- 7 Bamford J, Sandercock P, Warlow C, et al. A prospective study of acute cerebrovascular disease in the community: the Oxfordshire Community Stroke Project 1981-1986. I. Methodology, demography, and incident cases of first-ever stroke. J Neurol Neurosurg Psychiatry 1988;51:1373-80.
- 8 Hatano S. Experience from a multicenter stroke register: a preliminary report. Bull WHO 1976;54:541-53.
- 9 Rankin J. Cerebrovascular accidents in patients over 65 years of age. 2. Prognosis. Scott Med J 1957;2:200-15.
- 10 Office of Population Censuses and Surveys. Population projections. London: HMSO, 1985. (Series PP2, No 13.)
- 11 Skilbeck C, Wade D, Langton-Hewer R, Wood V. Recovery after stroke. J Neurol Neurosurg Psychiatry 1983;46:5-8.
- 12 Office of Population Censuses and Surveys. Mortality statistics. Area: England and Wales, London: HMSO, 1984. (Series DH5, No 10.)
- 13 Haberman S, Capildeo R, Rose F. Epidemiological aspects of stroke. In Greenhalgh R, Rose F, eds. Progress in stroke research I. Tunbridge Wells:
- 14 Fratiglioni L, Massey E, Schoenberg D, Schoenberg B. Mortality from cerebrovascular disease. Neuroepidemiology 1983;2:101-16.

- 15 Whelton P. Declining mortality from hypertension and stroke. South Med  $\mathcal J$ 1982;75:33-
- 16 Garraway W, Whisnant I, Drury I. The continuing decline in the incidence of
- stroke. Mayo Clin Proc 1983;58:520-3.

  17 Acheson R, Williams D. Epidemiology of cerebrovascular disease: some unanswered questions. In: Rose F, ed. Clinical neuroepidemiology. Tunbridge Wells: Pitman, 1980:88-104.
- 18 Haberman S, Capildeo R, Rose F. Diverging trends in cerebrovascular disease
- and ischaemic heart disease mortality. Stroke 1982;13:582-9.

  19 Broderick JP, Phillips SJ, Whisnant JP, O'Fallon WM. Stroke incidence in Rochester, Minnesota: the end of decline in stroke? Neurology 1988;38
- 20 Terent A. Increasing incidence of stroke amongst Swedish women. Stroke 1988-19-598-603
- 21 Van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJA, van Gijn J Interobserver agreement of handicap in stroke patients. Stroke 1988;19:

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# For Debate

## Does constitutional hypotension exist?

John Pemberton

While visiting the late Professor Dr Hans Jesdinsky, an epidemiologist, in Dusseldorf I noticed on his desk some sickness statistics which included details of patients who had been absent from work with a diagnosis of hypotension. I told him that I did not believe that hypotension existed as a primary condition in the United Kingdom and asked him to send me a photocopy of its description from a standard German textbook of medicine. This he kindly did. Under the heading "Constitutional hypotension" and paraphrased it stated that:

It exists if the systolic blood pressure is constantly under 110 mm Hg in men and under 100 mm Hg in women, with a diastolic pressure under 60 mm Hg. It is a disturbance of blood pressure control. The leading symptoms are bodily and mental tiredness, giddiness, a tendency to faint, and tightness round the heart. On standing up the pulse rate may go up to 100 or more, and the standing electrocardiogram may show a flattened or negative T wave and depression of the ST segment. It must be distinguished from coronary artery disease, a vasovagal attack, and a psychogenic fainting attack.

The treatment is systematic bodily exercises and the prescription of peripheral vascular constrictors such as dihydroergotamine or perhaps in severe cases sympathomimetic drugs.

Another German textbook' gives the same cut off points for blood pressure and includes among the symptoms:

tiredness, sleep disturbances, giddiness, blackouts, fainting, anxiety or depression, consciousness of the heart beat, and racing of the heart and sweating. The prognosis is not serious and treatment should include physical exercise and a high salt

Many antihypotensive drugs are taken in West Germany. In the Munich Blood Pressure Study of 1980-1, for example, it was found that 1.8% of men and 5.8% of women aged 30-69 in the population studied were taking antihypotensive drugs (U Keil, personal communication). In a study of the cost and burden of hypotension in West Germany it was reported that 9.5 million days were lost from work in 1978 from this cause, and the estimated cost of antihypotensive drugs for the country in 1979 was 380 million DM (roughly £120m).

