to reduce pain and the misery that goes with it. At the conference Hinton[8] was quoted: "We emerge deserving of little credit; we who are capable of ignoring the conditions which make muted people suffer. The dissatisfied dead cannot noise abroad the negligence they have experienced." Awareness is perhaps the most urgent need.

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Medical treatment of open-angle glaucoma

In the last decade much attention has been focused on finding the ideal drug for open-angle glaucoma. What we need is a non-toxic substance that will effectively lower the intraocular pressure over a long period without producing side effects.

Pilocarpine is a most effective drug, but it is inconvenient for patients because it causes miosis and alters accommodation. Some patients are affected more than others, especially the younger ones with myopia and those with central lens opacities. Is there a satisfactory non-miotic drug? Adrenaline is the obvious answer, and it has been a useful drug for glaucoma for many years. But it has a limited effect, and unfortunately, used alone, its action is seldom sufficient to bring the glaucoma under control.[1] Other catecholamines have been tried. Isoprenaline was effective, but it produced a tachycardia even when used topically and had to be abandoned.[2] Salbutamol was equally effective but caused extreme hyperaemia and discomfort and could not be tolerated.[3] Noradrenaline is less potent than adrenaline,[4] which remains the best compromise in this group of drugs.

The next approach was to attempt to potentiate the action of adrenaline. Among the agents tried in various countries were 6-hydroxydopamine, protriptyline,[5] and guanethidine. The combination of guanethidine with adrenaline provides a useful alternative to pilocarpine for patients with open-angle glaucoma.[6] The solution is instilled only twice a day and has little effect on vision. About a third of the patients using this regimen suffer from hyperaemia, which may occasionally mean withdrawing the treatment, but most prefer a slightly red eye to the visual disturbances caused by pilocarpine. Tachyphylaxis develops only rarely, and many patients have been using this combination for over five years.

The discovery that the adrenergic beta-blocking agents reduced intraocular pressure—with either systemic or topical administration—raised great hopes. Propranolol was the first compound investigated, and the early studies showed that when given by mouth it lowered intraocular pressure.[7] Unfortunately the solution for topical application was unsuitable: it acted as a local anaesthetic and was also extremely irritant.

Other beta-blocking agents investigated included topical practolol, which, used in Holland, produced successful results for over a year; but it had to be withdrawn when side effects were reported.[8] Topical atenolol gave promising results in initial studies. There was a profound fall in intraocular pressure, lasting six hours, after the early applications of the 4% solution.[9] The long-term effect, however, has been disappointing. A gradual reduction in the effect is seen in about 75% of patients and eventually complete tachyphylaxis occurs about six months after starting treatment. Thus only 25% of the patients with open-angle glaucoma are suitable for treatment with this drug alone. Those patients who do not develop tachyphylaxis with atenolol report no discomfort or side effects: the pupil diameter remains unchanged and there is no hyperaemia.[10] Timolol may prove a valuable alternative: it is more potent than atenolol and the incidence of tachyphylaxis appears to be lower. This drug is not yet available in Britain.

Systemically administered beta-blocking drugs are suitable for patients with both systemic and ocular hypertension. Propranolol has been used for several years for this group of patients. Tachyphylaxis is seen less often when the drugs are administered systemically.

The medical treatment of glaucoma is in a constant state of flux as new drugs are introduced and withdrawn; only time will tell which ones will find an established place. A hundred years after it was first used the place of pilocarpine is at last being seriously challenged.

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Cannabis and the cardiovascular system

The effects of cannabis on the cardiovascular system are worthy of study for at least three reasons. Firstly, cannabis smoking has become so widespread that we should know what effects it has on patients with heart disease. Reefer smoke commonly contains nicotine, carbon monoxide, and tar as well as the active principles of cannabis. Cannabis depresses cardiac contractility in patients with angina pectoris[1]; and even in the absence of heart disease long-term deleterious effects on the heart and blood vessels remain a possibility. Secondly, we need to know about any drug interactions that might occur when cannabis is taken with another drug. For example, in the presence of tetrahydrocannabinol (THC) atropine produces an appreciable pressor effect,[2] and anticholinergic drugs or local anaesthetic containing adrenaline could dangerously potentiate a cannabis-induced tachycardia.[3] Thirdly, among the many actions of cannabis, the hypotensive effect may conceivably have a clinical application—though

over 20 years have elapsed since Hardman *et al*[4] first described this effect of drugs related to THC, the most studied active principle of cannabis.

