http://www.harleystreet.sg/heart
Email **enquiries@harleystreet.sg**

BP – HOW LOW CAN YOU GO?

The treatment targets and thresholds for hypertension continue to evolve as new information becomes available. In 2013 the ESC recommended target was to treat patients to < 140/90. The 2013 guidelines also stated that there was no incremental benefit to lowering BP to < 130/80mmHg. Between 2013 and the updated ESC guidelines in 2018, new evidence emerged. This evidence largely came from trials, registries, and meta-analyses. In patients with high CV risk lowering BP to <130 in comparison to 130-139 was associated with reduction in the risk of stroke.

The question still remains as to how low you can go. The SPRINT trial compared 2 different targets <140mmHg v <120mmHg. More intensive lowering was associated with a 25% reduction in major CV events and a 27% reduction in all cause death. However, there were questions on the methods they used to measure BP in the participants. They used unattended automatic measurement of BP, that some critics said produced numbers much lower than standard office BP. Several meta-analyses since then have been published suggesting benefit in reaching lower targets of 120mmHg, but with an increase in treatment discontinuation due to side effects.

At the ESC congress 2020 some tantalizing new evidence on BP was presented. The Blood Pressure Lowering Treatment Trial Collaboration (BPLTTC) is an individual level patient data analysis in over 348.854 patients pooled from 48 hypertension trials. This is a remarkable dataset with incredible detail unseen before in meta-analyses. They examined the effect of BP lowering on MACE in people below the typical thresholds for hypertension in patients with and without CVD. They found that for every 5mmHg reduction of systolic BP they reduced the risk of CV events by 10%. There was also no evidence that this was affected by baseline BP, there was benefit even in patients with a baseline BP < 120mmHg. In addition, this benefit was seen in patients with and without CVD. This suggests that BP lowering regardless of your starting value and to levels below current targets reduces your risk of events. This paper has not yet been published, however, and so we should currently stick to guideline directed BP targets. But it does give us an indication of what the future might hold for future guidelines.

By **Dr. Michael MacDonald**
Senior Consultant Cardiologist
The Harley Street Heart & Vascular Centre

WHEN SHOULD DOCTORS INVESTIGATE FOR SECONDARY CAUSES OF HYPERTENSION?

Secondary hypertension are cases of arterial hypertension that are due to an identifiable cause- if the underlying cause is removed, then the hypertension can often resolve without the need for long term medication. It has been estimated that about 5 to 10% of cases of hypertension are due to secondary causes. However, accumulating evidence from tertiary centres suggests that the prevalence of secondary hypertension may be much higher (up to 35% in some series), but remain undiagnosed as the appropriate investigations are often not performed.

Although performing routine tests for secondary hypertension in every case of hypertension is time-consuming and not cost effective, there are certain clinical clues that could suggest a secondary cause. These include the following:

- Resistant hypertension- persistently elevated blood pressure greater than 140/90 mmHg despite using three different anti-hypertensives, including a diuretic, all at adequate doses.
- Worsening or labile blood pressure in a patient who had previously stable pressures.
- Hypertension diagnosed in younger patients (under 40 years) who do not have any other risk factors for hypertension, e.g., obesity, family history.
- Patients with severe hypertension (BP greater than 180/110 mm Hg) and patients with end-organ damage such as acute kidney injury, neurological manifestations, flash pulmonary oedema, hypertensive retinopathy, left ventricular hypertrophy.
- Hypertension that is associated with electrolyte disorders such as hypokalemia or metabolic alkalosis.
  Unusual blood pressure profiles on a 24-hour ambulatory blood pressure monitor- usually blood pressure is lower at night than during the day. The absence of this nocturnal "dip" in blood pressure or a "reverse dipping" pattern (when the dip is present during the day instead of at night) can be suggestive of a secondary cause of hypertension.

Recommendations:
Table 1 summarises the common secondary causes of hypertension and useful diagnostic tests which can be considered in patients with the clinical clues stated above. Even though primary hypertension is very common, the astute physician should bear in mind potential secondary causes, based on the profile and medical condition of the patient, and investigate appropriately if suspected.

If a secondary cause of hypertension is found, then the patient should be referred to the appropriate specialist for further evaluation and treatment. It can be very rewarding for the doctor to diagnose secondary hypertension and even more so for the patient who can be spared a life-time of anti-hypertensive medication if the cause can be treated.

At the Harley Street Heart and Vascular centre, we often perform a series of thorough investigations (most of which can be performed in-house) in newly diagnosed hypertensive patients (particularly young patients below the age of 40 years or those with very high or resistant hypertension) to look for secondary causes. These often include:

- A 24 hour ambulatory BP monitor - to confirm the severity and pattern of the hypertension.
- ECG and echocardiogram - to assess for left ventricular hypertrophy.
- Renal duplex ultrasound scan - to assess renal architecture and renal artery stenosis.
- Blood tests for renal function, renin, aldosterone and cortisol levels + urine tests.
- Home sleep study (if clinically indicated).

Table 1. Secondary causes of hypertension

Secondary cause of hypertension	Conditions	Useful tests to aid diagnosis
Endocrine	• Primary aldosteronism (PA) • Cushing' syndrome • Phaeochromocytoma • Hypo/hyperthyroidism	• Plasma Na+ and K+, aldosterone, renin and cortisol levels • Abdominal CT/MR scan • Adrenal vein sampling (for suspected PA) • Plasma or urinary catecholamine and metanephrines (for suspected phaeo) • Overnight dexamethasone suppression test (for suspected Cushing's syndrome)
Renal	• Renal parenchymal disease • Renin- producing tumour • Reno-vascular disease (fibromuscular dysplasia and atherosclerosis	• Renal ultrasound scan • Renal vascular duplex ultrasound scan • CT/MR renal angiogram • Conventional renal angiogram
Obstructive sleep apnoea	• Sleep disordered breathing • May be related to obesity and alcohol	• Sleep study (home sleep study usually sufficient for initial screening)
Iatrogenic	• Drug (e.g. NSAIDs, cancer therapies) • Exogenous hormones/ contraceptive pill	
Miscellaneous	• Aortic coarctation • Arteritis, vasculitis	• Echocardiogram • CT aortogram • Plasma inflammatory markers, autoimmune blood tests, vasculitic screen

By **Dr. Reginald Liew**
Senior Consultant Cardiologist
The Harley Street Heart & Vascular Centre

HYPERTENSION AND THE LATEST ISH 2020 GUIDELINES – MESSAGES FOR PRACTICE

Hypertension and the Latest ISH 2020 Guidelines – Messages for Practice

Hypertension remains the leading cause of death globally, accounting for 10.4 million deaths per year. Hypertension is a major contributor to cardiovascular disease in South Asia and it's prevalence continues to grow. This is a function of population aging, industrialization, adoption of Western lifestyles, high salt intake, and accumulation of precipitating factors such as obesity and tobacco use. In accordance with most major guidelines it is recommended that hypertension be diagnosed when a person's blood pressure in the office or clinic is ≥140/90 mm Hg following repeated examination.

In 2020, the International Society of Hypertension (ISH) has recently developed guidelines for the management of hypertension in adults aged ≥18 years. Conceptually, these 2020 ISH Guidelines are closer to the 2018 ESC/ ESH Guidelines rather than to the 2017 ACC/AHA Guidelines. The 2020 ISH Guidelines simplified the definition of BP categories by eliminating the 'optimal' BP category (BP<120/80mmHg), thereby defining as "normal" BP all values < 130/85 mmHg. The 2020 ISH Guidelines also eliminated the 'Grade 3' ESC category (≥ 180/110 mmHg), thereby assigning a 'Grade 2' to all subjects with office BP ≥160 mmHg systolic and/or 100 mmHg diastolic.

The 2018 ESC/ESH and 2020 ISH Guidelines recommend that hypertension can be diagnosed in a single visit only if BP if severely increased (≥180/110 mmHg). If BP is lower, the diagnosis should be confirmed in two or more clinical visits, or using home BP or 24-hour ABPM. Hence, home BP and 24-hour ABPM have been considered by the 2018 ESC/ESH and 2020 ISH Guidelines as almost equivalent tools to confirm the diagnosis of hypertension, in alternative to repeated clinical visits in patients with BP <180/110 mmHg.

Both guidelines recommend an initial free or fixed drug combination [ACE-inhibitors or angiotensin receptor blockers (A) combined with diuretics (D) or calcium channel blockers (C) -Figure 1].The 2020 ISH Guidelines expressed a preference for A + D after stroke, in the elderly, or in those with incipient heart failure or intolerance to C, as well as the preference for A + C in black patients.

The 2020 ISH Guidelines introduced some novel indications:

1. The BP range requiring drug therapy was set to ≥140/90 mmHg in all subjects, including those aged ≥80 years. The 2018 ESC/ESH Guidelines suggested a higher threshold (≥ 160/90 mmHg) for initiating drug therapy in subjects aged ≥ 80 years. Hence, the 2020 ISH Guidelines seem to support a more intensive approach in these subjects.

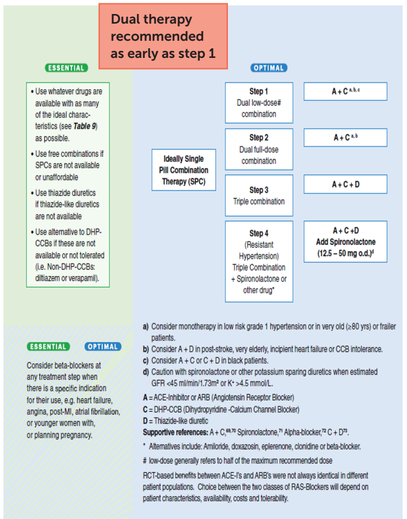
2. In patients with office BP persistently in the range 130–149/ 90–99 mmHg and without overt cardiovascular disease, chronic kidney disease, target organ damage or diabetes, drug treatment should be initiated in all subjects in case of drug availability.

3. In addition to an ideal BP target set to <140/90 mmHg, shared by the 2018 ESC/ESH guidelines, the definition of an 'essential' BP target included a 'BP reduction by at least 20/10 mmHg'. Such indication is reasonable, and based on the 50% reduction in the risk of cardiovascular mortality associated with a 20/10 mmHg BP difference.

4. In patients aged ≥65 years, the BP target is coupled with the indication to 'consider an individualized BP target in the context of frailty, independence and likely tolerability of treatment'. Thus, it seems that the lowest target value of 130 mmHg ('safety boundary'), included in the 2018 ESC/ESH Guidelines in the subset aged ≥65 years was replaced by a more individualized approach based on efficacy and tolerability. However, a safety boundary of 120/70 mmHg in the management of patients aged <65 years is included in both Guidelines.

In summary, the new developments arising from the ISH 2020 include:
i. Redefining hypertension
ii. Initiating treatment with a single pill combination therapy
iii. Advising wider out-of-office BP measurement
iv. Lower BP targets

Figure 1.



By **Dr. Rohit Khurana**
Senior Consultant Cardiologist
The Harley Street Heart & Vascular Centre

ERECTILE DYSFUNCTION AND HYPERTENSION – A DOUBLE-EDGED SWORD

Men with hypertension are almost twice as likely to have impaired penile blood flow and erectile dysfunction (ED) compared to men with normal blood pressure. Both hypertension and ED have an underlying disturbance of endothelial function with impaired production of nitric oxide in the endothelium. This can lead to an increase in vascular smooth muscle (VSM) contraction, arteriosclerosis in the penile vessels with apoptosis of VSM cells, failure of the VSM to relax in response to a sexual stimulus and decreased blood flow to the penis[1].

Stiffening of the vascular system includes the penile vasculature and is likely to be the underlying mechanism linking ED and hypertension especially during the aging process. In a sub-analysis in male participants to the SPRINT study[2], the International Index of Erectile Function Total Score (high scores mean good erectile function) was related negatively to systolic and positively to diastolic BP, confirming the importance of assessing the hemodynamic pattern in the hypertensive patient with sexual dysfunction. The relationship can be seen in figure 1 which is the Erectile dysfunction hemodynamic study of a patient with poor blood pressure control.

However, previous studies have shown that erectile dysfunction is more common in treated, than untreated men with high blood pressure. And certain antihypertensive drugs – notably thiazide diuretics and beta blockers – have been linked with deterioration in sexual function[3]. All medications with potent vasodilator and no counter-regulating activities (including ACE-inhibitors, Angiotensin Receptor Blockers, Ca++-Channel Blockers and **α**-blockers) are not reported to be associated with ED. In fact, they might be protective, as reported for doxazosin and Angiotensin Receptor Blockers. Other medications reducing BP without direct vasodilator effect can worsen sexual function. The possible mechanism is related to the reduced BP, not counterbalanced by vasodilation of penis arterioles and arteries, with consequent reduction of blood flow, and lack of sufficient trapping of incoming blood flow into corporal sinusoids to initiate an erection[4].

These imply that many long-standing hypertensive patients already have significant structural damage in the penile arteries and adding antihypertensive drugs may not further reduce penile blood flow. But in men with normal or high-normal blood pressure, the penile arteries have minimal structural damage. Here medications, particularly beta-blockers and thiazide diuretics, could have a negative impact on penile blood flow.

For men with as yet untreated hypertension, beta blockers and diuretics are not ideal and should be used only if absolutely indicated. However, if a co-existing disease dictates using a specific drug category (for example, beta blockers for coronary artery disease and heart failure, diuretics for heart failure), then switching is not advocated. Alternatives might be considered if patients are at risk of stopping lifesaving therapy because of the detrimental impact of erectile dysfunction on their life. Nebivolol, for example is a highly cardio selective beta-blocker with potent vasodilator properties and increases the secretion of nitric oxide from endothelial cells (a mechanism that, however, has a fundamental assumption in the integrity of endothelial cells). Nebivolol also exerts a synergic effect with type 5 phosphodiesterase inhibitors (PD5-I) in the treatment of ED, with reported beneficial effects on adherence[4].

It is also important to note that switching to another drug class does not guarantee either the restoration or improvement of erectile function. This must be carefully explained to patients in advance to avoid unreasonable expectations. High blood pressure can be treated without causing erectile dysfunction and patients and doctors need to have open discussions to find the best treatment option.

References

1. Hernández-Cerda J, Bertomeu-González V, Zuazola P, Cordero A. Understanding Erectile Dysfunction in Hypertensive Patients: The Need for Good Patient Management. Vasc Health Risk Manag. 2020;16:231-239
2. Foy C.G., Newman J.C., Berlowitz D.R. et al. Blood pressure, sexual activity, and erectile function in hypertensive men: baseline findings from the systolic blood pressure intervention trial (SPRINT). J Sex Med. 2019; 16: 235-247
3. Nunes KP, Labazi H, Webb RC. New insights into hypertension-associated erectile dysfunction. Curr Opin Nephrol Hypertens. 2012 Mar;21(2):163-70
4. Giovanni de Simone, Costantino Mancusi. Erectile dysfunction and arterial hypertension: Still looking for a scapegoat. EJIM. 2020 Nov; 81:22-23

Figure 1. ED hemodynamic study at the Harley Street vascular lab of a hypertensive patient.
Note the high brachial pressure (161 mmHg), low dorsal penile arterial pressures and a poor amplitude (vasodilatory) response to a Caverject injection in the penile vessels compared to the digital vessel waveform above it.

By **Dr. Sriram Narayanan**

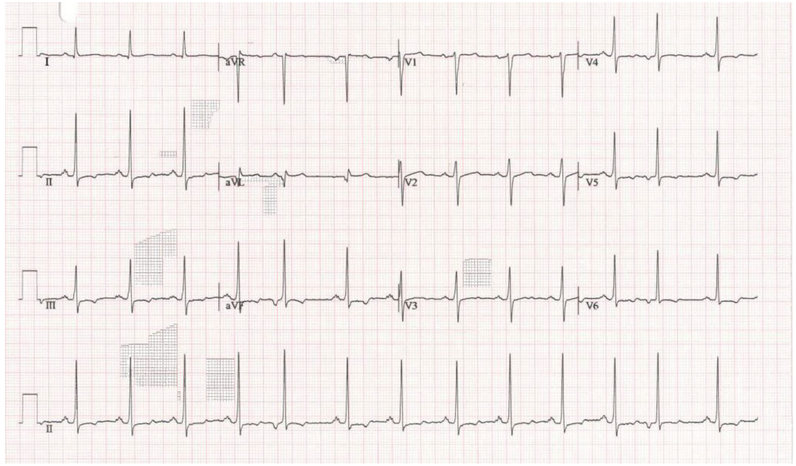
Senior Consultant Vascular & Endovascular Surgeon
The Harley Street Heart & Vascular Centre

QUIZ

51 year old male found to have high BP on routine screening. No other significant past medical history. BP in clinic 180/100.

1. What does the ECG show?
2. What condition does he have based on these blood tests?

Alosterone	531.6 (ref: 3.7-43.2ng/dl)
Renin	2.7 (ref:5.3 – 99.1 uU/ml)
Aldosterone/Renin ratio	196.9 (Ref: <=31)



Answer is available on our website:
http://www.harleystreet.sg/quiz - answers/medbulletin-Mar-2021/

By **Dr. Michael MacDonald**

Senior Consultant Cardiologist
The Harley Street Heart & Vascular Centre

MEDBULLETIN
MARCH2021

THE HARLEY STREET
HEART & VASCULAR CENTRE

INTRODUCTION

In this issue of the newsletter we are focusing on hypertension. This is a big part of everyone's practice, and it is an increasing problem in Singapore, with a prevalence of 18.9% in 2010 rising to 21.5% in 2017 in adults age 30-69. More worrying is the prevalence in young patients; 1 in 5 males in the 40-49 age group have hypertension increasing to 1 in 2 people age 60-69. We know that adequate treatment reduces CV risk, yet <50% of patients currently achieve a target of <140mmHg. In this short series of articles, I explore the future of BP targets, with new evidence presented at the ESC in 2020 from a 350000 patient meta-analysis. Dr Liew summarizes when and how we should be looking for secondary causes. There have been recent updates to the guidelines in 2020, and Dr Rohit provides an update on the key take home messages. Finally, Dr Sriram discusses the effect of hypertension on erectile dysfunction and how we should approach it. We hope you find this short series of articles useful.

From The Harley Street Heart and Vascular Centre

From left to right:
Dr. Sriram Narayanan, Dr. Reginald Liew
Dr. Michael MacDonald, Dr. Rohit Khurana

http://www.harleystreet.sg/heart
Email **enquiries@harleystreet.sg**

LICENSE: MCI (P) 022/02/2021

Mount Elizabeth Novena Specialist Centre
#05-30, 38 Irrawaddy Road
Singapore 329563

Gleneagles Hospital #02-38/41 (Annexe Block)
6A Napier Road
Singapore 258500

Mount Elizabeth Medical Centre
#11-07, 3 Mount Elizabeth
Singapore 228510