patients with hypertension baseline systolic blood pressure was 148 ± 2 mm Hg, rising to 207 ± 5 mm Hg at 6000 N m. Baseline diastolic pressure was 100 ± 1 mm Hg, increasing to 111 ± 2 mm Hg at 6000 N m ($p < 0.01$) and falling to 95 ± 2 mm Hg and 93 ± 3 mm Hg after one and five minutes' rest. The diastolic pressure in the hypertensive compared with the normotensive subjects showed a distinctly different pattern of response at maximum exercise: in the patients it rose by 11 ± 2 mm Hg while in the normotensive subjects there was no change. A repeat test in eight hypertensive patients three to six months later yielded nearly identical results.

Blood-pressure response to graded exercise in untreated hypertensive subjects ($n=35$) plotted against nomogram obtained from results in normal individuals ($n=28$). Unbroken line of nomogram represents mean blood pressures; broken line represents mean $+1.65$ SD; and hatched area shows upper boundary of 95% confidence limit.

Conversion: SI to traditional units—1 N m ≈ 0.1 kp m.

Comment

It has recently been claimed that changes in blood pressure during exercise may be better correlated with ambulatory measurements than with casual resting blood pressure.¹ Moreover, assessment of ambulatory pressure may have a predictive value for cardiovascular risks (M Soklow, D Perloff, R Cowan, unpublished observations). Hamer *et al*² suggested that during exercise the effect of nervous influences on arterial tone is abolished; therefore, measurements made during exercise may offer a more reliable estimate of the degree of hypertensive vascular changes.

The present study serves as a model for evaluating the blood-pressure response to exercise in normotensive and hypertensive subjects. Hypertensive patients were characterised by a rise in diastolic pressure, while in normotensive subjects diastolic pressure remained unchanged. This rise in diastolic pressure may be attributable to an inability of hypertensive patients to reduce peripheral resistance to the same extent as normotensive subjects during exercise, a phenomenon reported by other workers.³ In contrast to these findings, Lund-Johansen³ reported a rise in diastolic blood pressure in normotensive subjects, but other workers have observed a fall.⁴ The discrepancy between these studies may be partly due to different methodological approaches, since the position of the body during exercise influences the pattern of response.³

In the present study the mean age was slightly higher in the hypertensive than the normotensive subjects; therefore a comparison was made with an age-matched group of normotensive subjects. The pattern of response showed the same differences, excluding the possibility of age as a contributing factor to the different responses.

Fourteen hypertensive patients retested after drug treatment had achieved normal resting blood pressures. On repeat exercise testing six manifested a normotensive response while eight maintained a hypertensive response irrespective of type or dose of medication. These preliminary data indicate that exercise testing may be a useful tool for assessing hypertension and evaluating the efficacy of treatment.

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Hypertension Unit, Department of Medicine, Hadassah University Hospital, Jerusalem, Israel

B LEIBEL, MPH, research assistant

I KOBRIN, MD, lecturer in medicine

D BEN-ISHAY, MD, professor of medicine

Transient monoclonal gammopathy in hydralazine-induced lupus erythematosus

Hydralazine-induced lupus erythematosus was observed commonly when the drug was used at high doses, and the daily dose is now customarily limited to 200 mg to avoid this complication. The syndrome still, however, occurs in 3-4% of patients when the dose is limited in this way.^{1,2} It occurs almost exclusively in slow acetylators. We describe a case of hydralazine-induced lupus erythematosus with transient monoclonal gammopathy, an association that to our knowledge has not been reported before.

Case report

Severe hypertension (250/140 mm Hg) was diagnosed in 1972 in a woman aged 57 years. She had stable mild renal impairment (blood urea concentration 13-15 mmol/l (78-90 mg/100 ml)) and in 1979 suffered a small stroke. In January 1979 hydralazine was started, and she was maintained on 50 mg twice daily from April 1979. In addition she took atenolol, methyldopa, and cyclopentiazide. In July 1980 (when aged 65 years and after 18 months of treatment with hydralazine, the total dose being about 52 g) she was admitted with a further small stroke, from which she made an uncomplicated recovery. She complained also of anorexia and general ill health and had lost 15 kg in weight over 18 months (table). She had noted mild pain in her right shoulder but did not have pleurisy or a rash.

