from diabetes. We may have to adjust our expectations in these patients. We may have to accept less than perfect control and aim only to achieve reasonable control. Still if we can bring down their HbA 1c we already reduce their risks of further complications and mortality rates.

Most patients would come already treated with combinations of oral agents. Most patients are reluctant to go to insulin. Some may be already on insulins. The first step is usually to identify possible problem area like diet, lack of compliance, exercise, etc. The appropriate advice should be given. Once all this has been done, we have to consider if pharmacological means have to be employed to improve control. I find the fasting blood glucose as a reasonable indicator of whether the drugs are working. Generally a very high fasting blood glucose indicates drug failure. These patients need higher doses of drugs or they need insulin. Weight loss is often an indication of insulin requirement.

Change of oral agents may not bring about much improvement although it is commonly employed and I sometimes do that as well. There may be some improvement due to improved enthusiasm and it is worthwhile to give it a try. Many patients also need to be convinced that even other oral agents do not work.

The next step is to put the patient on insulin. It is worthwhile explaining that insulin is not the pinnacle of diabetes treatment. Even insulin may fail to control the blood glucose. I am not averse to the idea of switching back to oral agents, if very good control is achieved. Again sometimes this serves to reinforce in the patient's mind that really oral agents cannot work and they will then be more willing to accept insulin indefinitely. I am also not averse to switching back to oral agents if control is equally dismil on insulin. If control is dismal on both oral agents and on insulin, at least the patient need not suffer the pain of daily injections.

CONCLUSION

To manage diabetes is to be willing to fail. With regards to the goal of maintaining good glycaemic control (HbA 1c less than 7%), I think we fail more often than succeed. At least that has been my own experience. We have to keep trying making use of all the imperfect means at our disposal.

Finally it is very important to mention that glycaemic control is not the only thing we need to be concerned about when we see diabetic patients. It is equally important to control blood pressure, to normailise lipid profiles, to encourage patients to adopt a healthy lifestyle and to monitor for long-term diabetic complications. If we cannot achieve good glycaemic control we can still do all these other things to improve the long-term outcomes of our patients.

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The Singapore Family Physician

Psychosis - Everyone's Concern: The Early Psychosis Intervention Programme (EPIP) In Singapore

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SUMMARY

One of the most severe forms of psychosis and a leading cause of disability worldwide is schizophrenia. Recent research has demonstrated that the first episode of schizophrenia is a critical therapeutic opportunity. If patients are treated promptly and effectively, good outcomes can be achieved.

Early this year, the Early Psychosis Intervention Programme (EPIP) was initiated at the Institute of Mental Health with financial support from the Ministry of Health. EPIP uses a multidisciplinary approach with a team of psychiatrists, psychologists, social workers, occupational therapists, and nurses working closely together to provide a comprehensive, accessible and rapid service. One of the aims of EPIP has been to increase awareness and recognition of psychosis among the primary health care physicians and also, more importantly to involve them as partners in the continued care of patients. The opportunity of making a real difference to the lives of patients and families should be a challenge that we must collectively respond.

***Key Words:** Early Psychosis, EPIP, Schizophrenia*

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INTRODUCTION

One of the most severe forms of psychosis is schizophrenia. According to the World Health Organization it is one of the leading cause of disability worldwide. The lifetime prevalence of schizophrenia is about 1%. A review of annual incidence rates of schizophrenia show a median rate of 0.2 per 1,000 [1]. It is estimated that every year, 600 people in Singapore will develop schizophrenia. Although not a very common condition, the disability and cost are disproportionately high.

The symptoms of schizophrenia are generally categorised into positive symptoms, negative symptoms and disorganised symptoms. Positive symptoms refer to the presence of mental features that should not be normally present. These include delusions and hallucinations. Negative symptoms refer to a lack of certain emotional and psychological characteristics that are normally present. These include affective flattening (difficulty in expressing emotions), alogia (limited speech with consequent difficulty in maintaining a continuous conversation or saying anything new), avolition (extreme apathy with lack of initiation, drive and energy which result in academic, vocational and social deterioration), anhedonia (lack of pleasure or interest in life), asociality (social withdrawal and few social contacts) and attentional impairment. Disorganised symptoms include disturbances in thinking and speech, disorganised or bizarre behaviour, and incongruous affect.

