

remove some of the problems and inevitable distress from predictive testing for Huntington's disease.

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- 1 Gusella JF, Wexler NS, Conneally PM, *et al*. A polymorphic DNA marker genetically linked to Huntington's disease. *Nature* 1983;306:234-8.
- 2 Youngman S, Sarfarazi M, Quarrell OWJ, *et al*. Studies of a DNA marker (G8) genetically linked to Huntington disease in British families. *Hum Genet* 1986;73:333-9.
- 3 Haines J, Tanzi R, Wexler N, *et al*. No evidence of linkage heterogeneity between Huntington's disease and G8 (D4S10). *Am J Hum Genet* 1986;39(suppl):461.
- 4 Wasmuth JJ, Hewitt J, Smith B, *et al*. A highly polymorphic locus very tightly linked to the Huntington's disease gene. *Nature* 1988;332:734-6.

- 5 Gilliam TC, Bucan M, MacDonald ME, *et al*. A DNA segment encoding two genes very tightly linked to Huntington's disease. *Science* 1987;238:950-2.
- 6 Youngman S, Shaw DJ, Gusella JF, *et al*. New DNA probes localised to the region 4p15.1-pter. *Cytogenet Cell Genet (Human Gene Mapping 9)* 1987;46:724-5.
- 7 Gusella JF, Tanzi RE, Bader PI, *et al*. Deletion of Huntington's disease-linked G8 (D4S10) locus in Wolf-Hirschhorn syndrome. *Nature* 1985;318:75-8.
- 8 Pritchard C, Casher D, Uglum E, *et al*. Physical mapping studies of the region surrounding the Huntington disease locus. *Am J Hum Genet* 1988;43(suppl):A155.
- 9 Anonymous. Presymptomatic detection of Huntington's chorea [Editorial]. *Br Med J* 1972; iii:540.
- 10 Thomas S. Ethics of a predictive test for Huntington's chorea. *Br Med J* 1982;284:1383-9.
- 11 Quarrell OWJ, Tyler A, Meredith AL, Youngman S, Upadhyaya M, Harper PS. Exclusion testing for Huntington's disease in pregnancy with a closely linked DNA marker. *Lancet* 1987;ii:1281-3.
- 12 Meissen GJ, Myers RH, Mastromauro CA, *et al*. Predictive testing for Huntington's disease with use of a linked DNA marker. *N Engl J Med* 1988;318:535-42.
- 13 Harper PS, Sarfarazi M. Genetic prediction and family structure in Huntington's chorea. *Br Med J* 1985;290:1929-31.
- 14 Harper PS. A genetic marker for Huntington's disease. *Br Med J* 1983;287:1567-8.
- 15 Morris M, Tyler A, Meredith L, Harper PS. Predictive testing for Huntington's disease: methods and problems. *J Med Genet* 1988;25:640.
- 16 Morris M, Tyler A, Harper PS. Adoption and genetic prediction for Huntington's disease. *Lancet* 1988;ii:1069-70.

Aetiology of peripheral atherosclerosis

Smoking seems especially important

Patients with intermittent claudication are up to four times more likely than normal people to have coronary artery disease^{1,2} and about half will die from a heart attack.³ Conversely, patients with coronary artery disease have at least a fivefold greater risk of developing intermittent claudication.^{4,6} These findings reflect the diffuse nature of atherosclerosis. But why are some people more prone to disease in their peripheral arteries than their coronary arteries?

Vascular surgeons are justified in believing that smoking is almost a prerequisite for developing peripheral arterial disease because over 90% of their patients may give a history of smoking.⁷ Studies of intermittent claudication in the community provide a different perspective: the population attributable fraction—that is, the percentage of disease prevalence that may be caused by cigarettes—varies between a fifth and three quarters. Many subjects have apparently never smoked. But smoking does seem to have an independent effect greater than other risk factors^{5,6} and to be a more important aetiological variable than in ischaemic heart disease.⁶ Most epidemiological studies have shown that raised blood pressure is also likely to be a major risk factor for peripheral arterial disease.^{1,2,5,6} The direction of a possible causal association has not, however, been confirmed.

The particularly high incidence of peripheral arterial disease in patients with florid diabetes mellitus is well known, but the extent to which impaired glucose tolerance in the general population is a risk factor is less obvious. A raised casual blood glucose concentration in the Framingham study was more closely related to developing intermittent claudication than heart disease and had an independent effect when other risk factors were taken into account.⁹ Conflicting results have, however, been obtained in other population studies.^{2,4,5,10} In Oxford, for example, Hughson *et al* found that patients with intermittent claudication did not have a higher fasting blood glucose concentration than controls.² Furthermore, in a study in Basle that excluded known diabetes an inverse association was found between the degree of glucose intolerance and the occurrence of disease.¹⁰ These results are important because, unlike those from most other studies,^{2,5,9} they are based on a glucose tolerance test. They do, however, have the disadvantage of being derived from cross sectional and not longitudinal data, and more evidence is

needed on whether impaired glucose tolerance is a risk factor in the general population.

