College of Family Physicians Singapore

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New Horizons In Hypertension

RASILEZ® PROVIDES PROFOUND BP REDUCTIONS, ALONE AND IN COMBINATION[1]

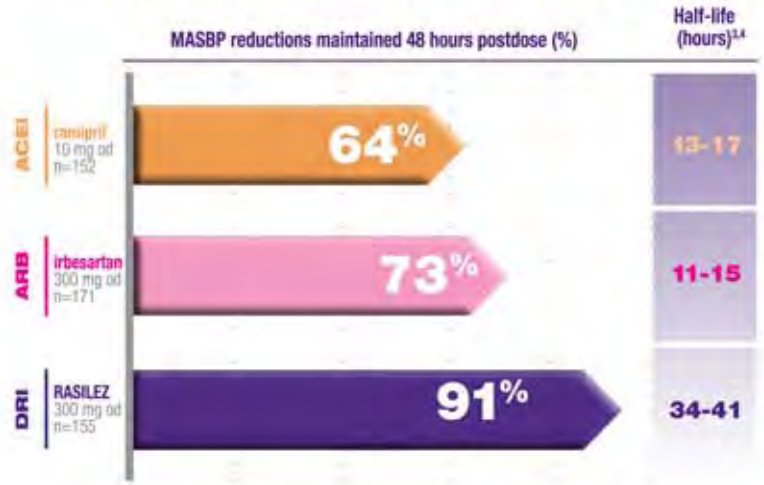
[1]This 12-week, double-blind randomized trial assessed the efficacy of aliskiren as monotherapy compared with the combination of aliskiren and hydrochlorothaizide in 688 patients with mean sitting SBP 160-<180mmHg. Patients were randomized to once daily aliskiren 150mg or Aliskiren /HCT 150/12.5mg. After 1 week, doses were doubled (forced titration) and treatment continued for an additional 11weeks

When Rasilez or HCT is not enough,

prescribe **RASILEZ *HCT*®**

RASILEZ® PROVIDES LONGER-LASTING EFFICACY THAN RAMIPRIL OR IRBESARTAN[2]

Percentage of BP efficacy maintained after a missed dose[2]



- **Provides long-lasting coverage if patients forget to take a tablet[2]**

[2]Adapted from Palatini P et al, *J Clin Hypertens*. 2008;10(suppl A):A31.

References: 1. Black HR, Kirkpatrick A, Palatini PA, et al. Aliskiren as monotherapy or in combination with hydrochlorothiazide provides effective BP lowering in patients with systolic BP 160-<180 mm Hg (ACQUIRE study) [Abstract PO-13]. J Clin Hypertens. 2010;12(suppl 1):A24. 2. Palatini P, Jung W, Schlaepfer E, et al. Blood pressure reduction following a simulated missed dose of aliskiren, irbesartan or ramipril: a comparative ambulatory blood pressure monitoring study. J Clin Hypertens. 2008;10(suppl A):A31-A32. Abstract P-62. 3. Lacy CF, Armstrong LL, Goldman MP, Lance LL. Drug Information Handbook: A Comprehensive Resource for All Clinicians and Healthcare Professionals. 14th ed. Hudson, Ohio: Lexi-Comp Inc; 2006. 4. RASILEZ (summary of product characteristics). Basel, Switzerland: Novartis Pharma AG; 2007.

RASILEZ® Presentation: Aliskiren. Film-coated tablets containing 150 mg and 300 mg of aliskiren. **Indications:** Treatment of essential hypertension. **Dosage:** 150 mg to 300 mg once daily, alone or in combination with other antihypertensive agents. **Contraindications:** Hypersensitivity to aliskiren or to any of the excipients, pregnancy, history of angioedema with aliskiren. **Precautions/Warnings:** Not recommended with cyclosporin. Not recommended during pregnancy or when planning to become pregnant. To be discontinued if pregnancy occurs. Rare cases of hypotension after initiation of treatment. Close medical supervision in patients with an activated renin-angiotensin system (e.g. volume- and/or salt-depleted patients). Caution in patients with severe renal dysfunction, renal artery stenosis, a history of dialysis, nephrotic syndrome, or renovascular hypertension. **Interactions:** Monitoring when used concomitantly with furosemide. Interactions with cyclosporin, ketoconazole, atorvastatin, verapamil. Concomitant treatment with drugs that may increase serum potassium levels. **Adverse Drug Reactions:** Common: Diarrhea, uncommon: Rash. Serious/rare: Angioedema. Laboratory values: decrease in haemoglobin and haematocrit, increase in serum potassium. Post-marketing reports: frequency unknown: Peripheral oedema.

RASILEZ HCT® Presentation: Film coated tablets containing 150 mg aliskiren (a renin inhibitor) and 12.5 mg hydrochlorothiazide (a thiazide diuretic), or 300 mg aliskiren and 12.5 mg hydrochlorothiazide or 150 mg aliskiren and 25 mg hydrochlorothiazide, or 300 mg aliskiren and 25 mg hydrochlorothiazide. **Indications:** Treatment of essential hypertension in adults. Indicated in patients whose blood pressure is not adequately controlled on aliskiren or hydrochlorothiazide used alone. Indicated as substitution therapy in patients adequately controlled with aliskiren and hydrochlorothiazide given concomitantly, at the same dose levels as in the combination. **Dosage:** One tablet of Rasilez HCT 150/12.5 mg or 300/12.5 mg or 150/25 mg or 300 mg/25 mg daily. **Contraindications:** • known hypersensitivity to the components of this product or to sulfonamides • pregnancy • severe hepatic impairment • severe renal impairment (creatinine clearance < 30 mL/min) • refractory hypokalaemia • hypercalcaemia • History of angioedema with aliskiren • Lactation • Concomitant use of aliskiren with ciclosporin, a highly potent P-glycoprotein (P-gp) inhibitor, and other potent p-gp inhibitors (quinidine, verapamil) **Warnings/Precautions:** • Avoid use in women planning to become pregnant and while breast-feeding • Risk of hypotension in sodium- and/or volume-depleted patients • Caution is advised when administering Rasilez HCT to patients with renal artery stenosis, renal and liver impairment or systemic lupus erythematosus. • Disturbance of serum electrolyte balance (monitoring recommended), glucose tolerance and serum levels of cholesterol, triglycerides and uric acid. • Not recommended when patient treated with ciclosporin • Caution in driving or operating machinery. • Caution with patients with history of allergy and asthma. • Not recommended in patients below 18 years of age. **Pregnancy:** Contraindicated **Breast-feeding:** Contraindicated **Driving and using machines:** Caution when driving or using machinery **Excipients:** Contains lactose **Interactions:** • Monitoring when used concomitantly with furosemide • Monitoring when used concomitantly with lithium • Caution when used concomitantly with drugs that may increase potassium levels. • Caution if combined with other antihypertensives, curare derivatives, NSAIDs, corticosteroids, ACTH, sympathicolytic, carbenoxolone, Penicillin G, Digoxin, anticiabetic agents, allopurinol, amantadine, diazoxide, cytotoxic drugs, anticholinergic agents, methyldopa, cholestyramine, vitamin D, calcium salts, , ketoconazole, atorvastatin, verapamil and ciclosporin **Adverse reactions:** Common (1 to 10%): Diarrhoea. For the aliskiren component, other reported adverse reactions include: Uncommon: Rash. Serious/rare: Angioedema. Laboratory values: decrease in haemoglobin and haematocrit, increase in serum potassium. For the hydrochlorothiazide component, other reported adverse reactions include: Urticaria and other forms of rash, decreased appetite, mild nausea and vomiting, postural hypotension Dizziness, photosensitivity reaction, abdominal discomfort, constipation, headache, sleep disorder, depression, paresthesia, visual disturbance, jaundice, arrhythmia, thrombocytopenia, waterborne with purpura, vasculitis necrotising and toxic epidermal necrolysis, cutaneous lupus erythematosus-like reactions, reactivation of cutaneous lupus erythematosus, pancreatitis, leukopenia, agranulocytosis, bone marrow depression, haemolytic anaemia, respiratory distress including pneumonitis and pulmonary oedema. Laboratory values: Neutropenia, elevations in and breakdowns. Electrolyte and metabolic disorders. (Nov 2007 SIN)

Important note: Before prescribing, consult full prescribing information.

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Rasilez® aliskiren

RasilezHCT® aliskiren/hydrochlorothiazide

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HYPERTENSION IN SINGAPORE

Adj Asst Prof (Dr) Tan Ngiap Chuan

SFP2011; 37(4) (Suppl I): 3-4

Hypertension affects a quarter of Singaporeans aged 30 to 69 years and is the commonest chronic disease that is managed in primary care. What is stunning was a local study which showed that 38.5% of hypertensive patients were previously undiagnosed. Age, male gender, obesity, smoking and diabetes are known risk factors for hypertension. It is more prevalent amongst Chinese men and Malay women. Salt ingestion is associated with hypertension. A survey revealed that 90% of Singaporeans exceeded the recommended daily salt intake.

Clinical blood pressure (BP) measurement is the most common method used for detection and monitoring of hypertension. However BP varies according to circadian rhythm and affected by the white-coat effect. Hypertensive patients with abnormal BP variability have increased risk of end organ damage and poorer outcome. Home BP monitoring (HBPM) and Ambulatory BP Monitoring (ABPM) eliminates the white-coat effect but requires patient involvement and added costs. Both HBPM and ABPM can better predict end organ damage and cardiovascular risk than clinic BP. Using validated HBPM devices, home BP can be measured at trough level of treatment to check on the therapeutic coverage throughout the dose-to-dose time interval. Patients are likely to achieve treatment target rapidly and the readings will reflect the effectiveness of their prescribed medications. ABPM is more costly and needs to be performed by cardiac technicians, which will restrict its use in the community.

Beyond the diagnosis, it is critical for hypertensive patients to have their BP treated to target levels. For hypertensive patients without diabetes mellitus and cardiovascular complications, they should aim to control their BP to be below 140/90 mm Hg, regardless of their age. Those with diabetes and other vascular diseases should target below 130/80 mm Hg. Every increase of 20 m Hg in systolic BP and 10 mm Hg in diastolic BP result in doubling of mortality from ischemic heart disease or stroke and this relationship is similar across all age groups between 40 to 89 years old.

Patients should thus be informed that their risks of complications rise significantly if they fail to meet their BO control target. However, studies have shown that only slightly more than a third of them achieve such good control and many succumb to complications such as cerebrovascular diseases (CVD) and peripheral vascular diseases (PVD).

TAN NGIAP CHUAN, Honorary Editor, Singapore Family Physician

The battle to combat hypertension is multi-pronged. Effective antihypertensive drug therapy should lower BP to below target level whilst maintaining normal 24-hour BP variability. Recent clinical trials have shown that combination therapy provides better 24-hour BP control. Such therapy has the combined efficacy of each component at lower dosages and thus with lesser side-effects and single pill combination improves patient adherence. Recent development includes renal sympathetic denervation therapy. It is a procedure with potential in controlling BP amongst patients who are already on multiple BP lowering drugs.

In the event that patients present with early symptoms of stroke, most will present to their primary care physicians (PCP). It is critical for PCP to recognize these early presentations of CVA so that patients are managed with appropriate emergency care in specialized Stroke Units in major hospitals in Singapore. Tools such as FAST and ABCD2 have been developed to assist PCP in early recognition of CVA and decision support to determine urgency of referral respectively.

PCP must not forget to screen periodically for PVD amongst their hypertensive patients. PVD is largely asymptomatic; amongst the minority with symptoms, presentation may be atypical. Apart from a good history, the Edinburgh Claudication Questionnaire can be used as a screening tool. Examination includes feeling for the peripheral pulses, recognition of signs of arterial insufficiency and measurement of ankle-brachial index (ABI). PVD is a signature for systemic atherosclerosis. PCP should proceed with other assessment of cardiovascular risks once PVD is diagnosed. Management of PVD includes aggressive risk factor modification (smoking cessation, treating diabetes, BP and LDL-cholesterol to control targets), a regular exercise program, anti-platelet therapy and referral for revascularization based on guidelines.

Patients are also educated to embark on self management of their BP control, such as home BP monitoring and to undertake regular cardiovascular exercises and selection of healthier food options.

PCP plays pivotal role in engaging these patients and motivating them to change their behavior to take on these recommended activities. PCP can make use of the Transtheoretical Model and Motivational Interviewing techniques to facilitate this change. Recognizing the heterogeneity of patients in terms of their stages of change will prompt the PCP to use different strategies to facilitate change. The use of guiding style, focusing on collaboration and respect for patient's autonomy, allows the PCP to explore and facilitate

patient's personal motivation to change. Such approaches will form a framework and methods for the PCP to modify their patient's behavior towards mutually agreed specific and achievable treatment targets.

Achieving treatment targets and permanent adoption of these healthy lifestyles are proven ways to reduce the plethora of hypertension related complications. This issue provides a good coverage of these strategies to enable the PCP to decrease the cardiovascular risks for their patients.

Distance Learning Course on "New Horzions in Hypertension"

- Overview of "New Horizons in Hypertension"
- Unit 1 : Overview & Epidemiology of Hypertension in Singapore
- Unit 2 : Reduction of Cardiovascular Risk through Detection and Treatment of Episodic Hypertension and Blood Pressure Variability
- Unit 3 : Cerebrovascular and Peripheral-vascular Complications
- Unit 4 : Behaviour Modification
- Unit 5 : Therapeutic Considerations
- Unit 6 : Renovascular Complications

OVERVIEW OF "NEW HORIZONS IN HYPERTENSION" FAMILY PRACTICE SKILLS COURSE

A/Prof Goh Lee Gan

SFP2011: 37(4) (Suppl I): 6-7

INTRODUCTION

In Singapore, hypertension is the most common condition seen at the Government outpatient clinics and also a commonly encountered condition in GP clinics. Just over 50% of all strokes and about half of all ischaemic heart diseases are attributable to hypertension. Yet, the number of patients whose blood pressure is well controlled is less than 40% in a 2006 survey in Singapore. Clearly, there is a lot of improvement to be made. The readings on new horizons in hypertension care in 2011 are contributed by the panel of speakers in this Family Practice Skills Course: they cover Home BP monitoring, preferred choices of antihypertensives, the single pill combination, and renal sympathetic denervation therapy for the multidrug resistant hypertension, motivational interview, as well as information on cerebrovascular complications, peripheral artery disease, and renal vascular complications. The College thanks Novartis (Singapore) Pte Ltd for sponsoring this Family Practice Skills Course for primary care doctors. Come and update yourself and push up the prevalence of good BP control in your patients to far beyond 50%.

COURSE OUTLINE AND CME POINTS

This Family Practice Skills Course is made up of the following components. You can choose to participate in one or more parts of it. The CME points that will be awarded are also indicated below.

Components and CME Points

- Distance Learning Course – 6 units (6 Core FM CME points upon attaining a minimum pass grade of 60% in Distance Learning Online MCQ Assessment).
- 2 Seminars (2 Core FM CME points per seminar).
- 2 Workshops (1 Core FM CME point per workshop).
- 10 Readings – read 5 out of 10 recommended journals (maximum of 5 CME points for the whole CME year).

Distance Learning Course

Unit 1: Overview & Epidemiology of Hypertension in Singapore
A/Prof Terrance Chua Siang Jin

Unit 2 : Reduction of Cardiovascular Risk through Detection and Treatment of Episodic Hypertension and Blood Pressure Variability
Dr Goh Ping Ping

Unit 3 : Cerebrovascular and Peripheral-vascular Complications
Dr Chadachan Veerendra Melagireppa, Dr Tay Jam Chin

Unit 4 : Behaviour Modification
Dr Tan Yew Seng

Unit 5 : Therapeutic Considerations
Dr Akira Wu

Unit 6 : Renovascular Complications
Prof A Vathsala

COURSE TOPIC DETAILS

Unit 1: Overview & Epidemiology of Hypertension in Singapore

- Prevalence
- Undiagnosed hypertension
- Risk factors
- Blood Pressure Control
- Complications of hypertension
- Chronic disease programs

Unit 2: Reduction of Cardiovascular Risk through Detection and Treatment of Episodic Hypertension and Blood Pressure Variability

- Introduction
- What is BP variability
- Role of blood pressure variability in the development of cardiovascular risk
- Role of blood pressure monitoring in tracking and controlling BP variability
- Home BP monitoring (HBPM) and ambulatory BP monitoring (ABPM)
- Normal values
- Choice of antihypertensive agents

Unit 3: Cerebrovascular and Peripheral-vascular Complications

Cerebrovascular complications of hypertension

- Background
- Clinical evaluation
- Diagnosis
- Management of cerebrovascular complications
- Management in the pre-admission phase
- Management in the post-discharge phase
- Referral guidelines

Peripheral vascular complications of hypertension

- Background
- Clinical evaluation
- Diagnosis
- Management of patients with peripheral vascular disease
- Referral guidelines

GOH LEE GAN, Associate Professor, Division of Family Medicine, University Medicine Cluster, National University Health System
Senior Consultant, Institute of Family Medicine, College of Family Physicians Singapore

Unit 4: Behaviour Modification
- Changing health threatening behaviours
- Understanding how change takes place
- What's in TTM for the practitioner?
- But the patient is just not motivated to change!
- How can we do it better?
- Is there a best way to behaviour change?
- Will I be able to have the time to do this?

Unit 5: Therapeutic Considerations
- Introduction
- Causes of hypertension
- Single pill combination therapy
- Renal denervation therapy

Unit 6: Renovascular Complications
- Prevalence of hypertension in the Singapore Population
- Renal effects of hypertension
- Management of hypertension

FACE-TO-FACE SESSIONS

Seminar 1: 15 October 2011
2.00pm – 4.15pm

Unit 1 : Overview & Epidemiology of Hypertension in Singapore
A/Prof Terrance Chua Siang Jin

Unit 2 : Reduction of Cardiovascular Risk through Detection and Treatment of Episodic Hypertension and Blood Pressure Variability
Dr Goh Ping Ping

Unit 3 : Cerebrovascular and Peripheral-vascular Complications
Dr Chadachan Veerendra Melagireppa

Workshop 1: 15 October 2011
4.30pm – 5.45pm

Global Assessment on Cardiovascular Risks
Dr Goh Ping Ping

Seminar 2: 16 October 2011
2.00pm – 4.15pm

Unit 4 : Behaviour Modification
Dr Tan Yew Seng

Unit 5 : Therapeutic Considerations
Dr Akira Wu

Unit 6 : Renovascular Complications
Prof A Vathsala

Workshop 2: 16 October 2011
4.30pm – 5.45pm

DASH Diet Application
Gladys Wong

UNIT NO. 1

OVERVIEW & EPIDEMIOLOGY OF HYPERTENSION IN SINGAPORE

A/Prof Terrance Chua Siang Jin

ABSTRACT

In Singapore, hypertension is the most common condition noted at outpatient visits, present in 16.6% of all polyclinic attendances in 2009. Close to a quarter of all Singaporeans aged 18 to 69 have hypertension. Based on successive National Health Surveys, the crude prevalence of hypertension was 22% in 1992, rising to 27% in 1998 and falling to 24.9% in 2004. In this survey, 38.5% of hypertensives were previously undiagnosed and undiagnosed hypertension was more common in men (44%) compared to women (30%). Blood pressure screening, both in opportunistic settings when patients seek medical care for unrelated problems and as part of mass public health screening is therefore important. Apart from increasing age, other factors such as gender (men), obesity, and diabetes are established risk factors for hypertension. The percentage of hypertensive patients with good BP control (<140/90 mmHg) was 49.5% from the 2004 National Health Survey, with better control in Chinese compared to Malays and Indians. However, only 37.7% of hypertensives had good control in a 2006 survey of hypertensive patients in 9 polyclinics. This was much worse in an elderly population, with 64% not being optimally controlled. Effective treatment of hypertension has been clearly shown to reduce the risk complications, even in the elderly. Screening for hypertension and effective treatment remains an important goal for all of us. There is growing evidence of the importance of effective patient education and home monitoring in the control of hypertension.

