What's new in hypertension

Is it time to forget about diastolic blood pressure? Should we abandon the mercury sphygmomanometer? Is non-pharmacological intervention a waste of time? These were some of the questions discussed at the first Primary Care Cardiovascular Society (PCCS) meeting of 2002 which was carried out jointly with the British Hypertension Society (BHS) on 26th February. The meeting – chaired by Professors Bryan Williams (Leicester Royal Infirmary) and Richard Hobbs (University of Birmingham) – focused on practical advice and trial evidence. Ola Soyinka reports.

The global burden and status of hypertension in the UK

Cardiovascular disease is a major contributor to the global burden of disease. Furthermore, the contribution of stroke and coronary heart disease to this burden is set to rise. This, Professor Poulter, Director of the Cardiovascular Studies Unit, Imperial College, London, explained, is a result of longer life expectancy combined with a poor diet, a tendency to exercise less, drink more alcohol and smoke.

One of the major risk factors in this global problem is hypertension. In absolute terms, he pointed out, we see more strokes among people with more modestly elevated blood pressures – a systolic blood pressure of 130–160 mmHg, for example - than at the extremes. This, he argued, suggests the need for a population-based strategy. "With a high-risk strategy we are not going to solve the problem," he said, recommending that our thresholds for intervention should be lower.

Professor Poulter expressed dismay at government policy in the UK which, he said, has seen successive cuts in alcohol tax plus an increase in pub licensing hours and recommended 'sensible' drinking limits. He felt that this had undoubtedly contributed to the observed increase in drinking, particularly among women. "Boozing and body weight are going up so the population is going to have to do something pretty clever to bring blood pressure down on average," he warned.

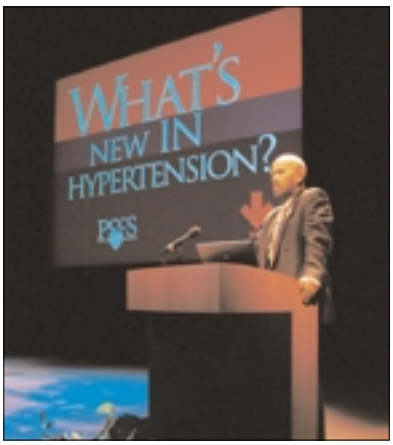
The PCCS and the BHS joined forces for a meeting at the International Convention Centre in Birmingham

Commenting on international coronary heart disease death rates, Professor Poulter said: "Only Czechoslovakia and Hungary die of this disease more than we do".

He did, however, feel that things were moving in the right direction. He quoted the results of a survey which shows that, for hypertension, the rule of halves had been supplanted by a 'rule of two thirds' by 1994. Furthermore, data for 1998 suggested that the percentage of controlled hypertensives had risen from 30% to 39%. "In four years that is a fantastic improvement, largely attributable to the primary care sector," he said.

He cautioned, however, over using the current blood pressure target of 140/90 mmHg, highlighting that the percentage of patients currently controlled is only about 9%. He also pointed out that we are performing particularly badly in the elderly.

Speaking about the reasons for the persisting gap between theory and practice, Professor Poulter listed a range of likely causes, but stressed that doctors must accept final responsibility. "There is an unholy alliance between doctor and patient in which they continuously find an excuse to postpone action and change treatment regimes," he said.



'Only Czechoslovakia and Hungary die of this disease more than we do'

Neil Poulter

Concluding, Professor Poulter encouraged doctors to begin prescribing the number of drugs that are necessary to get patients to target and to place more emphasis on non-pharmacological interventions.

Systolic hypertension and the elderly

Introducing his lecture, Professor Gareth Beevers of the Department of Medicine, City Hospital, Birmingham, criticised the tendency to regard the elderly as a separate category or minority. "The concept of the elderly is a spurious one and should be abolished," he said.

Moving on to discuss blood pressure, Professor Beevers challenged convention by arguing for the irrelevance of diastolic pressure in management decisions. "The Framingham Study showed us very early on – while we were more obsessed with diastolic pressure – that over the age of 45, systolic blood pressure had more predictive power for coronary risk," he said.

More recent data and new methods of statistical analysis confirm this. They also suggest that diastolic pressure is minimally predictive and show that pulse pressure is important as a predictor of coronary risk. Professor Beevers stopped short of claiming diastolic pressure was totally redundant but suggested it was only relevant at higher pressures of over 120 mmHg.

On the importance of isolated systolic hypertension (ISH), Professor Beevers discussed evidence which shows that ISH produces the same degree of left ventricular hypertrophy as systo-diastolic elevation, suggesting that this shows we should not differentiate between the conditions. ISH should be controlled and we should not worry about reducing blood pressure too far, he said.

Arguing the case for ignoring diastolic blood pressure

Gareth Beevers

He went on to point out that the fear of adversely affecting coronary artery filling during diastole, a theoretical problem for people suffering from coronary heart disease, has been laid to rest by trials such as Syst-Eur. These have shown that there is no 'J curve' and that there are dramatic benefits to be had from treating ISH, he said.

Concluding, Professor Beevers levelled his sights at another target – the quality of evidence provided by observational studies. "We have a revolution in thinking based on facts," he said. "These facts come from randomised controlled prospective studies which provide proof, unlike retrospective case-control studies which are merely interesting."

Protecting the brain

"Every five minutes, someone in the UK has a stroke," said Dr Gordon McInnes, Consultant Physician, Western Infirmary, Glasgow, explaining that stroke, while less prevalent than CHD, is a particular problem because of the degree to which individuals may be disabled. He pointed out that the management of stroke and its consequences consumes approximately 4.3% of all NHS resources.

The relationship between stroke and blood pressure is continuous, he believes, without a lower threshold, which holds for diastolic as well as systolic blood pressure. Dr McInnes referred to evidence that reducing blood pressure is beneficial in the primary prevention of stroke. "It is absolutely cast iron," he said.

Syst-Eur has also shown that blood pressure control can help to preserve cognitive function and reduce the incidence of dementia. Furthermore, he said, the rigour of control is important. Evidence shows that maintaining diastolic blood pressure at 85 to 80 mmHg can result in further gains in stroke prevention; systolic blood pressure should be kept under 140 mmHg.

Regarding the choice of drug, Dr McInnes advised that "although the data suggest a minimal though significant advantage for calcium channel blockers and ACE inhibitors over conventional treatments, whichever drug you use, you are likely to get similar results". For the newer angiotensin II antagonists, more data are in the pipeline, he said, with LIFE (see news section pages 198-9) and SCOPE due to report in 2002.

Secondary prevention is a more complex area, he said, with data being scarce. Traditionally doctors have been unsure of the safety of lowering blood

'Blood pressure control can help to preserve cognitive function and reduce the incidence of dementia'

Gordon McInnes

pressure in stroke patients because of worries about brain perfusion, particularly of ischaemic areas.

The PROGRESS trial with perindopril and indapamide has shown that, regardless of the type of stroke and the systolic or diastolic blood pressure beforehand, there was a significant benefit obtained by reduction of blood pressure with these agents. Treatment started from two weeks after the event will significantly reduce the risk of further events.

Although the advantage of particular drugs is uncertain, multiple drugs in combination will usually be required. Dr McInnes suggested that the BHS targets of 140/85 mmHg (a diastolic blood pressure of 80 mmHg for diabetic patients) should be used, with all stroke patients being treated to target or having their individual systolic and diastolic blood pressures reduced by at least 9/4 mmHg respectively.

Protecting the heart

Hypertension is only one of the risk factors contributing to coronary heart disease, Dr Adrian Brady, Royal Infirmary, Glasgow, reminded the audience, pointing out that cholesterol is perhaps a more important risk factor. Trials with antihypertensive agents, such as in the EWPHE, MRC, SHEP and the recent Syst-Eur and UKPDS studies, have shown effective risk reduction for stroke but more modest benefits in reductions of coronary events, except in diabetic patients.

Dr Brady discussed the contrasting success in the control of hypertension and cholesterol levels in Europe. Data from EUROASPIRE 2 shows that blood pressure control is improving rapidly but there is slower progress with cholesterol. Similarly in the UK, audit of GP data from the Healthwise database showed that in over 24,400 patients with established (and recorded) coronary heart disease, two thirds of the men and over half the women had well controlled blood pressure, but about a third of the men and more than half the women had never had a cholesterol measurement. "This shows that blood pressure has been much more sorted than cholesterol," said Dr Brady.

The 4S study showed that very large reductions in coronary events could be achieved with statins in patients with established coronary heart disease. Subgroup analysis, he said, showed that "if you've got hypertension and you lower cholesterol with statins, you get important benefits". The Heart Protection Study has recently provided more important evidence of the cardiovascular benefits to be gained from lowering cholesterol levels with statins.