On examination she was ill and anaemic and had hepatosplenomegaly. Blood pressure was 160/80 mm Hg. Investigations showed a high erythrocyte sedimentation rate (130 mm in the first hour); pancytopenia (haemoglobin concentration 7.8 g/dl, white cell count $3.4 \times 10^9/l$, and platelets $108 \times 10^9/l$); low serum albumin concentration (24 g/l); high globulin concentration (43 g/l); presence of antinuclear factor (titre of 1/500); and a weak positive titre of antibody to double-stranded DNA. She was a slow acetylator. Tests for haemolysis and deficiency of iron, vitamin B₁₂, and folate yielded negative results. An IgM kappa monoclonal was present at a concentration of 16.7 g/l. Further investigation suggested that this was a benign monoclonal as concentrations of IgG (12.6 g/l) and IgA (2.3 g/l) were normal, Bence-Jones protein was absent, skeletal x-ray films showed no evidence of myeloma, and the bone marrow showed plasma cells normal in both number and morphology. Plasma viscosity was slightly raised at 1.94 mPa s (cP) (normal 1.5-1.72 mPa s).

A presumptive diagnosis of hydralazine-induced lupus erythematosus with a coincidental benign monoclonal gammopathy was made, and hydralazine was stopped. The symptoms, signs, and laboratory abnormalities associated with the lupus syndrome resolved completely over the next few months (table). During the same period the concentration of the IgM monoclonal decreased and eventually disappeared. She subsequently remained in good health.

Comment

An illness characterised by weight loss, ill health, hepatosplenomegaly, a high erythrocyte sedimentation rate, pancytopenia, low albumin and high globulin concentrations, and a high titre of antinuclear factor occurring in a slow acetylator 18 months after the start of treatment

Changes in weight and selected haematological values over time. Hydralazine was started in January 1979 and stopped in July 1980

	Normal range	January 1978	July 1980	August 1980	October 1980	April 1981	April 1982
Weight (kg)		72.7	56.0	52.5	57.2	63.4	77.6
Haemoglobin (g/dl)	11.5-16.5	14.2	7.8	9.8	13.6	12.4	11.8
White cell count ($\times 10^9/l$)	4-11	6.1	3.4	6.3	5.4	7.0	6.0
Erythrocyte sedimentation rate (mm in 1st h)	<7	12	130	103	24	20	44
Albumin (g/l)	35-53	42	24	29	40	41	ND
Globulin (g/l)	16-33	29	43	ND	33	30	ND
IgM (g/l)			16.7*	14.0*	12.0*	3.5	2.3

ND = Not done.

* Monoclonal.

with hydralazine strongly suggests hydralazine-induced lupus erythematosus; and the patient's complete recovery after the drug was stopped also supported this diagnosis rather than that of idiopathic lupus erythematosus. Increases in plasma immunoglobulin concentrations are common in hydralazine-induced lupus erythematosus,³ but a monoclonal gammopathy has not been reported. Benign monoclonal gammopathies are not uncommon, occurring in about 2% of the population aged over 60⁴; the monoclonal generally persists in unchanging concentration over many years. In the present case, however, the IgM kappa monoclonal disappeared gradually and completely after hydralazine was stopped, suggesting that the monoclonal was part of the lupus syndrome and not a coincidental finding. Transient monoclonals may occur rarely—for example, in response to infection or in patients with primary immunodeficiency diseases⁵—and this case suggests that they may also be caused by drug-induced immunological illness.

Hydralazine-induced lupus erythematosus is readily diagnosed when it presents with arthritis, pleurisy, or rash. It may, however, present as an insidious illness characterised by general ill health, considerable weight loss, a high erythrocyte sedimentation rate, and blood dyscrasia. In these circumstances the diagnosis is easily delayed or missed completely and there is a danger that advanced malignancy may be diagnosed incorrectly. The presence of a paraprotein would tend to reinforce this error, and it is important to recognise that monoclonal gammopathy may be a feature of this reversible illness.

¹ Bing RF, Russell GI, Thurston H, Swales JD. Hydralazine in hypertension: is there a safe dose? *Br Med J* 1980;280:353-4.

² Freestone S, Ramsay LE, Silas JH. Incidence of hydralazine-associated autoimmune disease. *Br J Clin Pharmacol* 1982;13:291-2P.

³ Perry HM Jr. Late toxicity to hydralazine resembling systemic lupus erythematosus or rheumatoid arthritis. *Am J Med* 1973;54:58-72.

⁴ Axelsson U, Bachmann R, Hallen J. Frequency of pathological proteins (M-components) in 6,995 sera from an adult population. *Acta Med Scand* 1966;179:235-47.

