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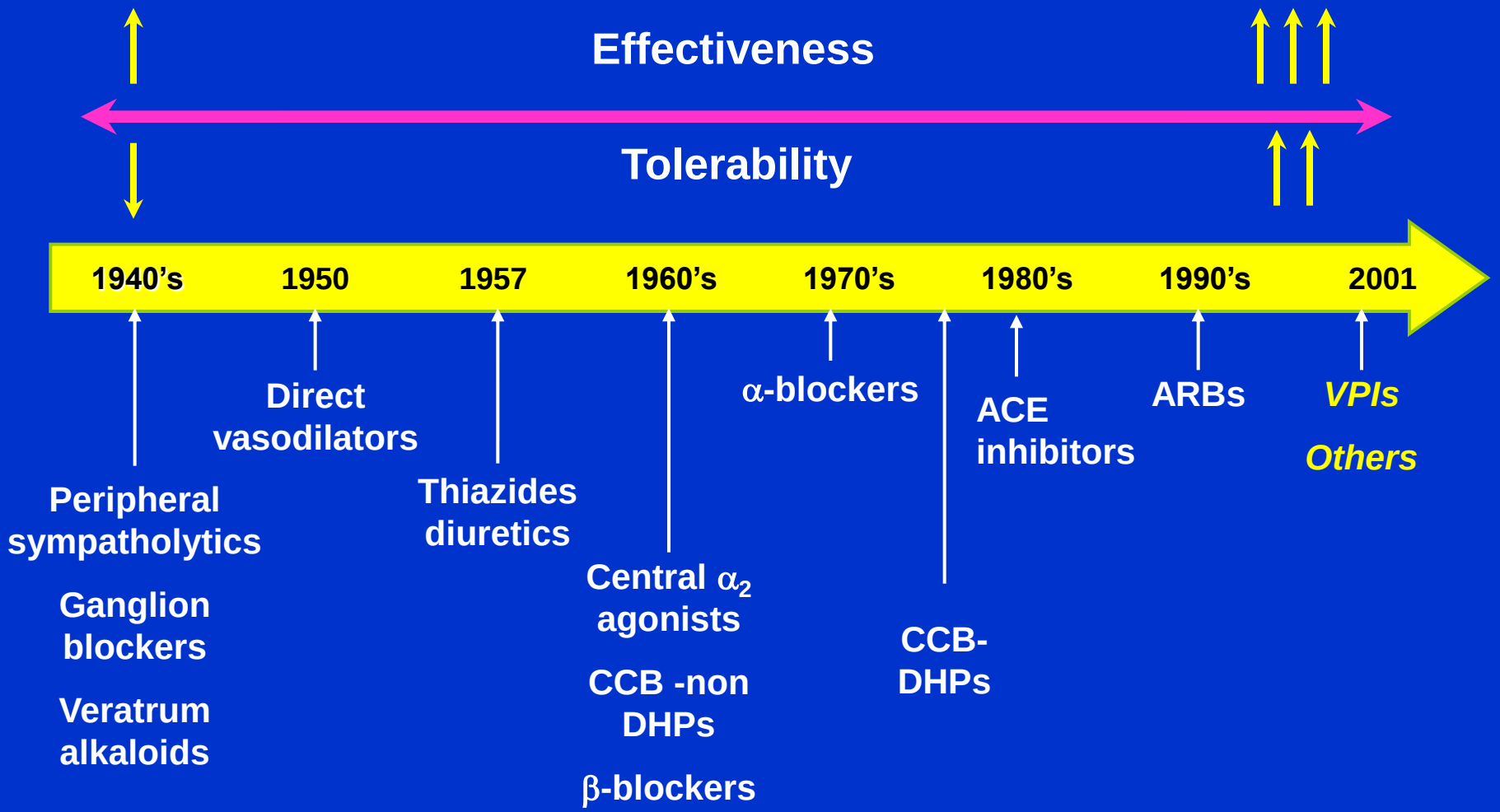
Development of Antihypertensive Therapies



Treatment Goal

- The *short-term goal* is to achieve the recommended goal BP by using the least *intrusive* means possible

- *Intrusive* has several interpretations: *economic, office visits, adverse effects, and convenience*

Hurst, 2004

Treatment Goal

- The ***ultimate goal*** of hypertension treatment is to
  - reduce CV and renal morbidity and mortality

Hurst, 2004

The Ideal Antihypertensive

"… those therapies that not only effectively decrease BP but also reduce the ultimate endpoints, namely, they decrease rates of hypertension-related cardiovascular complications."

