

Malaysia Urological Association
and
MEDACT

Clinical Practice
Guide in

Erectile
Dysfunction

MUA / MEDACT CLINICAL PRACTICE GUIDELINE COMMITTEE :

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7. Dr. David Quek Kwang Leng
8. Dr. Loh Chit Sin
9. Dr. Sahabudin Raja Mohamed
10. Dato' Dr. Siti Zaliha Zainal

CLINICAL PRACTICE GUIDELINES ON ERECTILE DYSFUNCTION (ED):

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SUMMARY OF GUIDELINES

**(A) The key to The Diagnosis of
Erectile Dysfunction**

**(B) The Key to The Treatment of
Erectile Dysfunction**

SUMMARY OF GUIDELINES

Definition: "Erectile Dysfunction" is defined as the consistent or recurrent inability of a male to attain and/or maintain a penile erection sufficient for sexual performance.

Erectile dysfunction is a symptom based on the patient's complaints. Objective testing (or partner reports) may be used to support the diagnosis of erectile dysfunction. Cultural factors and patient-physician communication will be important determinants in defining and diagnosing the disorder.

It is noteworthy that erectile dysfunction might not be the primary complaint (and / or) be associated with other sexual problems.

The rational selection of therapy for patients is only possible following appropriate education, including information about sexuality and all treatments for erectile dysfunction.

In contrast to most other medical conditions, the various treatments for ED have to be considered in the context of traditions, ethnicity and socio-economic conditions and also the patient and partner's preference, expectations and psychological status. However, due to the huge diversity of the Malaysian culture, this consensus does not attempt to cover the details of the ethical sensitivities involved when dealing with ED patients.

(A) The key to The Diagnosis of Erectile Dysfunction

The cornerstone of clinical assessment of all men with ED is an initial diagnostic work-up and evaluation. This evaluation should be performed by a physician knowledgeable in male sexual function and dysfunction with sensitivity toward cultural, ethnic and religious factors.

The diagnostic tests utilized in the assessment of the patient with ED may be stratified as:

- Routine and necessary: an assessment necessary in all patients
 - a comprehensive sexual, medical and psycho-social history are the most important elements in the evaluation of ED.
 - a focused physical examination should be performed on every patient with ED.
 - Symptom intensity and impact scales could be used for several purposes: (i) to aid clinicians in recognizing and diagnosing the disorder, (ii) to permit patients to acknowledge the problem in routine office settings, and (iii) to assist researchers in the collection of epidemiological and clinical trial data.
- Recommended: tests of proven value in the evaluation of most patients. Their use is strongly encouraged during initial evaluation. These would include the fasting blood glucose and lipid profile and an evaluation of the hypothalamic-pituitary-gonadal axis with a testosterone assay
- Optional: tests of proven value in the evaluation of specific patient profiles, at the discretion of the attending physician.
- Specialized: tests of value in select patient profiles in specialized settings.

(B) The Key to The Treatment of Erectile Dysfunction

The first step in the management of the patient with ED is to facilitate the patient's and partner's (if available) understanding of the condition, the results of the diagnostic assessment and to identify patient's and partner's needs, expectations, priorities and preferences. The identification and recognition of ED's associated medical and psychological factors in the individual patient must be emphasized.

Prior to direct intervention, good medical practice recognizes the value of altering modifiable risk factors which may benefit selected patients to various degrees.

(1) Alter Modifiable Risk Factors or Causes

These potentially modifiable risk factors and causes include the following:

- Lifestyle and psychosocial factors
- Prescription or non-prescription drug use
- Hormone replacement therapy for hormonal abnormalities

(2) Direct Treatment Interventions for ED

The vast majority of patients will need to consider direct treatment options for ED. It is reasonable to discuss the benefits, risks, and costs of the available treatment strategies with the patient and have the patient actively participating in the choice of therapy (shared decision making)

The treatment selected by a patient will be influenced not only by issues such as efficacy and safety but also by the patient's cultural, religious and economic background. Additionally, such factors as (1) ease of administration, (2) invasiveness, (3) reversibility, (4) cost, (5) the mechanism of action (peripheral vs central, inducer vs enhancer) and (6) legal regulatory approval and availability; may all critically influence the individual patient's selection of therapy.

An important issue prior to the institution of any therapy and the subsequent resumption of sexual activity is the overall cardiovascular condition of the patient. Is this patient able to resume the exercise of sexual activity? If not, priority cardiovascular assessment and intervention may be appropriate.

Sexual counseling and education

Sexual counseling and education (sex therapy, psychosexual therapy or marital therapy) for individuals or couples addresses specific psychological or interpersonal factors such as relationship distress, sexual performance concerns, dysfunctional communication patterns and comorbid sexual conditions that are likely to impact sexual functioning.

Oral Agents

When indicated oral therapies will probably become the first line treatment for the majority of patients because of potential benefits and lack of invasiveness.

Historically, prior to the advent of sildenafil, oral medications such as yohimbine have been utilized empirically without the support of rigorous clinical trial data on efficacy and safety.

Sildenafil citrate, a selective inhibitor of phosphodiesterase V (PDE V), has been approved in many countries for the treatment of ED. In clinical trials, sildenafil has shown broad spectrum efficacy in a majority of patients regardless of the underlying etiology of the ED, the baseline severity of the ED or the age of the patient. In general, sildenafil when prescribed appropriately, has demonstrated broad efficacy and an acceptable safety profile.

Apomorphine, a dopaminergic agonist acting at the central nervous system level and phentolamine, an alpha-adrenergic blocking agent with both central and peripheral activity, are under review at the time of this writing.

Other drugs under investigation include IC 351, a PDE V inhibitor, melanotan II, an alpha-MSH analogue and the combination of L-arginine and yohimbine.

Local Therapy

They include intracavernosal injection therapy, intraurethral therapy and the use of vacuum devices. Patients who fail oral drug therapy, who have contraindications to specific oral drugs or who experience adverse events from oral drugs might consider these local therapies. Additionally, individual preferences may direct a patient to consider local therapies prior to or as an alternative to oral drug therapy.

Intracavernosal injection therapy is a well established medical therapy for ED. Injection therapy with alprostadil or a combination of drugs is effective in a large majority of patients, although discontinuation rates are usually high.

The intraurethral application of alprostadil is an alternative to injection therapy. Intraurethral therapy is associated with significantly less efficacy than direct injection of alprostadil.