### Evidence in other countries

In France I asked a retired French general practitioner if he recognised the condition. "Oh yes indeed," he said, "my wife here suffers from it." I inquired after her symptoms and treatment and learnt that her main complaints were vertigo and fatigue and that he treated her with a derivative of ergot. He said he had treated many other patients with similar symptoms in his practice. I have not found clear evidence in French publications that low blood pressure is regarded as a disease in itself, apart from its association with posture -that is, orthostatic hypotension. The condition is recognised in Italy where it is called chronic primary hypotension and ephedrine or amphetamine is recommended for treatment. In Spain a condition of essential hypotension has been described with symptoms of fatigue, vertigo, sweating, and fainting. Recommended treatment included ephedrine, coffee, Swedish drill, and cold showers.6

British textbooks of medicine describe hypotension as a symptom of acute conditions such as coronary thrombosis, shock, vasovagal attacks, orthostatic fainting, and drop attacks in the elderly, as a symptom of chronic conditions such as Addison's disease, cachexia, tuberculosis, Parkinson's disease, diabetes, and anorexia nervosa, and as a side effect of taking levodopa and antihypertensive and antidepressive drugs.78 A rare condition of degeneration in the autonomic nervous system, the Shy-Drager syndrome, which is characterised by hypotension, is also described. They do not describe a chronic constitutional disease of hypotension. Three British general practitioners whom I have spoken to do not diagnose or recognise the condition, and textbooks of general practice of do not mention it.

In Australia according to one authority "hypotension is significant only when associated with symptoms" such as "dizziness or giddiness upon standing." In the United States one authoritative textbook states: "Although many patients have been treated for chronic 'low blood pressure', most of them, with systolic pressures in the range 90-110 mm Hg are normal and may actually have a greater life expectancy than those with 'normal pressures'."12

### Two explanations

There are two possible explanations of the difference between the practice of British and West German doctors. The first is that British doctors are failing to recognise a disease of chronic constitutional hypotension or are calling it by another name. The second explanation is that West German and other European

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doctors are assuming that a group of symptoms such as giddiness, fatigue, and anxiety when accompanied by low blood pressure constitute a chronic specific disease that requires treatment, often with antihypotensive drugs. Patients with these symptoms are often seen in general practice in the United Kingdom. In the past neurasthenia or anaemia was diagnosed often without confirmation by laboratory tests. Today these symptoms are probably attributed to psychogenic causes. It is probably the view of most British doctors that blood pressures around or a little below 110/60 mm Hg are normal values at the lower end of the distribution and are in fact a healthy sign.

The other possibility—that British doctors are missing a real disease—must be considered. It is biologic-

TABLE 1-Numbers (and percentages) of men and women with low blood pressure in three community surveys

	Melbourne	Caerphilly	Renfrew and Paisley
Men:			
Age (years)	55-66	39-61	55-64
Size of sample	463	2508	3224
Systolic blood pressure < 110 mm Hg	12 (2.6)	68 (2.7)	52 (1.6)
Diastolic blood pressure <60 mm Hg	5 (1·1)	25 (1.0)	35 (1·1)
Women:			
Age (years)	55-66	39-61	55-64
Size of sample	102	222	3976
Systolic blood pressure < 100 mm Hg	2 (2.0)	8 (3.6)	12 (0.3)
Diastolic blood pressure < 60 mm Hg	2 (2.0)	6 (2.7)	48 (1.2)

TABLE II - Symptoms attributed to hypotension by level of systolic blood pressure

Systolic blood pressure* (mm Hg)		No (%) of subjects reporting:			
	Population	Palpitations	Dizziness	Fainting	Tiredness
Men:					
<100	9	2 (22)	3 (33)	4(11)	0(0)
100-109	167	13 (8)	15 (9)	0(0)	13(8)
110-119	667	73 (11)	53 (8)	7(1)	80 (12)
120-129	1066	149 (14)	107 (10)	9 (0.8)	117 (11)
130-139	754	106 (14)	68 (9)	4 (0.5)	68 (9)
140-149	394	59 (15)	51(13)	3 (0.8)	47 (12)
>149	250	48 (19)	25 (10)	3(1)	18(7)
χ†		12.78	2.14	0.05	0.96
		p<0.001	NS	NS	NS
Women:					
< 100	115	6(5)	25 (20)	5 (4)	25 (22)
100-109	347	52 (15)	52 (15)	14(4)	66 (19)
110-119	362	54 (15)	58 (16)	11(3)	62 (17)
120-129	239	41 (17)	31 (13)	7(3)	36 (15)
130-139	95	26 (27)	11 (12)	2(2)	10(11)
140-149	51	9(18)	8(16)	1(2)	4(8)
>149	49	14 (29)	8(16)	3 (6)	6(12)
χ'†		17.88	1.12	0.05	7.77
7. I		p<0.001	NS	NS	p<0.01

<sup>\*</sup>Mean of two readings at "screening" visit and at "medical visit" two weeks later.