Keywords: Hypertension, Prevalence, Singapore, Screening, Treatment, Elderly

SFP2011; 37(4) (Suppl I): 8-9

PREVALENCE

In Singapore, hypertension is the most common condition noted at outpatient visits, present in 16.6% of all polyclinic attendances in 2009. Close to a quarter of all Singaporeans aged 18 to 69 have hypertension[1]. Based on successive National Health Surveys, the crude prevalence of hypertension was 22% in 1992, rising to 27% in 1998 and falling to 24.9% in 2004 [1]. The prevalence rises with age, from 8% between 30-39 years to 56% for those aged 60 to 69 years old in the 2004 survey. Comparing our figures to the west, age- and sex-adjusted prevalence of hypertension was 28% in North American countries and 44% in the European countries at the 140/90 mm Hg threshold[2,3].

TERRANCE CHUA SIANG JIN, Deputy Director, Senior Consultant, Cardiology, National Heart Centre Singapore

UNDIAGNOSED HYPERTENSION

One major concern at the 2004 survey 1 was that 38.5% of hypertensives were previously undiagnosed, though this represents some improvement over 1998, when 53% were undiagnosed. Undiagnosed hypertension was more common in men (44%) compared to women (30%). Hence the importance of screening, both in opportunistic settings when patients seek medical care for unrelated problems and as part of mass public health screening.

RISK FACTORS

Age is an obvious risk factor for hypertension. In one survey of elderly Singaporeans (age > 60 years), 73% were hypertensive [4], 30.8% were unaware of the condition, and 32% were not being treated. In contrast, in a military survey [5] of young conscripts in Singapore, hypertension was found to be uncommon (1.6%).

Among the few that had hypertension in this age-range, there were strong associations with obesity and low socio-economic status. Apart from increasing age, other factors such as gender (men), obesity, and diabetes are established risk factors for hypertension.

There are also survey data to suggest a higher prevalence of hypertension in low-income neighborhoods [6]. There is also an established link between obstructive sleep apnoea and hypertension, and this has also been demonstrated in Singapore populations [7]. Ethnicity also appears to influence the prevalence of hypertension.

In the 2004 survey, the highest prevalence of hypertension was in Chinese men, then Indians, and Malays, whereas for women, it was more common in Malays, then Chinese and Indians [1]. Salt intake is clearly linked to hypertension. The 1998 National Nutrition Survey revealed that 9 out of 10 Singaporeans exceeded the recommended allowance of salt.

BLOOD PRESSURE CONTROL

The percentage of hypertensive patients with good BP control (<140/90 mmHg) was 49.5% from the 2004 National Health Survey 1, with better control in Chinese compared to Malays and Indians. However, only 37.7% of hypertensives had good control in a 2006 survey of hypertensive patients in 9 polyclinics.[8] This was much worse in an elderly population,

with 64% not being optimally controlled [4]. There is the pervasive belief that elevated blood pressure is "normal" as one grows older, and therefore no treatment is needed. Yet randomized controlled trials have clearly shown benefit, even in elderly patients [9]. Care should be taken to avoid orthostatic hypotension, though, in this population.

COMPLICATIONS OF HYPERTENSION

Apart from stroke, heart failure and myocardial infarction, renal damage is a well established consequence of hypertension, hence the value of screening for microalbuminuria as a marker of end-organ damage. One local study found that 48.5% of hypertensive diabetics had microalbuminuria [10].

CHRONIC DISEASE PROGRAMS

There is growing evidence of the importance of effective patient education and home monitoring in the control of hypertension. One local pilot study in diabetics found significantly better control of diabetes and hypertension using a comprehensive chronic care program in a primary care setting [11].

CONCLUSIONS

- Although there are encouraging trends based on serial national health surveys, hypertension continues to be a highly prevalent condition afflicting one-quarter of Singaporeans, and a major risk factor for stroke, heart failure, myocardial infarction and renal failure.
- Despite awareness of this condition, close to 40% of patients were undiagnosed, and only half had good control in 2004.
- Yet hypertension today is easily treated with a wide array of medications available. Moreover effective treatment of hypertension has been clearly shown to reduce the risk complications, even in the elderly.
- Therefore screening for hypertension and effective treatment remains an important goal for all of us.

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LEARNING POINTS

- **In Singapore, hypertension is the most common condition noted at outpatient visits, present in 16.6% of all polyclinic attendances in 2009.**
- **In 2004, close to 40% of patients were undiagnosed, and only half had good control.**
- **Apart from increasing age, other factors such as gender (men), obesity, and diabetes are established risk factors for hypertension.**
- **Only 37.7% of hypertensives had good control (<140/90 mmHg) in a 2006 survey of hypertensive patients in 9 polyclinics. This was much worse in an elderly population, with 64% not being optimally controlled.**
- **Effective treatment of hypertension has been clearly shown to reduce the risk complications, even in the elderly.**
- **There is growing evidence of the importance of effective patient education and home monitoring in the control of hypertension.**
- **Screening for hypertension and effective treatment remains an important goal for all of us.**

UNIT NO. 2

REDUCTION OF CARDIOVASCULAR RISK THROUGH DETECTION AND TREATMENT OF EPISODIC HYPERTENSION AND BLOOD PRESSURE VARIABILITY

Dr Goh Ping Ping

ABSTRACT

Optimal treatment of hypertension includes both achieving target blood pressure and maintaining normal diurnal variation. Home blood pressure monitoring and ambulatory blood pressure monitoring provide multiple readings in an out-of-office setting and enable the clinician to identify subsets of patients at increased risk despite normal clinic readings. Effective antihypertensive agents are available, especially in combination therapy, to reduce abnormal fluctuations in blood pressure and improve outcome.

Keywords: diurnal variation, home blood pressure monitoring, ambulatory blood pressure monitoring, combination therapy

SFP2011; 37(4) (Supp 1): 10-14

INTRODUCTION

Hypertension is highly prevalent in developed countries and is a major risk factor for cardiovascular and renal diseases. In Singapore, up to 25% of adults aged 30 to 69 years old are reported to be hypertensive by a Ministry of Health survey 1. In a meta-analysis of 61 prospective studies, every increase of 20 mmHg in systolic blood pressure (BP) and 10 mmHg in diastolic BP correlate with doubling of mortality from ischemic heart disease or stroke, and the relationship is similar across all age groups between 40 to 89 years old [2]. Control of BP is an important component of an overall strategy to improve cardiovascular health.

WHAT IS BP VARIABILITY

Hypertension treatment guidelines recommend lowering BP to below target level to reduce end organ damage. Besides achieving the target level of 140/90 mmHg for the general population, it is equally important to assess and control BP variability. In normal circadian rhythm, night-time BP is 10-20% lower than day-time, with a steeper increase in early morning and followed by more gradual increase throughout the awake hours.

This normal circadian rhythm can be disrupted in various subsets of hypertensive patients.

GOH PING PING, Cardiologist, Cardiac Specialist Centre, Mount Elizabeth Medical Centre, Chief and Senior Consultant, Department of Cardiology, Changi General Hospital

Some important terminology to note:

- Non-dipper: failure of nocturnal BP to decrease by at least 10% of daytime BP.
- Riser: paradoxical increase of nocturnal BP above the daytime BP.
- Extreme dipper: extremely large night-time BP drop.

ROLE OF BLOOD PRESSURE VARIABILITY IN THE DEVELOPMENT OF CARDIOVASCULAR RISK

Hypertensive patients who exhibit abnormal BP variability have increased risk of end organ damage and poorer outcome. In 2 large hypertension treatment trials, the United Kingdom Transient Ischemia Attack (UK-TIA) and ASCOT-Blood Pressure Lowering Arm (ASCOT-BPLA) trials, excessive variability in systolic BP was associated with increased risk of cardiovascular events [3, 4]. This was postulated to be linked to arterial stiffness, changes in peripheral vascular resistance and structural remodelling of arteries. In particular, the early morning surge in BP is associated with a higher risk of acute myocardial infarction, sudden death and stroke. Hence, cardiovascular risk can remain high in the individual patient whose average BP (usually assessed during clinic visits) falls below target BP but who may still exhibit significant BP variability, especially with an early morning surge. In the ASCOT-BPLA substudy, it was further shown that treatment to reduce BP variability was associated with reduction in cardiovascular event rate.

ROLE OF BLOOD PRESSURE MONITORING IN TRACKING AND CONTROLLING BP VARIABILITY

Clinic BP is the most common method used for detection and monitoring of hypertension. However, it may be fraud with the problem of white coat effect, which may affect as many as up to 20% of patients [5]. On the other hand, some patients with normal BP in the clinic may have pressures that spike to dangerous levels in other situations.

Home BP Monitoring (HBPM) and Ambulatory BP Monitoring (ABPM) eliminate the problem of white coat hypertension but requires greater patient involvement and added costs. They also have the advantage of being able to detect diurnal variation and early morning surge of BP. Both HBPM and ABPM have been shown to provide better prediction of end organ damage and cardiovascular risk compared to clinic BP [6, 7, 8]. These modalities are particularly useful in the elderly who are more prone to BP variability and

white coat effect, as well as patients with diabetes, kidney disease and pregnant women. The advantages of HBPM and ABPM are summarised in Table 1.

The European Society of Hypertension recommends validated, semi-automated devices with self-inflating cuffs for home BP measurement. When done properly, it is a better reflection of BP control compared to isolated clinic BP. Home BP can be taken at trough level of treatment to check on the therapeutic coverage throughout the dose-to-dose time interval. Patients are likely to achieve goals more quickly and be confident that medicines are working for them.

ABPM needs to be performed by a cardiac technician or nurse. It is more costly and less repeatable than HBPM. However, it provides a complete picture of diurnal variation especially the night-time BP profile. The latter has been shown to be superior to day-time ambulatory BP as a predictor of cardiovascular outcome 9. Figures 1 and 2 are examples of a normal and abnormal ABPM tracing respectively.

Table I. Advantages for Ambulatory and Home BP monitoring

Home BP monitoring

- useful for initial diagnosis when suspect white coat effect
- convenient, able to do multiple readings
- easy to perform by self or caregiver
- low-cost monitors are available
- improves adherence and BP control

Ambulatory BP monitoring

- useful for initial diagnosis when suspect white coat effect
- true assessment of diurnal variation
- identifies high risk subgroups (non-dipper, inverse dipping)
- can detect hypotensive episodes especially in elderly and diabetics
- large body of evidence for prognostication

NORMAL VALUES

For Home BP monitoring, 3 readings are recommended, taken 1 minute apart. Although the first reading is typically the highest, an average of the 3 readings is used as the BP reading. The American Society of Hypertension recommends an upper limit of 135/85 mmHg for Home BP [10].

For Ambulatory BP monitoring, the upper limits of normal are 135/85 mmHg for daytime, 120/70 mmHg for night-time and 130/80 mmHg for average BP over 24 hours [5]. As with clinic BP monitoring, a lower goal is advisable for special groups such as diabetes, renal failure and pregnancy.

Choice of Antihypertensive Agents

Effective antihypertensive treatment should lower BP to below target level while maintaining normal 24-hour BP variability. In particular, BP control should prevent the high risk early morning spike when most cardiovascular and cerebrovascular events occur.

Recent data has shown that combination therapy can provide superior 24-hour BP control. In the ASCOT study, a combination of calcium channel blocker (Amlodipine) and ACE-I (Perindopril) was shown to be more effective than beta-blocker/thiazide in reducing systolic BP variability [3]. This resulted in reduction of stroke and coronary events between the two treatment groups. This approach is similar to the NICE hypertension guideline, which recommended starting with a calcium channel blocker (CCB) or thiazide diuretic for patients 55 years old or older and an ACE-I (or Angiotensin Receptor Blocker if intolerant of ACE-I) for patients below 55 years old. Subsequently if control is suboptimal, a combination of the CCB and ACE-I or diuretic with ACE-I can then be used.

Combination therapy has the combined efficacy of the individual components used at lower dosages and thus with fewer side effects. Furthermore, single pill combination has been shown to improve patient adherence.

It is useful to note that combination of antihypertensive agents have been categorised by the American Society of Hypertension in order of preference as "Preferred", "Average" or "Unacceptable". This recommendation also includes the newest class of antihypertensive i.e. Renin Inhibitors [11].

"Preferred" combinations are ACE-Inhibitor (ACE-I)-Diuretic, Angiotensin Receptor Blocker(ARB)-Diuretic, ACE-I-Calcium channel blocker(CCB) and ARB-CCB.

"Average" combinations are betablocker-diuretic, CCB (dihydropyridine)-betablocker, CCB/diuretic, Renin-inhibitor-diuretic, Renin-inhibitor-ARB, Thiazide diuretic-Potassium sparing diuretic.

"Unacceptable" combinations are ACE-inhibitor-ARB, ACE-ihhibitor-betablocker, ARB-betablocker, CCB (nondihydropyridine)-betablocker, centrally acting agent-beta blocker.

Ultimately, the choice of therapy also depends on patient factors such as tolerability and cost.

CONCLUSIONS

Optimal hypertension care should include BP monitoring to provide the clinician with a comprehensive BP profile of the patient. To this end, ABPM and HBPM have complementary roles. This approach draws the clinician's attention to particular area of vulnerability for each patient. Together with wider and better choices of antihypertensive agents, especially combination therapies with proven efficacy, the clinician is able to achieve better and more individualised care for hypertensive patients.

Illustrations

Figure 1. 24 –hour Ambulatory BP Monitoring of a patient with well controlled BP and normal diurnal variation. Note that the BP falls during sleep (arrowed line).

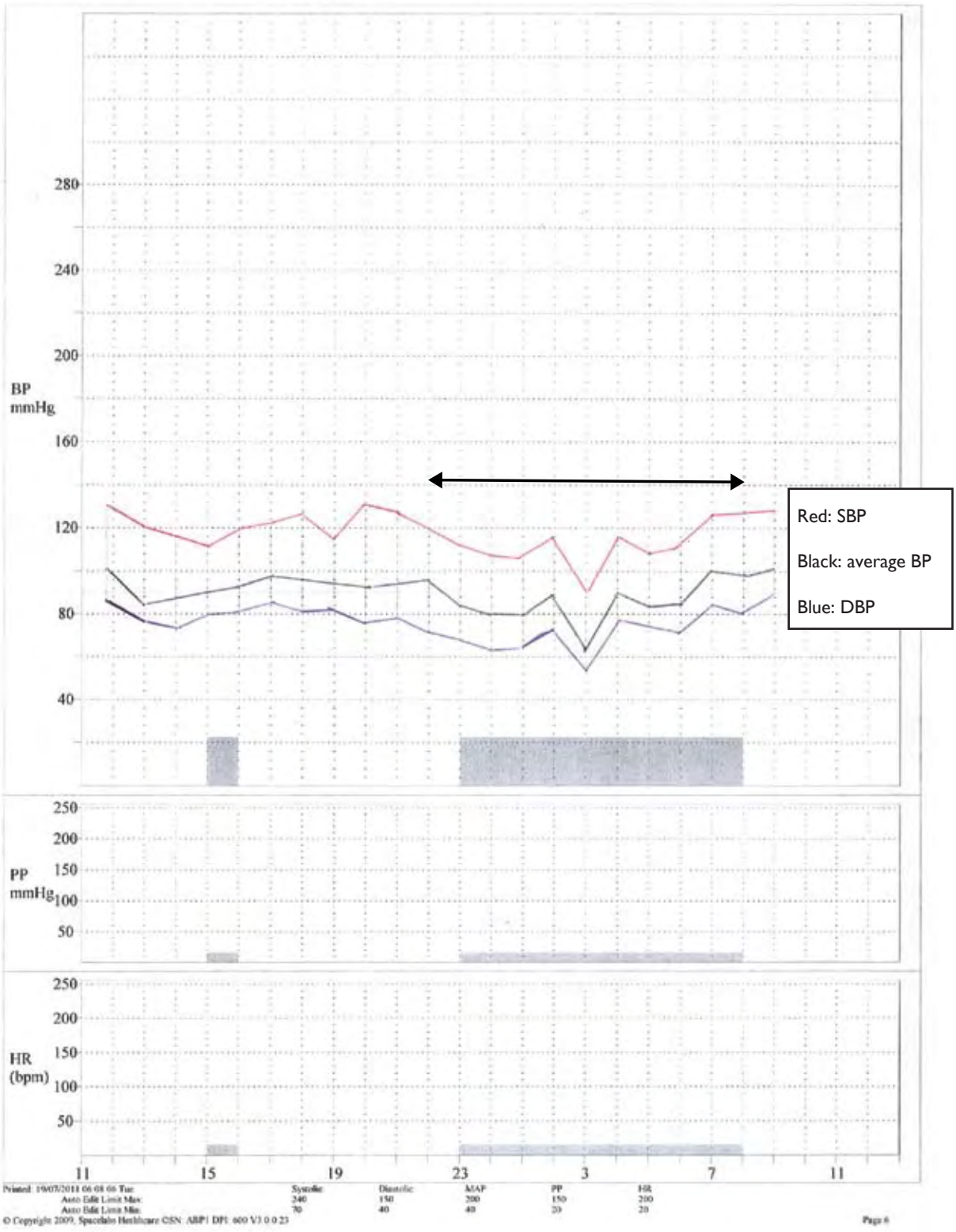
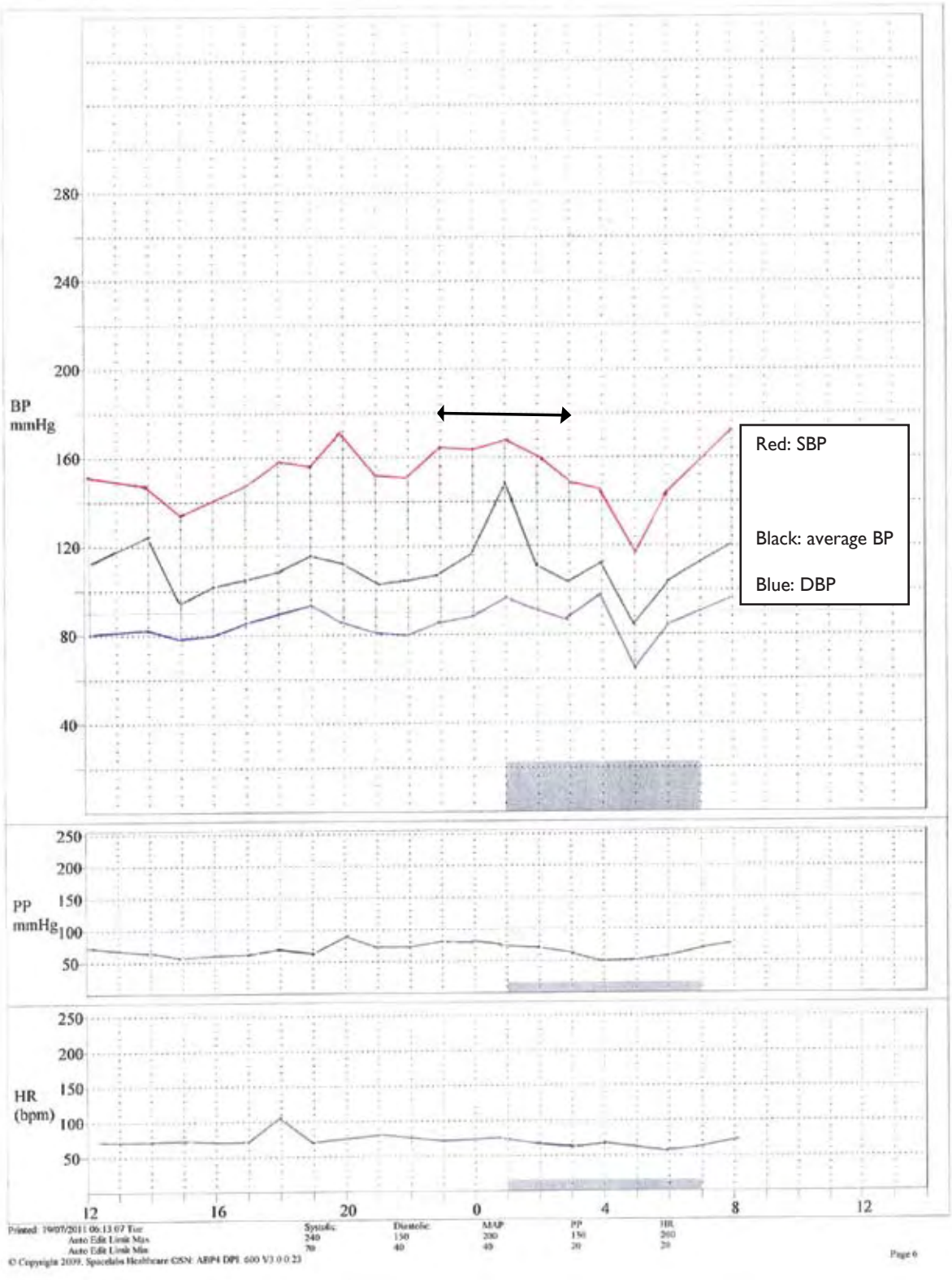


Figure 2. 24 –hour Ambulatory BP Monitoring of a patient whose BP is not well controlled.
There is loss of diurnal variation and BP rises paradoxically during first half of sleep time (arrowed line).