The advantages of Vacuum Device Therapy (VCD) include its nonpharmacologic nature, on demand use, lack of contraindications and cost. The disadvantages of VCD therapy include their cumbersome utilization and minor local side-effects.

Surgical Therapy

Microvascular arterial bypass and venous ligation surgery may achieve the goal of increasing arterial inflow and decreasing venous outflow. Certain young patients with vascular insufficiency may be candidates for surgical cure or at least significant improvement of their ED.

The final treatment option for ED is the surgical implantation of a malleable or inflatable penile prosthesis. This option is highly invasive and irreversible and should therefore be reserved for select cases failing other treatment modalities. When properly selected, penile prosthesis may be associated with high rates of patient satisfaction.

Reassessment and Follow-Up

Reassessment and follow-up should be conducted at regular intervals with every patient receiving treatment for ED.

INTRODUCTION

Definition of Erectile Dysfunction (ED)

Impact of ED

Prevalence and Association with Age

**Misconception of ED and
the Importance of Communication**

INTRODUCTION

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Definiton of Erectile Dysfunction (ED)

Erectile dysfunction is defined as the persistent or recurrent inability, for at least 3 months duration, to achieve and/or maintain an erection sufficient for satisfactory sexual performance ^(1,2).

Erectile Dysfunction is currently the preferred term instead of 'impotence' as the latter term lack specificity and has negative connotations ⁽¹⁾.

ED does not refer to penile curvatures, spontaneous or drug-induced prolonged erections and painful erections. ED must also be distinguished from other sexual disorders such as premature ejaculation, anorgasmia and lack of desire, although ED may occur concurrently with these other sexual disorders.

Erectile Dysfunction is a symptom based on the patient's complaints. Objective testing (or partner reports) may be used to support the diagnosis of erectile dysfunction, but these measures cannot substitute for the patient's self-report in defining the disorder or establishing the diagnosis. The necessary reliance on patient reports implies that cultural factors and patient-physician communication will be important determinants in defining and diagnosing the disorder. Consistency is a part of the definition of erectile dysfunction. Erectile difficulties must be reported to occur on a consistent or recurrent basis in order to qualify for the diagnosis of erectile dysfunction. At present, a minimum duration of three months is generally accepted for establishment of the diagnosis.

Erectile dysfunction may occur regardless of the post-pubertal age and there are many underlying aetiological factors. It is noteworthy that erectile dysfunction might not be the primary complaint and/or be associated with other sexual problems.

Sexuality, including erection, is a complex biopsychosocial process. The physician and collaborating specialists should possess broad knowledge about human sexuality. In the case of erectile dysfunction, problems may be lifelong or acquired, global or situational. Adequate attention to these details during the history will educate the often uninformed patient regarding the complex nature of sexuality, and prepare him for understanding treatment and outcome realities. Patient and partner expectations, needs and priorities will be significantly influenced by cultural, social, ethnic, religious and national/regional perspectives. The rational selection of therapy by patients is only possible following appropriate education, including information about sexuality and all treatments for erectile dysfunction. Although not always possible on the first visit, every effort should be made to involve the patient's primary sexual partner early in the therapeutic process.

In contrast to most other medical conditions, the various treatments for ED have to be considered in the context of traditions, ethnicity and socio-economic conditions and also the patient and partner's preference, expectations and psychological status.

Impact of Erectile Dysfunction (ED)

Erectile Dysfunction is a significant and common medical problem affecting many men worldwide.

Cause-specific assessment and treatment of male sexual dysfunction will require recognition by the public and the medical community that erectile dysfunction is a part of overall male sexual dysfunction. Erectile dysfunction is a very common medical condition leading to fear, loss of image and self-confidence and depression. The multifactorial nature of erectile dysfunction, comprising both organic and psychologic aspects, may often require a multidisciplinary approach to its assessment and treatment. This consensus report addresses these issues, not only as isolated health problems but also in the context of social and individual perceptions and expectations.

Erectile dysfunction is often assumed to be a natural concomitant of the aging process, to be tolerated along with other conditions associated with aging. This assumption may not be entirely correct. For the elderly and for others, erectile dysfunction usually occurs as a consequence of specific illnesses or of medical treatment for certain illnesses.

Physicians, health educators, and patients and their families are sometimes unaware of this potential complication. Whatever the causal factors, the embarrassment among patients and health care providers in discussing sexual issues becomes a barrier to pursuing treatment.

Erectile dysfunction can be effectively treated with a variety of methods. Many patients and health care providers are unaware of these treatments, and the dysfunction thus often remains untreated, compounded by its psychological impact. Concurrent with the increase in the availability of effective treatment methods has been increased availability of new diagnostic procedures that may help in the selection of an effective, cause-specific treatment. This guideline was designed to address these issues and to define the state of the art.

Prevalence and Association with Age

There is an estimated 100 million men having ED worldwide⁽³⁾.

In the USA, the Massachusetts Male Aging Study, reported in 1994, provide data on the prevalence of erectile dysfunction in a general population of men who were 40 to 70 years of age⁽⁴⁾.

The combined prevalence of all degrees of erectile dysfunction was 52%. The category with the highest prevalence was moderate erectile dysfunction with a rate of 25%, followed by minimal erectile dysfunction at 17% and complete erectile dysfunction at 10%⁽⁴⁾.

The Cross National Prevalence Study on ED, was jointly carried out by the National Population and Family Development Board of Malaysia and the New England Research Institute from the USA in 1998. Based on this survey, ED was defined as mild (occasional), moderate (most of the time) and complete ED (all the time)⁽⁵⁾. The prevalence of moderate to complete erectile dysfunction in Malaysian men aged 40 and above is 16%. Based on these statistics, the number of men with moderate and complete ED is 448,000. If we include the mild ED cases, the prevalence is raised to 60% in this survey, which is 1.68 million men aged 40 and above⁽⁵⁾.

Misconception of ED and the Importance of Communication

A number of survey on attitudes to ED have been reported. One recent important survey was conducted by the Market and Opinion Research Institute (MORI) of London in 1998, involving 10 countries, of which 4 were Asian countries⁽⁶⁾.