- Canadian Hypertension Society

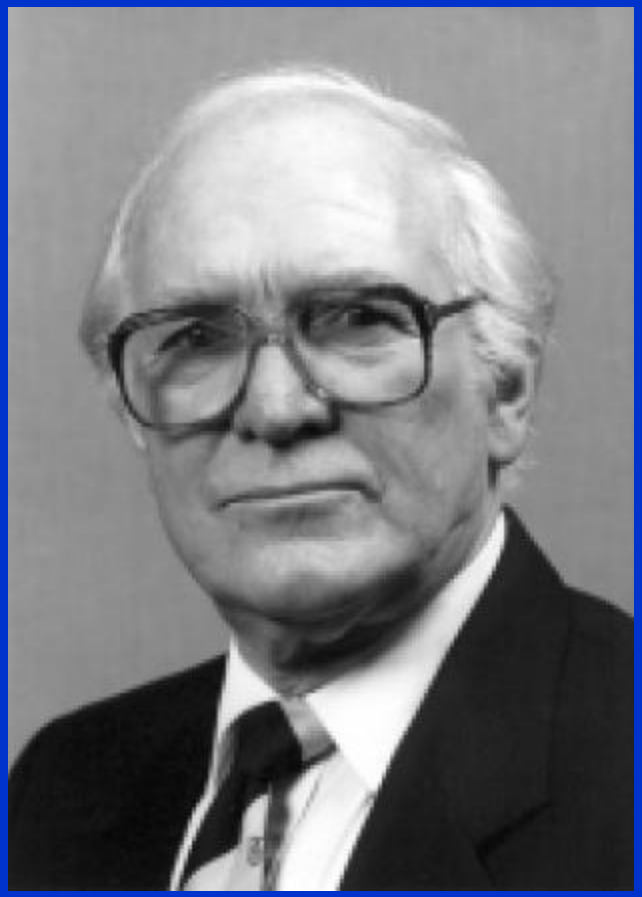
Blood Pressure Reduction + End-organ Protection = Prolonged Survival (Efficacy)

Feldman RD, et al. *Can Med Assoc J* 1999; 161(Suppl. 12).

Beta Blocker

Over the past 4 decades, national and international guidelines have proposed beta-blockers to be used on an equal footing with diuretics for initial therapy of Hypertension

Beta-Blockers



Sir James Black, the pharmacologist who invented propranolol, the beta adrenergic receptor antagonist that revolutionized the medical management of ischemic heart disease

Most important contributions to clinical medicine and pharmacology of the 20th century

Propranolol

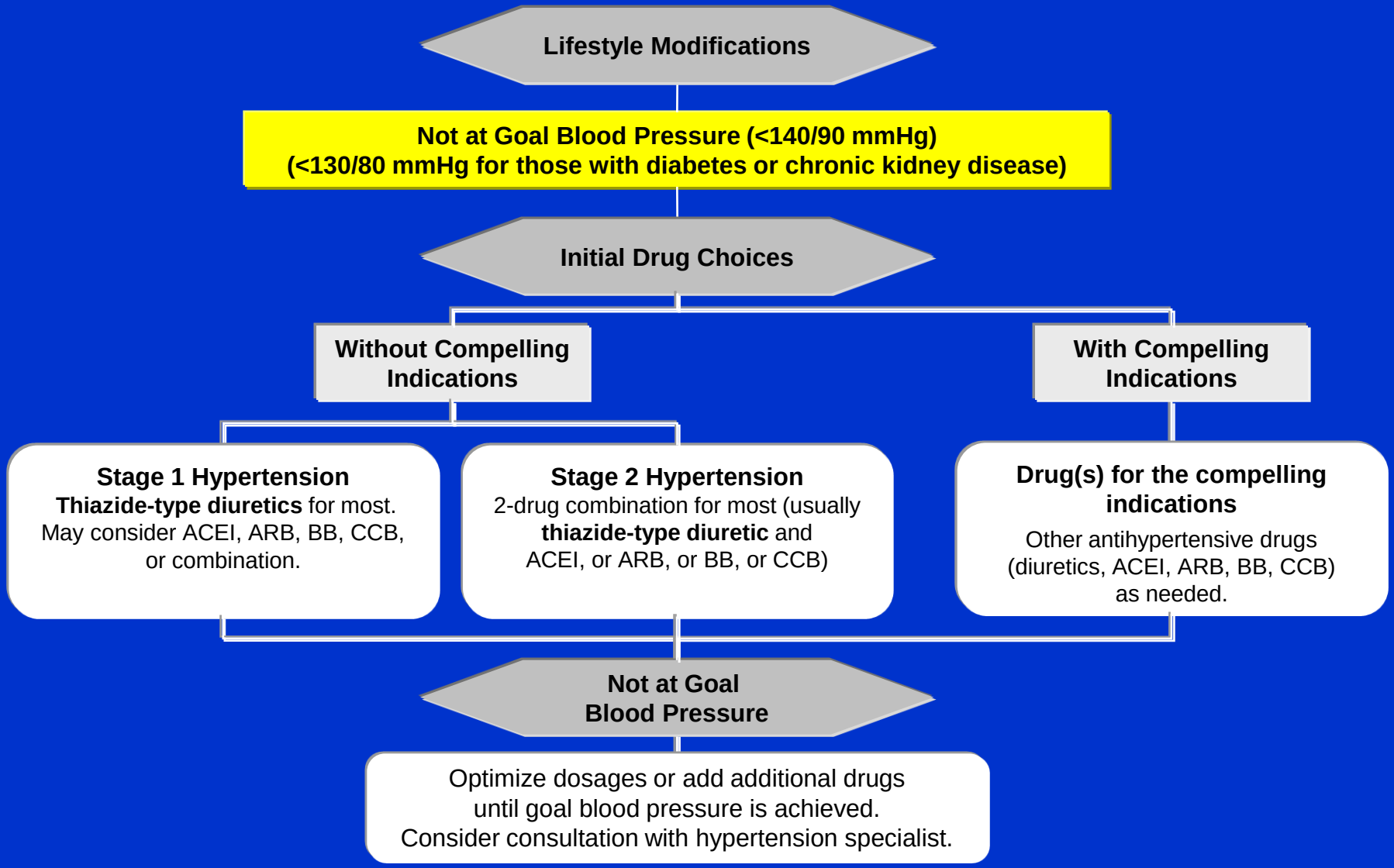
1964 - as Inderal by ICI in IHD
1967 - United States in angina
Much later than in most other countries
1976 - indicated for Hypertension
1984 - included in 1st line therapy along with diuretics in JNC III
1988 - James Black got Noble prize