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LEARNING POINTS

- **Optimal hypertension care should include BP monitoring to provide the clinician with a comprehensive BP profile of the patient.**
- **Hypertensive patients who exhibit abnormal BP variability – non-dipper, riser, extreme dipper -- have increased risk of end organ damage and poorer outcome.**
- **The American Society of Hypertension recommends an upper limit of 135/85 mmHg for Home BP**
- **Choice of antihypertensive agents are grouped in order of preference into "preferred combinations", "average combinations", and "unacceptable combinations".**

UNIT NO. 3

CEREBROVASCULAR AND PERIPHERAL VASCULAR COMPLICATIONS

Dr Chadachan Veerendra Melagireppa, Dr Tay Jam Chin

ABSTRACT

Hypertension is one of the most important global public health challenges and is among the most common conditions seen at the primary care office setting. Hypertensive patients are at increased risk of developing cerebrovascular diseases (CVD) and peripheral vascular diseases (PVD). Patients who have established CVD and PVD are not only associated with significant morbidity and mortality in short term from the disease itself, but also in long term from recurrent events and from associated cardiovascular disease. While in patients with CVD, the primary disease is by itself life-threatening, in patients with PVD, the major life threatening problems are more from associated cardiovascular disease and CVD. Hence primary care physicians are often faced not only with challenges of diagnosing and managing these complications in the short term, as well as with secondary prevention of recurrent events in the long term. In this article, we will present guidelines on diagnosis, clinical evaluation and management of these complications of hypertension at a primary care office testing. We will also present guidelines on when to refer patients with the complications to Specialist services.

Keywords: Cerebrovascular Complications, Peripheral Vascular Complications, Face Arm Speech Test, Transient ischaemic attack, ABCD2 score.

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CEREBROVASCULAR COMPLICATIONS OF HYPERTENSION

Background

Hypertension is the single most important modifiable risk factor for stroke [1]. There is a close linkage between hypertension and cerebrovascular disease. It has been estimated that about 54% of strokes worldwide are attributable to hypertension [2]. The degree of elevation of blood pressure (BP) is also tightly correlated with the risk of stroke. Detailed analysis of large cohort studies have shown that the relationship between BP and risk of stroke is continuous, consistent and independent of other risk factors [3].

It has also been shown that hypertension increases the risk of both ischemic as well as hemorrhagic strokes [4]. Among the ischemic strokes, although hypertension-related strokes are mainly lacunar infarcts from small-vessel disease, hypertension also plays a key role in the pathogenesis of large artery atherosclerosis, which in turn causes ischemic stroke due to thrombotic arterial occlusion, artery-to-artery embolism, or a combination of both these factors.

In this section of the article we will review the clinical evaluation and management of cerebrovascular disease in hypertensive patients at a primary care setting.

Clinical Evaluation

Most (95%) people will have their first symptoms of cerebrovascular accidents outside the hospital and may initially present to the primary care physician. Therefore it is vital that the primary care physicians can recognise stroke as accurately as possible to facilitate appropriate emergency care. It is also essential that they treat patients with symptoms suggestive of an acute stroke as an emergency and organise urgent transfer to a centre with specialised hyperacute stroke services such as a Stroke unit. This is especially true for those patients who are seen within the first three hours of the onset of stroke symptoms, who require to be transferred directly to a specialised hyperacute stroke unit for assessment for the need for thrombolysis.

Diagnosis Of Cerebrovascular Accidents (CVA)

Stroke is defined as an acute onset of neurological symptoms which result from impaired cerebral vascular perfusion and persist for more than 24 hours. Transient ischemic attack is defined as transient and acute onset of neurological symptoms which recover within 24 hours and most of the times within one hour [5].

Initial diagnosis of CVA is based mainly on the history and physical examination. At a primary care office setting, when a patient presents with a sudden onset of neurological symptoms, a validated tool, such as FAST (Face Arm Speech Test), should be used to screen for diagnosis of stroke or TIA (See Table 1) [6].

Of course it is important to exclude hypoglycemia in all patients who present with sudden onset of neurological symptoms. If a patient is suspected to have stroke, further management is determined by the type of stroke. Hence the process of diagnosis will need to establish whether or not the stroke is due to ischaemia (approximately 80% of all strokes) or due to intracerebral haemorrhage (approximately 20% of all strokes). Moreover, those with ischaemic strokes presenting within three hours of onset of symptoms should be assessed for thrombolysis in centres with staff and systems in place to deliverthis intervention. Therefor all patients with suspected stroke should be referred for admission to a specialised acute

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stroke unit. There is also evidence that stroke patients have better long term outcomes if they are managed in a Stroke units rather than in a general ward or in the community [7].

Table 1. FAST screening tool for diagnosis of CVA

Facial weakness	Can the person smile? Has their mouth or eye drooped?
Arm weakness or numbness	Can the person raise both arms? Is there numbness in either arm?
Speech problems	Can the person speak clearly and understand what you say?
Time: Act FAST	Stroke is a medical emergency Call Ambulance – early treatment can prevent further brain damage

If a patient is diagnosed to have TIA symptoms, then he/she should be referred to the Specialist Neurology clinic as soon as possible. The urgency of referral depends upon the risk of recurrent TIA or stroke after the initial TIA event. This risk can be assessed using the ABCD2 score computation (See Table 2) [8].

Table 2. ABCD2 Score for estimation of Stroke Risk after TIA

Age	≥ 60 yrs	1 point
	< 60 yrs	0 points
Blood pressure	≥ 140/90	1 point
	< 140/90	0 points
Clinical Features	Speech impairment without weakness	1 point
	Unilateral weakness	2 points
Duration of symptoms	10-59 mins	1 point
	≥ 60 mins	2 points
Diabetes	Yes	1 point

ABCD2 algorithm predicts a patient's very early risk of stroke following a TIA. The corresponding 2- day risks for a subsequent stroke are shown in Table 3 [9].

Table 3. ABCD2 Score and Risk of subsequent stroke

ABCD2 score	Risk of stroke at 2 days	Urgency of Referral
0-3	1%	Within 7 days
4-5	4%	Within 24 hours
6-7	8%	Within 24 hours

High risk patients (ABCD2 score 4 and above) should be assessed at the Specialist Neurology clinic within 24 hours of first presentation to the primary care doctor.

Low risk patients (ABCD2 score 3 or lower) should be assessed at the Specialist clinic within 7 days of first presentation to the primary care doctor.

Management Of Cerebrovascular Complications

Role of primary care physicians in CVA is biphasic. First phase is management of stroke (or TIA) before admission to hospital (or before specialist consultation for TIA). Second phase is the long term management of stroke patients after they are discharged from the hospital.

Management In Pre-Admission Phase

Acute Stroke

All patients with suspected stroke should be referred for admission to a specialised acute stroke unit.

Brain imaging (CT scan or MRI/MRA) should be performed immediately, if available at the Family practice setting, for patients with acute stroke to determine the type of stroke.

All people presenting with acute stroke who have had a diagnosis of primary intracerebral haemorrhage excluded by brain imaging should, as soon as possible but certainly within 24 hours, be given aspirin 300 mg orally [10].

All patients with acute stroke should have their swallowing screened before being given any oral food, fluid or medication.

Management of hypertension in the acute stroke situation is a matter of debate. Most guidelines recommend antihyper tensive treatment in the acute setting of stroke in patients scheduled for thrombolysis if blood pressure is above 185/110 mmHg. If thrombolysis is not indicated antihypertensive treatment is recommended when blood pressure is above 220/110 mm Hg or if there is a hypertensive emergency.

Subsequent management of patients with acute stroke is carried out in-patient at the Specialised Stroke units.

Transient Ischemic Attacks (TIA)

Patients with suspected TIA who are at high risk of stroke (that is, with an ABCD2 score of 4 or above) should have aspirin (300 mg daily) started immediately and referred to Specialist assessment and investigation within 24 hours of onset of symptoms. Measures for secondary prevention introduced as soon as the diagnosis is confirmed, including modification of individual risk factors [11].

Patients with crescendo TIA (two or more TIAs in a week) should be treated as being at high risk of stroke, even though they may have an ABCD2 score of 3 or below [11].

Patients who have had a suspected TIA who are at lower risk of stroke (that is, an ABCD2 score of 3 or below) should have aspirin (300 mg daily) started immediately and referred to Specialist assessment and investigation as soon as possible, but definitely within 1 week of onset of symptoms. Measures for secondary prevention again should be introduced as soon as the diagnosis is confirmed, including modification of individual risk factors [11].

Patients who have had a TIA but who present late (more than 1 week after their last symptom has resolved) should be treated as though they are at lower risk of stroke [11].

Management In Post-Discharge Phase

Poststroke outpatient care largely focuses on rehabilitation and secondary prevention of recurrent stroke.

Rehabilitation

Rehabilitation planning and initiation begins within the first day of the acute stroke. Recent research has demonstrated the benefits of early and aggressive mobilization.

Secondary prevention of recurrent stroke or TIA

From the moment a person has an acute cerebrovascular event, that person is at an increased risk of further stroke and other vascular events. The risk of further stroke is highest early after stroke or TIA and may be as high as 10% within the first week, 20% within the first month, and between 30% and 43% over the next five years.

For each patient, an individualised and comprehensive long-term strategy for stroke prevention should be implemented as soon as possible following a TIA or stroke.

Life-style recommendations

1. All patients who smoke should be advised to stop smoking.
2. All patients should be advised to eat the optimum diet.
3. All patients should be advised to take regular exercise as far as they are able to.

Blood pressure recommendations

1. All patients should have their blood pressure checked, and should be treated in keeping with the recommended guidelines. An optimal target BP for patients with established cardiovascular disease is 130/80 mmHg.

2. In hypertensive patients aged 55 or older, the first choice for initial therapy should be either a calcium-channel blocker or a thiazide-type diuretic. In hypertensive patients younger than 55, the first choice for initial therapy should be an angiotensin-converting enzyme (ACE) inhibitor (or an angiotensin-II receptor antagonist if an ACE inhibitor is not tolerated). An ACE inhibitor, calcium-channel blocker or a thiazide-type diuretic should be added if target BP is not achieved with the initial choice

3. Beta blockers should not usually be initiated as first or second-line for the prevention of recurrent stroke (unless there are other specific clinical indications).

Lipid lowering therapy recommendations

All patients who have had an ischaemic stroke or a transient ischaemic attack should be treated with a statin drug unless contraindicated, if the total cholesterol is more than 3.5mmol/L, or LDL cholesterol is more than 2.6mmol/L

REFERRAL GUIDELINES

Stroke

1. All patients with suspected stroke should be referred to a hospital with a specialist acute stroke unit to allow medical stabilization and assessment of factors that may lead to complications. With the advent of thrombolysis, speed of admission is paramount.

2. The primary care physician is also responsible for the general medical care of people who have had a stroke and have been discharged from hospital. They should ensure that problems related to stroke are detected early and, when necessary, referred to the appropriate community health service, local social services, and specialists in secondary care, including an occupational therapist, a physiotherapist, and a speech therapist.

3. Remember to address psychosocial issues as depression is common, affecting up to half of all those who have suffered a stroke. If depression is detected then a prompt referral should be considered for psychiatric evaluation.

Transient Ischaemic Attack

1. If a patient presents with TIA symptoms they should be referred to the Specialist Neurology clinic as soon as possible. The risk of recurrent event is assessed using the ABCD2 score computation.

2. High risk patients (ABCD2 score 4 and above) should be assessed at the Specialist's clinic within 24 hours of first presentation to a primary care doctor.

3. Low risk patients (ABCD2 score 3 or lower) should be assessed at the Specialist's clinic within 7 days of first presentation to the primary care doctor.

PERIPHERAL VASCULAR COMPLICATIONS OF HYPERTENSION

Background

Hypertension is an important risk factor for the development of Peripheral vascular disease (PVD). There is a strong link between blood pressure and the risk of developing PVD in the future. In the Framingham Heart Study, the higher an individual's blood pressure, the more likely he/she was to develop PVD [12]. On the other hand, the patients with PVD also have higher prevalence of hypertension. About 70-80% of patients with PVD have hypertension. And finally, the presence of peripheral vascular disease carries an increased risk of developing cardiovascular events [13]. This risk is further shown to

be augmented by the presence of hypertension. Thus it is very important to look for PVD in patients with hypertension. Unfortunately, PVD remains under-diagnosed in primary care settings. Many a times, PVD remains asymptomatic with only a quarter of patients having symptoms. Secondly, most patients with PAD do not present with typical symptoms, which may contribute to less frequent diagnoses. Finally, ABI measurements are rarely performed at the primary care office settings. In this section of the article we will review clinical evaluation and management of PVD in hypertensive patients in a primary care setting.

CLINICAL EVALUATION FOR PERIPHERAL VASCULAR DISEASE (PVD)

Clinical evaluation for PVD in patients with hypertension should include accurate diagnosis of PVD and assessment of cardiovascular risk.

DIAGNOSIS OF PERIPHERAL VASCULAR DISEASE

Diagnosis of PVD is based mainly on the history and physical examination, with ankle brachial pressure index being used to confirm the diagnosis and assess the severity of the disease.

History Taking

A diagnosis of intermittent claudication can usually be made on the basis of the history. Intermittent claudication presents with a characteristic history of pain in the muscle, typically in the calf, thigh or buttock, which is elicited by exertion and relieved within a few minutes of rest. The Edinburgh claudication questionnaire is highly specific (91%) and sensitive (99%) for the condition (See Table 4) [14].

The location of pain helps to determine the level of PVD and the amount of exercise needed to elicit pain determines the severity of PVD. The distal lesions in the femoral, popliteal or tibial arteries produce a cramping pain in the calf muscles, while proximal or aorto-iliac lesions usually produce an aching discomfort in the hips, buttocks or thigh. And the more severe the disease, the lesser the amount of exercise is needed to produce pain. Development of rest pain or non-healing or delayed healing wounds or ulcers in the feet indicates a more severe or critical limb ischemia.

Table 4. Edinburgh Claudication Questionnaire

Questions	Correct Answer
1. Do you get pain or discomfort in your legs(s) when you walk? o Yes o No o Unable to walk If you answered "yes" to question 1, go to the following questions	Yes
2. Does the pain ever begin when you are standing or sitting still? o Yes o No	No
3. Do you get it when you walk fast or uphill? o Yes o No	Yes
4. Do you get it when you walk at an ordinary pace on the level? o Yes o No	Yes
5. Does the pain disappear if you stand still for up to 10 minutes? o Yes o No	Yes
Definition of positive classification requires all correct responses: "Yes" to (1), "No" to (2), "Yes" to (3), "Yes" to (4), "Yes" to (5). If these criteria are fulfilled go to question (6)	
6. Where do you get this pain or discomfort? Classic claudication - when the pain is in the calf. Atypical claudication - when the pain is in the thigh or buttock, in the absence of any calf pain.	

It is also important to differentiate intermittent claudication of PVD from venous claudication and neurogenic claudication (See Table 5).

Table 5. Differential diagnosis of Intermittent claudication

Type	Intermittent claudication	Venous claudication	Neurogenic claudication
Characteristic of pain	Cramping sensation	"Bursting" sensation	Electric shock-like sensation
Onset	Gradual, consistent	Gradual, can be immediate	Can be immediate, inconsistent
Relieved by	Standing still	Elevation of leg	Sitting down, bending forward
Location	Muscle groups (buttock, thigh, calf)	Whole leg	Poorly localised, can affect whole leg
Legs affected	Usually one	Usually one	Often both

Physical Examination

A detailed physical exam should be performed with emphasis on:

1. The quality of the femoral, popliteal, dorsalis pedis, and posterior tibial arterial pulses.

2. Signs of arterial insufficiency, e.g., coolness, scaling, paleness (especially with leg elevation), and ulceration.

3. Measurement of ankle-brachial index (ABI).

The ABI measurement is a simple, highly specific, noninvasive screening and diagnostic test for PAD. The actual performance time for an ABI in a primary care setting takes an average of 5 minutes. All physicians providing routine care to patients with hypertension should be able to measure the ABI. ABI is

measured by the higher of the systolic blood pressures in the pedal arteries (usually the dorsalis pedis or posterior tibial artery) divided by the higher of the systolic blood pressures in the brachial arteries of the two arms. The ABI cannot pinpoint the area of stenosis but it is a very accurate indicator of the presence of PVD. It is also a simple measure of the severity of lower extremity PVD (See Table 6) [15].

Table 6. Interpretation of ABI results

ABI	Interpretation	Clinical implications
>1.30	Non-compressible calcified vessels	PAD need to be evaluated with other tests.
0.90 to 1.30	Normal	No symptoms
0.40 to 0.89	Mild to moderate PVD	Patients usually present with intermittent claudication.
<0.40	Severe PVD	Patients may present with rest pain or non-healing ulcers.

ASSESSMENT OF CARDIOVASCULAR RISK

Peripheral vascular disease is a marker of systemic atherosclerosis; the risk to the limb in claudication is low, but the risk to life is high because of increased prevalence of cardiovascular events in patients with PVD [16]. Therefore, assessment of patients with PVD should also include evaluation for other cardiovascular risk factors (in addition to hypertension), evaluation for other target organ damages (in addition to PVD) and evaluation for presence of other cardiovascular diseases:

Evaluation for other Cardiovascular risk factors

1. Family history of coronary artery disease,

2. History of Smoking,

3. Fasting lipid profile

4. Presence of diabetes and status of its control

Evaluation for other Target organ damages associated with hypertension

1. Ask for any symptoms of vascular disease in other vascular territories – coronary artery disease, cerebrovascular disease, etc.

2. Test for the presence of protein in the urine by sending a urine sample for estimation of the albumin:creatinine ratio and test for haematuria using a reagent strip.

3. Measure plasma creatinine with electrolytes and estimate glomerular filtration rate (eGFR).

4. Examine the fundi for the presence of hypertensive retinopathy.

5. Arrange for a 12-lead electrocardiograph to be performed.

Evaluation for presence of other cardiovascular diseases

1. Coronary artery disease – history of angina, myocardial infarction, features of heart failure, ECG.

2. Cerebrovascular disease – history of TIAs, strokes, presence of carotid bruit.

3. Renovascular disease – presence of renal artery bruits, severe resistant hypertension, worsening renal failure with ACE inhibitors.

4. Abdominal aortic aneurysm – pulsatile abdominal masses.

MANAGEMENT OF PATIENTS WITH PVD

Management of patients with PVD includes risk factor modification, a regular exercise program, pharmacologic therapy and referral for revascularisation [17].

Risk factor modification

1. Hypertension control. Strict control of hypertension slows the progression of PVD and reduces cardiovascular events. There is no consensus about what type of antihypertensive drugs to use in patients with PVD. Beta-blockers used to be avoided, but most experts now believe that their benefits outweigh the risk. Based on the HOPE trial, angiotensin-converting enzyme (ACE) inhibitors would be the agents of choice [18].

2. Management of dyslipidemia. Angiographic studies have confirmed that lipid-lowering retards the progression of femoral atherosclerosis. All hypertensive patients with elevated lipid levels should be on lipid-lowering therapy, and the target LDL level should be less than 100 mg/dL. Statins have shown benefit in reduction of incidence of PVD as well as improvement of claudication symptoms [19].

3. Encourage patients to quit smoking. The progression of peripheral vascular atherosclerosis is significantly greater in patients who continue to smoke. Complete cessation of tobacco use should be the goal. Stopping smoking can reduce the 5-year amputation risk tenfold and decrease the mortality rate by 50% [20].

4. Control of diabetes mellitus. The combination of diabetes mellitus and PVD is ominous, because PVD rapidly progresses to ischemic pain at rest and ulceration in these patients. Optimal glycaemic control should be a consideration.

