The presence and distribution of pharmacological receptors in the human prostate, and specifically in the prostate showing the changes of benign hypertrophy, were noted in an earlier chapter. The presence of a high α-adrenergic receptor content in the adenoma, and an even higher content in the prostatic capsule, has been described. This finding proved to be the starting point of the development of a method of symptomatic pharmacological treatment that has offered, probably for the first time, a truly effective means of providing help for a large proportion of these patients.

Urologists have long been aware of the fact that symptoms in the prostatic patient typically vary from time to time, often altering within a short period. Thus, for example, a patient may be experiencing relatively little obstructive trouble with micturition and then quite suddenly have an exacerbation of his symptoms, which after a few hours or days settles down again to their previous state. Similarly, the degree of frequency of micturition and urgency is often variable. In its extreme form the sudden increase in difficulty can actually lead to complete retention, which may then pass either spontaneously or following bladder decompression, with the return of micturition to its previous state. The latter occurrence is dealt with in detail in Chapter 45. It is logical to deduce that the variations in symptoms are probably not due to rapid changes in the anatomical configuration of the prostate; it therefore follows that in addition to the mechanical factor in prostatic obstruction due to benign prostatic hypertrophy (BPH), there must also be a dynamic component, variations in which produce the rapid variations in the patient’s symptomatology. Certain factors are commonly recognized by the patient and the urologist as giving rise to these variations clinically. A change in ambient temperature often produces them, cold exacerbating the symptoms and warmth relieving them; it has long been the practice to advocate hot baths to alleviate prostatic symptoms. Mental stress and tension or allowing the bladder to fill to excess can increase symptoms. The administration of sympathomimetic drugs (e.g., ephedrine or phenylpropanolamine, which may be included in a cough mixture, or phenylephrine in nose drops) have long been known to worsen the difficulty in micturition. The common denominator in all these factors is an increase in the level of sympathetic activity in the body. Considering the demonstration of the high α-adrenergic receptor content in the prostate, it seemed logical to conclude that the variable dynamic component in prostatic obstruction could be due to variations in the degree of stimulation of these alpha receptors, resulting in corresponding variations in the tone of the prostatic and capsular muscle and corresponding variations in the closure pressure exerted by the prostate on the urethra.

It follows logically from this hypothesis that inactivation of the α-adrenergic receptors by pharmacological blockade should abolish the sympathetic effect on this muscle and reduce the dynamic obstructive component to a minimum, thus leaving the patient with only the organic mechanical blockage and the symptoms due to that alone. It is clear that the degree of benefit to be expected depends on the underlying level of dynamic obstruction present in a given patient. For those in whom this is high, one can anticipate a greater improvement, but for those in whom it is low or
virtually absent one can expect only minimal benefit or even none at all.

Based on this hypothesis, symptomatic treatment of BPH patients by means of $\alpha$-adrenergic blocking agents has now been used for a number of years and has shown itself to be effective in a high proportion of patients. The drug normally used is phenoxybenzamine (Dibenzyline, Dibenamine), an effective blocking agent that is absorbed after oral administration and has a cumulative effect in the body for about a week.

Effects of Phenoxybenzamine in BPH

Owing to the spontaneous variations that occur in prostatic symptomatology and the placebo effect of many medications, the effectiveness of any drug treatment for prostatic hypertrophy can be reliably assessed only on the basis of properly controlled observations. A number of such studies has now appeared in the literature. In a double-blind placebo-controlled series we found statistically significant improvement in both the peak flow rates and the mean flow rates, as well as a significant reduction in the diurnal and nocturnal frequency of micturition. Abrams and his colleagues, in another study of this type, also found a statistically significant improvement in the maximal flow rate and in the symptoms of hesitancy and slow stream, as well as a reduction in residual urine. In addition, they showed a significant reduction in the height and area of the prostatic plateau on urethral pressure profile recordings. They were not able to confirm an improvement in frequency or an effect on bladder instability as demonstrated by cystometry. Gerstenberg and his colleagues performed detailed urodynamic studies that showed significant decreases in residual urine, all voiding pressure parameters, and both diurnal and nocturnal frequency. There were increases in the bladder capacity, and in both the maximal and mean urine flow rates. In addition, bladder hyperreflexia was improved or abolished in the three patients in whom it was present. Their series was not placebo-controlled because of ethical problems involved in carrying out the detailed urodynamic studies on patients not receiving treatment, but it was controlled in the sense that all evaluations were made “blind” by an independent observer.

The results of such studies as these may be summarized as showing that there is reliable objective evidence that phenoxybenzamine can reduce the outflow obstruction in BPH, resulting in a better urine flow and improved bladder emptying, and that the site of action corresponds to the prostatic segment of the urethra. In addition, there is evidence of a reduction in hyperreflexia, an increase in bladder capacity, and a reduction in the frequency of micturition.

Clinical Experience

Clinical experience with the use of alpha blockers in BPH has now accumulated over many years and in several hundred patients, and there can be no doubt that alpha blockers can afford symptomatic relief in a high percentage of cases. Boreham and his colleagues, in a 1-week trial in 30 cases, found improvement in 60%. Kondo and co-workers reported overall symptomatic improvement in 91% of 46 patients taking the drug for 2–69 weeks. We recently reviewed the results in 200 consecutive cases of BPH treated for several months or years and found an overall relief of symptoms in 80%: relief of obstructive symptoms was experienced in 78.7%; nocturnal frequency was reduced in 75.9% and diurnal frequency in 66.9%. Uroflowmetry carried out in 102 patients showed the flow to be more than doubled in 46% of patients and increased by 50–100% in a further 25.5%.

The improvement in symptoms is usually noted within the first day or two but does not reach its maximum for about 7 days or more because of the cumulative nature of the drug. Similarly, on stopping administration, the beneficial effects persist for a variable time, usually up to about 2 weeks, until the drug is completely freed from the receptors and eliminated from the body.

Indications for Use

It should be clear from the mode of action discussed above that $\alpha$-adrenergic blockers are in no sense a curative treatment for BPH but are used only to abolish the dynamic component of the obstruction and correspondingly to improve the patient's symptoms in accordance with the part played by this component. It must be stressed to the patient that the treatment in no way reduces the size of the prostate, nor does it prevent a con-