INTRODUCTION

The continuing development of antihypertensive drugs

The concept of alpha and beta adrenoceptors as applied to current cardiovascular pharmacotherapy was first described by Ahlquist in 1948. Regarding the cardiovascular system, alpha receptors mediate vascular smooth muscle contraction and therefore mediate vasoconstriction. Beta receptors, on the other hand, cause smooth muscle relaxation and therefore cause vasodilation, bronchodilation, and cardiac stimulation. The first beta blocker to be used clinically was pronethalol but was not widely accepted because of its carcinogenicity in mice. It was soon replaced by propranolol, which currently represents the standard by which all subsequent beta blockers are assessed.

■ *See Prichard (pp 337-350).*

While these agents were used initially to treat angina pectoris and cardiac arrhythmias, Dr. B.N.C. Prichard was among the first to describe the antihypertensive efficacy of beta-adrenergic blocking agents. These early reports initiated a new era in the treatment of arterial hypertension.

Since the primary hemodynamic abnormality in hypertension is an elevated peripheral vascular resistance, and since alpha-adrenoceptor antagonists are potent vasodilators, it follows that these agents would be investigated as potential antihypertensive drugs. The classical nonselective alpha blockers, such as phentolamine and phenoxybenzamine, have not proved useful in long-term treatment of hypertension because of adverse effects, including reflex tachycardia and fluid retention. A key development in the history of alpha blockers was the discovery of prazosin, the first selective $alpha_1$-blocking agent. A major advantage of this drug over classical nonselective alpha blockers is the absence of reflex tachycardia.

In the accompanying review article, Dr. Prichard has provided our readers with a practical clinical overview of the beta-adrenergic blockers together with the selective $alpha_1$-blocking agents currently used so extensively in the treatment of hypertension. Further, he has addressed the continuing development of multiple action beta-blocking drugs, demonstrating features of both traditional beta blockade together with peripheral vasodilating effects in hypertensive patients.

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