A growing body of evidence suggests that delays in providing effective treatment for patients with psychosis has significant negative effects on the outcome. These include more hospitalisations with longer periods of inpatient care [2], slower and less complete recovery [3], and increased rate of relapses [4]. Another consequence of delaying antipsychotic treatment is that the cost of such treatment when it is finally initiated may be higher than if it had been started earlier [5].

A controversial hypothesis suggests that untreated psychosis may result in neurotoxicity that induces irreversible brain damage which may be clinically manifested as deterioration in functioning and treatment resistance [6, 7]. If this hypothesis is correct, a long duration of untreated psychosis can have serious consequences, including enduring and perhaps lifelong deficits and disability. Furthermore, undiagnosed and untreated psychosis can give rise to terror and distress to patients and their families [8]. The onset of schizophrenia is usually in the late adolescence

and early adulthood. This is a time when the individual has to undertake the tasks of adulthood such as establishing relationship outside the family and achieving independence. The emergence of psychosis at this critical stage can subvert this development and often alter the course of a young person's life in a way that is not easily repaired. In additions, an untreated person with psychosis is at risk for episodes of violence, drug abuse, and suicide.

EARLY PSYCHOSIS: A CRITICAL THERAPEUTIC OPPORTUNITY

Recent research has demonstrated that the first episode of schizophrenia is a critical therapeutic opportunity. If patients are treated promptly and effectively, good outcomes can be achieved. However, these same studies have shown that there is an alarming length of time between the onset of psychotic symptoms and the initiation of treatment [8]. Further, patients with first-episode schizophrenia might have multiple contacts with other services before effective assistance is provided [9].

The causes for this delay are still not well understood. For instance, how much of untreated psychosis is accounted for by patient delay i.e. the time between onset of symptoms and actually initiating contact with a health professional, and how much by diagnostic delay which is the time between first contact and the time when definitive diagnosis and treatment is achieved [8].

The early recognition of the disorder is to an extent dependent on the type of symptoms that first emerge. Like many other illnesses, schizophrenia in most instances has a prodromal stage. However, the prodromal symptoms are varied and include attenuated psychotic symptoms like illusions, ideas of reference, magical thinking; mood disturbances like anxiety, depression, behavioural changes like social withdrawal, obsessive-compulsive behaviour, and cognitive impairment like concentration difficulty and memory impairment [8]. These symptoms are therefore non-specific and diagnosis at this stage is difficult. An insidious onset and the mode of presentation may also hinder early detection and treatment. A study reported that negative symptoms at time of presentation predicted longer delays compared to those with positive symptoms [10].

Other important determinants of duration of untreated psychosis (DUP) are sociocultural factors of which ethnicity, cultural beliefs and values most certainly determine patterns of help seeking [11]. Social and supernatural explanations are associated with the more traditional cultures of the non-Western societies [12]. Practitioners of traditional medicine are common in Singapore and so are faith healers. A study done among 100 Chinese patients referred to a psychiatric unit of a general hospital reported that 36% of them had consulted a traditional healer [13]. A study among Malays in a rural state in Malaysia showed that more than 80% of patients with mental disorders had consulted a bomoh (indigenous Malay medicine man or traditional healer) and that relatives of patients with schizophrenia believed that the illness was caused by supernatural factors [14].

In a recent study, we found that amongst individuals with a first episode of psychosis, the mean DUP was 31 months with a SD of 57 months and a median of 12 months. Twenty-five percent of them had first sought help from a faith or traditional healer while 19% had consulted a general practitioner, and 23% had consulted a psychiatrist.

EARLY PSYCHOSIS INTERVENTION PROGRAMME (EPIP), SINGAPORE

There is therefore an urgent need to reduce this DUP, which is unacceptably long in our local context, through a specialised service that is designed to reduce delays and secondary morbidity by maximising the number of high-risk people targeted through comprehensive and integrated treatment programmes. There is a growing awareness of the need for such services, which have already been implemented in Australia, Canada, United Kingdom and United States of America. Early this year, the Early Psychosis Intervention Programme (EPIP) was initiated in the Institute of Mental Health with financial support from the Ministry of Health.