The MORI findings showed from Europe, Asia to Latin America, men share many similar views and misconceptions about ED. Not one of the main organic risk factors is included in the top four perceived causes of ED - even among those who reported having the condition. Half of men aged 40 and above, the highest proportion, consider ED to be 'a natural part of aging'. In contrast, far fewer (around one in five) are aware that diabetes and hypertension - both significant risk factors - are causes of ED. ED is not solely a psychological condition, nor an inevitable result of aging, and communication is needed about the underlying medical conditions that can result in ED. The survey also highlighted the low likelihood of men being asked by their doctors about sexual functioning. Eighty-three percent of men aged 40 and above said their doctors had never asked them about their sexual functioning and 84% said they had never initiated a discussion with their doctors about these topics. And 40% of men aged 40 and above identified ED as the health issue that men their age would be least likely to approach health professionals for help with. ED came highest on the list of 12. However, two in three men agree that talking about ED would help lift the stigma associated with the condition and result in more men with ED being helped.

PHYSIOLOGY OF ERECTION

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A normal erectile mechanism entails an intact nervous system and adequate blood supply to the penis and a competent veno-occlusive mechanism of the penis.

Penile erection and detumescence are haemodynamic events that are regulated by corporal smooth muscle relaxation and contraction respectively.

In the flaccid state, a dominant sympathetic influence prevails, and the arteries and corporal smooth muscle are tonically contracted. There is a constant but minimal blood flow into the lacuna spaces (sponge-like penile tissue).

After sexual stimulation, parasympathetic activity increases resulting in vasodilatory effects. This decreases the peripheral resistance bringing about tremendous increase in blood flow through the cavernous and helicine arteries.

Relaxation of corporal smooth muscle increases compliance and the expansion of the lacuna spaces compresses the outflow veins (subtunical veins) resulting in maintenance of erection.

Detumescence occurs when sympathetic activity (following orgasm) increases the tone of the helicine arteries and the corporal smooth muscle.

Normal erectile process begins with sexual stimulation in the brain (perception, desire, etc) from where impulses are transmitted via the spinal cord and the pelvic nerve to the penile corpus cavernosum (corporal smooth muscle).

In the corpus cavernosum, a gaseous neurotransmitter, nitric oxide (NO) acts as a physiological mediator, activating the enzyme, guanylate cyclase through the cell membrane of the corporal smooth muscle cells. This enzyme guanylate cyclase is responsible for converting guanosine triphosphate (GTP) into cyclic guanosine monophosphate (cGMP). Cyclic GMP then induces calcium to leave the corporal smooth muscle cells. These cells relax syncitally and penile erection results. Penile erection is maintained by continuous central and local stimuli. The local stimuli act through the sacral cord reflex pathway. When sexual stimulation is terminated, the NO stimulus is removed or ceased, cGMP is no longer produced and the erection subsides with cGMP being degraded by the enzyme phosphodiesterase type V (PDE V).

ERECTILE DYSFUNCTION

Causes And Risk Factors

ERECTILE DYSFUNCTION

ERECTILE DYSFUNCTION

Erectile dysfunction can occur as a result of a neurological disorder affecting the central nervous system or anywhere in the erection pathway, an arterial disorder, as in generalised arteriopathy or localised as seen after pelvic surgery or radiotherapy, or a defective veno-occlusive mechanism, either congenital or acquired. Less commonly, ED can result from endocrinological factors (abnormal hormonal milieu) and penile or cavernosal factors (e.g. fibrosis, curvatures).

Psychological processes such as depression, anxiety, and relationship problems can impair erectile functioning by reducing erotic focus or otherwise reducing awareness of sensory experience. This may lead to inability in initiating or maintaining an erection. Aetiologic factors for erectile disorders may be categorized as neurogenic, vasculogenic, psychogenic, endocrinologic or cavernosal, but most commonly, they appear to derive from various combinations of these factors.

Causes and Risk Factors

Psychogenic

- Performance anxiety
- Loss of attraction
- Relationship difficulties
- Stress

Psychiatric

- Anxiety disorders
- Depression

Neurogenic

Trauma
Myelodysplasia (spinal bifida)
Intervertebral disc lesions
Diabetes mellitus
Alcohol abuse
Pelvic surgery

Endocrine

Hyperprolactinaemia
Hypo- and hyperthyroidism
Hypogonadism leading to testosterone deficiency

Arteriogenic

Hypertension
Smoking
Diabetes mellitus
Hyperlipidaemia
Peripheral vascular disease

Penile disorders

Peyronie's disease

Drugs and substance abuse

Narcotics
Antihypertensives (thiazides, beta blockers, methyldopa, spironolactone)
Antidepressants and tranquilisers
NSAID's
H₂ antagonists (cimetidine)
Miscellaneous drugs (ketoconazole, hyoscine, anti-cancer agents)

EVALUATION AND ASSESSMENT

Standard Questionnaires

Comprehensive Sexual, Medical &
Psychosocial History

Physical Examination

Laboratory Studies

Cardiac Status Evaluation

EVALUATION AND ASSESSMENT

Patients usually do not volunteer their problem with ED. Screening should be employed if the doctor suspects that his patient has ED. Screening is advised for males around 40 years of age, especially if they have risk factors viz.:

- a. Diabetes
- b. Hypertension
- c. Hyperlipidaemia
- d. Heavy smoking
- e. Cardiac disease
- f. Depression

Standard Questionnaires

An acceptable screening tool using a 5 question questionnaire is as follows (see *Table I*)^(7,8)

Table I^(7,8)

1. How often were you able to get an erection during sexual activity?

Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always
1	2	3	4	5

2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)?

Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always
1	2	3	4	5

3. When you attempted intercourse, how often were you able to penetrate (enter) your partner?

Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always
1	2	3	4	5

4. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?

Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always
1	2	3	4	5

5. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?

Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult
1	2	3	4	5

* All questions are preceded by the phrase ' Over the past 4 weeks.'

Instructions for Scoring: Add the scores for each item 1-5 (total possible score =25). ED Severity Classification : Total score 5-10 (severe); 11-15 (moderate); 16-20 (mild); 21-25 (normal).

Note: The following questions should only be completed by individuals who have been sexually active and have attempted sexual Intercourse in the past 3 months. For sexually inactive individuals, the questionnaire may be answered for the last period of time (3 months or longer) during which the individual was sexually active.

