TABLE II—*Variability in blood pressure measurements expressed as coefficient of variability*

		Patients in sinus rhythm (n=50)	Patients in atrial fibrillation (n=50)	p Value (Mann-Whitney U test)
	Interobserver variability			
Systolic blood pressure (mm Hg)	Range	2·0-11·8	1·5-28·0	0·0013
	Median	5·0	7·0	
	Median difference between groups (95% confidence interval)	1·9 (0·3 to 3·2)		
Diastolic blood pressure (mm Hg)	Range	1·6-33·6	3·4-27·4	0·0009
	Median	5·90	9·65	
	Median difference between groups (95% confidence interval)	3·3 (1·5 to 4·9)		
	Intraobserver variability			
Systolic blood pressure (mm Hg)	Range	0·7-14·3	0·4-18·2	0·140
	Median	3·8	5·3	
	Median difference between groups (95% confidence interval)	1·0 (−0·3 to 2·2)		
Diastolic blood pressure (mm Hg)	Range	0·8-18·0	1·0-26·3	0·012
	Median	4·15	6·15	
	Median difference between groups (95% confidence interval)	1·7 (0·3 to 3·2)		

TABLE III—*Sources of observer variability. Correlation of degree of variability with other factors*

	SD systolic blood pressure	Systolic blood pressure	Age	Pulse rate
	Sinus rhythm			
SD systolic blood pressure	—	0·28	0·004	−0·100
Systolic blood pressure	—	—	0·057	−0·098
Age	—	—		−0·007
	p>0·05			
	Atrial fibrillation			
SD systolic blood pressure	—	0·195	−0·066	−0·151
Systolic blood pressure	—	—	0·125	0·066
Age	—	—	—	−0·045
	p>0·05			

bias, digit preference, and auditory acuity.[5 10 11] No study has sought to exclude these sources of error and look specifically at the influence of cardiac rhythm on observer variation. The important finding of our study is that atrial fibrillation is associated with a greater interobserver variability in the measurement of blood pressure but does not seem to affect intraobserver variability to the same extent. This suggests that the source of the increased variability is individual doctors' different interpretation of Korotkoff sounds. In atrial fibrillation there is baseline variation in blood pressure and the onset and disappearance of the sounds are more difficult to identify with a specific pressure reading.

There are at present no recommendations for measuring blood pressure in atrial fibrillation, so that some doctors may record systolic pressure at the first appearance of sounds whereas others may wait until these are consistently present. A similar problem may arise with the disappearance of sounds and the recording of diastolic pressure. Guidelines should make it possible to overcome this increased observer variation by using the first appearance and final disappearance of the sounds to record systolic and diastolic pressures. This, however, may result in the overestimation of the effective systolic pressure and an artificially lowered reading for the diastolic pressure. The order of magnitude of the variability found is 10%, which would certainly be enough to affect clinical management decisions. The difficulties in setting guidelines for a single estimate of blood pressure suggest that a more prudent course would be to use repeated recordings. This reinforces the importance of not making decisions on the basis of a single recording, particularly in the presence of atrial fibrillation.

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Postural hypotension related to zidovudine in a patient infected with HIV

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Disease of the adrenal glands is common in patients with AIDS.[1 2] Clinical adrenocortical insufficiency, though less common, is increasingly recognised.[3] We report a case in which adrenocortical insufficiency was brought to our attention by symptoms repeatedly precipitated by zidovudine.

Case report

A 49 year old homosexual first presented in October 1987 with an eczematous rash and mild oral candidiasis. His rash cleared after a short course of 0·025% betamethasone ointment. He had serological evidence of past hepatitis B infection and of antibodies to HIV. In April 1988 he received a two week course (his first) of ketoconazole for oral candidiasis.

Because of tiredness, weight loss (body weight 53 kg), and a reduced CD4−lymphocyte count (0·055 × 10⁹/l) he was started on zidovudine 200 mg every four hours in June. Within an hour after his first oral dose he experienced hunger and dizziness for about 30 minutes, and these recurred after every subsequent dose. He was monitored before and after his dose, at 8 am, before breakfast. Twenty eight minutes after the dose he experienced his usual symptoms. Blood pressure (while he was seated) had decreased from a baseline of 115/65 mg Hg to 90/50 mm Hg and was 90/60 and 86/60 mm Hg 15 and 30 minutes thereafter, increasing to 110/74 mm Hg two hours after the dose. He was pale, but his pulse remained regular and stable, ranging from 76 to 84 beats/min. Plasma sodium, potassium, calcium, albumin, and phosphate concentrations 0, 30, 60, 90, 120, and 150 minutes after the dose were normal and did not change appreciably; the corresponding fasting blood glucose values were 3·9, 3·7, 3·5, 3·5, 3·7, and 3·6 mmol/l.

Symptoms related to blood pressure, pulse rate, and blood concentrations of cortisol, zidovudine, and the 5-O-glucuronide of zidovudine (GAZT) in patient given zidovudine 200 mg and placebo

Time (min)	Patient supine: Blood pressure (mm Hg)	Patient supine: Pulse (beats/min)	Patient erect: Blood pressure (mm Hg)	Patient erect: Pulse (beats/min)	Plasma cortisol (nmol/l)	GAZT (μmol/l)	Zidovudine (μmol/l)	Symptoms
			Zidovudine 200 mg given at time 0					
−30	113/72	87	112/69	98		<2·0	<0·25	None
0	112/69	84	115/69	91	204	<2·0	<0·25	None
30	131/74	76	108/68	89		24·2	5·6	Slightly dizzy
40	111/65	80	Unrecordable					Very giddy, hungry, pale
50	123/74	74	118/65	83				
60	107/70	81	119/69	98	139	19·1	2·5	Less giddy, hungry
75	111/73	76	112/71	93				Not giddy, hungry
90	116/70	80	118/75	90	120	7·7	1·4	None
120	125/75	77	126/74	100	111	4·3	1·0	
150	129/77	73	123/67	89	171	2·5	0·6	
			Placebo given at time 0					
−30	108/66	86	109/58	93	233	<2·0	<0·25	
0	114/72	82	105/66	92	191	<2·0	<0·25	
30	119/73	81	117/74	92	147	<2·0	<0·25	
40	124/72	82	119/70	88				
50	120/71	79	122/69	90				
60	124/77	80	120/69	90	125	<2·4	<0·30	
75	114/72	78	117/66	94				
90	116/68	77	124/67	95	94	<2·0	<0·25	
120	117/71	75	115/68	90	99	<2·4	<0·30	
150	117/73	75	120/64	98	88	<2·0	<0·25	

Seven weeks later, at 7 am on consecutive mornings, a double blind placebo controlled challenge was performed. An intravenous cannula was inserted with the patient resting on an examination couch. Blood pressure and pulse rate were recorded with an electronic Colin sphygmomanometer (103 N Mark 3) half an hour before the drug was given; when the patient took two unmarked capsules; and at set intervals thereafter. The patient independently recorded any symptoms. Blood (20 ml) was taken via the cannula at set intervals and aliquots of plasma and serum immediately frozen at − 20°C. Blinded specimens were assayed for both zidovudine (limit detection 0·25 μmol/l) and a major metabolite, the 5-*O*-glucuronide of zidovudine (3-azido-3-deoxy-5-*B*-D-glucopyranuronosylthymidine; GAZT) (limit of detection 2·0 μmol/l), by high performance liquid chromatography (table). There was no appreciable abnormality or fluctuation in serial concentrations of sodium, potassium chloride, bicarbonate, urea, creatinine, calcium, phosphate, albumin, and magnesium.

There was no evidence of autonomic neuropathy: the response of blood pressure and pulse to the Valsalva manoeuvre was normal. The short tetracosactrin stress test showed a suboptimal response from a baseline value of 362 nmol/l to 517 nmol/l at 30 minutes.

Comment

Postural hypotension related to zidovudine has not been reported previously. Dizziness, however, was reported in a small number of patients in both the group given zidovudine and the group given placebo in a controlled trial, but the nature and timing of the symptoms were not stated.[4] In our patient the symptoms occurred only after he took zidovudine and coincided with the raised blood concentrations of both zidovudine and the metabolite that we measured. This drug profile corresponds with the published data on the pharmacokinetics and bioavailability of zidovudine in humans.[5]

We postulate that zidovudine or its metabolites, or both, have a direct but transient vasomotor effect related to dose that is not clinically apparent unless there is underlying adrenocortical insufficiency. Even allowing for normal diurnal variation, the mid-morning plasma cortisol concentrations were subnormal and there was no increase in cortisol concentration related to stress. Alternatively, zidovudine may have a direct effect on the autonomic system. We do not think that the patient's previous short course of ketoconazole and weak topical betamethasone were contributory.

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Dupuytren's contractures in patients infected with HIV

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A free radical mechanism for the pathogenesis of Dupuytren's contracture has been established,[1] and there is evidence for increased activity of free radicals in patients infected with HIV.[2] We compared the prevalence of Dupuytren's contractures in such patients with that in patients negative for HIV.

Patients, methods, and results

Fifty men (age range 19-54) serially admitted to hospital with complications of HIV infection were examined independently by two doctors for clinical evidence of Dupuytren's contractures. These were regarded as present only if both doctors agreed. A control group of 50 men seen as outpatients in a sexually transmitted disease clinic, who were negative for HIV antibody, were examined similarly.

The men's occupational histories and histories of alcohol consumption, epilepsy, diabetes mellitus, and all current medicines were obtained. Their livers were examined for hepatomegaly clinically and by ultrasonography or computed tomography; liver function was assessed by measurement of aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase activities; and fasting blood glucose concentration was measured. In the patients with HIV infection the date on which HIV antibody had first been detected was noted and plasma p24 antigen concentrations and CD4+ lymphocyte counts were measured (table).

All 50 patients with HIV antibodies had advanced disease (48 had stage IV, as classified by the Centers for Disease Control, and two stage III). Eighteen of these patients had Dupuytren's contractures (nine bilateral). One clinician thought that a thickening of the palmar aponeurosis was present in a further six patients (these were not included in the analysis). None of the 50 control patients had Dupuytren's contractures. Among the patients infected with HIV raised fasting blood glucose concentrations, biochemical abnormalities of liver function, hepatomegaly, high alcohol