⁵ Seligmann M, Danon F, Clauvel JP. Natural history of monoclonal immunoglobulins. *Br Med J* 1971;ii:321-2.

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University Department of Therapeutics, Royal Hallamshire Hospital, Sheffield S10 2JF

S FREESTONE, MB, MRCP, research fellow

L E RAMSAY, MB, MRCP, consultant physician and associate in medicine

Branhamella catarrhalis infection of the lower respiratory tract: reliable diagnosis by sputum examination

Branhamella catarrhalis, an oropharyngeal commensal, has been isolated from the lower respiratory tract by transtracheal puncture in acute exacerbations of chronic chest disease.¹ Sputum may be contaminated by oropharyngeal commensals while transtracheal puncture enables reliable identification of lower respiratory tract pathogens² but causes discomfort to the patient. We compared sputum and transtracheal aspirates to investigate the reliability of sputum examination in the diagnosis of lower respiratory tract infection with *B catarrhalis*.

Patients, methods, and results

Ten men and one woman (mean age 61.5 years, range 35-78) were studied. Ten had chronic chest disease, including chronic bronchitis (3) with emphysema (1) or with asthma (3), bronchiectasis (2), and asthma (1). One, without chronic chest disease, was a heavy cigarette smoker; five were smokers, five ex-smokers, and one a non-smoker. Six were receiving oral corticosteroids for chronic chest disease and, of these six, one also had multiple myeloma and one diabetes mellitus.

B catarrhalis was presumptively identified in sputum by the presence of Gram-negative diplococci in leucocytes and by colonial morphology after growth in direct and quantitative culture on 5% sheep blood agar and chocolate agar. Transtracheal punctures were then performed and transtracheal aspirates Gram stained and cultured aerobically and anaerobically on 5% sheep blood agar and aerobically on chocolate agar. *B catarrhalis* was positively identified in sputum and transtracheal aspirates by the criteria of Doern and Morse³ and confirmed by the National Health Institute, Wellington.

B catarrhalis was isolated from 10 of 11 transtracheal aspirates from 11 patients in whom *B catarrhalis* was identified in sputum. It was isolated in pure culture in four specimens and with other bacteria in six (table). All 10

Bacteriological analysis of tracheal aspirates

Bacterial isolates	No of aspirates
<i>B catarrhalis</i> (alone)	4
<i>B catarrhalis</i> + <i>H influenzae</i>	3
<i>B catarrhalis</i> + <i>H influenzae</i> and <i>Streptococcus pneumoniae</i>	2
<i>B catarrhalis</i> + <i>S pneumoniae</i>	1
<i>Enterobacter</i> sp	1

isolates of *B catarrhalis* from transtracheal aspirates were susceptible to erythromycin, co-trimoxazole, tetracycline, and cefuroxime, and five of the 10 isolates produced β -lactamase. In four of the five patients with a β -lactamase-producing *B catarrhalis* infection amoxycillin or ampicillin was prescribed before antibiotic susceptibilities were known. In two patients β -lactamase-producing *B catarrhalis* persisted in sputum for two and seven days, and in the remaining two patients amoxycillin-sensitive *Haemophilus influenzae* also persisted in sputum for two and seven days despite treatment with amoxycillin or ampicillin.

Comment

We recognise *B catarrhalis* as a pulmonary pathogen because of its isolation in pure as well as mixed culture from the lower respiratory tract by transtracheal puncture and from frankly purulent sputum during acute exacerbations of chronic chest disease. Also, the presence of *B catarrhalis* within leucocytes in sputum suggests pathogenicity.

An exacerbation of chronic chest disease by infection with β -lactamase-producing *B catarrhalis* may be treated with an inappropriate antibiotic unless this micro-organism is looked for and identified. We have seen two cases of persisting clinical infection during treatment with amoxycillin or ampicillin until β -lactamase-producing *B catarrhalis* was recognised and an alternative antibiotic used. Furthermore, the production of β -lactamase by *B catarrhalis* may protect other pathogens from the action of penicillins. In two cases of β -lactamase-producing *B catarrhalis* infection treated with amoxycillin or ampicillin *H influenzae* as well as *B catarrhalis* persisted in sputum for two and seven days despite in-vitro sensitivity of *H influenzae* to amoxycillin.

B catarrhalis is a recognised pathogen causing pneumonia in immunosuppressed patients.⁴ In our 11 cases, five had no cause of generalised immunosuppression and none had a risk of aspiration from the oropharynx.