Should the patient be found to have ED from the above questionnaire (i.e. total score 20 or less, a subjective bothersome questionnaire (*Table II*) may be useful:

Table II ⁽⁹⁾

	Very dissatisfied	Rather dissatisfied	Mixed, about equally satisfied	Rather satisfied	Very satisfied
If you were to spend the rest of your life with your erectile condition, the way it is now, how would you feel about that?	1	2	3	4	5

For patients suspected to be suffering from depression, a two-question screening tool (*as shown in Table III*) may be useful:

Table III ⁽¹⁰⁾

- During the past month, have you often been bothered by feeling down, depressed or hopeless?
- During the past month, have you often been bothered by little interest or pleasure doing things?

Although normal aging can result in a decline in sexual performance, persistent erectile dysfunction should be investigated. The appropriate evaluation of all men with erectile dysfunction should include a comprehensive sexual, medical and psychosocial history, physical examination and focused laboratory studies.

Comprehensive Sexual, Medical & Psychosocial History

A sexual history is needed to accurately define the patient's specific complaint and to distinguish between true erectile dysfunction, changes in sexual desire, and orgasmic or ejaculatory disturbances.

The patient should be asked specifically about perceptions of his erectile dysfunction, including the nature of onset, frequency, quality, and duration of erections; the presence of nocturnal or early morning erections; and his ability to achieve sexual satisfaction. Psychosocial factors related to erectile dysfunction should be probed, including specific situational circumstances, performance anxiety, the nature of sexual relationships, details of current sexual techniques, expectations, motivation for treatment, and the presence of specific discord in the patient's relationship with his sexual partner. The sexual partner's own expectations and perceptions should also be sought since they may have an important bearing on diagnosis and treatment recommendations.

Other essential components of history taking should cover the following :

- **Altered sexual desire**
- **Ejaculation**
- **Orgasm**
- **Sexual related genital pain**
- **Lifestyle factors**
- **Smoking**

- **Chronic medical illness :**
 - hypertension
 - diabetes mellitus
 - atherosclerosis and cardiovascular risk factors including hyperlipidaemia
 - renal and hepatic dysfunction
- **Pelvic / perineal / penile trauma :**
 - bicycling injury
 - motor vehicle accident etc.
- **Medications / recreational drug use :**
 - antihypertensives
 - antidepressants
 - alcohol
 - cocaine
- **Past surgery :**
 - radical prostatectomy
 - laminectomy
 - vascular bypass surgery
- **Neurological illnesses :**
 - spinal cord injury
 - multiple sclerosis
 - lumbosacral disc injury
- **Endocrinological illnesses :**
 - hypogonadism
 - hyperprolactinaemia
 - thyroid disease
- **Sexually transmitted diseases :**
 - gonorrhoea
- **Psychiatric illnesses :**
 - depression
 - anxiety

Psychosocial history should cover symptoms of depression (*Table III*), altered self esteem, past and present partner relationships, past and present sexual practices, history of sexual trauma / abuse, job and social position satisfaction, economic position and educational attainment.

Sample Psychosocial Assessment Questions

- "Do you suffer from depression or other mood problems?"
- "How are your relationships with family members and other important people in your life?"
- "Do you have any difficulties in your work situation?" (if applicable)
- "How is your current relationship with your partner? How was it in the past?"
- "Were you ever the victim of sexual abuse (forced to have sex)? If yes, what effect did this have on you then or now?"

Sample Sexual History Questions

- "Many men of your age start to experience sexual difficulties, if you have such a problem, I would be happy to discuss this further":
- "Could you describe your sexual problem?"
- "When did your erection problems begin?" "Please describe the circumstances."
- "How was your sexual functioning prior to this time?"
- "How are your erections that you achieve with masturbation or those that occur with sleep or upon awakening early in the morning?" (The discussion of masturbation is a sensitive issue that is often influenced by cultural and religious perspectives).
- "How strong is your desire for sex, now and in the past?"
- "Do you have difficulties in ejaculating, either too fast or slow, either now or in the past?"
- "Is your partner able to become aroused and reach climax when you have sex together?"
- "What has been your partner's reaction to your current sexual difficulties?"
- "What has been the effect of your sexual difficulties on your partner relationship?"
- "What has been the effect of your sexual difficulties on your overall lifestyle?"

Physical Examination include the following:

- **General Appearance**

Secondary sexual characteristics

- **Cardiovascular System**

Blood pressure
Peripheral pulses

- **Neurological system**

Reflexes, bulbocavernosus reflex
Penile sensation

- **Genito-urinary system**

Penile examination : circumcision, deformity, plaques,
phimosis, hypoaesthesia
Testes examination : size and consistency
Rectal examination : sphincter tone and prostate examination

Laboratory Studies

The physician must tailor the laboratory work up based on patient complaints and risk factors outlined by the history and physical examination. One should also take into consideration the cost and availability of testing resources.

Recommended Tests

- Urine analysis
- Fasting blood glucose
- Testosterone

If indicated - full blood count, lipid profile, renal profile, serum prolactin, LH, TSH, free T4, liver profile, PSA.

Further Specialised Tests include :

- Office Intracavernosal Injection Tests
- Nocturnal Penile Tumescence (NPT) Tests
- Penile Doppler Ultrasonography
- Dynamic Infusion Cavernosometry, Cavernosography
- Angiography

Cardiac Status Evaluation ⁽¹¹⁾

- Sexual activity is no more stressful to the heart than when compared with a number of other natural daily activities e.g. walking one mile on the level in 20 minutes.
- The cardiac risk of sexual activity, in patients diagnosed with cardiovascular disease, is minimal in properly assessed and advised patients.
- Erectile dysfunction (ED) is common, affecting 10% of men aged 40-70 years and increases in frequency with age.
- ED and cardiovascular disease share many of the same risk factors and often coexist.
- ED in patient with cardiovascular disease, should be identified by routine questioning in general practice. Modern therapies can restore a sexual relationship in the majority of patients with ED and can lead to a substantial improvement in quality of life.
- The majority of patients assessed to be at low or intermediate cardiac risk, as defined in Table V, can be effectively managed in primary care. Primary care treatment for ED in patients defined as high risk can be initiated following a specialist opinion and/or confirmation that the patient's cardiovascular condition is stable.
- There is no evidence that currently licensed treatments for ED add to the overall cardiovascular risk in patients with or without cardiovascular disease.