NS = not significant.

TABLE III—Symptoms attributed to hypotension by level of diastolic blood pressure

Diastolic blood pressure* (mm Hg)		No (%) of subjects reporting:			
	Population	Palpitations	Dizziness	Fainting	Tiredness
Men:					
< 60	112	21 (19)	16 (14)	0(0)	8(7)
60-69	487	54(11)	29 (6)	3 (0.6)	54 (11)
70-79	1119	134 (12)	90(8)	6 (0.5)	123 (11)
80-89	1008	131 (13)	101(10)	10(1)	111(11)
90-99	471	80 (17)	66 (14)	4 (0.8)	42 (9)
100-109	90	17 (19)	11(12)	1(1)	7(8)
>109	20	2(10)	2(10)	0(0)	2 (10)
x <sup>:</sup> †		3.84	10.52	1.37	0.41
7. 1		p = 0.05	p<0.01	NS	NS
Women:					
< 60	156	17(11)	25 (16)	5(3)	30 (19)
60-69	407	49 (12)	53 (13)	12(3)	73 (18)
70-79	418	75 (18)	71 (17)	13(3)	67 (16)
80-89	192	42 (22)	29 (15)	8(4)	27 (14)
90-99	66	16 (24)	9(14)	1(2)	6 (9)
100-109	15	5 (33)	4 (27)	0(0)	2(13)
>109	4	0(0)	0(0)	0(0)	0(0)
χ:†		17-37	0.26	0.02	5.07
		p<0.001	NS	NS	p<0.05

<sup>\*</sup>Mean of two readings at "screening" visit and two readings at "medical visit" two weeks later.

NS=not significant.

ally plausible to think that it is probably unhealthy to be at either extreme of a biochemical or physiological measurement. This is true, for example, in the case of concentrations of haemoglobin and blood sugar, body weight, or temperature: why not blood pressure? If we accepted the view that blood pressures under 110/60 mm Hg in men and 100/60 mm Hg in women are abnormal how big a problem would that represent in the population?

#### Frequency of low blood pressure in the population

Several well designed studies have been done of blood pressure in the community, mainly aimed at discovering the prevalence of high blood pressure in unselected samples of the population. The full distribution including the low blood pressures is not always published, although in at least one study it was. The authors of some other published studies have kindly supplied me with the figures in table I (P C Elwood, Caerphilly Heart Disease Study and F A Boddy, M Jangobhani, and H Gilmour, survey of blood pressure in Renfrew and Paisley, personal communications), which show the percentages of middle aged men and women falling into the low blood pressure categories in these population surveys.

If we take the criteria of under 110 mm Hg systolic blood pressure for men and under 100 mm Hg for women then from these data between 1.6% and 2.7% of men and between 0.3% and 3.6% of women would be classed as hypotensive. If we take the criterion of under 60 mm Hg diastolic blood pressure then the percentages are between 1.0 and 1.1 for men and between 1.2 and 2.7 for women.

These figures are approximate, but they suggest that there are probably hundreds of thousands of people in these categories in the countries mentioned, and if hypotension defined in this way is considered a disease and doctors and patients think that it should be treated with drugs to raise the blood pressure a large demand for and market in these drugs would be created, as in West Germany.

Who then is right? The doctors in the Western European countries who recognise chronic hypotension as a disease and treat it or the doctors in the UK who do not? Are we perhaps missing a disease and depriving those who suffer from it from treatment or are the doctors in European countries incorrectly attributing certain symptoms to low blood pressure and giving unnecessary treatment?

In a large population survey of blood pressure carried out in Australia<sup>13</sup> the presence or absence of the symptoms that have been associated with low blood pressure was recorded. Tables II and III show the numbers and percentages of subjects who complained of palpitation of the heart, dizziness, fainting, and tiredness at different levels of systolic and diastolic blood pressures.

