*ABC of Blood Pressure Reduction*LIAM T BANNAN
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NOEL WRIGHTVASODILATOR DRUGS AND
RESISTANT HYPERTENSION

Step 1	Non-drug management
Step 2	Thiazide <u>or</u> β -blocker
Step 3	Thiazide <u>and</u> β -blocker
Step 4	Thiazide + β -blocker + vasodilator

Initial treatment for most hypertensives is a thiazide diuretic or a β -receptor blocker. If these fail alone they can be given together. Most hypertensive patients can be controlled by this means. If blood pressure is not reduced adequately it is worth checking that the patient is actually taking his pills. If drug compliance is not a problem then the next step is to add a vasodilator.

Vasodilators are used mainly as additional treatment in patients who are not controlled by thiazides and beta-blockers. They may also be used as initial treatment in special circumstances, particularly in patients suffering from congestive cardiac failure.

They act either directly on the smooth muscle of the vessel wall or on the postganglionic sympathetic fibres. Examples are hydralazine, prazosin, minoxidil, nitroprusside, and diazoxide.

Hydralazine

Hydralazine is a direct-acting vasodilator. Its main action is on arterioles and it has little or no action on the venous side of the circulation. It therefore causes a drop in peripheral resistance followed by reflex tachycardia and increased cardiac output. It also causes fluid retention, and both these effects tend to counteract its antihypertensive action. Rapidly and completely absorbed from the gastrointestinal tract, it is mainly excreted through the kidneys. Hydralazine is eliminated from the plasma more rapidly in "fast acetylators" than in "slow acetylators." This leads to both a greater hypotensive effect and a greater risk of developing a systemic lupus-type syndrome in slow acetylators. Apart from a systemic lupus syndrome, the other major side effect is an acute rheumatoid state. Physiological side effects include tachycardia, palpitations, headache, fluid retention, flushing, and nasal congestion.

The physiological side effects can be counteracted by simultaneously administering a beta-blocker and a diuretic. The acute rheumatoid state and the systemic lupus-type syndrome occur in 10-20% of those treated with more than 400 mg/day and rarely occur with doses under 200 mg/day. Stopping the drug reverses the syndrome but positive tests for antinuclear antibodies may persist for years.

Hydralazine should be given twice a day in doses up to a maximum of 200 mg/day in association with thiazides and beta-blockers.

Prazosin

Prazosin acts by blocking peripheral postsynaptic α -receptors—that is, those supplying the vasculature. This leads to a drop in peripheral resistance and a reduction of venous tone with little or no change in cardiac output or heart rate. The physiological side effects that occur with hydralazine are less likely to occur with prazosin. Initial dosage with prazosin should be low, as it occasionally causes a severe reduction in blood pressure with associated collapse. This can be avoided by giving a tiny first dose in bed at night. It is well absorbed after oral administration.

Treatment should be started with an initial dose of 0.5 mg and thereafter prazosin should be given twice daily, increasing up to a maximum of 20–30 mg/day.

Side effects are similar to those of hydralazine, although lupus and tachycardia do not occur. In addition to the first-dose effect some patients complain of urinary incontinence and frequency. Postural hypotension occurs in a few patients and may be troublesome. This is most likely to occur as a response to an initial dose of the drug or an increase in the dose and tends to clear up as the drug is continued.

Drugs for resistant hypertension

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Step 5	Thiazide + β -blocker + minoxidil or diazoxide or Thiazide + β -blocker + hydralazine + methyldopa

If diastolic blood pressure is still over 110 mm Hg despite treatment with a thiazide, a beta-blocker, and hydralazine or prazosin prognosis is poor. These patients are probably best managed in hospital clinics.

Often, however, the failure is on the part of the doctor in prescribing over-complex regimens or on the part of the patient in not taking tablets, rather than failure of the drugs.

If the hypertension is genuinely resistant, either a fourth drug—methyldopa, guanethidine, or bethanine—may be added or minoxidil or diazoxide may be substituted for hydralazine. Both minoxidil and diazoxide have major side effects and their use is justified only occasionally. Minoxidil causes retention of fluid, tachycardia, and hirsuties and is available only in hospital practice. It should always be given in conjunction with a diuretic and a beta-blocker. Diazoxide causes diabetes, tachycardia, fluid retention, and occasionally extrapyramidal central nervous system signs.

1. Are tablets being taken ?
2. Are side effects preventing adherence ?
3. Check again for underlying causes

Other antihypertensive drugs

Most hypertensive patients can be controlled using beta-blockers with thiazides and vasodilators. This regimen has largely superseded the following drugs in routine management. Nevertheless, these drugs may be necessary in some difficult cases. Usually, however, their side effects limit their usefulness.

Clonidine is an α -receptor stimulator which lowers blood pressure by acting on the central nervous system to lower sympathetic outflow. It may cause drowsiness, dry mouth, and retention of fluid. Sudden withdrawal of the drug is associated with rebound hypertension, which may be dangerously severe. If patients miss taking their tablets rebound rises in blood pressure may occur often. For this reason this drug has little place in modern treatment of hypertension.

Spironolactone is a mild diuretic with potassium-sparing qualities which acts as an aldosterone antagonist. It is usually prescribed with other diuretics to prevent loss of potassium. In patients with impaired renal function it may cause hyperkalaemia. Side effects include gynaecomastia and menstrual disorders and abdominal pains.

Reserpine acts by depleting the postsympathetic neurones of noradrenaline. It commonly causes sedation, lassitude, and depression. Extrapyramidal symptoms, diarrhoea, and postural hypotension also occur.

Amiloride and *triamterene* are potassium-retaining diuretics, acting mainly in the renal tubules. They have few side effects, but hyperkalaemia may occur.

Phenoxybenzamine is an alpha-blocker and may be used in association with other drugs, especially the beta-blockers, to treat resistant hypertension or hypertension secondary to a pheochromocytoma. It causes sedation, postural hypotension, and failure of ejaculation.

Guanethidine, *bethanidine*, and *debrisoquine* all prevent the release of noradrenaline from the postganglionic sympathetic neurone. They produce a gradual fall in peripheral resistance and are very potent hypotensive agents. Their use is limited, however, because of their side effects and they should be considered only when more conventional drug treatment has failed. Side effects are postural hypotension, diarrhoea, impaired ejaculation or impotence, and fluid retention. These drugs have been largely superseded by beta-blockers.

Labetalol is a combined alpha- and beta-blocking agent, which combines the benefits of reducing peripheral resistance with those of beta-blockade. Side effects are few, but the contraindications are the same as for conventional beta-blockers, though labetalol may have advantages in treating patients with obstructive airways disease and congestive heart failure.

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