Table IV: METs Equivalentents ⁽¹²⁾

Daily Activity	METs Score Rating
Sexual intercourse with long-standing partner - lower range ('normal') - upper range (vigorous activity)	2-3 5-6
Lifting and carrying objects (9-20kg)	4-5
Walking one mile in 20 minutes on the level	3-4
Golf	4-5
Gardening (digging)	3-5
DIY, wallpapering, etc	4-5
Light housework e.g. ironing, polishing	2-4
Heavy housework e.g. making beds, scrubbing floors	3-6

Table V: Management Algorithm according to Graded Risk ⁽¹¹⁾

Grading of Risk	Cardiovascular Status upon Presentation	ED Management Recommendations for the Primary Care Physician
Low Risk	<ul style="list-style-type: none"> • Controlled hypertension • Asymptomatic ≤ 3 risk factors for CAD - excluding age & gender • Mild valvular disease • Mild stable angina • Post successful revascularisation 	<ul style="list-style-type: none"> • Manage within the primary care setting • Review treatment options with patient and their partner (where possible)
Intermediate Risk	<ul style="list-style-type: none"> • History of recent MI or CVA (less than 6 weeks) • ≥ 3 risk factors for CAD - excluding age and gender • LVD/CHF (I, II) • Murmur of unknown origin • Moderate stable angina 	<ul style="list-style-type: none"> • Specialised evaluation recommended (e.g. exercise test for angina, echocardiogram for a murmur) • Patient to be placed in high or low risk category depending upon outcome of testing
High Risk	<ul style="list-style-type: none"> • Unstable or refractory angina • Uncontrolled hypertension (SBP > 180mmHg) • CHF (III, IV) • Recent MI*, CVA • High risk arrhythmias • Hypertrophic cardiomyopathy • Moderate/severe valve disease 	<ul style="list-style-type: none"> • Refer for specialised cardiac evaluation and management • Treatment for ED to be deferred until cardiac condition stabilised and/or specialist evaluation completed
	* Recent MI = within last 14 days	

Glossary of Terms:**New York Heart Association
Classification of CHF**

- Coronary Artery Disease, CAD	Class I	Patients with cardiac disease but with no limitation during ordinary physical activity
- Myocardial Infarction, MI		
- Cerebral Vascular Accident, CVA		
- Congestive Heart Failure, CHF	Class II	Slight limitations caused by cardiac disease. Activity such as walking causes dyspnoea.
- Left Ventricular Dysfunction, LVD		
- Systolic Blood Pressure, SBP		
- Erectile Dysfunction, ED	Class III	Marked limitation. Symptoms are provoked easily, e.g. by walking on the flat
	Class IV	Breathlessness at rest

Management algorithm of ED in the patient with diagnosed cardiovascular disease ⁽¹⁾

ASSESSMENT

- Consider level of normal daily activities compared with the level of exertion associated with resuming sexual activity (*Table IV*)
- Conduct routine ED investigations
- Grade as low, intermediate or high risk using simple criteria in *Table V*

IS IT SAFE FOR THE PATIENT TO RESUME SEXUAL ACTIVITY?

YES

NO

ED TREATMENT OPTIONS

- Oral sildenafil
- Injectable alprostadil
- Intraurethral alprostadil
- Vacuum constriction devices
- Psychosexual/couple therapy

• KEY CONSIDERATIONS

- 1. Informed patient choice**
 - discuss advantages and disadvantages of all available options with patient and partner (where possible)
- 2. Patients taking warfarin**
 - consider increased risk of bruising with injectable alprostadil and bleeding with intraurethral alprostadil
 - consider increased risk of haematoma with vacuum constriction devices
- 3. Patients taking nitrates**
 - if patient is on nitrate therapy, stop his nitrate before sildenafil is initiated.

ACTION

- Optimise management of the cardiovascular disease
- Discuss with the patients, and if possible the partner, the reasons for management decision
- Consider psychosexual/couple therapy
- Re-assess cardiovascular status and reconsider treatment of the ED.

FOLLOW-UP

- Arrange initial follow-up to assess efficacy of therapy and tolerability of patient to resuming sexual activity
- After initial follow-up ED assessments can be conducted as routine checks for cardiovascular symptoms - discuss compliance and any recurrence of spontaneous erections.

PREVENTION

PREVENTION

PREVENTION

ED is not an inevitable consequence of aging. Modifying any known risk factors can help reduce the risk of ED. This includes regular review of the use of any drug that may cause ED. Lack of sexual knowledge and anxiety about sexual performance are common contributing factors to erectile dysfunction. Education and reassurance may be helpful in preventing the cascade into serious erectile failure in individuals who experience minor erectile difficulty due to medication or common changes in erectile functioning associated with chronic illnesses or with aging. Contrary to popular belief, an active sex life does not contribute to ED.

TREATMENT FOR ERECTILE DYSFUNCTION (ED)

General Considerations

Altering Modifiable Risk Factors or Causes

Direct Treatment Interventions

- Sexual Counseling and Education
- Oral Agents
- Local Therapy
- Surgical Therapy

TREATMENT FOR ERECTILE DYSFUNCTION (ED)

General Considerations

The first step in the management of the patient with ED is to facilitate the patient's and partner's (if available) understanding of the condition, the results of the diagnostic assessment and to identify patient's and partner's needs, expectations, priorities and preferences. The identification and recognition of associated medical and psychological factors in the individual patient must be emphasized.

Clearly, the selection of therapy is strongly influenced by personal, cultural, ethnic, religious and economic (affordability) factors. The presentation and stratification of therapies may therefore vary from individual to individual, culture to culture, religious persuasion to religious persuasion and from one economic tier to another. Sensitivity to these factors is important in determining the long-term success of any selected therapeutic course. Prior to direct intervention, good medical practice recognizes the value of altering modifiable risk factors, and this step alone may be of some value in selected patients.

Altering Modifiable Risk Factors or Causes

Potentially modifiable risk factors and causes include the following:

- 1. Lifestyle and psychosocial factors** (e.g. partner conflict, cigarette smoking, substance abuse or depression, sexual misinformation)
- 2. Prescription or non-prescription drug use** (e.g. most commonly antihypertensives, psychotropic drugs including antidepressants and anti-psychotics, as well as anti-arrhythmics, anti-androgens and steroids)
- 3. Appropriate therapy** for hormonal abnormalities (e.g. hypogonadism, hyperprolactinemia)

Although the quantitative benefits of altering modifiable risk factors or causes, particularly when associated with the need to modify behaviour, are not documented, good clinical practice mandates attention to these issues either prior to or along with direct therapies as a key to treating ED. Alterations in drug dosages or classes may be of significant benefit in select patients but this should be coordinated with the primary physician managing, for example, the patient's hypertension or depression. Lifestyle factors such as relationship issues or substance abuse may require priority management specific to the particular issue.