The data were analysed using  $\chi^2$  techniques to test for a trend in the proportions of subjects reporting symptoms in relation to blood pressure and also whether any trends that did exist were linear or not. The analysis indicated that in both sexes the prevalence of palpitation of the heart showed a trend with increasing blood pressure. In men dizziness also showed a similar trend with diastolic blood pressure. Significant negative trends were found for both systolic and diastolic blood pressure in women for tiredness.

The association of tiredness with low blood pressure in women gives some support to the view that hypotension may be a specific illness. But the fact that only a fifth of the women with the lowest blood pressures had this symptom, that there was no relation between tiredness and low blood pressure in men, and that none of the other symptoms were associated with low blood

<sup>†</sup>x² value of test for trend with one degree of freedom.

by value of test for trend with one degree of freedom

pressure lends little support to accepting hypotension as a primary disease.

#### **Conclusions**

The chief symptoms ascribed to persistent hypotension—tiredness, dizziness, palpitations of the heart, anxiety, and depression—are commonly encountered in general practice and in the UK would probably be attributed in most cases to psychogenic factors and treated accordingly, even if the blood pressure was found to be low. In West Germany and some other European countries the same symptoms are often attributed to hypotension when the blood pressure is low, and the patients are treated with antihypotensive drugs.

The data from the Australian study suggest that these symptoms are not uncommon at all blood pressure levels and, with the exception of tiredness in women, are not more common at low levels of blood pressure. At the present time there seems to be insufficient evidence for accepting the view that there is such a disease as primary chronic hypotension.

These findings raise two general questions. Are there other "diseases" recognised in some countries of the European Community but not in others? And will this lead to difficulties in diagnosis and treatment after the further integration of these countries which is due to take place in 1992?

One unwelcome result of recognising low blood pressure as a primary disease in the UK might be attempts by pharmaceutical companies to persuade doctors to prescribe antihypotensive drugs. If this were done on the scale practised in West Germany it could lead to a substantial increase in the cost of drugs in the NHS.

Perhaps there is a case for creating an organisation within the European Community that would look for major discrepancies in the practice of medicine within the community and which would instigate research to elucidate them.

I thank Dr Bervl Edve of the National Institute of Occupational Health and Safety, New South Wales, for providing me with the data in tables II and III; Emeritus Professor of History, W Carr and Emeritus Professor of Spanish, F Pierce, University of Sheffield, for translations from German and Spanish texts; and Mrs Linda Westlake, Medical Care Research Unit, Department of Community Medicine, for the statistical analysis.

- 1 Schettler G, ed. Innere medizin. Stuttgart: Thieme, 1976;233-7.
- 2 Vosschulte K, Lasch HG, Heinrich F, eds. Innere medizin und chirurgie. Stuttgart: Thieme, 1979:173-6.
- 3 Beske F, Boschke WL, Ruschmann HH. Effizienanalyse der medikam hypotonie therapie. Kiel: Institut für Gesundheits-System-Forshung, 1983.
- 4 Ninet J, Annat G, Boisson D. L'hypotension orthostatique: aspects actuels Rev Med Interne 1984;5:51-61.
- 5 Anguissola AB, Pandolfo G, Sindromi ipotensive. In: Teodori U, ed. Trattato di patalogia medica. Rome: Società Ed Universitaria-Roma, 1981:2825-33.
- Valenti FF, Mazzei ES. Medicina interna. Barcelona: Manuel Marin, 1956.
   Scott RB, ed. Price's textbook of the practice of medicine. Oxford: Oxford
- University Press, 1987. 8 Weatherall DJ, Ledingham JGG, Warrell DA, eds. Oxford textbook of
- medicine. 2nd ed. Oxford: Oxford University Press, 1987. 9 Fry J, Byrne PS, Johnson S, eds. A textbook of medical practice. Lancaster: MTP Press, 1976.
- 10 Taylor RB, ed. Family medicine. New York: Springer, 1978.
- 11 Kochar MS. Chapter 18. In: Hunyor S, ed. Hypotension in cardiovascular drug therapy. Sydney: Williams & Williams ADIS, 1987:149-57.
- 12 Braunweld E, ed. Harrison's principles of internal medicine. 11th ed. New York:
- 13 National Institute of Occupational Health and Safety Blood Pressure Study. Handbook of tables. Canberra: Australian Government Publishing Service,
- 14 Armitage P. Statistical methods in medical research. Oxford: Blackwell, 1971.