Exercise Program

A regular walking regimen is extremely helpful. It has been shown to increase the claudication distance by 180 to 400% [21]. Initially, patients should be enrolled in a supervised exercise regimen. In these programs, patients walk on a treadmill initially set to a speed and grade that bring on the pain of claudication within 3 to 5 minutes. They walk at this rate until they experience claudication of moderate severity, rest until the claudication abates, and then resume walking. The sessions typically last 60 minutes and are monitored by a skilled nurse or technician. Subsequently, patients are encouraged to continue walking at home. They should walk at least three times a week (preferably every day) for 30 to 45 minutes, and keep up this regimen for at least 6 months. They should walk as far as possible using near-maximal pain as a signal to stop, and resume walking when the pain goes away.

Pharmacologic therapy

1. Two agents have been approved by US FDA for the symptomatic treatment of intermittent claudication. The first agent shown to be useful was pentoxifylline. But unfortunately, only about 20% of patients benefit from pentoxifylline, but a trial of 2 to 3 months in most patients is reasonable. Cilostazol, a newer antiplatelet and vasodilating agent, may be more effective than pentoxifylline for patients with intermittent claudication [22]. However, cilastozol being a phosphodiesterase inhibitor is absolutely contraindicated in patients with congestive heart failure, because studies have shown increase mortality with the use of phosphodiesterase inhibitors in patients with congestive heart failure.

2. Antiplatelet agents reduce both the risk of limb loss and the need for surgical revascularization in patients with intermittent claudication. Antiplatelet therapy also substantially reduces the risk of myocardial infarction, stroke, or death in patients with PVD. Therefore all patients with PVD should be started on aspirin or other antiplatelet agents unless contraindicated [23].

Revascularization

PVD patients should be referred for revascularization (i.e., percutaneous angioplasty or surgery) if they have lifestyle-limiting claudication, rest pain, ischemic ulceration, and gangrene. In general, angioplasty is favored for shorter lesions, while surgery is reserved for chronic long-segment occlusions and after failure of angioplasty [24,25] .

REFERRAL GUIDELINES

Patients should be referred to a Vascular medicine/ Vascular surgery specialist for an assessment if they have any of the following:

1. Lifestyle-limiting claudication

2. Any sign of potential critical limb ischemia, such as foot or limb ulceration, skin changes (nail or skin atrophy, dependent rubor), or gangrene

3. An ABI less than 0.50 at rest

4. An incompressible ankle artery (systolic ankle pressure > 300 mm Hg); incompressible ankle arteries suggest significant medial wall calcification and likely reflect significant PVD

5. Blood pressure more than 75 mm Hg higher in the ankle than in the arm.

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LEARNING POINTS

- **Hypertension is the single most important modifiable risk factor for stroke and about 54% of strokes worldwide is attributable to hypertension.**
- **At the primary care setting, when a patient presents with a sudden onset of neurological symptoms, a validated tool, such as FAST (Face Arm Speech Test) should be used to screen for diagnosis of stroke or TIA.**
- **Patient with crescendo TIA (two or more TIAs in a week) should be treated as being at high risk of stroke, even though they may have an ABCD2 score of 3 or below.**
- **Poststroke outpatient care focuses on rehabilitation and secondary prevention of recurrent stroke.**
- **All patients who have had an ischaemic stroke or a transient ischaemic attack should be treated with a statin drug unless contraindicated, if the total cholesterol is more than 3.5mmol/L, or LDL is more than 2.6mmol/L.**
- **High risk patients (ABCD2 score 4 and above) should be assessed at the specialist's clinic within 24 hours of first presentation to a primary care doctor.**
- **Diagnosis of peripheral vascular disease is based mainly on the history and physical examination, with ankle brachial pressure index being used to confirm the diagnosis and assess the severity of the disease.**
- **Management of patients with peripheral vascular disease includes risk factor modification, a regular exercise program, pharmacologic therapy and referral for revascularization.**

UNIT NO. 4

BEHAVIOUR MODIFICATION

Dr Tan Yew Seng

ABSTRACT

Addressing health threatening behaviours will be an increasingly important issue in general practice. However, it is known that simply telling or advising patients to change is insufficient to change behaviour. This article will focus on two key approaches, the Transtheoretical Model and Motivational Interviewing, which are known to be useful in facilitating such changes, and their implications to everyday clinic practice. An understanding of the process of changes highlights the heterogeneity of patients in terms of their stages of change which suggests the need for different strategies to facilitate change. The practitioner is also more likely to succeed by adopting a guiding style as opposed to either being directive or passive. The guiding style, which emphasizes collaboration and respecting the patient's autonomy, enables the practitioner to explore and enhance the patient's own motivation to change. Together with the setting of specific and achievable goals, such approaches may provide the framework and methods for the busy practitioner to respond effectively and efficiently to health threatening behaviours.

Key words: behaviour change; general practice; transtheoretical model; motivational interviewing; chronic disease management

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CHANGING HEALTH THREATENING BEHAVIOURS

The trouble with health related behaviours is that they matter significantly in disease and death. In the United States, behavioural causes account for 40% of premature deaths, with the pair of obesity and inactivity, and smoking being the top two behavioural causes of premature deaths[1]. But beyond the "big four" lifestyle habits (smoking, excessive drinking, lack of exercise and unhealthy diet), change may also be desired to enhance health related activities such as the use of aids, devices and medicines[2]. Therefore, to manage a patient's condition adequately, the practitioner is often required to address the topic of behavior change. The traditional approach employed by many practitioners is one of "directing" the patient to change. This generally comprise highlighting the risk of developing a disease and the consequent need to change, followed perhaps by prescriptions about how to change. The actual manner in which it is done vary according to the practitioner's style and temperament as well as whom is being helped to change. These include explaining, reasoning, cajoling, instructing, lecturing, preaching, admonishing, and even pleading and threatening. Unfortunately, those who have attempted to do so would be familiar with these common replies:

"My grandfather smokes like a chimney and he lived to 93 years old"

"My friend was diagnosed with cancer the year he decided to stop smoking"

"I know it is important for me to watch my diet, but…"

"We only live once, so what's the point of living if you can't enjoy eating"

"Yes, I'll try" (As a somewhat polite way of NOT agreeing but helps avoid an otherwise protracted consultation)

While some patients do seem to respond to practitioners telling them to change their behavior, most consultations about changing unhealthy behaviours are more likely "heart-sink" experiences that threatens the practitioner-patient relationship. It is not surprising that many practitioners choose either to deal with it cursorily, or just avoid it altogether. Sometimes, when change remains elusive despite the practitioner's well-meaning efforts, these patients are labeled as "stubborn" or "recalcitrant" - perhaps only to mitigate the practitioner's impotence as this does nothing to resolve the deadlocked situation. Wouldn't it be wonderful if there were a "magic pill" to deal with unhealthy behaviours!

But it is known that just simply telling patients that they are at risk of developing a disease is rarely sufficient to change behavior [2,3]. Behaviours can be said to be products of complex interactions between an individual's biological, social, developmental and psychological processes, and the environment[4]. The biomedical context at the clinic is only a part of the wider web of equations that the patient has to contend with consciously or unconsciously when contemplating or attempting a behavior change. Fortunately, much is now known about how people change their health behaviours and this has improved our understanding about change and refined our strategies to change health behaviors. This article will first introduce some concepts about changing unhealthy behaviours and later, discuss strategies that the practitioner can use to obtain better outcomes in facilitating the patients' health

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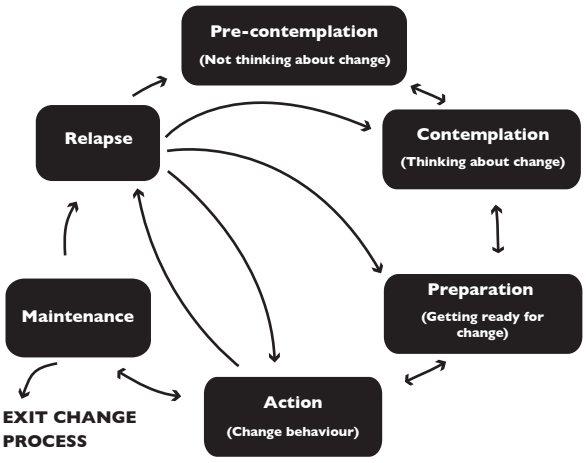
behavior change.

Figure 1. The Trans-theoretical Model



UNDERSTANDING HOW CHANGE TAKES PLACE

When people change behaviours, they tend to go through a number of fairly stereotypical psychological processes before the change becomes sustained. Change that is evoked by intervention or therapy resembles that which occurs spontaneously. A framework that describes this natural sequence is the Transtheoretical Model (TTM) or Stages of Change model, described by Diclemente and Prochaska in the late 1970s and the 1980s. In this model [5,6,] the person attempting to change navigates gradually through processes that may be classified into five stages: from being uninterested or uninformed about change (precontemplation), to considering change (contemplation), to preparing for change (preparation), to taking genuine steps in changing (action) and finally actively incorporating the change (maintenance/relapse prevention) (Figure 1). During the course of change, the person can move backwards or regress to the previous stages; relapse can also be expected after change occurs, thereafter starting another round of change stages. Several cycles of change and relapse may be necessary before the behaviour change is completed and stable. While this model was first described in patients with addictive behaviours, it has since been found to provide a useful framework for understanding change in many other health related behaviours [7, 8].

Precontemplation Stage

During the precontemplation stage, patients do not consider changing in the foreseeable future, usually measured as the next six months. They may be in this stage because they are uninformed or under-informed about the consequences of their behaviour. Or they may have tried to change a number of times and become demoralized about their ability to change. Both groups tend to avoid reading, talking or thinking about their high risk behaviours. During discussions, they may downplay the seriousness of their condition ("All my family members are obese"), or fail to make the link between their condition and the complications ("I don't believe it will happen to me"). They may be defensive in the face of other people's efforts to pressure them to quit. These patients are frequently labelled as being resistant or unmotivated.

Contemplation Stage

During the contemplation stage, patients are more aware of the personal consequences of their bad habit and they spend time thinking about their problem. In this stage, the patients considers the benefits and costs of the behaviour change, so that ambivalence results. The possible barriers to change include time, financial costs, inconvenience, loss of pleasure, change of routines etc. The ambivalence may be so profound that the patient can remain in this stage for a long time.

Preparation / Decision Stage

Patients in the preparation stage get ready for change in the immediate future, usually measured as within the next month. The preparation may involve experimenting with small changes, reading self-help books, talking to their practitioner about change, or trying out low-fat foods or low tar cigarettes.

Action Stage

The action stage is one in which the patient takes active steps to change their behaviour by a variety of techniques. The changes are generally specific overt modifications. In this stage, relapse is common.

Maintenance / Relapse prevention

This is the stage in which the patient starts to incorporate the new behaviour into the lifestyle with efforts being directed to maintain the new status and prevent relapse. Most patients may find themselves recycling through the stages before the new behaviour is eventually established.

WHAT'S IN TTM FOR THE PRACTITIONER? (IT ISN'T ALWAYS BAD WHEN THERE'S NO "CHANGE")

Firstly, the TTM acknowledges that patients who need or even seek change are not homogenous and may be in different stages of change. Some will therefore respond to gentle reminders while others are probably not ready to process anything told to them. This implies also that different strategies may be required at each stage. It is notable that many of the common strategies to encourage change tend to work well with people who are already in the preparation or action stages, in contrast to those in the pre-contemplative or contemplative stages. An approach tailored to the patient's stage may be necessary. Some stage-specific

strategies are shown in Table I.

Secondly, a rather simple truism that some practitioners just have to get over: the stage that the patient is in is determined by the patient and not the practitioner. This may avert the often frustrating question about why some patients are so hard to change – Q: Why can't they change? A: Because they are not at a stage where the behavior change happens. An important corollary to this fact is that the pace of change is also patient determined. The more appropriate role of practitioners is therefore the facilitation of the patient's movement through the stages.

It also follows that when there is resistance during the change process, which is usually defined from the practitioner's perspective of the patient becoming less responsive to his intervention, the cause may be one of mis-matching of patient's stage and the practitioner's perception of his stage, or the use of interventions which is not appropriate for the stage. This underlies the need for the practitioner to actively assess for the changes in the patient's stage, and respond accordingly. In other words, if the patient does not change, the practitioner changes (his ideas, expectations and methods).

Thirdly, when we survey the continuum in the stages of change, it may be evident that an overt change in behaviour may be observed only in the preparation or action stages. In other words, the patient may be proceeding positively along the stages of changes but yet there is little in the way of a changed behaviour. What should not be ignored is the increased positive intention or readiness to change; one can be gratified when the patient is assessed to have moved along the stages, whether the behaviour has changed or not. This beats frustrating oneself and the patient with the unrelenting expectation and pressure to see an overt change in the patient's behaviour.

By now, one would realise that the patient's stages in the TTM, tend to be fluid and dynamic. The flux of the stage of change is often determined by the patient's context outside the clinic. Hence, even after a rousing pep talk that appears to have convinced the patient that a change in his diet is in order, by the time he returns home, passing by his favourite restaurant and settling down in the sofa, the enthusiasm may be blunted and doubts about wanting to change resurface. And even when a behaviour change has occurred, it is still not permanent. There is a need to maintain the change until it becomes integrated into the person's routine or lifestyle.

Finally, practitioners and patients alike should be pleased to

Table 1. Stages of Change and approaches that are most appropriate at each stage [9]

Stage	Explanation of stage	Approach suitable for stage
Pre-contemplation **(Not thinking of change)**	Stage during which a person does not even consider the need to change: • Have not had sufficient experience with negative consequences • Tipped toward negatives	Reflective listening • Empathy • Effective questioning • Provide objective information in a non-judgmental manner • Explore barriers (Action-oriented messages are not appropriate)
Contemplation **(Thinking of Change)**	In this stage, a person considers changing a specific behaviour: • Beginning to seek relevant information • Re-evaluating behaviour • Obtaining help of others to support future attempts • Still weighing up options • Not ready to take action	• Reflective listening • Empathy • Effective questioning • Provide non-judgmental objective information that may be taken away • Encourage the patient to accept ownership of the problem • Increase awareness of negative questions • Recognise how situations effect illness
Preparation/Determination **(Ready for change)**	The stage where a person makes a serious commitment to change • Ready to take action in the next 30 days • Need to set goals and develop priorities in order to manage illness	• Encouragement • Empathy • Goal setting • Support of self-efficacious behaviour
Action **(Changing Behaviour)**	Change begins (this can be large or small changes) • Efforts made to modify habits and environment • Increased use of behavioural processes of change (eg restructuring one's environment, removing alcohol)	Encourage stimulus control • Skills training interventions • Encourage support from others
Maintenance **(Maintaining change)**	Change is sustained over a period of time • Substituting alternatives for problem behaviours eg relaxation • Taking responsibility for actions • Susceptible to relapse. Need to remain aware of stimuli that may trigger problem behaviours	• Do not view relapse as failure, but as a way to gain knowledge of triggers • Decrease environmental and internal stimuli that trigger problem behaviours

know that in TTM, relapse does not equal failure. In fact, a relapse is an excellent opportunity to help the patient learn about their own life circumstances, the precipitants of the relapse and the weaknesses of the change strategy. In other words, a relapse provides learning about how things may be done to secure a more sustainable change. It is known that for a behaviour change to take place, it may be necessary for one to cycle through the stages of change several times. However, relapse if not dealt with properly is not innocuous either, as repeated episodes may lead to loss of confidence and motivation to try to change again.

BUT THE PATIENT IS JUST NOT MOTIVATED TO CHANGE!

When patients do not respond positively to the sound advice of practitioners, it is frequently assumed that the patient has "poor" or "no" motivation, as if deficient motivation is a stable personal trait. Such beliefs are simply untrue as no one is truly unmotivated; patients may just be more motivated NOT to change due to circumstances unknown to the practitioner. They may also be motivated to change in ways that are more ecological to their circumstances. For example, a patient may be motivated to stop cigarette smoking most times but not ready to decline cigarettes when with his business friends. Being able to explore, understand and enhance the patient's motivation therefore becomes important steps in facilitating patient's change in behaviour.

Motivational Interviewing (MI) offers another model for understanding and dealing with the readiness for change. MI was developed by Rollnick and Miller as a strategy for addictive behaviour change, and like TTM, MI has found many applications in helping patients change other health related behaviours[10-12]. MI was initially defined as a client-oriented, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence[10]. It was updated in 2008 as a collaborative, person-centred form of guiding to elicit and strengthen motivation for change[13]. The idea of the practitioner as a guide in a consultation for change contrasts with the more commonly subscribed role of the practitioner as the "expert" directing the change process, but neither does it imply submitting to the patient's wishes. The guiding stance, whilst respecting the patient's autonomy and the patient as the agency of change, maintain controls of the direction and structure of the consultation to evoke the patient's own arguments and strategies for change. The guiding process thus avoids the struggle or "fights" with the patient over changing behaviour and has been likened more to "dancing" with the patient-partner[13].

The core communication skills that the practitioner needs to employ in MI are

"Asking"	Open questions that invite the patient to consider why and how they might change	
"Listening"	Not only to understand their experience, but also to respond actively with statements of interest, understanding or acknowledgement e.g. using summaries of what was said, Or with reflective listening statements; All of which conveys empathy and encourages the patient to further elaborate, and could also reduce resistance from the patient	("Hmm, please tell me more") ("There are many things you wished you could do, and these are _____") ("You are tired of people expecting you to change_____, you have tried so hard")
"Informing"	Giving information and then asking about the impact of the information on the patient	("There is another way of achieving what you wanted; I am wondering if you would like to hear about it?" then "How does knowing _____affect the way you look at/feel about changing?")

Using the core skills, MI explores the patients' inner motivations and helps them to recognize and be responsible for it. It also directs them towards the discrepancies that already exist between what they want and how their behavior impacts these goals. Such discrepancies reflect a state of ambivalence that many patients have about changing. In MI, ambivalence is a natural state that patients can be expected to pass through (but not stay) as they change. Ambivalence is therefore not generally interpreted as an undesirable state, and patients (and practitioners) can therefore feel comfortable about discussing about their conflicting issues and dilemmas. The practitioner assists the patients work through their ambivalence and guides them to decide for change.

Another important concept in MI is the idea of self-efficacy. Bandura describes self-efficacy as "people's beliefs about their capabilities to produce designated levels of performance that influence over the event that affect their lives" [14]. It is therefore more about a "belief" or psychological state than just the presence or absence of skills. The latter, also known as capability, differs from the former in that it may be more simply remedied by the imparting of skills. For example, a smoker who has relapsed many times may suffer not from a lack of knowledge or skills about quitting cigarettes but from being demoralised after the repeated "failures", hence the belief that change is not possible. Setting achievable goals may be one of the strategies that restore the sense of self-efficacy, and therefore the likelihood of eventual successful behaviour change.

Talking about change

What is also known to reflect the patient's motivation to change is the patient's use of commitment language in a dialogue about change[15]. Generally, those who talk about change, in particular about the desire, ability, reasons, need, and commitment for change tend to change. Conversely, those who talk against change are less likely to do so. Facilitating the patient to process and speak more about why and how to change then becomes one of the strategies to motivate change. In MI, this is known as change talk. Change talk may not be so peculiar when we reflect that people often self-talk before doing something they are not so confident or capable of doing, such as speaking on stage or an athletic event. The content of such self-talk often includes expressions of the **importance** and **confidence** to change, which are the determinants of readiness to change in the MI model. Knowing that patients can literally talk themselves into or out of behaviour change, evoking commitment language becomes a key part of change dialogue.

Yet, it is also not uncommon that conversations between practitioners and patients often suppress change talk instead. One of the common impediments is the practitioner's behaviour of trying to fix the "unhealthy" lifestyle or behaviour of the patient for "his/her sake". Examples of such behaviour include attempts to convince patients that they have a problem; arguing for the benefits of change; telling clients how to change; and warning them of the consequences of not changing. This behaviour has been termed the righting reflex in MI. And while it may have originated from positive intentions, it failed to recognise the phenomenon of ambivalence - an ambivalent patient would in such circumstances be encouraged to respond by arguing against changing. An example of such a conversation is shown in Table 2.

In MI understanding, the practitioner has played the wrong role by encouraging the patient to speak against change. The person who should argue for change is the patient and not the practitioner. Evoking the patient's own arguments for change is therefore the appropriate role of the practitioner.