At least 20 studies have examined the relation between blood cholesterol concentration and peripheral arterial disease, and a consistent picture has not emerged; many studies have found no relation.⁸ The role of high density lipoprotein cholesterol has not been widely investigated, but lower mean plasma concentrations have been found in those with disease.^{11,12} What is of particular interest is that almost without exception serum triglyceride concentrations have been found to be higher in patients with peripheral arterial disease than in controls. It would be tempting to assume that triglycerides are an important risk factor for atherosclerosis affecting the peripheral arteries and not the coronary arteries, but the independent effect of triglycerides has not been examined adequately in peripheral arterial disease. In line with the findings in coronary arterial disease the association might well disappear when adjusted for other risk factors—especially since triglyceride concentrations are related inversely to concentrations of high density lipoprotein cholesterol.¹³

Any suggestion therefore of a unique risk profile for peripheral atherosclerosis is not supported by the evidence. Smoking seems to be particularly important, but we should be wary that an apparently differential effect of smoking on peripheral arterial disease and coronary arterial disease detected in retrospective studies may simply be a manifestation of a dose response relation in which more smoking is associated with a more severe form of disease. Indeed, claudication tends to occur in older age groups,^{4,9} when generalised atherosclerosis is presumably more advanced. On the other hand, people with claudication might represent an attenuated cohort because many of those with severe peripheral atherosclerosis might die from coronary disease at an earlier age. Studies on symptomless subjects in the community may give a clearer picture of the importance of smoking.

Numerous hypotheses have been put forward to explain the atherogenic effects of smoking,¹⁴ but the different anatomical structures and haemodynamics of the peripheral and coronary arteries may explain the differential effects of smoking at these sites. Atherosclerosis occurs most commonly at

bifurcations and bends and may be related to low velocity low shear areas forming.¹⁴⁻¹⁶ This might result in local accumulation of lipids and other constituents, and activated platelets and white cells might spend longer at the site, promoting their interaction with the endothelium. Smoking is associated with an increased packed cell volume, increased circulating fibrinogen concentrations, and blood viscosity^{17 18} and hence might encourage further blood stagnation in these areas.¹⁹ Thus a combination of smoking and haemodynamic factors might promote atherogenesis in specific sites of the arterial tree and perhaps more in peripheral than in coronary arteries.

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- 1 Reid DD, Holland WW, Humerfelt S, Rose G. A cardiovascular survey of British postal workers. *Lancet* 1966;i:614-8.
- 2 Hughson WG, Mann JI, Garrod A. Intermittent claudication: prevalence and risk factors. *Br Med J* 1978;ii:1379-81.

- 3 Widmer LK, Stahelin HB, Nissen C, da Silva A. *Venen-, Arterien-Krankheiten, koronare Herzkrankheit bei Berufstätigen*. Bern: Huber, 1981.
- 4 Reunanen A, Takkinen H, Aromaa A. Prevalence of intermittent claudication and its effect on mortality. *Acta Med Scand* 1982;211:249-56.
- 5 Schroll M, Munck O. Estimation of peripheral arteriosclerotic disease by ankle blood pressure measurements in a population study of 60 year old men and women. *J Chronic Dis* 1981;34:261-9.
- 6 Dawber TR. *The Framingham study*. Cambridge, Massachusetts: Harvard University Press, 1980.
- 7 Lord JW. Cigarette smoking and peripheral atherosclerotic occlusive disease. *JAMA* 1965;191:249-51.
- 8 Fowkes FGR. Epidemiology of atherosclerotic arterial disease in the lower limbs. *European Journal of Vascular Surgery* 1988;2:283-91.
- 9 Kannel WB, McGhee DL. Update on some epidemiological features of intermittent claudication: The Framingham Study. *J Am Geriatr Soc* 1984;33:13-8.
- 10 Da Silva A, Widmer LK, Ziegler HW, Nissen C, Schweizer W. The Basle longitudinal study: report on the relation of initial glucose level to baseline ECG abnormalities, peripheral artery disease, and subsequent mortality. *J Chronic Dis* 1979;32:797-803.
- 11 Meerloo JM, Billimoria JD. High density lipoprotein cholesterol levels in peripheral vascular disease and in women on oral contraception. *Atherosclerosis* 1979;33:267.
- 12 Bihari-Vargi M, Szekeley J, Gruber E. Plasma high density lipoproteins in coronary, cerebral and peripheral vascular diseases. The influence of various risk factors. *Atherosclerosis* 1981;40:337-45.
- 13 Hulley SB, Rosenman RH, Bawol RD, Brand RJ. Epidemiology as a guide to clinical decisions: the association between triglyceride and coronary disease. *N Engl J Med* 1980;302:1383-9.
- 14 Woolf N. *Pathology of atherosclerosis*. London: Butterworth, 1982.
- 15 Schettler G, Nerem RM, Schmid-Schonbein H, Mori H, Diehm C, eds. *Fluid dynamics as a localising factor for atherosclerosis*. Berlin: Springer-Verlag, 1983.
- 16 Goldsmith HL, Karino T. Microthology and clinical medicine; unravelling some problems related to thrombosis. *Clinical Hemorheology* 1982;2:143-56.
- 17 Ernst E, Matrai A, Schmolzl C, Magyarosy I. Dose effect relationship between smoking and blood rheology. *Br J Haematol* 1987;65:485-7.
- 18 Meade TW, