to age the standard deviation ranged from 2.2 to 4.9 years, indicating an even distribution of the patients. The standard deviation of the means ranged from 0.84 to 1.25 kPa for arterial oxygen tension and from 0.7 to 2.1% for oxygen saturation. No clinically important differences were found for other variables (multiple analysis of variance for haemoglobin, packed cell volume, mean cell volume, arterial carbon dioxide tension, bicarbonate concentration, pH, and smoking habits (<10 cigarettes/day)). There were no sex differences, except for persistently higher packed cell volumes in men.

Comment

Most studies of blood gas concentrations have shown a linear decrease in oxygen tension with age.¹ This would suggest hypoxaemia in advanced age even in the absence of disease, but most of these studies included few patients over the age of 60.

The findings in our series of healthy inpatients are likely to represent the minimal estimate of the effect of age. Although the arterial oxygen tension declined significantly ($p<0.001$) with age, this decline was not linear in advanced age. Elderly patients did better, probably following the "survival of the fittest" concept. Minor activity had a pronounced effect on oxygen tension, which was less evident on oxygen saturation because of the S shaped oxygen dissociation curve.

To define hypoxaemia one must rely on normal values related to age and activity. In the elderly determination of the oxygen saturation is helpful in differentiating a normal from a pathological state.

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Relation between arterial oxygen tension, arterial oxygen saturation, and age in samples obtained from patients at rest and after activity

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Occult AIDS: *Pneumocystis carinii* pneumonia in elderly people

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The common understanding of AIDS is that it affects young homosexuals and intravenous drug addicts. In a young man presenting with an acute respiratory illness the diagnosis of an infection related to AIDS would be considered. We describe two patients, aged 64 and 73, who presented with chest infections; the diagnosis of AIDS was initially overlooked on the basis of both their age and the history.

Case reports

Case 1—A previously fit 73 year old bachelor presented with a two week history of increasing breathlessness and dry cough. He denied homosexuality. He was dehydrated and there were bilateral basal crackles. His temperature was normal. His haemoglobin concentration was 129 g/l and his white cell count $4.9 \times 10^9/l$ with a normal differential. A chest x ray film showed extensive, predominantly left sided consolidation. Culture of sputum and blood yielded negative results. Titres of antibody to legionella, mycoplasma, coxiella, and chlamydia during the acute and convalescent phases of his illness and results of screening for respiratory viruses were negative. Despite seven days' treatment with ampicillin and erythromycin his condition continued to deteriorate. On further questioning he admitted to having had a

few homosexual relationships. After counselling he was tested for human immunodeficiency virus (HIV) antibody; the result was positive. Bronchoscopy with bronchoalveolar lavage and transbronchial biopsy did not show any pathogen. High dose intravenous co-trimoxazole for 14 days produced clinical and radiological resolution, and he was discharged taking oral maintenance treatment with co-trimoxazole. The titre of antibody to *Pneumocystis carinii* rose from 1/32 to 1/128. He died 18 months later. *P. carinii* was found in the lung at necropsy.

Case 2—A 64 year old man presented with a two month history of increasing breathlessness and dry cough. He had a 10 year history of chronic obstruction of the airways. He had taken amiodarone 200 mg daily intermittently for two months for paroxysmal atrial fibrillation. He was divorced and on admission denied homosexuality. He was centrally cyanosed and dyspnoeic and had a fever (38.5°). His chest was hyperinflated with a poor air entry throughout and no added sounds. His haemoglobin concentration was 166 g/l and white cell count $5.6 \times 10^9/l$ with a normal differential. The oxygen tension was 6.7 kPa and the carbon dioxide tension 4.0 kPa. A chest x ray film showed diffuse bilateral reticulonodular shadowing, predominantly in the mid and upper zones. Sputum and blood cultures yielded negative results. Titres of antibody to legionella, mycoplasma, coxiella, and chlamydia during the acute and convalescent phases of his illness and results of screening for respiratory viruses were negative. After seven days' treatment with ampicillin his condition deteriorated, and on direct questioning he admitted having had occasional homosexual relationships. After counselling he was tested for HIV antibody and found to be positive. Bronchoscopy with bronchoalveolar lavage and

Age (years)	No of patients
0-19	2
20-24	19
25-29	26
30-34	48
35-39	57
40-44	33
45-49	31
50-54	7
55-59	6
60-64	2
≥65	4

transbronchial biopsy did not show any pathogen. He was treated with co-trimoxazole and hydrocortisone. After 14 days of co-trimoxazole he had improved clinically and radiographically and was discharged receiving maintenance treatment.