Table 2. Talking against change

Practitioner	Patient
Do you smoke?	Yes
How much are you smoking now?	About 20 cigarettes a day
Do you intend to stop smoking now?	Not really
Not really?	Yeah
Why not?	I just don't feel like stopping cigarettes at this time. I tried stopping last time and I can't concentrate at work after that.
I must inform you that the cough and breathlessness that you are having is caused by smoking As your doctor, I must tell you that smoking is harmful to you and your family. Don't you care for them?	It isn't so bad. It is just a temporary cough; it gets better with the cough mixture. I can still carry on doing my work in spite of the cough. My family is not really complaining since I cut down from 2 packs to one and a half a day.
I think you should start on medication to stop smoking	No need lah! I think I can stop smoking when I really want to.

Table 3. How a change consultation may be done

How a change consultation may be done
1. Build rapport
2. Remember the key principles
- Be curious and interested
- Resist the righting reflex
- Guide rather than direct
3. Set the agenda for discussion collaboratively
4. Exploring about and enhancing readiness to change
- Change talk
- Others:
o Providing information
o Exploring importance
o Enhancing confidence
5. Setting goals and action plans
- Specific
- Proximal
- Enhance the action plans with step 4. Strategies
6. Review and follow-up

HOW CAN WE DO IT BETTER?

With the background information about how change happens and the different ways in which change may be facilitated, we can attempt to derive a neat model of practice for the busy practitioner, bearing in mind that responding to the patient and in accordance to the principles are probably more important than following a cook-book manner of implementation (Table 3).

1. Build rapport

This is an indispensable step to set up an open and honest exchange in a healthy therapeutic alliance. Without any rapport, attempts at change may be misconstrued as intrusive or coercive, and resistance invariably results. Rapport is also not an all-or-none entity. The level of rapport can fluctuate during the consultation depending on what has transpired and how the practitioner responded to the patient. Constant monitoring of the rapport is necessary to ensure the strength of the therapeutic alliance.

2. Remember the key principles

Be curious about the patient as a unique individual with his/her set of behaviours! To explore aspects of what is presented at the consultation, one has to be non-judgemental and sensitive. Resist the righting reflex. Remember that you are only the "guide". The patient is the one who has to justify the change, decide how to change, and more critically, live out the behaviour change, NOT you. Use the core skills of asking, active listening and informing.

3. Setting an agenda collaboratively

Many health behaviours do not exist alone, for example, dietary behaviour and sedentary lifestyle; cigarette smoking and alcohol consumption and so on. Not only do they coexist, they also influence one another. Patients too, may have other issues when they express a desire for 'change'. Examples of hidden agendas include mending relationships by quitting cigarettes, or losing weight to keep a boyfriend. If ignored, the efforts to change may be sabotaged by these external factors. The practitioner should be mindful that extra-therapeutic/patient factors have been shown to have significant influences on change outcomes [16, 17]. Be interested in the circumstances of the patient, even if it means having to go beyond the realms what is commonly perceived as "medicine". Sometimes, dealing with what is troubling the patient elsewhere may also change an unhealthy behaviour, such as dealing with a social issue when managing hypnotic dependence.

It is therefore useful to set the agenda from the start. This is a good way of laying out what are the possible behaviours that need attention as well as other issues that the patient feels are important to him or her. An agenda can also alert the practitioner to an area of avoidance by the patient, and sometimes the practitioner. The consultation may start off with something like: "With respect to the daily management of diabetes, we can talk about diet, exercise, tablets, smoking, and so on. Which of these would you like to discuss, or is there something else which is on your mind?" Agenda setting is therefore not totally hands-off or laissez-faire. The role of the practitioner remains directive, by negotiating goals and the agenda, and directing focus onto areas of neglect. The approach, however, remains one that considers patient choice and decision making.

4. Exploring and enhancing the readiness to change

Getting patients to talk about changing

Maintain a sensitive curiosity about the stage of change or state of readiness that the patient presents with, e.g. Why is it important for them to change now? What's difficult about staying unchanged? How do they think they can change? Understand the motivation of the patient and reflect it back to them. Elicit "change talk", the content of which includes acknowledging the problems of remaining the same, recognising the benefits of change, intent and commitment to change, and optimism for change. Once change talk is elicited, the ways by which the practitioner can respond are:

- Elicit more (with open questions)
- Affirm
- Reflect
- Summarise

Some other helpful strategies include:

Providing information

While simply telling or giving advice to patients has not been found to be useful, patients nevertheless need appropriate information in order to self-manage. One technique is "elicit, provide, elicit". In this technique, after the patient's understanding about a matter is elicited, the practitioner provides some other supporting information and then checks back with the patient, the personal implications of the information that has been provided [2]. For example, "Can I check what's your understanding about the control of your diabetes so far?"; then "You are quite right about…, and in addition, other similarly important aspects might be…"; and finally, "So, now knowing these aspects about care, how might that affect the way you deal with your diabetes condition?".

Another similar technique is the "ask, tell, ask" technique that Bodenheimer and his colleagues described[18]. The technique is similar in the first two steps of the earlier technique but in the final step the practitioner asks whether the patient had understood and what additional information is desired. The technique therefore addresses the problem of a lack of information in a manner directed by the patient so that only information is that is useful for the patient is given without information excess. Hence, using the earlier example, the final "ask" may be "So, of all these aspects of care at home, which one would you like to know more about?"

Exploring importance

We can explore and assess the importance for change with the following questions:

- "How important is keeping up with the medication daily for you right now?" (Explores the patient's sentiments, fears and possible competing issues)
- "On a scale of 0 to 10, where 0 is not important and 10 is extremely important, what would you say the level of importance for changing is?"
- "Can you tell me why you have given yourself a score of x instead of 1?" (Elicit patient's positive reasons for change); "How can you go higher?" (Explores perceived options); "What stops you from moving up from x to [higher number]?" (Explores the perceived obstacles)

Another way is to examine the costs and benefits of changing or staying the same. This process helps the patient self-reflect on the internal-external discrepancies, and the ambivalence about change. Doing so can generate tensions within the patient's internal "world views" which can motivate the patient to change [10]. This process may be achieved with the visual aid of a 'decision grid' as shown in Figure 2.

After listing down in the boxes, ask: "What are your thoughts as you look at the advantages and disadvantages of changing and not changing?" You may also reflect to the patient the considerations involved in changing.

Figure 2. Decision Grid

	No change	Change
Cost		
Benefits		

Enhancing confidence

The following sequence may help assess and enhance confidence:

- "How confident are you right now in changing?"
- "On a scale of 0-10, how confident would you say you are now?"
- "Why had you scored x instead of 1?"; "How can it go higher?"; "What would help you to become more confident?"; "What stops you moving up from x to [higher number]?"

Another method is to brainstorm with the patient the possible courses of action and then allow the patient to choose what is suitable. The purpose is to help the patient realise that there is choice among the many possible courses of action, while conveying optimism. Sometimes, it may be appropriate to talk about the patient's past efforts and his or her successes and failures – to affirm previous attempts at change and past successes. It should not however be misconstrued as emphasizing the success or dismissing the failures. Rather, the practitioner's task is to help the patient appreciate a balanced appraisal of the past performances (not the person).

Similarly, it is vital not to over inflate the importance of change or the patient's confidence about change. Premature and ill-prepared attempts may lead to disappointments and a sense of failure. The goals for the patient should be realistic and specific, even if they are "small gains" in the eyes of the practitioner. What is important is that they represent the patient's choice and context.

Other interventions

Sometimes, it is necessary to provide certain specific interventions before the patient can proceed to make specific changes. For example, relaxation techniques may be useful for patients who are under 'stress' or anxiety. Social interventions should also be considered if mundane needs such as housing rental, child care, marital counselling, job placement etc are wanting. Depending on culture and social status, many such basic needs may rank above health concerns. Adopting this stance may be easier said than done, as many practitioners can feel compelled to revert back to the directing style because of time constraints or if they perceive an urgent need to impose change because of dire medical state of the patient.

Some useful questions in talking about change are shown in Table 4.

Table 4. Top 10 useful questions [2]

Top 10 useful questions [2]
What changes would you most like to talk about?
What have you noticed about …?
How important is it for you to change…?
How confident do you feel about changing…?
How do you see the benefits of …?
How do you see the drawback of …?
What will make the most sense to you?
How might things be different if you…?
In what way…?
Where does this leave you now?

5. Setting goals and action plans

An important component of behaviour change is goal setting, a process which has been associated with improved health-related behaviours [19, 20]. As discussed earlier, goals that are unachievable only frustrates and demoralises the patient, some of whom eventually becoming precontemplators[10]. On the other hand, a well set series of achievable goals can increase the patient's sense of self-efficacy and put the patient on track for a successful change of behaviour. The following recommendations come from our understanding of how goal-setting affects performance:

- Goals that are specific ("I will walk for 30 minutes on Mondays, Wednesdays and Fridays in the park"), preferably including aspects of what, when, how much and how often, are more likely to succeed than vague ones ("I will try to control my food intake", "I will lose some weight")

- Proximal (short term and specific) goals are associated with better performance than distal (long-term and general goals). Short-term goals, also known as action plans, are more likely to result in early success (which enhances self-efficacy), which in turn leads to setting of higher level goals subsequently. Hence, a proximal goal may be "I will bring my own drinking water to work and not consume any soft drinks during lunch", which while not really achieving a holistic dietary modification, may be more useful in the long run than the goal of "I will lose 10kg of my body weight".

Needless to say, the goal setting process must be done in collaboration with the patient, with the patient having the final say.

Once the goal or action plan is set, continue to enhance the likelihood to doing it by applying Step 4 ("Exploring and enhancing the readiness to change") discussed earlier.

6. Review and follow-up

Finally, even when goals are set, it is important to follow-up and review the outcomes. Remember that the inability to achieve the goal at the next review does not equate failure. Learning from the episode and dealing with the identified barriers or changing direction altogether will enable the patient to try again. The same approach applies in a situation of relapse. Conversely, TTM tells us that even if the behaviour appears to have changed, it may not be permanent and other steps or behaviours may need to be installed to maintain the change.

CONCLUDING COMMENTS – ALL THESE SEEM RATHER DIFFICULT

Changing behaviour is not easy, but the stakes in changing unhealthy behaviours in patients with chronic medicalconditions are high. Yet, even as the practitioner feels the urgency to get the patient to change, the reality is that once outside the hospital or clinic setting, it is the patients who decide what and how much to eat, whether to exercise or take medication; and how much cigarettes or alcohol they will use. It is not possible to install or reasonably force lasting or meaningful change onto people. What practitioners can do is only to enable patients to help themselves, and we need to learn new skills to do so.

Some practitioners may find applying these ideas and methods awkward. This is to be expected in the initial stages as it requires a different way of thinking about and talking to patients. Such an experience is not so different from learning a new language or learning to swim or cycle (where every movement seems strange to the body). For those who feel these methods are rather "unnatural", "artificial" or "unreal", it is probably so because we have long been accustomed to the "usual" doctor-centric relationship which is incidentally more suited to the sporadic and exceptional situations of acute medical care provision and less applicable to caring for patients living in the community with chronic disease. In other words, maintaining the status quo, where patients have to abide by the practitioner's model, is in reality more contrived, and hence the difficulties faced by practitioners because of the resulting tensions and dilemmas in care.

Is there a best way to behaviour change?

No one style fits all patients. Indeed, some patients may respond best with a directing style or relationship. Ultimately, the practitioner needs to have a respectful attitude to the patients and be open to changing styles and methods to be in tandem with the patient's responses. Imposing the practitioner's ideas about change, even if this in accordance with some well used guideline may not necessarily lead to successful change. Duncan and his colleagues have gathered evidence to show that rather than the type of therapeutic intervention provided or the techniques used, the factors that determine outcomes may have more to do with the patient's perceptions of the therapeutic relationship, how consistent the method used is with the patient's own theory about change, whether they feel comfortable and respected, and the level of active participation. In other words, the practitioner's ability to find a

complementary 'fit' with his patient affects these factors [16, 17, 21].

Will I be able or have the time to do this?

By now, it should be obvious that it takes time for the patient to change his/her behaviour. It also requires that the practitioner spend time guiding the patient. But this investment in time may be more efficient and sound, when compared with the time spent on futile advice, or the situation where the patient has repeated consultations for complications arising from the failure to change.

Fortunately, the practitioner may find some solace that even brief interaction, if skilfully done, may have a significant impact on the patient's behaviour change[7, 12]. Understanding and applying what we know about the processes of behavioural change, and making the shift towards a guiding style, which encapsulates principles such as collaboration, negotiation, respecting patients' autonomy, and supporting self-efficacy, might be good beginning steps. The guiding style, on which MI is based, would be within the reach of the busy practitioner[2].

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LEARNING POINTS

- **Telling or advising patients to change is insufficient to change behaviour.**
- **The transtheoretical model (TTM) highlights the heterogeneity of patients in terms of their stages of change which suggests the need for different strategies to facilitate change.**
- **Motivational interviewing is a guiding style which emphasizes collaboration and respecting the patient's autonomy, enables the practitioner to explore and enhance the patient's own motivation to change.**
- **Together with the setting of specific and achievable goals, the transtheoretical model provides the framework and the motivational interview the method for the busy practitioner to respond effectively and efficiently to health threatening behaviours.**

UNIT NO. 5

THERAPEUTIC CONSIDERATIONS

Dr Akira Wu

ABSTRACT

Just over 50% of all strokes and about half of all ischemic heart disease are attributable to hypertension. Blood pressure lowering results in significant reduction in coronary artery disease events and stroke. Although all classes of antihypertensive agents are effective in blood pressure reduction, choice of drugs should be based on compelling indications, contraindications & patient factors. Single pill combination therapy can dramatically achieve BP targets and offer benefit in a high percentage of patients. Controlling blood pressure can sometimes be challenging in resistant hypertension. Recent introduction of renal sympathetic denervation therapy looks promising in the management of resistant hypertension.

Keywords: Single pill combination, sympathetic denervation therapy, hypertension, causes, resistant hypertension

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INTRODUCTION

According to the Global Burden of Disease 2000 study, approximately 54% of all strokes and 47% of all ischemic heart disease are attributable to high blood pressure (BP)[1]. Another interesting aspect of the report is that approximately one-half of the BP-attributable deaths were due to systolic BP levels between the optimal systolic BP level (defined in the report as ≤ 115 mm Hg) and the current therapeutic intervention threshold of ≥140/90 mm Hg as advocated in guidelines. Placebo-controlled trials have shown that reductions in BP of 10 to 20 mm Hg systolic and 5 to 6 mm Hg diastolic for a few years conferred relative risk reductions of 38% for stroke and 16% for coronary heart disease [2]. However, the blood pressure control rates in most countries are still sub-optimal. The purpose of this brief review is to highlight the role of single pill combination therapy and the minimally invasive renal denervation therapy in influencing the current therapeutic management of hypertension.

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CAUSES OF HYPERTENSION

Although 90% of hypertension is essential or idiopathic, the rest is caused by kidney disease, vascular (arterial) stenosis, endocrinopathies, obesity and poly-pharmacy. An integral part of the assessment for hypertension should include the patient's cardiovascular (CV) risk and co-morbidities, and target organ involvement in the heart (LVH) or in the kidney (proteinuria).

Some of the key patho-physiologic considerations which may influence therapeutic approach, are volume regulation (sodium and fluid balance, ADH, aldosterone etc), sympathetic nervous system, renin-angiotensin-aldosterone system (RAAS), vasoactive substances (nitric oxide, prostaglandins, endothelium-derived hyperpolarizing factor [EDHF], endothelin), associated co-morbidities such as obesity, sleep apnoea and genetic factors. The kidney plays a pivotal role in salt and water intake and excretion which have a direct influence on volume status. The INTERSALT Study confirmed a direct relationship between sodium and mean blood pressure[3]. Hypertensive patients can have chronically increased levels of renin despite feedback mechanisms[4]. Aldosterone promotes hypertension by sodium retention contributing to volume expansion, up-regulation of angiotensin II (Ang II) receptors and potentiation of pressor responses of Ang II [5].

Over-activity of the sympathetic nervous system may contribute to hypertension. Alpha 1, alpha 2 and beta receptors mediate cellular responses to catecholamines. Activation of alpha 1 receptors results in vasoconstriction contributing to increased blood pressure[6]. Vasoactive substances synthesized in the vascular wall also play a vital role in the pathogenesis of hypertension. The key vasoactive substances are nitric oxide (vasodilation), prostaglandins (vasoconstriction), enthothelin (ET)-1 which counters the effects of nitric oxide and EDHF which is vasodilatory[7]. Some of the important co-morbidities in hypertensive patients are obesity and insulin resistance[8].

Table 1. ACCOMPLISH: Primary and secondary end points

End point	Hazard ratio (95% CI)
Cardiovascular morbidity / mortality*	0.80 (0.72-0.90)
Individual components	
• Cardiovascular mortality	0.80 (0.62-1.03)
• Fatal and nonfatal MI	0.78 (0.62-0.99)
• Fatal and nonfatal stroke	0.84 (0.65-1.08)
• Hospitalization for unstable angina	0.75 (0.50-1.10)
• Coronary revascularization	0.86 (0.74-1.00)
• Resuscitation after sudden cardiac arrest	1.75 (0.73-4.17)

*Primary end point

Jamerson K et al. N Engl J Med 2008; 359: 2417-2428.

Table 2. ONTARGET: Key results

ONTARGET: Key results

Outcome	Ramipril, n=8576 (%)	Telmisartan n=8542 (%)	Combination n=8502 (%)
CV death/MI/ stroke/ CHF hospitalization[a]	16.5	16.7	16.3
CV death /MI/stroke[b]	14.1	13.9	14.1
MI	4.8	5.2	5.2
Stroke	4.7	4.3	4.4
CHF hospitalization	4.1	4.6	3.9
CV death	7.0	7.0	7.3
Any death	11.8	11.6	12.5
Renal impairment	10.2	10.6	13.5

a. Primary end point
b. Primary end point in the HOPE trial

Yusuf S et al.N Engl J Med 2008: 358:1547-1559.

SINGLE PILL COMBINATION THERAPY

The currently available antihypertensive agents and appropriate life style modification should be able to control BP in most hypertensive patients. Yet, most surveys showed only a minority of patients achieved optimal BP control, especially in those who need tight control. Reasons for poor control include poor adherence to therapy, side-effects of medications, clinical inertia, sub-optimal intensity, inappropriate selection and timing of therapy.

In complicated hypertension, more than 2 antihypertensive agents were usually required to reach goal BP levels as specified in various trials (ALLHAT, LIFE, ASCOT) on hypertension [9,10,11]. JNC7 was the first guideline advocating first-line combination therapy for those subjects requiring ≥0/10mmHg blood pressure reduction (stage 2 hypertension)[12]. The recognition of the need for several drugs to achieve control led to the development of single-pill combination therapies involving almost all newer classes of antihypertensive agents.

Single pill combinations offer many advantages which include ease of administration, minimisation of side effects due to lower doses of component drugs, synergistic mechanisms of drug actions, and improved compliance. However, if they include a patent-protected drug, the total cost to the patient may exceed that of 2 generics. The choice of drugs in a combination therapy is influenced by their favourable outcomes in clinical trials, their favourable effects on co-morbid conditions, expert committee recommendations, once daily therapy, compelling indications and other factors.

The recently published ACCOMPLISH trial [13] started to address the issue of the impact of different combinations of antihypertensive agents on the outcomes of hypertensive subjects at high risk. The combination of agents with different but synergistic mechanisms of action is most logical. The most rationale is a diuretic, an ACEI or ARB or DRI, and a CCB. For example, the activation of renin-release by a diuretic will potentiate the antihypertensive effect of any blocker of the RAAS such as ACEIs, ARBs and the DRI. When comparing against diuretics or BBs or ACEIs, all types of CCBs except for the short-acting agents, are effective in protecting against major CV events[14] .

In patients with high CV risk, ACEI and ARB are virtually identical in providing CV protection[15] . The renal data from the ONTARGET study suggest that an ACEI/ARB combination has no advantages and should not be routinely used for hypertensive patients without severe heart failure or chronic renal disease with heavy proteinuria. However, in hypertensive diabetic patients already treated with an ARB, the addition of a DRI-based treatment significantly reduced the mean urinary albumin/ creatinine ratio by 20% compared to the ARB-based treatment[16].