EPIP uses a multidisciplinary approach with a team of psychiatrists, psychologists, social workers, occupational therapists, and nurses working closely together to provide a comprehensive, accessible and rapid service in various treatment settings. The initial goal of the treatment plan is to bring about a rapid remission of the psychosis using the most effective and best tolerated drugs. However, even after optimum intervention with medications, most patients have difficulty in readjusting and reintegrating into the community. They may have difficulties with schooling, employment and interpersonal relationships. Psychosocial interventions minimise these impairments and may be particularly relevant in the early phase of the illness. These interventions include various forms of psychotherapy e.g. cognitive behavioural therapy, which has been shown to be useful for individuals with persistent hallucinations and delusions. Psychoeducation is used as a strategic tool to promote recovery, to strengthen the coping ability of patients and their families, and to reduce the risk of early relapse. It is also important to work with families since are they often the principal caregivers and majority (81%) of patients with first-episode psychosis live with their families. We consider the family to be an essential part in the assessment, treatment and recovery process in episodes of acute psychosis. The needs of families of patients with first-episode psychosis differ from those of families with established psychotic illness. This involves working with families to develop practical strategies for dealing with an acutely ill relative and later changing expectations, setting realistic, achievable goals for recovery, providing tangible support, and monitoring for early warning signs of relapse. This will also prevent "fatigue" of the caregivers setting in resulting in the subsequent rejection of patients.

For those patients who have difficulties reintegrating into community, EPIP runs a Day Programme. It is a goal-oriented, recovery-focused programme facilitating re-integration of patient into community. It provides psychoeducation, emotional support, social and vocational recovery. The initial period following a psychotic episode presents the greatest opportunity to introduce measures to prevent development of subsequent social disability. The Day Programme has the advantages of reducing prolonged hospitalisation and thereby costs, as well as offering recovering patients a supervised and structured environment.

In cases where a patient is likely to take several weeks to recognise the need for treatment and develop sufficient motivation to attend regular appointments, home-based treatment and support is provided through an Outreach Team. If inpatient treatment is necessary, the use of ambulances and involvement of the police is kept to a minimum. In cases where police needs to be involved, the Outreach Team will liaise with them to reduce their impact.

Training, consultation and education are all necessary to bring about change within a service and to develop a new approach successfully. Within EPIP, there are peer support/supervision groups to maintain and upgrade skills and to sustain morale. We have established links with established centres in Australia and Canada. Site visits and use of expert speakers/consultants from these and other overseas centres are being effected to provide programme-centred administrative consultation.

One of the key component of EPIP is a strategy for early detection and includes an educational programme and an assessment system. An extensive public education campaign to destigmatize schizophrenia through public forums/workshops, talks with school personnel (educators, students), and dissemination of information by posters and the mass media is being undertaken.

Further, a service that has prevention and early intervention as its focus will not succeed unless good links exist with the primary health care professionals. Primary care practitioners (GPs, doctors in Polyclinics and SAF medical services) are the 'gatekeepers' to our health care system and the first medical contact for most people. Their role is essential in early recognition of psychosis. The aims of EPIP are not only to increase awareness and recognition of psychosis

among the primary health care physicians but also to involve them as partners in the continued care of patients. One of our first tasks has been to develop a network with primary care practitioners through workshops and direct consultations.

Evaluation and quality assurance in health services is an important issue for the policy makers and for those who use services. Because preventive intervention in early psychosis as described here is a relatively new area, evaluation of outcome and quality control in service provision are particularly important. Naturalistic studies of treatment interventions are more useful for determining effectiveness than studies of efficacy in controlled experimental conditions as they can be implemented in similar real-world clinical settings. An integral part of EPIP is a research programme that will assess the effectiveness of our various interventions, help us understand the help-seeking behaviour in individuals with psychosis, and contribute to the understanding of the pathophysiology of psychosis.

The prospect of being able to positively alter the course of a devastating and crippling illness is a ray of hope for many. The opportunity of making a real difference to the lives of patients and families should be a challenge that we must collectively respond.

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- Normally the text should not exceed 2000 words and the number of illustrations should not exceed eight.
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- Make all necessary corrections before submitting the final typescript. Headings and subheadings may be used in the text. Indicate the former by capitals, the latter in upper and lower case underlined.
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- The summary should state the purpose of and give the main argument or findings.
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The text should have the following sequence:

- **Introduction:** State clearly the purpose of the article.
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  Drugs must be referred to generically; all the usual trade names may be included in parentheses.

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