Comment

Both these patients were positive for HIV antibody and had a clinical and radiological presentation suggestive of *P carinii* pneumonia that responded to treatment; thus the criteria for a diagnosis of AIDS were satisfied.¹ In case 2 the diagnosis was complicated by the previous amiodarone treatment, though pneumonitis induced by amiodarone is unusual at a daily dosage less than 400 mg.^{2,3} Chest infections are common in the elderly. The increasing incidence of HIV infection and a reluctance of older homosexuals to admit to at risk behaviour may mean that elderly

patients will die without AIDS being diagnosed. In the United States 10% of patients with AIDS are over 50, 2·5% over 60, and 0·4% over 70. The table shows the age distribution of our patients with AIDS up to October 1987. Six of 235 (2·5%) patients were over 60. *P carinii* pneumonia should be considered in all patients with atypical chest infections, even when there are no apparent risk factors.

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Parkinsonism, tremor, and depression induced by cinnarizine and flunarizine

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Cinnarizine and flunarizine are piperazine derivatives with antihistamine properties and calcium channel blocking activity. Several recent reports have described extrapyramidal reactions and depression associated with their use.¹⁻³

Methods and results

In Spain a system of spontaneous reporting of adverse drug reactions has been operating since 1983. Around 5000 reports have been received, of which 86 refer to cinnarizine as the suspected drug, 25 to flunarizine, and five to both drugs taken simultaneously. Of these 116 reports 87 described extrapyramidal symptoms or depression, or both: cinnarizine had been taken in 70 cases, flunarizine in 13, and both drugs in four.

Seventy patients developed tremor and parkinsonism while being treated with cinnarizine (see table). They were not taking other drugs likely to induce parkinsonism, except for three patients, one of whom was also taking sulpiride, one thiethylperazine and dimenhydrinate, and one thioridazine (he subsequently recovered when cinnarizine was withdrawn without stopping thioridazine). Eight additional patients (two men, six women) presented with parkinsonism and three men presented with tremor while being treated with flunarizine (5 mg/day in one patient and 10 mg/day in 10). Four other patients developed parkinsonism (two men) or tremor (one man, one woman) while treated simultaneously with both drugs.

Four patients (two men, two women, aged 24 to 67) presented with depression while taking flunarizine (three patients, one of them also with tremor) or cinnarizine (one patient, who also presented with parkinsonism). The daily dose of flunarizine was 10 mg and of cinnarizine 150 mg. The intervals between starting drug treatment and the appearance of the first symptoms ranged from two days (in this patient tremor was also noted) to 10 months. The four patients

Characteristics of 70 patients with parkinsonism or tremor induced by cinnarizine. Unless otherwise stated, results are numbers (and percentages) of patients

	Parkinsonism	Tremor
No of patients:	39	31
Women*	24	20
Men*	13	11
Median age (range) (years)	78 (53-90)	68 (38-85)
Dose (mg):		
<150	3 (8)	12 (39)
150	28 (72)	14 (45)
>150	6 (15)	5 (16)
Unknown	2 (5)	
Induction period:		
<1 month	7 (18)	6 (19)
1-6 months	6 (15)	6 (19)
6-12 months	6 (15)	10 (32)
1-3 years	10 (26)	5 (16)
>3 years	5 (13)	0
Unknown	5 (13)	4 (13)
Recovered after withdrawal of drug:		
Within 1st 3 months	13 (33)	17 (55)
In 3-6 months	9 (23)	0
In 6-18 months	2 (5)	1 (3)
Unknown	4 (10)	5 (16)
Not within 1st 3 months	4 (10)	6 (19)
Not in 3-6 months	1 (3)	0
Not in 6-12 months	1 (3)	0
Not in >1 year	1 (3)	0
Unknown	4 (10)	2 (7)

*The sex of two patients with parkinsonism was unknown.

improved when treatment stopped; three of them improved during the first month, but no exact information was available about the fourth. None of these patients were taking any other drug which could have contributed to their depression.

Comment

In Spain cinnarizine is marketed in 10 pharmaceutical preparations, eight of which are fixed dose combinations with other drugs. The most common indications are cerebral and peripheral arterial insufficiency. The top selling preparations contain 75 mg per tablet, and the recommended dose is 75 mg twice a day. Approved indications for flunarizine are the same as for cinnarizine. In the United Kingdom cinnarizine is marketed as 15 mg tablets for vestibular disorders and motion sickness, with a maximum recommended dose of 30 mg three times a day.⁴ In Spain 5-7% of the population over the age of 60 may be receiving long term cinnarizine.⁵ The consumption of flunarizine is also high: in 1986, 1·2 million units were dispensed. Not surprisingly therefore a large number of cases of extrapyramidal symptoms and depression attributed to these drugs have been assembled by our national scheme.