Appropriate therapy for hormonal abnormalities

Appropriate therapy in the presence of a documented deficiency (e.g. androgen deficiency and hypogonadism), may not necessarily improve ED and thus one may need to consider direct intervention therapy even in this patient population. The issue of androgen replacement therapy is complicated. There is a statistical decline of testosterone levels, particularly free testosterone, in aging men. While this fall is only moderate, aging men show clinical signs of hypogonadism (loss of muscle mass / strength, reduction in bone mass and an increase in visceral fat).

Testosterone replacement or supplement therapy may improve bone mass, muscle mass, strength and frequently nocturnal erections as well in this age group. However, the effects on sexual function, mood and cognition are less clear but may be meaningful in certain men. The identification of that segment of the aging male population that might possibly benefit from androgen supplementation remains difficult. Questions still remain regarding the magnitude and longevity of these potential beneficial effects. More importantly, the long-term risks of androgen therapy in this age group really are now known, especially in the areas of cardiovascular and prostate diseases⁽¹³⁾. Despite increasing evidence that patients with subnormal or borderline normal levels of testosterone could be considered as candidates for testosterone treatment, until more information is available, testosterone and androgens in general should not be recommended as supplemental therapy.

Direct Treatment Interventions

The patient and his partner (if available) should be informed of all of the available and acceptable treatment options applicable to his clinical condition and the related benefits, risks, and costs of each modality. The development of ED can significantly affect the quality of life, but it is not a life-threatening disease. Consequently, it is reasonable to discuss the benefits, risks, and costs of the available treatment strategies with the patient and have the patient actively participate in the choice of therapy (shared decision making). An important issue prior to the institution of any therapy and the subsequent resumption of sexual activity is the overall cardiovascular condition of the patient. Is this patient able to resume the exercise of sexual activity? If not, priority cardiovascular assessment and intervention may be appropriate. The partner's sexual function if possible should be considered prior to initiating therapy.

The vast majority of patients will need to consider direct treatment options for ED. Only those pharmacological treatments that have been thoroughly tested in randomized clinical trials, with subsequent publication of results in peer-reviewed literature, should be considered for general use. Long-term follow-up of all treatment options must be performed to demonstrate durability and continued efficacy and safety as well as patient and partner acceptability. Additionally, new treatment options that enter the arena will need to meet not only the above efficacy and safety criteria but also should be compared to available therapies for cost-effectiveness.

The treatment selected by a patient, will be influenced not only by issues such as efficacy and safety, but also by the patient's cultural, religious and economic background. Additionally, such factors as (1) ease of administration, (2) invasiveness, (3) reversibility, (4) cost and (5) the mechanism of action (peripheral vs. central, inducer vs. enhancer) and (6) availability, may critically influence the individual patient's selection of therapy. As previously mentioned, affordability is a prime factor in influencing patient acceptance and utilization of a specific therapy for ED.

The use of the internet to prescribe therapies for erectile dysfunction should be strongly discouraged since it fails to meet the need for direct physician-patient contact in the assessment of all patients presenting with this complain.

- **Sexual Counseling and Education**

Sexual counseling and education (sex therapy, psychosexual therapy or marital therapy) for individuals or couples addresses specific psychological or interpersonal factors such as relationship distress, sexual performance concerns, dysfunctional communication patterns and comorbid sexual conditions that are likely to impact sexual functioning. Modified sex therapy may serve as an adjunct to the other direct therapies for ED to address psychological reactions to these medical or surgical therapies which may be perceived as temporary, unnatural or unacceptable by the patient and / or partner. The advantages of psychosexual therapy include its noninvasive nature and broad applicability. The disadvantages of psychosexual therapy include its variable efficacy in the treatment of ED, cost and acceptability by the patient or the couple.

- **Oral Agents**

When indicated oral therapy will probably become the first line treatment for the majority of patients because of potential benefits and lack of invasiveness. Historically, prior to the advent of sildenafil, oral medications such as yohimbine have been utilized empirically without the support of rigorous clinical trial data on efficacy and safety. Oral agents may act centrally as dopaminergic agonists; some may act both centrally and peripherally, like the alpha adrenergic blockers; and yet others like the phosphodiesterase type V (PDE V) inhibitors or nitric oxide (NO) precursors, act only peripherally. Sildenafil citrate, a selective inhibitor of PDE V⁽¹⁴⁾, has been approved in many countries for the treatment of ED. Phosphodiesterases are the enzymes responsible for the breakdown of the intracellular second messenger of nitric oxide i.e. cyclic guanosine monophosphate (cGMP)^(15,16) and PDE V is the predominant isoform of phosphodiesterase found in the corporal smooth muscle^(15,17). In clinical trials, sildenafil has shown broad spectrum efficacy in a majority of patients regardless of the underlying aetiology of the ED, the baseline severity of the ED or the age of the patient⁽¹⁸⁾. Recently, studies on patients with specific disorders such as diabetes mellitus, hypertension, spinal cord injury, multiple sclerosis and depression have also shown sildenafil to be effective^(3,19,20,21,22). Side effects include transient headache, flushing, dyspepsia, nasal stuffiness and transient altered color vision (due to PDE VI inhibition)⁽¹⁸⁾. A relatively small number of deaths have been reported in association with sildenafil usage but the specific relationship to the drug is uncertain⁽³⁾. This underscores the need for cardiovascular assessment prior to the treatment of ED and regular follow up. A small percentage of these deaths occurred with concomitant use of nitrates and are presumed to be due to severe hypotension that may ensue following this combination⁽¹¹⁾. In addition, patients with possible or

active coronary heart disease or other significant cardiovascular diseases such as aortic stenosis should undergo cardiac evaluation and management prior to considering sildenafil usage⁽¹¹⁾. To date, there is no physiological reason to indicate sildenafil exerts a direct effect on the myocardium⁽³⁾. In general, sildenafil when prescribed appropriately has demonstrated broad efficacy and an acceptable safety profile.