Practice Guidelines for Hypertension

Recent Practice Guidelines

- WHO-ISH : 1999
- USA (JNC-7) : 2003
- ESH-ESC : 2003
- UK (BHS IV) : 2004
- BHS-NICE Guideline : 2006

Algorithm for Treatment of Hypertension
(JNC 7)



JAMA 2003;289:2560-2572

Compelling Indications for Individual Drug Classes

High-Risk Conditions With Compelling Indication	Recommended Drugs					
	Diuretic	β-Blocker	ACEI	ARB	CCB	Aldosterone Antagonist
Heart failure	•	•	•	•		•
Post-myocardial infarction		•	•			•
High CAD risk	•	•	•		•	
Diabetes	•	•	•	•	•	
Chr. kidney disease			•	•		
Recurrent stroke prevention	•		•			

JAMA 2003;289:2560-2572

Doubt on Beta-blockers

Journal of Human Hypertension (1998) 12, 807–810

http://www.stockton-press.co.uk/jhh

FOR DEBATE

Beta-blockers for hypertension: time to call a halt

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Beta-blockers are not very effective at lowering blood pressure in elderly hypertensive patients or in Afro-Caribbeans and these two groups represent a large proportion of people with raised blood pressure. Furthermore they do not prevent more heart attacks than the thiazide diuretics. Beta-blockers can also be dangerous in many hypertensive patients and even when these drugs are not contraindicated, they cause subtle and depressing side effects which should preclude their usefulness. The time has come therefore to reconsider the endorsement of beta-blockers by the British Hypertension Society and other guidelines committees, except possibly for severe resistant hypertension, high risk post-infarct patients and those with angina pectoris. The time has come to move across to newer, safer, more tolerable and more effective antihypertensive agents whilst continuing to use thiazide diuretics in low doses in the elderly as first choice, providing there are no contraindications.

Keywords: beta-blockers; hypertension

Doubt on Beta-blockers

Systematic analysis of all available outcome studies found no evidence that beta-blockers reduced the risk of heart attacks or strokes

The inefficacy of beta-blockers is well documented

The incidence of adverse effects is also substantial.

Adverse effects

Compared with other drugs, beta-blockers have a long list of side effects, including

lethargy,

reduced exercise capacity,

sleep disturbance,

vivid dreams,

cold hands and feet, and

reduction in peak expiratory flow rates.

Ancillary evidence from effects on surrogate endpoints

Beta-blockers are least efficient in reducing left ventricular hypertrophy and vascular hypertrophy.

Beta-blockers have been shown to cause systematic weight gain, to increase the risk of developing de novo diabetes, and to have unfavorable effects in patients with metabolic syndrome.

Adverse effects

The MRC allows us to calculate that for every heart attack or stroke prevented, three patients withdrew from the study because of impotence and another seven withdrew because of fatigue.

This is hardly an acceptable risk/benefit ratio for a completely asymptomatic disease such as mild essential hypertension

Are you still astonished?

THANK YOU