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### ANY QUESTIONS

A woman in her 20s has the Kleine-Levin syndrome (periodic somnolence, morbid hunger, and motor unrest) and also suffers from epilepsy. She has been given an oestradiol implant (100 mg) to treat the syndrome and cyclical norethisterone to promote uterine bleeding. What contraceptive advice should she be given?

The Kleine-Levin syndrome is characterised by periodic attacks of excessive appetite followed by sleepiness that may last for days.1 The syndrome mainly affects adolescent men, though it has been described in women, and treatment is usually with psychoactive drugs such as amphetamines.2 If oestradiol has helped this woman her condition may be a variant of the premenstrual syndrome, for which oestradiol implants are effective. These implants also have a contraceptive action, and in one study of 1668 treated cycles only two pregnancies occurred.3 In a recent study 100 mg oestradiol implants were given to 10 ovulating premenopausal women along with cyclic oral progestogens. During the first three cycles follicular development continued in almost half the women but only one woman ovulated. (She was given a second implant at three months and this suppressed ovarian activity.) By the sixth cycle no woman ovulated, and when at six months a second implant was given to the remaining women ovarian activity was completely suppressed. This patient, however, may not be able to rely on her oestradiol implants for contraception if she is also taking anticonvulsants, most of which alter oestrogen metabolism by inducing liver enzymes. - JAMES OWEN DRIFE, senior lecturer in obstetrics and gynaecology, Leicester

- 1 Walton JN. Brain's diseases of the nervous system. 8th ed. Oxford: Oxford University Press,
- 2 Duffy IP, Davison K. A female case of the Kleine-Levin syndrome, Br 7 Psychiatry 1968;114:
- 3 Greenblatt RB, Asch RH, Mahesh VB, Bryner JR. Implantation of pure crystalline pellets of estradiol for conception control. Am J Obstet Gynecol 1977;127:520-4.

  4 Magos AL, Collins WP, Studd JWW. Effects of subcutaneous oestradiol implants on ovarian
- activity. Br J Obstet Gynaecol 1987;94:1192-8.

What treatment is advised for occasional recurrent attacks of pancreatitis in a woman in her 20s? Can such attacks be prevented?

I strongly suspect that this patient has gall stones, but the difficulty may lie in proving it. Gall stones are present in at least half of British patients with acute pancreatitis, the exact percentage reflecting the diligence of the search. The calculi incriminated in acute pancreatitis originate within the gall bladder, migrate down the cystic duct, and lodge transiently at the ampulla. They therefore tend to be small and can escape diagnosis on conventional investigations such as biliary ultrasonography and oral cholecystography. Endoscopic retrograde cholangiopancreatography should probably be performed after any attack of acute pancreatitis labelled as "idiopathic"—without overt gall stones, alcoholism, or other clear cut cause-but in recurrent attacks it becomes mandatory. A negative endoscopic retrograde cholangiopancreatogram still does not rule out tiny gall stones. It is possible to pursue the diagnosis by sieving the stools for stones during convalescence from pancreatitis or by looking for cholesterol crystals in bile retrieved by duodenal intubation. For practical purposes, however, it may be simpler and more effective to carry out cholecystectomy in a fit young woman with recurrent acute pancreatitis confirmed by repeatedly raised serum concentrations of amylase.

Although I have emphasised the likelihood of gall stones, there are other possible explanations for recurrent acute pancreatitis. Various drugs have been blamed, often on rather sketchy evidence. Hyperlipidaemia, hyperparathyroidism, and sundry viral infections are rarely associated. Other surgical causes include ampullary tumour, pancreas divisum, and pancreatic ductal stricture, all of which can be shown by thorough endoscopic retrograde cholangiopancreatography and cured by appropriate operations.2 One thing is clear: the matter must be taken further. Sooner or later one of these attacks could develop into a severe, even life threatening illness. - R C N WILLIAMSON, professor of surgery, London

- 1 Corfield AP, Cooper MJ, Williamson RCN. Acute pancreatitis: a lethal disease of increasing incidence. Gut 1985;26:724-9.

  Williamson RCN. Surgical aspects of acute pancreatitis. In: Salmon PR, ed. Key developments in
- gastroenterology. London: John Wiley, 1988:113-36.