Apomorphine is a dopaminergic agonist acting at the central nervous system level. It was initially administered subcutaneously. However intolerable adverse events prompted the development of a sublingual pill. Apomorphine has shown efficacy in placebo-controlled fixed and dose escalation studies⁽²³⁾. In responders, erection usually begins within 20 minutes. Its principal adverse effect is nausea which is usually minimal at lower dosages (2mg and 4 mg). Other adverse effects are dizziness, sweating, somnolence and yawning as well as rarely, syncope.

Phentolamine is an alpha adrenergic blocking agent with both central and peripheral activity. In placebo controlled studies, it has been found to have modest efficacy in patients with mild to moderate ED. Adverse reactions include dizziness, nasal stuffiness and tachycardia. These events are minimal at the usual dose of 40mg^(24,25).

Other drugs under investigation include IC 351 a more selective and longer acting PDE V inhibitor; melanotan II, an alpha-MSH analogue and the combination of L-arginine and yohimbine.

In the future, combination oral therapy may be employed for potentially additive or synergistic actions (e.g. sildenafil and apomorphine). However, clinical trials are required to evaluate not only efficacy but also safety.

The advantages of oral drug therapy include broad patient acceptance, ease of administration and relative efficacy. The disadvantages include specific contraindications such as the concomitant use of nitrates with respect to sildenafil and the relative cost.

- **Local Therapy**

Local therapy include intracavernosal injection therapy, intraurethral therapy and vacuum device therapy. Patients who fail oral drug therapy, who have contraindications to specific oral drugs or who experience adverse events from oral drugs might consider these. Additionally, individual preferences may direct a patient to consider local therapy prior to or as an alternative to an oral drug therapy.

Intracavernosal Injection Therapy

Intracavernosal injection therapy is a well-established medical therapy for ED. The delivery, by penile injection, of agents that directly relax corporal smooth muscle such as papaverine, phentolamine or more recently alprostadil (prostaglandin E1) is associated with broad efficacy and relative safety. Alprostadil is widely approved worldwide as alprostadil sterile powder or alfadex. Combinations of agents have established efficacy and safety based upon common usage. Injection therapy with alprostadil or a combination of drugs is effective in a large majority of patients, although discontinuation rates are usually high⁽²⁶⁾. The side effects associated with injection therapy are primarily local and include pain, priapism and scar tissue formation over time. This therapy is contraindicated in patients with sickle cell anemia and with other conditions that predispose them to priapism. The advantages of penile injection therapy include broad efficacy, relative safety and the rapidity of onset of action. The disadvantages include invasive local administration and relative cost.

Intraurethral Therapy

The intraurethral application of alprostadil is an alternative to injection therapy. Intraurethral therapy is associated with significantly less efficacy than direct injection of alprostadil. The efficacy may be increased by using an elastic band placed at the base of the penis. The associated side effects include pain as well as systemic hypotension. The advantages of intraurethral therapy include its less invasive nature. The disadvantages include local as well as systemic side-effects, relative cost and partner related vaginal irritation.

Transdermal penile delivery of vasoactive drugs is currently under investigation at the time of writing.

Vacuum Constriction Devices

Vacuum constriction devices (VCD) are widely available and may be sold over-the-counter (without prescription) in some countries. They are of appeal to a group of men that are not interested in pharmacological therapy or have specific contraindications to these therapies. VCD's apply a negative pressure to the pendulous penis, thus drawing blood into the penis, which is then retained by the application of an elastic band at the base of the penis. The side effects associated with VCD therapy include penile pain, penile numbness, bruising and retarded ejaculation. The advantages of VCD therapy include its nonpharmacologic nature, on demand use, lack of contraindications and cost. The disadvantages of VCD therapy include their cumbersome utilization and minor local side effects⁽²⁷⁾.

- **Surgical Therapy**

Vascular Surgery

Microvascular arterial bypass and venous ligation surgery may achieve the goal of increasing arterial inflow and decreasing venous outflow. Certain young patients with vascular insufficiency may be candidates for surgical cure or improvement of ED. These patients must be evaluated by specialized testing and should be treated by an experienced surgeon, usually in research centres.

Penile implants

The final treatment option for ED is the surgical implantation of a malleable or inflatable penile prosthesis. This option is highly invasive and irreversible and should therefore be reserved for select cases failing other treatment modalities. However, under unique and uncommon circumstances a penile implant could be selected as a primary option. When properly selected, penile prostheses may be associated with high rates of patient satisfaction⁽²⁸⁾. Penile implant surgery is uncommonly associated with prosthesis infection but such cases usually require explanation and may result in severe scarring and penile deformity. The advantages of penile prosthesis implantation include relative efficacy and a 'long term solution'. The disadvantages of penile prostheses include irreversibility, invasiveness, surgical complications and mechanical failure.

**REASSESSMENT AND
FOLLOW-UP**

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Reassessment and follow-up should be conducted at regular intervals (the recommendation is six-monthly) for every patient receiving treatment for ED. The goals of follow-up include:

1. The need for dose titration or substitution of another treatment intervention may be considered when necessary. Patients may change treatment preferences, seek new information, or wish to reevaluate their current treatment choices.
2. Patient communication. Patients may have concerns regarding treatment administration, other sexual dysfunction problems (e.g. premature ejaculation), partner issues (e.g. anorgasmia) or lifestyle factors (e.g. emotional stress) and these should be addressed.
3. Patients may change medication regimens, either for ED or a concomitant medical disorder. The possibility of adverse drug reactions or drug interaction effects with oral medications for ED should be carefully monitored.
4. General medical and psychosocial reassessment should occur at regular intervals, depending upon the patient's health, physical and psychosocial needs. Follow up also provides an additional opportunity for patient education.

SHARED CARE CONCEPT ⁽²⁹⁾

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SHARED CARE CONCEPT⁽²⁹⁾

Currently only about 10% of the ED sufferers seek treatment. This low figure is expected to change radically in the near future because of the increasing population of the aging men, who are better educated, more affluent and have higher expectations of maintaining good quality of life.

A high percentage of this graying population has concomitant disease leading to ED. With widespread awareness that ED is a disease and is currently easily treatable with effective oral medication and many other easy-to-administer therapies, a huge population of sufferers will be expected to come forward to seek treatment. The primary care physicians who are the frontline health care providers will be exposed to most of the ED patients. These primary care physician who understand the background of their patients will be the ideal persons to raise the subject of ED and proceed on to a comprehensive work-up which entails a full medical and sexual history, relevant physical examination and order focussed laboratory tests.