In anaesthetised animals, THC and cannabis extracts consistently produce bradycardia and hypotension.[5] In man, on the other hand, a single dose of cannabis (smoked or ingested) or intravenous THC produces a tachycardia (up to 160/min) with either no change or a slight increase in systolic and diastolic blood pressures[3 6-9] and an increase in limb blood flow.[3] The tachycardia is dose related[10] and is detectable[8] at 50 μg of THC per kg body weight. It reaches a maximum within 30 minutes and persists for longer than 90 minutes.[6 11] After a single oral dose of THC (300 μg/kg) the tachycardia may persist for as long as 12 hours[12]; electrocardiographic changes may also occur.[6 13] Occasionally, large single doses of cannabis taken by mouth[14 15] or smoked[16] produce orthostatic hypotension in man.

The tachycardia induced by taking cannabis for short periods appears to be due to increased sympathetic tone, because it is abolished by β-adrenoceptor blockade.[3 15 17] If, in the short term, cannabis acts through a β-adrenergic mechanism, then it should increase the strength as well as the rate of contraction; and, indeed, in tests on healthy volunteers cannabis caused shortening of the pre-ejection period, lengthening of the left ventricular ejection time, and an increase in stroke volume, suggesting an enhancement of left ventricular performance.[17] In another investigation,[18] however, the only changes found in left ventricular function were secondary to tachycardia. These discrepancies may have been due to differences in dose and tolerance.

When cannabis is taken for long periods the effects are different. Both bradycardia and hypotension develop, probably as a result of decreased sympathetic tone in the peripheral blood vessels[19] with resulting parasympathetic dominance.[20 21] The bradycardia is reversed by vagotomy, ganglion block, and anticholinergic drugs.[20] THC also reduces venous tone,[20] so explaining the orthostatic hypotension. Men given 210 mg of THC daily for 18-20 days showed a decrease in heart rate and a fall in systolic and diastolic blood pressure[22] accompanied by impaired cardiovascular responses to standing, exercise, Valsalva's manoeuvre, and cold pressor tests—all suggesting sympathetic insufficiency. Other effects included fluid retention and gain in weight; tolerance developed to the orthostatic but not the supine hypotension. During ingestion of THC[22] responses to both an alpha-agonist (phenylephrine) and a beta-agonist (isoprenaline) were unchanged, while parasympathetic block with atropine alone or with the beta-adrenoceptor blocker propranolol caused the heart rate to increase, suggesting that cannabis acts centrally to produce both sympathetic insufficiency and enhanced parasympathetic activity. More recent evidence[23] suggests that cannabis modulates sympathetic outflow by a dual mechanism: it reduces spontaneous sympathetic efferent activity and (like barbiturates) it suppresses inhibitory mechanisms. This accounts for the apparent increase or decrease in sympathetic outflow in different species or within the same species under different experimental conditions—such as with and without anaesthesia.

Has cannabis any clinical potential? Dimethylheptyltetrahydrocannabinol produces in man a long lasting tachycardia and supine and orthostatic hypotension, with a virtual absence of psychological effects[24]; in contrast, the synthetic cannabis derivative nabilone (Lilly 109514) produces a dose-related euphoria and postural hypotension without tachycardia, but with rapidly developing tolerance.[25] The pharmacological properties of the cannabinoids can thus be separated —though the prospect of new hypotensive drugs that produce postural hypotension, with or without tachycardia, and the possibility of tolerance is not encouraging. With better hypotensive agents already available the time has perhaps come to take a broader look at the whole group of lipophilic drugs[9] rather than concentrating on the cannabinoids.

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Algodystrophy

Sudeck's atrophy and the shoulder-hand syndrome are rare conditions, but most clinicians will remember seeing a case. Not many will have made the diagnosis themselves. In fact, these conditions are usually not diagnosed in their early stages, and since treatment becomes more difficult and less effective in the later stages this group of disorders remains a cause of serious chronic and permanent disability.

A workshop held recently at the Royal College of Physicians under the auspices of the British Association for Rheumatology and Rehabilitation decided that there were three essential diagnostic features of algodystrophy—the name by which the condition is known in France, and the one recommended for general use, being non-committal about aetiology and yet emphasising the clinical combination of pain and dystrophic changes. Characteristically there is, firstly, intense, ill-defined pain and hyperaesthesia; secondly, vasomotor changes and disturbance of sweating; and, thirdly, osteoporosis.

Algodystrophy may occur in virtually any part of the locomotor system,[1] though the hand and foot are the parts most commonly affected. Pain, always prominent, is particularly distressing and constant, with associated hyperaesthesia and tenderness. Vasomotor changes[2] are usually, but not always, a