The importance of component drugs in single pill combination therapy is suggested by the ACCOMPLISH trial[13] which showed a significant ≈20% reduction in the primary CV end point in favour of the ACEI-CCB treated to the diuretic-CCB treated group (Table 2). Patients in both treatment arms received excellent blood-pressure control, with blood pressures of 132/73 mm Hg in the ACEI-CCB arm and 133/74 mm Hg in diuretic-CCB arm. More importantly, the blood pressure control rates of fixed drug combinations were superior to that achieved by free drug combinations. This study has established that combining a CCB with ACE inhibition, or presumably other forms of RAS blockade, is a very effective treatment option for high-risk patients with hypertension.

Antihypertensive treatment adherence varies with drug class as evident by a recent 17-study meta-analysis involving 935,920 patients with a mean age of 61.7 years. The results showed that the mean adherence to prescribed antihypertensive agents varied from 28% for beta blockers to 65% for ARBs. Patient adherence was greatest for ARBs, with rates 33% and 57% higher for this class than for ACE inhibitors and CCBs, respectively [17]. was greatest for ARBs, with rates 33% and 57% higher for this class than for ACE inhibitors and CCBs, respectively [17].

Resistant Hypertension

Resistant hypertension is defined as an elevated office blood pressure exceeding 140/90 mmHg in patients under 3 or more antihypertensive agents with an adequate dosage, including a diuretic. It is more common in the elderly, diabetics, obese and those with hypertensive heart disease or chronic kidney disease [18]. It is important to exclude pseudo-resistance such as white coat effect, blood pressure measurement problems, non-compliance, odd drug combinations, interfering drugs and under-dosing of anti-hypertensive agents. Every resistant hypertensive subject requires exclusion of a concealed undiagnosed cause of secondary hypertension, despite the lack of clinical clues to suspect it. This requires complex and expensive biochemical and radiological testing.

Primary aldosteronism has been documented in about 20% of resistant hypertension [19]. Standard triple drug regime for resistant hypertension is ACEI or ARB, diuretic preferably a thiazide and long acting CCB. Diuretics potentiate the effect of other antihypertensive agents, and contribute a specific effect to individuals with salt-sensitivity of blood pressure [20] . If blood pressure remains uncontrolled, other agents such as AAs (spironolactone, aldactone, eplerenone), vasodilating BBs, centrally acting agent or vasodilating agents (hydrallazine, minoxidil) may be added as last resort. Spironolactone may be particularly effective in obese subjects [21], on the basis of possible stimulation of inappropriate adrenal release of aldosterone by adipocyte secretagogues [22]. Although effective, these strategies are not devoid of risk, particularly in populations that are likely to have both resistant hypertension and risk for thiazide-inducedhyponatremia as in the elderly or for hyperkalemia which may affect subjects with diabetes, who commonly have renal tubular acidosis IV, and those with chronic renal insufficiency.

There are 2 interventional approaches that are being developed for patients with resistant hypertension. The Rheos® Hypertension Therapy system (CVRx, Inc; Minneapolis, Minnesota) is an implantable device that has been shown in clinical trials to lower blood pressure through activation of carotid baroreceptors [23]. The renal sympathetic denervation is a catheter-based interventional procedure which has been shown to be effective and can safely be used to substantially reduce blood pressure in treatment-resistant hypertensive patients [24]. The substantial reduction in BP was sustained out to 2 years of follow-up, without significant adverse events [25].

RENAL DENERVATION THERAPY

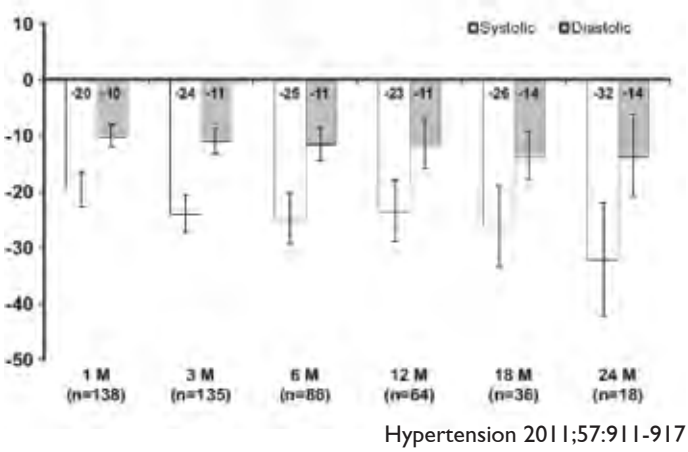
The sympathetic innervation of the kidney is implicated in the pathogenesis of hypertension through effects on rennin secretion, increased plasma rennin activity that leads to sodium and water retention, and reduction of renal blood flow (RBF) [26,27]. Complete bilateral renal denervation decreases the level of blood pressure in several experimental models, such as spontaneously hypertensive rats, DOCA hypertensive rats, two-kidney one-clip rats, obesity-induced hypertensive dogs, and aortic coarctation dogs [26]. Renal denervation, a minimally invasive procedure that disables sympathetic nerves located in the renal artery walls. The system consists of a generator and a flexible catheter. The catheter is introduced through the femoral artery in the upper thigh and is threaded up into the renal artery near each kidney. Once in place, the tip of the catheter delivers low-power radio-frequency (RF) energy according to a proprietary algorithm, or pattern, to affect the surrounding sympathetic nerves. The procedure does not involve a permanent implant.

Results from SYMPLICITY HTN-2 [24], a randomized, controlled clinical trial of 106 patients in Europe, Australia and New Zealand, showed that patients with resistant hypertension (systolic BP ≥160 mm Hg on ≥3 antihypertension drugs, including a diuretic) randomized to renal denervation achieved a mean blood pressure reduction of 32/12 mmHg at 6 months, whereas the patients in the control group randomised to anti-hypertensive medications alone had blood pressures that did not vary from baseline (1/0 mmHg). The overall occurrence of adverse events did not differ between groups.

In the recently published 24-month follow-up of 153 patients in SYMPLICITY HTN-2 (38), post-procedure office BPs were reduced by 20/10, 24/11, 25/11, 23/11, 26/14, and 32/14 mm Hg at 1, 3, 6, 12, 18, and 24 months, respectively (Figure 1). The median time from first to last radiofrequency energy ablation was 38 minutes. The procedure was without complication in 97% of patients (149 of 153). The 4 acute procedural complications included 3 groin pseudoaneurysms and 1 renal artery dissection, all managed without further sequelae.

Based on the findings of Symplicity HTN-1 [24], the indications for renal denervation therapy are systolic blood pressure of 160 mmHg or greater on 3 or more antihyper tensive medications and eGFR >= 45 mL/min. The contra-in dications are renal artery abnormalities and known secondary hypertension attributable to a cause other than sleep apnea.

Figure 1. Mean systolic and diastolic BP changes after renal sympathetic denervation procedure over 24-months of follow-up



Hypertension 2011;57:911-917

CONCLUSIONS

In conclusion, hypertension is a significant but modifiable risk factor for atherosclerotic events and mortality. Early achievement of target BP levels maximizes cardiovascular protection. Multiple antihypertensive agents are often required to achieve target BP levels in hypertension with co-morbidities. Multi-mechanism therapies offer many advantages over free pill combinations. Single pill combinations are becoming the

therapy of choice for optimal management of hypertension. The renal sympathetic denervation therapy looks promising in controlling blood pressure in multi-drug resistant hypertension.

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LEARNING POINTS

- **Blood pressure lowering results in significant reduction in coronary artery disease events and stroke.**
- **Multiple antihypertensive agents are often required to achieve target BP levels in hypertension with co-morbidities.**
- **Single pill combinations are becoming the therapy of choice for optimal management of hypertension.**
- **The renal sympathetic denervation therapy looks promising in controlling blood pressure in multi-drug resistant hypertension.**

UNIT NO. 6

RENOVASCULAR COMPLICATIONS

Prof A Vathsala

ABSTRACT

Hypertension is an important risk factor for cardiovascular morbidity and mortality and can lead to chronic kidney disease (CKD) as manifested by proteinuria, renal dysfunction (eGFR <60 ml/min/1.73 m^2) and end stage renal failure. From the results of a survey in the US general population, over 17% were demonstrated to have proteinuria or renal dysfunction. On the other hand, hypertension was present in a significant proportion of those with underlying CKD: among survey participants, 51% of those with proteinuria and over 60% of those with eGFR < 60 ml/min/1.73 m^2, had hypertension. From the National Health Survey Singapore, 2004, the prevalence of hypertension in adults was 24.9%. Thus there is a strong association between hypertension and CKD and a significant proportion of the Singapore population is at risk for CKD. Regardless of whether hypertension is the cause or the result of CKD, one of the most difficult problems in managing patients with CKD is the achievement of blood pressure (BP) targets recommended by guidelines. Management of hypertension in CKD includes lifestyle measures such as sodium restriction as well as pharmacologic measures. A treatment regimen that optimises BP control while reducing proteinuria is necessary to reduce progression of kidney disease while minimising the risks of heart disease and stroke.

Keywords: chronic kidney disease, eGFR, microalbuminuria, end stage renal failure, Singapore Renal Registry, hypertension.

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PREVALENCE OF HYPERTENSION IN THE SINGAPORE POPULATION

According to the last National Health Survey (NHS), Singapore, 2004 [1], the prevalence of hypertension in adults aged 30 to 69 years in 2004 was 24.9%. Hypertension was more prevalent in males (29.5%) than females (20.4%) and more prevalent among Chinese (25.6%), compared with Malays (22.7%) and Indians (21.6%). The age specific prevalence of hypertension rose dramatically above the age of 40 years (prevalence of 8.8%, 21.6%, 36.2% and 56.1%, for those of 30-39 years, 40-49 years, 50-59 years and 60-69 years respectively). However, among those found to have hypertension, only 61.5% had been previously diagnosed, with 49.5% of these having good blood pressure control, as defined by systolic blood pressure < 140 mm Hg and diastolic blood pressure < 90 mm Hg.

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RENAL EFFECTS OF HYPERTENSION

Hypertension is a risk factor for atherosclerosis and its attendant complications and is an independent risk factor for heart failure, coronary artery disease, stroke, kidney disease and peripheral arterial disease. It is the most important risk factor for cardiovascular morbidity and mortality. Given the high prevalence of hypertension in the population and the wide range of end organ damage associated with hypertension, it would be useful to quantitate the impact of hypertension on these co-morbidities in the Singapore population.

However the NHS, Singapore was not intended to evaluate the systemic effects of hypertension; contrariwise, similar surveys in the United States have evaluated the impact of hypertension on various organs including the kidney. The National Health and Nutrition Examination Survey (NHANES) III [2], is a cross-sectional examination survey of the US civilian non-institutionalised population. For those surveyed between 2005 and 2008, approximately 68 million (31%) US adults aged ≥18 years had hypertension. The prevalence of hypertension was 30% and 31.7% among males and females respectively and as with the Singapore population, the prevalence of hypertension was higher among those 40 years and older. Among those aged 18-39 years, 40-64 years and >65 years, the prevalence of hypertension was 7.4%, 35.6% and 69.7% respectively. Of these, 70% were receiving pharmacologic treatment and 46% had good control of blood pressure. The many similarities between hypertension in the Singapore and US populations permit extrapolation of renal complications from one population to the other.

NHANES survey participants were evaluated for evidence of chronic kidney disease (CKD) by determining urinary protein and renal function[3]. Urine albumin (mg/l) and urinary creatinine (mg/dl) were measured and the urinary albumin/creatinine ratio (ACR) calculated. Participants with ACR > 30 mg/g were classified as having microalbuminuria. Renal function as estimated with the glomerular filtration rate (ml/min/1.73 m^2, eGFR) utilised the stan¬dardised creatinine and the MDRD formula described by Levey et al. Presence of chronic kidney disease (CKD) was defined as an eGFR < 60 ml/min/1.73m^2, or an eGFR ≥ 60 in the presence of

microalbuminuria. CKD stages were defined as follows:

Stage 1	ACR ≥ 30 and eGFR ≥ 90
Stage 2	ACR ≥ 30 and 60 ≤ eGFR ≤ 89
Stage 3	30 ≤ eGFR < 60
Stage 4	15 ≤ eGFR < 30
Stage 5	eGFR < 15

Among those with self reported hypertension in the survey, 17.2% had eGFR < 60 ml/min/1.73 m^2 while 17.3% had ACR > 30 mg/g, in contrast to the prevalence of these findings of 7.8% and 9.9% in the non-hypertensive population. In comparison to those without hypertension, the Odds ratio for reduced eGFR and microalbuminuria among hypertensives were 1.9 and 1.6 respectively. Thus the overall prevalence of CKD was significantly increased in the hypertensive population.

Indeed, on the other side of the spectrum of relationship between hypertension and CKD, the prevalence of hypertension was higher among those with proteinuria or reduced eGFR. Hypertension was present in 24% of par¬ticipants with an ACR < 10 mg/g, compared to 51% of those with an ACR > 30 mg/g. Among NHANES participants with eGFR < 60 ml/min/1.73 m^2, approximately 64% to 68% had hypertension, compared to 26% of those with an eGFR > 60 ml/min/1.73m^2. The prevalence of hypertension also rose with increasing CKD severity. In participants with eGFR < 30 ml/min/1.73 m^2, 84 to 85 percent had hypertension, compared to 5% of participants with eGFR > 60 ml/min/1.73 m^2. Renal dysfunction further conferred mortality risk in this survey population: deaths per 1,000 patient years were 45, 7 and 4 respectively for those with eGFR <60, 60-89 and > 90 ml/min/1.73 m^2. Thus the overall prevalence of hypertension was significantly increased in the population with either reduced eGFR or proteinuria.

This survey data is clear evidence of the strong association of CKD with hypertension in the general population. In this context, hypertension has been described as both a "victim" and a "villain". As a villain, atherosclerotic, hypertension-related vascular lesions in the kidney primarily affect the afferent arterioles resulting in ischemic changes in the glomeruli. Glomerular hyperperfusion and hyperfiltration from hypertension may also cause glomerular injury by direct damage to the glomerular capillaries. Glomerular injury progresses to glomerulosclerosis and eventually to renal tubular ischemia and atrophy. These glomerular changes lead to renal abnormalities including proteinuria and renal dysfunction as demonstrated above. In cases of malignant hypertension, fibrinoid necrosis of the afferent arterioles sometimes extending into the glomerulus occurs and may result in focal necrosis of the glomerular tuft, eventually progressing to renal damage.

Apart from the effects of hypertension on the kidney as described above, CKD itself increases the prevalence and severity of hypertension as described above. Extracellular fluid expansion in CKD may contribute to exacerbation of hypertension, leading to accelerated glomerular injury. Other mechanisms of exacerbation of hypertension in CKD include

- Renin-angiotensin aldosterone system activation
- Renovascular disease
- Increased sympathetic activity
- Alteration in endothelium-derived factors (nitric oxide/endothelin).

Hypertension as a cause of end stage renal failure (ESRF) is estimated at 27% in the US, with the proportion being particularly high among African Americans. Hypertension as a cause of ESRF is however less common in Singapore, with its estimated contribution approximately 10% of ESRF from data from the Singapore Renal Registry[4].

MANAGEMENT OF HYPERTENSION

Regardless of whether hypertension is the cause or the result of CKD, one of the most difficult problems in managing patients with CKD is the achievement of blood pressure (BP) targets recommended by guidelines[5]. Post hoc analyses of randomised clinical trials in patients with proteinuria > 300 mg/day have demonstrated slower declines in kidney function with lower BP levels. Thus, international guidelines for treatment of hypertension published since 2003, including the Seventh Report of the Joint National Committee on Prevention,Detection, Evaluation, and Treatment of High Blood Pressure (JNC7), recommend BP targets below 130/80 mm Hg for those with CKD so as to reduce progression of kidney damage. Furthermore, based on post hoc analyses of several studies demonstrating maximal slowing of nephropathy only when proteinuria was reduced to at least 30% below baseline values, and in conjunction with BP reduction, therapy to reduce proteinuria has become a recommendation in the management of hypertension and CKD.

Management of hypertension in CKD includes lifestyle measures such as sodium restriction as well as pharmacologic measures. For the latter, first line therapy comprising of Renin Angiotensin Aldosterone Blockers (RAAS), Angiotensin Converting Enzyme Inhibitors (ACEi) or Angiotensin Receptor Blockers (ARB), together with diuretics and Calcium Channel blockers (CCB) so as to control blood pressure and reduce proteinuria is recommended (Table 1). Beta blockers may be substituted for CCBs if the patient has angina, heart failure or arrhythmia. Agents such as hydralazine, methyldopa or clonidine can be used as adjunctive agents to achieve BP goals. Apart from these, aldosterone antagonists may be useful in treating hypertension in those with hypertension and advanced heart failure and for reducing proteinuria in those with significant proteinuric kidney diseases. On the basis of several studies, multiple agents are often required to achieve satisfactory blood pressures (3.3 agents at maximally tolerated doses).

Table 1: Guidelines for Management of Hypertension in Chronic Kidney Disease

	Antihypertensive Drug Class
Preferred Initial Antihypertensive	Angiotensin Converting Enzyme Inhibitors, Or Angiotensin Receptor Blockers
Adjunctive Antihypertensives	
2nd Line	Thiazide Diuretics for GFR ≥ 30 mL/min
	Loop Diuretics for GFR< 30 mL/min
3rd Line	Beta Blockers, Or Calcium Channel Blockers
Target Blood Pressure	< 130/80 mm Hg
Precautions	
ACEI / ARB	- Hyperkalemia, K^+ > 5.5 mmol/L - GFR Decline ≥ 30% from Baseline Value - Renal Artery Stenosis - Pregnancy
Aldosterone Antagonists	- Chronic Kidney Disease - Hyperkalemia, K^+ > 5.5 mmol/L
Diuretics	- Gout
Beta Blockers	- Bradycardia - Heart Failure - Heart Block - Asthma, Chronic Obstructive Lung Disease - In combination with Non-Dihydropyridine Calcium Channel Blockers
Calcium Channel Blockers	- Heart Block
Special Indications for Adjunctive Antihypertensives	
Heart Failure with Systolic Dysfunction	- Thiazide or Loop Diuretics - Aldosterone antagonists - Selected Beta Blockers[a]
Post Myocardial Infarction	- Beta Blockers
Chronic Stable Angina	- Beta Blockers - Calcium Channel Blockers
Coronary Artery Disease	- Thiazide or Loop Diuretics - Beta Blockers - Calcium Channel Blockers
Stroke prevention	- Thiazide or Loop Diuretics
Supraventricular tachycardia	- Beta Blockers - Non Dihydropyridine Calcium Channel Blockers

[a] Selected beta blockers such as Carvedilol, bisoprolol, metoprolol
Adapted from Guidelines from the Joint National Commission on the Prevention, Detection, Evaluation, Treatment of Hypertension and National Kidney Foundation Kidney Disease Outcomes Initiative and American Society of Hypertension position paper[5,6].

CONCLUSIONS

A treatment regimen that optimises BP control while reducing proteinuria is necessary to reduce progression of kidney disease while minimising the risks of heart disease and stroke.

