complication. Absorption of any drug through the skin depends on several factors, including the state of the skin[4]—normal skin absorbing less of the topically applied drug than actively eczematous skin.

We are concerned also that the instability of some steroid preparations may cause them to deteriorate, so that the "dose" being given to the patient is lowered. The results of this could be disastrous. The *British National Formulary* obligation for expiry dates of two weeks applies to diluted creams but not to ointments. Nevertheless, it has been this hospital's practice over the past two years to list expiry dates even on diluted ointments. Patients with long-standing conditions do not like to bother their doctors for frequent repeat prescriptions and understandably like a supply to last some time. This is usually a sensible arrangement as long as the preparations are stable for a known period.

As a result of this case we think that the possibility of the complications of benign intracranial hypertension, although obviously uncommon, should not be forgotten in any patient on topical steroid treatment.

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Lead-induced hypertension: blunted beta-adrenoceptor-mediated functions

Hypertension is one of the possible sequelae of lead poisoning.[1] We describe here a case of severe lead poisoning with hypertension in which data on plasma catecholamines, the renin-angiotensin-aldosterone system, and beta-adrenoceptor sensitivity pointed to reduced beta-adrenoceptor responses similar to those observed in low-renin essential hypertension.

Case report

After cleaning his garage, which had once been a lead foundry, a healthy, normotensive 65-year-old man (a regular blood donor) developed pronounced lead poisoning as a result of inhaling lead dust. He at first complained of loss of appetite, intestinal spasms, and reduced capacity for exertion. Six weeks later the lead concentrations in his blood and urine were 12·46 μmol/l (258 μg/100 ml) and 38·64 μmol/l (800 μg/100 ml)—four to five times the acceptable upper limit. He had typical lead anaemia (haemoglobin 7·0 g/dl), with an increase in δ-aminolaevulinic acid in plasma (1·31 mmol/l (17·18 mg/100 ml)) and urine (1·45 mmol (190·15 mg) /24 h) —a usual result of inhibition of haem synthesis. In view of his temporarily reduced renal function (serum creatinine maximum concentration 150 μmol/l (1·7 mg/100 ml)), we did not treat the lead poisoning with edetic acid. His blood pressure rose to 160–170/100–105 mm Hg.

After twelve months the patient's blood pressure in the supine position was still 140–170/95–105 mm Hg. Plasma renin activity was suppressed to 352 pmol/l/h (271 pg/ml/h) after salt depletion (urinary sodium excretion 37 mmol (mEq)/24 h). After he had had a 30-minute rest lying down we determined the dose-response curve for isoprenaline hydrochloride and found the chronotropic dose 25 (CD_{25}, the dose required to increase heart rate by 25 beats/min).[2] Subsequently we investigated the patient before and during gradually increasing bicycle ergometric exercise up to 100 W in a sitting position (table). His maximal physical work capacity (PWC_{max}) was then 150 W.

Discussion

Lead poisoning appears to have been responsible for the rapid development of hypertension and the other abnormalities in our patient. The plasma noradrenaline concentrations were higher than in five normal controls; but his beta-adrenoceptor-mediated functions —for example, maximal heart rate, renin release, and isoprenaline-induced tachycardia—were blunted.

Lead binds reactive anions such as sulphur and phosphorus and thus affects enzymes associated with membranes. Consequently, it impairs the synthesis of haem and that of sodium-potassium-activated adenosinetriphosphatase,[3] and probably also interferes with the receptor-adenylate cyclase system. This would reduce beta-adrenoceptor-mediated vasodilatation as well as exercise tachycardia and renin release. On this hypothesis, reactive sympathoneural activity—reflected in the raised plasma noradrenaline—would cause alpha-adrenoceptor-mediated vasoconstriction and contribute to the rise in blood pressure.

Biochemical abnormalities similar to those induced by lead may be found in elderly subjects, especially those with essential hypertension. They too show a disturbance of the normal balance, with raised plasma noradrenaline concentrations[4] and hyporesponsive beta-adrenoceptor functions—for example, renin activity, exercise tachycardia,[5] and isoprenaline sensitivity. In patients with low-renin essential hypertension, adaptive changes of the receptor-effector complex may result from chronic sympathoneural hyperactivity or the usually prolonged hypertension, or both.

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High plasma noradrenaline concentration, low plasma renin activity, and low isoprenaline sensitivity in lead-induced hypertension: blunted response of beta-adrenoceptor-mediated functions to stimulation at rest and during ergometry. Values are means ± SD

	Patient with lead-induced hypertension		Five controls	
	Supine	Exercise at 100 Watt	Supine	Exercise at 100 Watt
Plasma noradrenaline (nmol/l)	2·21	11·35	1·57 ± 0·30	6·33 ± 2·34
Plasma adrenaline (nmol/l)	0·43	0·88	0·34 ± 0·61	0·83 ± 0·18
Plasma dopamine (nmol/l)	0·84	1·42	0·72 ± 0·14	1·09 ± 0·33
Plasma renin activity (pmol/l/h)	254	4·86	2539 ± 846	4091 ± 1340
Blood pressure systolic (mm Hg)	152	240	142 ± 4	164 ± 5
Blood pressure diastolic (mm Hg)	106	118	84 ± 3	94 ± 4
Heart rate (beats/min)	62	98	71 ± 2	114 ± 3
Heart rate at PWC_{max} (beats/min)	138		171 ± 6	
CD_{25} isoprenaline (nmol/m²)	76·6		5·2 ± 1·88	

Conversion: SI to traditional units—Noradrenaline: 1nmol/l ≈ 169·2 pg/ml. Adrenaline: 1 nmol/l ≈ 183·2 pg/ml. Dopamine: 1 nmol/l ≈ 153·1 pg/ml. Isoprenaline: 1 nmol/m² = 0·211 μ/gm².