On the question of whether there was evidence for any particular drug or class, Dr Brady discussed the HOPE trial. The results of the HOT trial suggest that the coronary benefits shown by HOPE can be explained by blood pressure lowering alone. "It is unlikely there is an additional drug-specific effect," he concluded.

Other studies looking for differences between newer and conventional drugs in the prevention of cardiovascular events, for example STOP 2 and a variety of meta-analyses, have not provided convincing evidence for a particular advantage of one class of drug over another.

"The bottom line," said Dr Brady in summary, "is that blood pressure lowering is what reduces the risk of events. Although benefit is to be gained from lowering blood pressure, lowering of cholesterol is more impor-

'Lowering cholesterol is more important for reduction in coronary events'

Adrian Brady

tant for the prevention of coronary events".

Protecting the kidney

Professor Bryan Williams, Leicester Royal Infirmary, outlined to the meeting the natural history of diabetic nephropathy from the preclinical stage to the development of persistent microalbuminuria (ie.30 mg protein excreted over 24 hours), at which point there is evidence of renal enlargement and blood pressure also begins to rise. Proliferative retinopathy and cardiovascular events are common at this stage, and patients have a massively increased risk of premature cardiovascular death. Diabetics with persistent microalbuminuria are 20 times more likely to develop end stage renal disease (ESRD), Professor Williams told the meeting.

'Angiotensin receptor blockade should complement blood pressure control in the diabetic patient'

Bryan Williams

The third stage is marked by the presence of proteinuria and the prognosis for such patients is poor. "This is virtually an ante-mortem state and the outlook for patients is appalling," said Professor Williams. "All these patients will end up on dialysis if they live long enough and all will die of a premature cardiac death."

He discussed new evidence on the effect of drugs on the course of type 2 diabetes focusing on three trials - IRMA 2, IDNT and RENAAL.

IRMA 2 was carried out in diabetic patients with hypertension and persistent microalbuminuria to see if irbesartan would decrease progression to overt proteinuria or nephropathy. The outcome showed a significant benefit in reducing the relative risk of progression.

IDNT investigated patients with overt proteinuria and concluded that irbesartan reduced proteinuria and the rate of progression to primary end point (doubling of baseline creatinine, ESRD or death) by 20% compared to controls and has an additional effect above that produced by the reduction of blood pressure. There were no mortality differences.

RENAAL was a trial in patients with hypertension and renal disease on conventional medication plus either losartan or placebo. There were significant reductions in proteinuria and the rate of progression of renal disease. It is the first ever trial to demonstrate a drug's ability to prevent the development of ESRD. There was also a reduction in hospitalisations for heart failure.

Professor Williams stressed that the prime objective in the diabetic patient must be to control blood pressure. He said a reasonable target is a systolic blood pressure of 140 mmHg, because even in trials, it was difficult to get patients below this. The evidence suggests that there is additional benefit to be gained from angiotensin receptor blockade, which should be a complementary therapy to blood pressure control in the diabetic patient.

Summarising, Professor Williams recommended that treatment for diabetic patients should begin with an angiotensin receptor antagonist (or ACE inhibitor). In patients with microalbuminuria, if renal function is normal, a thiazide should be added. Treatment should then include a calcium channel blocker (CCB) if required and then, finally, an alpha or beta blocker can be added, if needed. This strategy, he said, will reduce the rate of decline in glomerular filtration rate. For patients with proteinuria, a loop diuretic (often at high dose) is likely to be required. A calcium channel blocker, then an alpha or beta blocker can then be added.

Thresholds and targets – the rationale and combination therapy

Dr Henry Elliott, Department of Medicine and Therapeutics, Western Infirmary, Glasgow, was frank about our current levels of success in treating hypertension. "Both the primary and secondary care sectors are not doing enough," he said.

The BHS guidelines of 1999 have given us blood pressure treatment targets of 140/85 mmHg or less. The HOT study has shown that small gains in hypertension control can translate into big gains in relative risk. The Framingham data have shown us that patients with high normal blood pres-

'Both the primary and secondary care sectors are not doing enough'

Henry Elliott

sure have more events than those with normal blood pressure, he said. Despite this knowledge, according to a recent survey, less than 20% of hypertensives in the UK are in the 140/90 mmHg blood pressure range.