REFERENCES

1. National Health Survey 2004 Singapore. Epidemiology and Disease Control Division, Ministry of Health. Singapore: Ministry of Health Publishers, 2005.
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5. Khosla N, Kalaitzidis R, Bakris GL. The kidney, hypertension and remaining challenges. Medical Clinics of North America. 2009; 93: 697-715.
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LEARNING POINTS

- **Hypertension is an important risk factor for cardiovascular morbidity and mortality and is associated with renal complications.**
- **The prevalence of hypertension in adults aged 30 to 69 years in 2004 in the Singapore population was 24.9%, indicating a large burden of disease.**
- **Only 61.5% had been previously diagnosed and only 49.5% of those diagnosed with hypertension having good blood pressure control, as defined by systolic blood pressure < 140 mm Hg and diastolic blood pressure < 90 mm Hg.**
- **One of the most difficult problems in managing patients with CKD is the achievement of blood pressure (BP) targets recommended by guidelines.**
- **A treatment regimen that optimises BP control while reducing proteinuria is necessary to reduce progression of kidney disease while minimising the risks of heart disease and stroke.**

ASSESSMENT OF 30 MCQs

FPSC NO : 44
MCQs on NEW HORIZONS IN HYPERTENSION
Submission DEADLINE: 25 November 2011

INSTRUCTIONS

- **To submit answers to the following multiple choice questions, you are required to log on to the College On-line Portal (www.cfps2online.org).**
- **Attempt ALL the following multiple choice questions.**
- **There is only ONE correct answer for each question.**
- **The answers should be submitted to the College of Family Physicians Singapore via the College On-line Portal before the submission deadline stated above.**

1. Which of the following is a CORRECT list of established risk factors for hypertension?

A. Increasing age, female sex, and diabetes.
B. Increasing age, female sex, and menopause.
C. Increasing age, male sex, and andropause
D. Low socioeconomic status, male sex, and obesity.
E. Female sex, malnutrition, and diabetes

2. About hypertension in Singapore, which of the following statement is CORRECT?

A. Hypertension is the most common condition noted in hospital admissions.
B. Hypertension is more prevalent in Singapore compared to North America or European countries
C. Hypertension prevalence reaches a peak and plateaus off as the population gets older.
D. Hypertension is present in about a quarter of the population aged 18 to 69 years old.
E. ALL of the above are correct.

3. In population surveys conducted in Singapore in the last 15 years which of the following statement about hypertension is CORRECT?

A. About 38% of hypertensives were previously undiagnosed in the 2004 National Survey.
B. Undiagnosed hypertension was more common in females.
C. Amongst the men, hypertension was most prevalent among the Malays.
D. Amongst the women, hypertension is most common among the Indians.
E. ALL of the above are correct.

4. With regards to blood pressure control in Singapore, which of the following statement is CORRECT?

A. The 2004 National Survey showed good BP control. (<140/90mmHg) in about 37.7% of the population.
B. The 2006 polyclinic survey showed only 25% of hypertensives had good BP control.
C. The Chinese had better BP control than Malays and Indians.
D. In the elderly, 90 % of them had good BP control.
E. Elevated blood pressure is normal in the elderly and no treatment is needed.

5. In diabetics with hypertension, there is a high prevalence of microalbuminuria so there is a value in screening for this. One local study, found that X% of hypertensive diabetics had microalbuminria. What is X?

A. 43.5.
B. 48.5.
C. 53.5.
D. 58.5.
E. 63.5.

6. With regards to blood pressure (BP) variability, which of the following statement is CORRECT?

A. Night time BP is 10-20% higher than daytime BP. undiagnosed in the 2004 National Survey.
B. There is a steeper increase of BP in the early night hours
C. There is no increase of BP throughout the waking hours in normotensive subjects.
D. Hypertensive patients who exhibit BP variability have increased risk of end organ damage.
E. Late night surge in BP is associated with higher risk of acute myocardial infarction, sudden death and stroke.

7. With regards to blood pressure variability in the UK-TIA & ASCOT-BPLA trials, which of the following statement best describes the results from the studies?

A. Late evening surge in BP is associated with a higher risk of stroke.
B. So long as the average BP is below target, the risk of stroke is reduced.
C. Treatment to reduce BP variability has marginal effect in reducing cardiovascular risk.
D. Patients with normal BP in the clinic is at less risk to have pressures that spike to dangerous levels in other situations.
E. Excessive variability in systolic BP was associated with increased risk of cardiovascular events.

8. About Home BP monitoring (HBPM), which of the following statement is CORRECT?

A. HMBP does not eliminate the problem of white coat hypertension.
B. HMBP does not require much patient participation.
C. HMBP is not able to detect diurnal BP variation, surges and troughs.
D. HBPM has been shown to provide better prediction of end organ damage and cardiovascular risk compared to clinic BP.
E. HMBP is of limited use in monitoring the BP of elderly patients as BP variability decreases with age.

9. About Ambulatory BP monitoring, (ABPM) what is its advantage over Home BP monitoring (HBPM)? about hypertension is CORRECT?

A. ABPM provides a complete picture of BP diurnal variation.
B. ABPM provides day-time BP profile which is superior to night-time ambulatory BP as a cardiovasculr outcome predictor.
C. ABPM is cheaper to do than HBPM.
D. ABPM upper limits of normal for day-time readings is 120/70 mmHg.
E. ABPM is more repeatable than HBPM.

10. About the choice of drugs for BP control, which of the following statement is CORRECT?

A. ARB-CCB is an "average" combination in treating high BP.
B. ACE-inhibitor-Diuretic is a "preferred" combination in treating high BP.
C. Beta-blocker/ thiazide combination is more effective than calcium channel blocker / ACE-inhibitor in reducing systolic BP variability.
D. ACE inhibitor-beta-blocker is a 'preferred' combination in treating high BP.
E. ACE inhibitor-ARB is a "preferred" combination in treating high BP.

11. About risk factors for cerebrovascular diseases, which of the following statement is CORRECT?

A. About 54% of strokes worldwide are attributable to hypertension.
B. Increasing age is most important single modifiable risk factor.
C. Blood pressure level and risk of stroke is not consistent and continuous.
D. Hypertension increases the risk of haemorrhagic strokes but not ischaemic strokes.
E. Hypertension plays a key role in large artery atherosclerosis but not lacunae strokes.

12. In Singapore, with regards to the diagnosis of cerebrovascular accidents which of the following statement is CORRECT?

A. A patient with an acute onset of neurological symptoms persisting for more than 12 hours has a stroke.
B. Neurological symptoms from impaired cerebrovascular perfusion that recovers within 1 hour is by definition a stroke.
C. The Face, Arm, Speech Test (FAST) is a validated tool to screen for diagnosis of stroke or transient ischaemic attack (TIA).
D. Initial diagnosis of cerebrovascular accident is made by ultrasound scan.
E. It is important to exclude hyperglycaemia in all patients presenting with sudden onset of neurological symptoms

13. In patients suspected of having a transient ischaemic attack (TIA), which of the following statement on management is CORRECT?

A. A patient with ABCD2 score of 4 and above should be started on aspirin 100mg daily immediately.
B. Patients with 2 or more TIA's in a week should be treated as high risk only if the ABCD2 score is above 3.
C. Patients suspected of TIA but low risk score of 3 or below should be referred within 2 weeks to a specialist.
D. Patients who present to you with TIA symptoms that occurred more than 1 week ago should be referred to a specialist within 48 hours.
E. A patient with ABCD2 score of 4 and above should be referred to a specialist within 24 hours of onset of symptoms.

14. With regards to Peripheral vascular Disease (PVD), which of the following statement is CORRECT?

A. The risk of PVD is independent of blood pressure.
B. The presence of PVD increases the risk of cardiovascular events.
C. In PVD, the risk of intermittent claudication is high.
D. About half of patients with PVD have hypertension.
E. Ankle brachial index is a highly specific (91%) and sensitive (99%) for PVD.

15. About the management of Peripheral vascular Disease (PVD), which of the following is useful?

A. Decreasing exercise.
B. Lowering LDL to less than 4mmol/L.
C. Avoiding ACE inhibitors.
D. Prescribing pentoxifylline because it benefits 80% of patients.
E. Controlling blood pressure

16. With regards to changing unhealthy behaviours which of the following statement is CORRECT?

A. Unhealthy behaviours cause more than 60% of premature deaths.
B. Just telling patients that they are at risk of developing diseases is usually sufficient to change behaviour.
C. Most consultations about changing unhealthy behaviours are heart sink experiences.
D. The usual consultation taking place at the clinic is the main source of behaviour change.
E. Patients are changing their behaviour more readily nowadays compared to before.

17. In the process of changing unhealthy behaviours, patients usually go through a series of stages. Which of the following statement about these stages is CORRECT?

A. There are usually six stages that a person navigates or goes through in the transtheoretical model of change.
B. During the course of change, the person usually moves forward from one stage to the next stage.
C. In the action stage, relapse is uncommon.
D. Patients relapse only once or twice before behavior change is complete and stable.
E. A framework that describes the natural sequence of behaviour change is the Trans-theoretical Model (TTM) or Stages of Change model.

18. About behaviour change, which of the following statement is CORRECT?

A. Behaviour must be visible if durable change is to take place.
B. The patient must listen to the doctor in order to change.
C. The patient decides when he or she is ready for change.
D. The doctor should decide for the patient when is best time for change.
E. The patient who is motivated to change usually jumps over several stages.

19. With regards to relapse after a behaviour has succeeded in changing, which of the following statement is CORRECT?

A. Relapse is uncommon.
B. Relapse is an indicator for failure to change.
C. Relapse is reduced by inducing fear of complications.
D. It is seldom necessary to go through several cycles of changes before relapse is eliminated.
E. Relapse is an excellent opportunity to learn about the patient's own life circumstances.

20. About motivational Interviewing (MI), which of the following statement is CORRECT?

A. The patient has generally no motivation for change and needs to be motivated
B. MI is a doctor-centred and oriented directive method to elicit change.
C. In MI, the doctor acts as guide, facilitator and collaborator to elicit and strengthen motivation for change.
D. The doctor usually allows the patient to control and submits to patient's autonomy and wishes.
E. Openly challenging the patient is a core MI skill.

21. About core communication skills that the practitioner needs to employ in MI, which of the following is CORRECT?

A. Asking, exploring, and challenging.
B. Asking, directing, and listening.
C. Challenging, listening, and guiding
D. Asking, challenging, and directing.
E. Asking, listening, informing

22. According to the Global Burden of Disease 2000 study, X% of all ischaemic heart disease is attributable to high blood pressure. What is X?

A. 32
B. 37
C. 42
D. 47
E. 52

23. Figures on hypertension causes, deaths, and effect size of treatment are now available. About these figures, which of the following statement is CORRECT?

A. Reduction of 10 to 20 mm Hg systolic for a few years confers a relative risk reduction 16% for stroke.
B. Reduction of 5 to 6 mm Hg diastolic for a few years confers a relative risk reduction 38%% for coronary heart disease.
C. Blood pressure control in most countries is now optimal.
D. Essential or idiopathic hypertension accounts for 75% of all hypertension cases in a population
E. About half of BP-attributable deaths occur between systolic BP 115mmHg and 140mmHg.

24. About single pill combination therapy, which of the following statement is CORRECT?

A. A combination of 4 or more agents is often needed to achieve target control of BP.
B. JNC 6 was the first guideline to advocate first line combination therapy.
C. Single pill combination therapies are becoming more commonly used in achieving target control of BP.
D. Combination therapies almost always involve the older generation classes of drugs.
E. Single pill combinations always give more side effects than the individual drugs used by themselves.

25. About the effects of antihypertensives, which of the following is CORRECT?

A. In patients with high cardiovascular risk, ARB is contraindicated.
B. In patients with high cardiovascular risk, ARB is better than ACE inhibitors in giving CV protection.
C. Short acting calcium channel blockers protect against major cardiovascular events.
D. Diuretics activates renin-release and hence ACEI which is a blocker of the renin-angiotensin system is a good antihypertensive to be combined with it.
E. The ACE/ARB combination potentiates the antihypertensive effect of one another.

26. About prevalence of hypertension treatment in the United States, X% were receiving pharmacologic treatment. What is X?

A. 30
B. 40
C. 50
D. 60
E. 70

27. A 60-year-old patient with hypertension and diabetes mellitus of 15 years duration is now in stage 5 chronic kidney disease. His estimated GFR (eGFR) is expected to be less than Xml/min/1.73m^2. What is X?

A. 5
B. 10
C. 15
D. 20
E. 25

28. Based on the National Health and Nutrition Examination Survey (NHANES) III, conducted between 2005 and 2008, 17.3% of the population had an albumin-creatinine ratio of more than 30 mg/g if they are hypertensive compared to X% if they not hypertensive. What is X?

A. 6.9
B. 7.9
C. 8.9
D. 9.9
E. 10.9

29. In the management of hypertension in chronic kidney disease, which of the following is a preferred initial antihypertensive?

A. Thiazide diuretic.
B. Angiotensin converting enzyme inhibitor.
C. Beta blocker.
D. Calcium channel blocker.
E. Loop diuretic.

30. With regards to the use of a diuretic as adjunct antihypertensive, you would choose a loop diuretic if the GFR is less than X ml/min. What is X?

A. 30
B. 35
C. 40
D. 45
E. 50

FPSC No. 37 "Primary Care Mental Health" Answers to 30 MCQ Assessment		
1. B	11. B	21. B
2. E	12. D	22. C
3. C	13. B	23. D
4. A	14. E	24. D
5. C	15. C	25. E
6. B	16. D	26. A
7. E	17. E	27. B
8. C	18. C	28. A
9. E	19. D	29. A
10. D	20. B	30. D

FPSC No. 38 "Management of Family Violence" Answers to 30 MCQ Assessment		
1. A	11. C	21. C
2. D	12. B	22. E
3. D	13. E	23. A
4. E	14. D	24. D
5. C	15. D	25. B
6. B	16. E	26. A
7. E	17. E	27. C
8. B	18. A	28. D
9. E	19. A	29. B
10. C	20. B	30. A

FPSC No. 39 "Oral Health in Primary Care" Answers to 30 MCQ Assessment		
1. E	11. E	21. D
2. D	12. D	22. C
3. C	13. B	23. E
4. E	14. A	24. D
5. D	15. D	25. E
6. C	16. C	26. A
7. E	17. E	27. E
8. B	18. A	28. A
9. C	19. B	29. D
10. E	20. B	30. C

FPSC No. 40 "Online Notifications & E-Services Platform" Answers to 30 MCQ Assessment		
1. D	11. B	21. E
2. B	12. C	22. B
3. E	13. A	23. B
4. C	14. E	24. E
5. B	15. D	25. D
6. E	16. C	26. D
7. C	17. D	27. A
8. B	18. A	28. E
9. D	19. E	29. B
10. E	20. B	30. A

FPSC No. 41 "Management of Functional Decline in Older Adults" Answers to 30 MCQ Assessment		
1. C	11. E	21. B
2. D	12. C	22. A
3. E	13. E	23. B
4. C	14. D	24. E
5. B	15. B	25. D
6. A	16. B	26. C
7. D	17. A	27. B
8. C	18. C	28. E
9. B	19. E	29. D
10. E	20. D	30. E

READINGS

A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO
NEW HORIZONS IN HYPERTENSION

A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO NEW HORIZONS IN HYPERTENSION

some available as free full-text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – Non-pharmacological aspects of blood pressure management

Hedayati SS, Elsayed EF, Reilly RF. Non-pharmacological aspects of blood pressure management: what are the data? Kidney Int. 2011 May;79(10):1061-70. Epub 2011 Mar 9. Review. PubMed PMID: 21389976.

URL: http://dx.doi.org./10.1038/ki.2011.46 (payment required)

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ABSTRACT

Hypertension affects 29% of US adults and is a significant risk factor for cardiovascular morbidity and mortality. Epidemiological data support contribution of several dietary and other lifestyle-related factors to the development of high blood pressure (BP). Several clinical trials investigated the efficacy of non-pharmacological interventions and lifestyle modifications to reduce BP. Best evidence from randomized controlled trials supports BP-lowering effects of weight loss, the Dietary Approaches to Stop Hypertension (DASH) diet, and dietary sodium (Na(+)) reduction in those with prehypertension, with more pronounced effects in those with hypertension. In hypertensive participants, the effects on BP of DASH combined with low Na(+) alone or with the addition of weight loss were greater than or equal to those of single-drug therapy. Trials where food was provided to participants were more successful in showing a BP-lowering effect. However, clinical studies with long-term follow-up revealed that lifestyle modifications were difficult to maintain. Findings from controlled trials of increased potassium, calcium, or magnesium intake, or reduction in alcohol intake revealed modest BP-lowering effects and are less conclusive. The reported effects of exercise independent of weight loss on BP are inconsistent. PMID: 21389976 [PubMed - indexed for MEDLINE]

READING 2 – The effect of nutrition on blood pressure

Savica V, Bellinghieri G, Kopple JD. The effect of nutrition on blood pressure. Annu Rev Nutr. 2010 Aug 21;30:365-401. Review. PubMed PMID: 20645853.

URL: http://www.annualreviews.org/doi/pdf/10.1146/annurev-nutr-010510-103954 (payment required)

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ABSTRACT

The incidence and severity of hypertension are affected by nutritional status and intake of many nutrients. Excessive energy intake and obesity are major causes of hypertension. Obesity is associated with increased activity of the renin-angiotensin-aldosterone and sympathetic nervous systems, possibly other mineralcorticoid activity, insulin resistance,

salt-sensitive hypertension and excess salt intake, and reduced kidney function. High sodium chloride intake strongly predisposes to hypertension. Increased alcohol consumption may acutely elevate blood pressure. High intakes of potassium, polyunsaturated fatty acids, and protein, along with exercise and possibly vitamin D, may reduce blood pressure. Less-conclusive studies suggest that amino acids, tea, green coffee bean extract, dark chocolate, and foods high in nitrates may reduce blood pressure. Short-term studies indicate that specialized diets may prevent or ameliorate mild hypertension; most notable are the Dietary Approaches to Stop Hypertension (DASH) diet, which is high in fruits, vegetables, and low-fat dairy products, and the DASH low-sodium diet. Long-term compliance to these diets remains a major concern. PMID: 20645853 [PubMed - indexed for MEDLINE]

READING 3 – Ambulatory blood pressure monitoring

7: Kanbay M, Turkmen K, Ecder T, Covic A. Ambulatory blood pressure monitoring: from old concepts to novel insights. Int Urol Nephrol. 2011 Jul 6. [Epub ahead of print] PubMed PMID: 21732053.

URL: http://www.springerlink.com./content/4m6252043xr63t51/ (payment required)

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ABSTRACT

Ambulatory blood pressure monitoring (ABPM) is an out-of-office technique for the assessment of 24-h blood pressure measurements. ABPM is indicated to diagnose many conditions, including white-coat hypertension, resistant hypertension, episodic hypertension, nocturnal hypertension, autonomic dysfunction, hypotension secondary to excessive usage of antihypertensive medication, and masked hypertension. ABPM gives a better prediction of clinical outcomes in patients with hypertension and cardiovascular diseases when compared to office blood pressure measurements. Recently, several new indices have been introduced with the aim of predicting various clinical end-points in several patient populations. In this review, we aimed to determine the clinical utility of 24-h ABPM and its potential implications for the management of hypertension in patients with a high risk of cardiovascular mortality and morbidity, as well as various novel indices that can predict clinical end-points in different patient populations. PMID: 21732053 [PubMed - as supplied by publisher]

READING 4 – Coping style and lifestyle factors and hypertension

Ariff F, Suthahar A, Ramli M. Coping styles and lifestyle factors among hypertensive and non-hypertensive subjects. Singapore Med J. 2011 Jan;52(1):29-34. PubMed PMID: 21298238.

URL: http://smj.sma.org.sg/5201/5201a5.pdf (free full text)

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ABSTRACT

INTRODUCTION: The objective of this study was to investigate the relationship between hypertensive patients and their coping style and associated lifestyle factors.

METHODS: A total of 502 participants attending nine outpatient clinics completed the validated Bahasa Malaysia version of the Coping Inventory for Stressful Situations and sociodemographic questionnaires. The height, weight, pulse rate and blood pressure of all the participants were measured using standardized methods.

RESULTS: A total of 264 (52.6 percent) participants were hypertensive, while 238 (47.4 percent) were not. Participants with

a high task-oriented core showed a significantly lower risk of hypertension compared to those with a low score (odds ratio [OR] 0.546; 95 percent confidence interval [CI] 0.371-0.804). Those with a high emotion-oriented coping score were associated with an increased risk of hypertension (OR 1.691; 95 percent CI 1.107-2.582). Hypertension was also significantly associated with a higher mean body mass index, positive family history of hypertension, history of diabetes mellitus and hypercholesterolaemia. In multiple logistic regression analysis with hypertension status as the dependent variable, a high emotion-oriented coping score, a low task-oriented coping score, age, body mass index, positive family history of hypertension and history of diabetes mellitus remain significant factors in the final model.
CONCLUSION: These results indicated a significant relationship between hypertension and coping styles and lifestyle factors. They underscored the importance of further study as well as the development and implementation of intervention measures to improve coping skills among hypertensive patients, which may be incorporated into the management of hypertension. PMID: 21298238 [PubMed - indexed for MEDLINE]

READING 5 – Individualized guidelines in blood pressure management

Eddy DM, Adler J, Patterson B, Lucas D, Smith KA, Morris M. Individualized guidelines: the potential for increasing quality and reducing costs. Ann Intern Med. 2011 May 3;154(9):627-34. PubMed PMID: 21536939.