Most of today's easy-to-administer treatment options, can be handled by the primary care physicians. The urologist and other related specialists will play a supportive role in handling ED patients who have failed simple therapies and are keen to try more invasive forms of treatments. The urologists or other related specialists will also provide backup for any treatment complications, handle any abnormal clinical or laboratory results needing further evaluation and also carry out a full diagnostic work-up on the patient's request or for medico-legal purposes (See *Table*).

A share care approach to the management of ED patients will be most productive and beneficial to the patient, health care provider and health care financier.

Shared Care Management in ED

Indications for referral to specialists :-

- Contraindication to oral medication
- First line treatment failure
- Unexpected clinical and laboratory results
- Complicated psychiatric or psychosexual disorder
- Complicated endocrinopathy
- Significant penile curvature
- Pelvic / perineal trauma
- Cases requiring vascular or neurosurgical intervention
- Primary ED
- Request for specialized evaluation
- Medico legal issues

REFERENCES

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1. NIH Consensus Development Panel on Impotence. Impotence. JAMA. 1993; 270(1):83-90.
2. Montague DK, Barada JH, Belker AM, et al. Clinical guidelines panel on erectile dysfunction: summary report on the treatment of erectile dysfunction. J Urol. 1996; 156:2007-2011.
3. Pfizer. Data on file.
4. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol. 1994; 151:54-61.
5. Tambi I. Epidemiology of ED in Malaysia. Highlights of Symposium at 5th Asian Congress on Sexology. Nov 1998; Seoul Korea.
6. Corrado M. Man and Erectile Dysfunction: A Survey of Attitudes in 10 Countries. Survey by Market & Opinion Research International. Presented at The 8th World Meeting on Impotence Research, August 1998; Amsterdam, The Netherlands
7. Rosen RC, Riley A, Wagner G, et al. The International Index of Erectile Function (IIEF): A Multidimensional Scale for Assessment of Erectile Dysfunction. Urology 1997; 49:822-830.
8. Cappelleri JC, Rosen RC, Smith MD, et al. Diagnostic Evaluation of the Erectile Function Domain of the International Index of Erectile Function. Urology 1999; 54:346-351.
9. Wagner G, et al. Committee on 'Symptom Scores and Quality-of-Life'. Presented at 1st International Consultation on Erectile Dysfunction, July 1999; Paris.
10. Whooley MA, Avins AL, Miranda J, et al. Case-finding Instruments for Depression. Two questions are as good as many. J. Gen. Intern. Med. 1997;12:439-445.
11. Jackson G, et al. A Systematic Approach to Erectile Dysfunction in the Cardiovascular Patient - A Consensus Statement. Int. J. Clin. Pract. 1999; 53(6):445-451.
12. Eds Wilson PK, Farday PS, Froelicher V. Cardiac Rehabilitation - Adult Fitness and Exercise Testing. Formulating the exercise prescription. Chapter 14. Philadelphia: Lee & Fabiger 1981:333-353. National Heart Association of Malaysia - Consensus Statement on Use of Sildenafil in Patients with Cardiovascular Disease November 1999
13. Lei CCM, Kim YC. Hormonal Therapy for Erectile Dysfunction. APSIR Book on Erectile Dysfunction. Chapter 9. APSIR 1999:113-117.

14. Boolell M, Allen MJ, Ballard SA, et al. Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. *Int. J. Impotence Res.* 1996; 8(2);47-52
15. Beavo JA. Cyclic nucleotide phosphodiesterases: functional implications of multiple isoforms. *Physio. Rev.* 1995; 75:725-748.
16. McDonald LJ, Murad F. Nitric oxide and cyclic GMP signaling. *Proc. Soc. Exp. Biol. Med.* 1996; 211:1-6.
17. Andersson KE, Wagner G. Physiology in penile erection. *Physiol. Rev.* 1995; 75:191-236.
18. Morales A, Gingell, Collins M, et al. Clinical safety of Oral Sildenafil Citrate (ViagraTM) in the treatment of Erectile Dysfunction. *Int. J. Impotence Res.* 1998; 10:69-74.
19. Guiliano F, Hultling C, El Masry WS, et al. Randomised trial of Sildenafil for the treatment of Erectile Dysfunction in Spinal Cord Injury. *Ann Neurol.* 1999; 46:15-21
20. Rendell MS, Rajfer J, Wicker PA, Smith MD for the Sildenafil Diabetes Study Group. Sildenafil for the treatment of Erectile Dysfunction in Men with Diabetes. *JAMA.* 1999;281: 421-426
21. Feldman R. Sildenafil in the treatment of Erectile Dysfunction: efficacy in patients taking concomitant antihypertensive therapy (abstract). *Am. J. Hypertens.* 1998; 11:10A
22. Hargreave T. Efficacy of Sildenafil in the treatment of Erectile Dysfunction in patients with Depression. Paper presented at: Annual Congress of the Collegium Internationale Neuro-Psychopharmacologicum; 1998; Glasgow, UK.
23. Padma-Nathan H, et al. Efficacy and safety of apomorphine sl vs. placebo for male erectile dysfunction. *J. Urol.* 1998; 159:A920.
24. Becker AJ, Stief CG, Machtens S, et al. Oral phentolamine as treatment for erectile dysfunction. *J.Urol.* 1998; 159:1214-1216.
25. Goldstein I, et al. Efficacy and safety of oral phentolamine (Vasomax) for the treatment of minimal erectile dysfunction. *J. Urol.* 1998; 159:A919.
26. Ng PEP, Tan HM. The Use of Intracorporeal Self Injection of Prostaglandin E1 in Malaysian Men. *Int. J. Impotence Res.* 1994; 6:D105.
27. Mah PKK, Yap HW. Vacuum Erection Devices for Erectile Dysfunction. *APSIR Book on Erectile Dysfunction.* Chapter 11. APSIR 1999:126-133.
28. Tan HM, Ng PEP. The Malaysian Experience with Penile Implants. *Int. J. Impotence Res.* 1994; 6:D133.
29. Tan HM. Shared Care Concept in the Management of Erectile Dysfunction. 1st ASEAN Conference on Primary Healthcare, March 1999; Ipoh, Malaysia.

Notes

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