One reason, explained Dr Elliott, is that in the UK approximately 60% of patients are on only one drug, 33% of patients are on two drugs and 7% are on three or more. Yet trials have shown that at least 50% of patients will achieve satisfactory blood pressure control on a single drug. "Combination treatment is almost obligatory if we are to arrive at a situation where we have good blood pressure control," he said. Not only will it improve control but it will help to reduce the side effects of the individual agents. There is also an opportunity to harness the additional beneficial characteristics of the individual drugs.

Dr Elliott urged delegates to remember other risk factors and to pursue a strategy aimed at reducing overall cardiovascular risk using lipid lowering and aspirin treatment where appropriate.

Debate: Non-pharmacological intervention – is it worth the effort?

The meeting ended with the ever-popular debate which tackled the value of lifestyle changes. Speaking for the motion, Professor Graham MacGregor, St George's Hospital, London, said ideally, PCCS and BHS members should be more like the members of the Venezuelan Yanomani tribe.

He warned that about 95% of the meeting's delegates were at risk of developing cardiovascular disease, unlike the jungle-dwelling Yanomani who do not develop cardiovascular problems at all and who have been shown not to develop atherosclerosis in post-mortems. They have a diet low in salt and fats, with plenty of carbohydrate, fruit and vegetables. They get plenty of exercise, and their average blood pressure is 96/61 mmHg, he said.

"Our normal ranges are not normal, they are an average," claimed Professor MacGregor. He suggested that we need to get down to such levels if we want to avoid cardiovascular disease altogether.

Speaking for the motion

Graham MacGregor

Reducing salt and increasing potassium intake via fruit and vegetables, weight loss, alcohol (short lived) and regular physical exercise, have all been demonstrated to lower blood pressure in good quality studies.

Professor MacGregor recommended a population strategy, citing proof that it could work from The North Karelia project in northern Finland. This involved 14,000 men, who over 20 years managed to achieve a cholesterol reduction of 13%, a blood pressure reduction of 9% and a reduction in smoking by 15%. This led to impressive results – stroke was reduced by 66% and coronary heart disease was reduced by 55%.

Professor MacGregor admitted that this was a major educational challenge for the healthcare profession. Salt restriction, which can have a major impact in reducing blood pressure (and is additive to drug therapy), would require significant patient education, he said. Most doctors, nurses and dietitians are not able to give the necessary advice and, since time is at a premium, methods can vary from the use of whatever simple leaflets are available to more imaginative schemes, such as patient-run meetings.

Professor MacGregor felt that it was a lack of appreciation of the evidence and a lack of will that was stopping the profession placing more emphasis on lifestyle changes. "We can prevent cardiovascular disease if we want to. We just don't seem to want to," he concluded.

General practitioner, Dr Terry McCormack has a patient population somewhat different from the Yanomani Indians. Working 'at the medical coalface' in Whitby, his practice cares for a population of 16,000 people. Speaking against the motion, Dr McCormack presented some observational evidence that suggested that the Whitby populace did not like being told to be good.

Speaking against the motion

Terry McCormack

"There are 32 churches which are either empty or boarded up," he said. In contrast, there are 31 pubs which always seem to be full and Whitby's 20 fish and chip shops are always well patronised.

On patient education he noted that, although we may know that salt restriction and other measures work,

most patients are not enthusiastic or motivated. Trying to make patients change their behaviour could alienate them, he said.

Dr McCormack felt it was simply too late for most adults. "We need to target the next generation and get the message across at school," he told the meeting. He felt that this was a problem for the Department of Education, the Department of Trade and Industry and the food industry, not the Department of Health.

Referring to the clinical trial evidence, Dr McCormack pointed out that "volunteers are not real people". Apart from being more motivated than average, they get an unreal level of intervention. The reality of what can be achieved in real life is different, he maintained.

There is also a danger, with lifestyle modifications, that valuable time may be lost before effective drug treatment is initiated. In conclusion, he advocated that the best lifestyle intervention was drugs – these will deal with most of the risk factors from nicotine patches for the smoker to sibutramine for the overweight.

Although the delegates voted heavily in favour of non-pharmacological intervention, the poll showed that Dr McCormack did achieve a statistically significant absolute swing, of one vote.

- An innovation to the PCCS/BHS meeting this year was a session on 'Practical issues and difficult cases'. This will be covered in a future issue of the journal.