URL: http://www.annals.org/content/154/9/627.long (free full text)

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ABSTRACT

BACKGROUND: Current guidelines focus on a particular risk factor and specify criteria for categorizing persons into a small number of treatment groups. OBJECTIVE: To compare current guidelines with individualized guidelines (that use readily available characteristics from each person to calculate the risk reduction expected from treatment and to identify persons for treatment in ranked order of decreasing expected benefit), in the context of blood pressure management. DESIGN: Analysis of person-specific, longitudinal data. SETTING: The ARIC (Atherosclerosis Risk in Communities) Study. PARTICIPANTS: Persons aged 45 to 64 years without preexisting cardiovascular disease who currently do not receive antihypertensive treatment. INTERVENTION: Treatment according to the criteria of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7 guidelines); individualized guidelines, or treatment in decreasing order of expected benefit; and random care, or treatment of persons selected at random. MEASUREMENTS: Number of myocardial infarctions (MIs) and strokes and medical costs. RESULTS: Compared with treating people according to random care, individualized guidelines could prevent the same number of MIs and strokes as JNC 7 guidelines at savings that are 67% greater than using JNC 7 guidelines, or it could prevent 43% more MIs and strokes for the same cost as treatment according to JNC 7 guidelines. The superiority of individualized guidelines was not sensitive to a wide range of assumptions about costs, treatment effectiveness, level of risk for cardiovascular disease in the population, or effects on workflow. The degree of superiority was sensitive to the accuracy of the method used to rank patients and to its span (the proportion of the population for whom all of the outcomes of interest can be calculated). LIMITATIONS: Specific results apply to the effects of blood pressure management on MI and stroke in the ARIC Study population. The methods for calculating individual benefits require quantitative evidence about the relationships among risk factors, long-term outcomes, and treatment effects. CONCLUSION: Use of individualized guidelines can help to increase the quality and reduce the cost of care. PMID: 21536939 [PubMed - indexed for MEDLINE]

READING 6 – Role of vasodilating beta-blockers in controlling hypertension

Basile JN. One size does not fit all: the role of vasodilating beta-blockers in controlling hypertension as a means of reducing cardiovascular and stroke risk. Am J Med. 2010 Jul;123(7 Suppl 1):S9-15. Review. PubMed PMID: 20609697

URL: http://www.sciencedirect.com/science/article/pii/S0002934310003396 (payment required)

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ABSTRACT

Beta-blockers have played a key role in the management of hypertension-related cardiovascular disease for decades, and continue to be recommended as a mainstay of therapy in national guidelines statements. Recent data have shown less optimal reductions in total mortality, CVD mortality, and CVD events with beta-blockers compared with renin-angiotensin system-blocking agents or calcium channel blockers. The beta-blocker class, however, spans a wide range of agents, and the growing concern about the risk-benefit profile of beta-blockers should not be generalized to later-generation vasodilating beta-blockers such as carvedilol and nebivolol. A growing database from hypertension studies confirms the clinical efficacy and safety of vasodilating beta-blockers, and outcome studies indicate that these agents can play an important role in global CVD reduction in patients with hypertensive or ischemic heart failure. PMID: 20609697 [PubMed - indexed for MEDLINE]

READING 7 – Management of hypertension in older persons

Aronow WS. Office management of hypertension in older persons. Am J Med. 2011 Jun;124(6):498-500. PubMed PMID: 21605724.

URL:
http://www.sciencedirect.com.libproxy1.nus.edu.sg/science/article/pii/S0002934311001859 (payment required)

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ABSTRACT

Antihypertensive drug therapy reduces cardiovascular events in older persons. In the Hypertension in the Very Elderly Trial, at 1.8-year follow-up, patients aged 80 years and older treated with antihypertensive drug therapy had a 30% reduction in fatal or nonfatal stroke (P=.06), a 39% reduction in fatal stroke (P=.05), a 21% reduction in all-cause mortality (P=.02), a 23% reduction in death from cardiovascular causes (P=.06), and a 64% reduction in heart failure (P<.001). The goal of treatment of hypertension is to lower the blood pressure to less than 140/90 mm Hg in older persons and to less than 130/80 mm Hg in older persons with diabetes or chronic kidney disease if tolerated. The selection of antihypertensive drug therapy in persons with associated medical conditions depends on their medical conditions. Large meta-analyses of published trials show that thiazide diuretics, angiotensin-converting enzyme inhibitors, calcium channel blockers, angiotensin receptor antagonists, and beta-blockers do not significantly differ in their ability to lower blood pressure and to exert cardiovascular protection in older and younger persons. If the blood pressure is more than 20/10 mm Hg above the goal blood pressure, drug therapy should be initiated with 2 antihypertensive drugs. Other coronary risk factors must be treated. PMID: 21605724 [PubMed - indexed for MEDLINE]

READING 8 – Approach to patient with drug-resistant hypertension

Townsend RR. Attending rounds: a patient with drug-resistant hypertension. Clin J Am Soc Nephrol. 2011 Sep;6(9):2301-6. Epub 2011 Aug 18. PubMed PMID: 21852665.

URL: http://cjasn.asnjournals.org/content/6/9/2301.full.pdf+html (payment required)

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ABSTRACT

Drug-resistant hypertension is present in about one in eight patients with high BP. It can be a frustrating and expensive condition to pursue from an office-based perspective. In this review, utilizing the American Heart Association scientific statement on drug-resistant hypertension as a guide, a case of drug-resistant hypertension is presented and walked through exactly as encountered by the author. Woven into the discussion is a combination of insights from the literature on this topic, blended with the experience of the author. This is not intended as an exhaustive review of each step in the evaluation and management process but, rather, as an overview incorporating a few carefully chosen references and, hopefully, a logical and useful approach to a common clinical challenge. PMID: 21852665 [PubMed - in process]

READING 9 – Diagnosis of secondary hypertension

Viera AJ, Neutze DM. Diagnosis of secondary hypertension: an age-based approach. Am Fam Physician. 2010 Dec 15;82(12):1471-8. Review. PubMed PMID:21166367.

URL: http://www.aafp.org/afp/2010/1215/p1471.html (payment required)

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ABSTRACT

Secondary hypertension is a type of hypertension with an underlying, potentially correctable cause. A secondary etiology may be suggested by symptoms (e.g. flushing and sweating suggestive of pheochromocytoma), examination findings (e.g., a renal bruit suggestive of renal artery stenosis), or laboratory abnormalities (e.g., hypokalemia suggestive of aldosteronism). Secondary hypertension also should be considered in patients with resistant hyper- tension, and early or late onset of hypertension. The prevalence of secondary hypertension and the most common etiologies vary by age group. Approximately 5 to 10 percent of adults with hypertension have a secondary cause. In young adults, particularly women, renal artery stenosis caused by fibromuscular dysplasia is one of the most common secondary etiologies. Fibromuscular dysplasia can be detected by abdominal magnetic resonance imaging or computed tomography. These same imaging modalities can be used to detect therosclerotic renal artery stenosis, a major cause of secondary hypertension in older adults. In middle-aged adults, aldosteronism is the most common secondary cause of hypertension, and the recommended initial diagnostic test is an aldosterone/ renin ratio. Up to 85 percent of children with hypertension have an identifiable cause, most often renal parenchymal disease. Therefore, all children with confirmed hypertension should have an evaluation for an underlying etiology that includes renal ultrasonography. PMID: 21166367 [PubMed - indexed for MEDLINE]

READING 10 - Malignant middle cerebral artery (MCA) infarction

Treadwell SD, Thanvi B. Malignant middle cerebral artery (MCA) infarction: pathophysiology, diagnosis and management. Postgrad Med J. 2010 Apr;86(1014):235-42. Review. PubMed PMID: 20354047.

URL: http://pmj.bmj.com./content/86/1014/235.full.pdf (payment required)

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ABSTRACT

'Malignant MCA infarction' is the term used to describe rapid neurological deterioration due to the effects of space occupying cerebral oedema following middle cerebral artery (MCA) territory stroke. Early neurological decline and symptoms such as headache and vomiting should alert the clinician to this syndrome, supported by radiological evidence of cerebral oedema and mass effect in the context of large hemispheric infarction. The prognosis is generally poor, and death usually occurs as a result of transtentorial herniation and brainstem compression. Treatment options include general measures and pharmacological agents to limit the extent of oedema, and surgical decompression to relieve the pressure effects. Until recently there has been little evidence to guide appropriate treatment, though in the last few years randomised data have been published addressing the role of surgical decompression. A pooled analysis of three European randomised controlled trials suggests that hemicraniectomy performed within 48 h significantly reduces mortality, and improves functional outcome in selected patients, and this has been reflected in recent national guidelines. PMID: 20354047 [PubMed - indexed for MEDLINE]

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  Elder JT, Travakkol A, Klein SB, et al. Protooncogene expression in normal and psoriatic skin. J Invest Dermatol, 1990;94:19-20.

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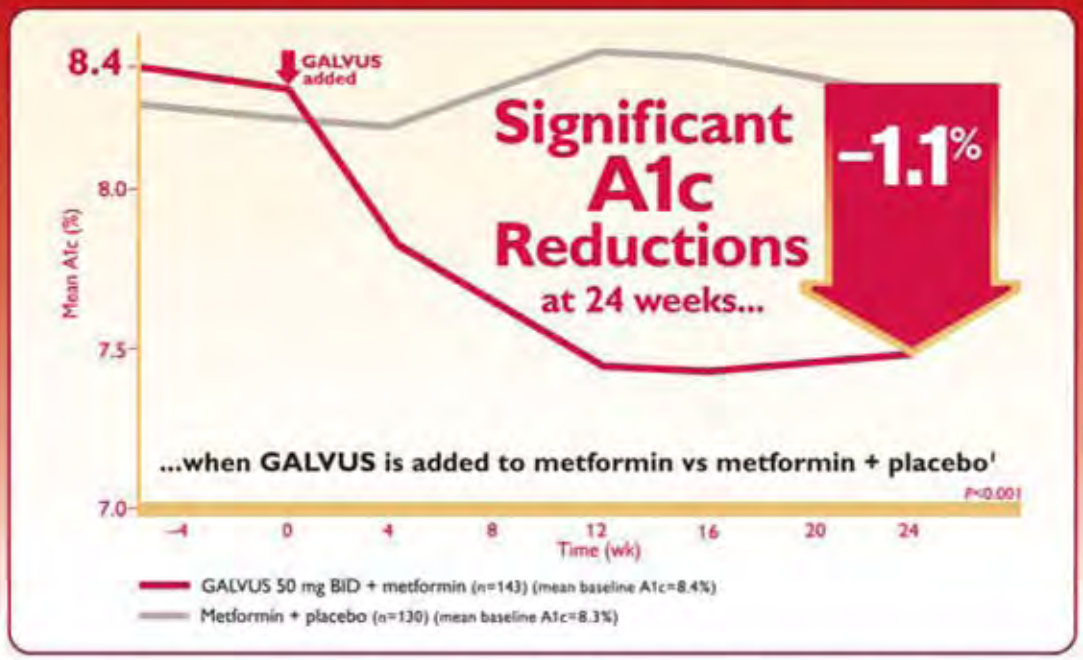

Trial design: 24-week, multicenter, double-blind, placebo-controlled study in patients with type 2 diabetes inadequately controlled with metformin monotherapy (≥1500 mg daily). 544 patients were randomized to receive GALVUS 50 mg BID plus metformin (n=185), or placebo plus metformin (n=182). Mean baseline A1c: 8.3%-8.4%. Mean metformin dosage at baseline was ~2100 mg daily in each arm. Sample sizes in chart represent primary ITT population.

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- 50 mg GALVUS/850 mg metformin BID
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References:
1. Bosi et al. Effects of Vildagliptin on Glucose Control over 24 weeks in patients with Type 2 Diabetes Inadequately Controlled on Metformin. Diabetes Care, 30: 890-895,2007. 2. Rosenstock J, et al. Vildagliptin clinical trials programme in monotherapy and combination therapy for type 2 diabetes. Int J clin Pract, 2008; 62 (1):59, 15-33

Presentation: Vildagliptin Tablets 50 mg. **Indications: •Galvus®** is indicated as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus (T2DM). It is indicated as monotherapy and in dual combination with metformin, a sulphonylurea (SU), a thiazolidinedione (TZD) or insulin when diet, exercise and a single antidiabetic agent do not result in adequate glycaemic control. **Dosage:** • The usual dose is 50 mg or 100 mg daily (in two divided doses of 50 mg) in monotherapy and in dual combination with metformin, a TZD or insulin. 50 mg daily in combination with a SU. •Galvus is not recommended in paediatric patients. **Contraindications:** • Hypersensitivity to vildagliptin or to any of the excipients. **Precautions/Warnings:** • Galvus should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. • Not recommended in moderate or severe renal impairment, or in patients with End Stage Renal Disease (ESRD) or haemodialysis. • Not recommended in patients with moderate hepatic impairment including patients with pre-treatment ALT or AST >2.5X the upper limit of normal. Liver function tests (LFT) to be performed prior to treatment initiation, at three-month intervals during the first year and periodically thereafter. Withdrawal of therapy with Galvus recommended if an increase in AST or ALT of 3X upper limit normal or greater persist. Following withdrawal of treatment with Galvus, if AST or ALT of 3X upper limit normal or greater persist, following withdrawal of treatment with Galvus and LFT normalisation, treatment with Galvus should not be reinitiated. • Contains lactose. **Pregnancy:** Should not be used unless the potential benefit justifies the potential risk to the foetus. **Breast-feeding:** Should not be used. **Interactions:** • Vildagliptin has a low potential for drug interactions. • No clinically relevant interactions with other oral antidiabetics (glibenclamide, pioglitazone, metformin, amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin were observed after co-administration with vildagliptin. **Adverse reactions:** • Rare cases of angioedema. Rare cases of hepatic dysfunction (including hepatitis). Vildagliptin monotherapy - Common: dizziness. • Uncommon headache, constipation, cerebral peripheral. • Combination with metformin - common: headache, tremor, dizziness. • Combination with a sulphonylurea - common: headache, tremor, dizziness, asthenia. • Combination with a thiazolidinedione - common: weight increase, oedema peripheral - uncommon: headache. • Combination with insulin - common: decreased blood glucose, headache, nausea, fatulence, gastroesophageal reflux disease. • Post-marketing experience: pancreatitis, urticaria. **Packs and prices:** Country specific. **Legal classification:** Country specific.

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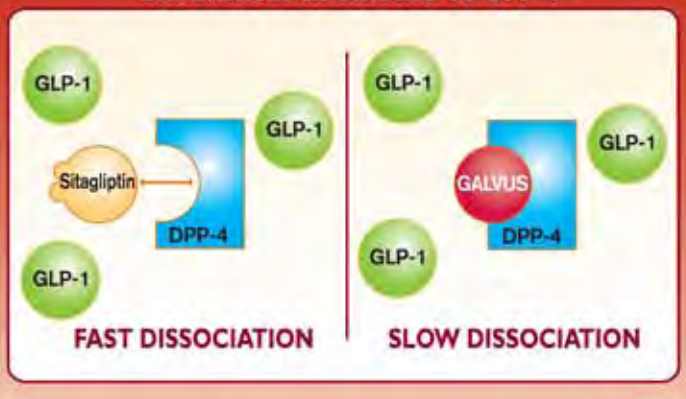
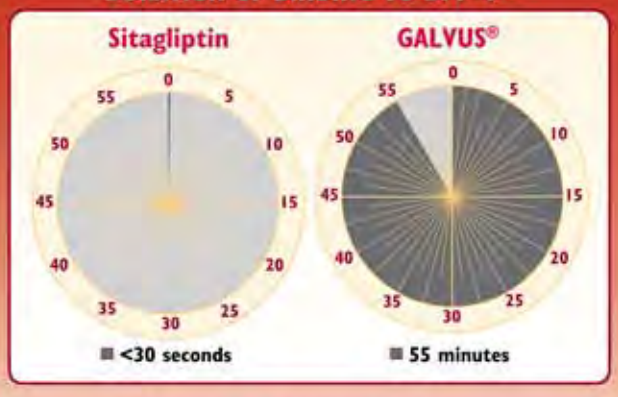
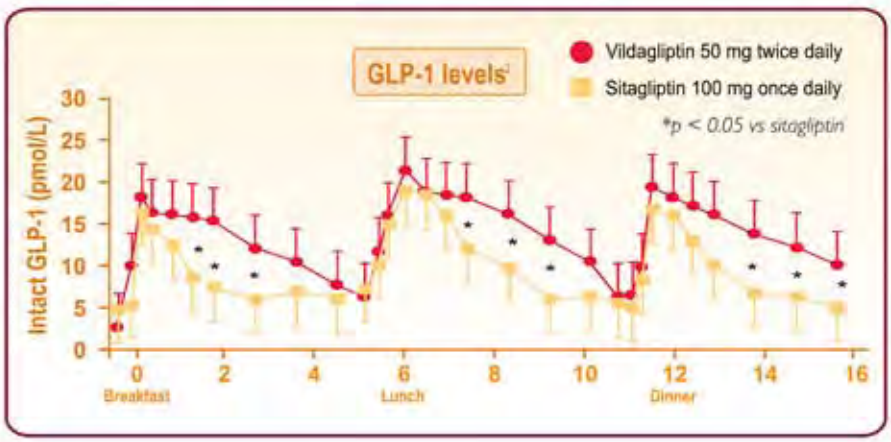


DURATION OF BINDING TO DPP-4[5-7]



Greater increases in active GLP-1 levels with GALVUS® compared with sitagliptin is likely due to tighter and longer-lasting binding[2,5-7]



• *Results from a 3-month exploratory mechanistic study of 48-hour continuous subcutaneous glucose monitoring (CSGM) in 38 patients receiving metformin plus GALVUS (n=18) or sitagliptin (n=20)*[6]

References:
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Presentation: Vildagliptin Tablets 50 mg. **Indications:** •**Galvus®** is indicated as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus (T2DM). It is indicated as monotherapy and in dual combination with metformin, a sulphonylurea (SU), a thiazolidinedione (TZD) or insulin when diet, exercise and a single antidiabetic agent do not result in adequate glycaemic control **Dosage:** •The usual dose is 50 mg or 100 mg daily (in two divided doses of 50 mg) in monotherapy and in dual combination with metformin, a TZD or insulin; 50 mg daily in combination with a SU. •Galvus is not recommended in paediatric patients.**Contraindications:** Hypersensitivity to vildagliptin or to any of the excipients. **Precautions/Warnings:** •Galvus should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. •Not recommended in moderate or severe renal impairment, or in patients with End Stage Renal Disease on haemodialysis. •Not recommended in patients with hepatic impairment including patients with a pre-treatment ALT or AST>2.5X the upper limit of normal. Liver function tests (LFT) to be performed prior to treatment initiation, at three-month intervals during the first year and periodically thereafter. Withdrawal of therapy with Galvus recommended if an increase in AST or ALT of 3X upper limit normal or greater persist. Following withdrawal of treatment with Galvus and LFT normalisation, treatment with Galvus should not be reinitiated. •Contains lactose **Pregnancy:** Should not be used unless the potential benefit justifies the potential risk to the foetus. **Breast-feeding:** Should not be used. **Interactions:** •Vildagliptin has a low potential for drug interactions. •No clinically relevant interactions with other oral antidiabetics (glibenclamide, pioglitazone, metformin), amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin were observed after co-administration with vildagliptin. **Adverse reactions:** •Rare cases of angioedema. Rare cases of hepatic dysfunction (including hepatitis) •Monotherapy - common: dizziness - uncommon: constipation, headache, oedema peripheral. •Combination with metformin - common: headache, tremor, dizziness. •Combination with a sulphonylurea - common: headache, tremor, dizziness, asthenia. •Combination with a thiazolidinedione - common: weight increase, oedema peripheral - uncommon: headache. •Combination with insulin - common: decreased blood glucose, headache, nausea, flatulence, gastroesophageal reflux disease. •Post-marketing experience: pancreatitis, urticaria. **Packs and prices:** Country specific. **Legal classification:** Country specific.

Before prescribing, please consult full prescribing information.

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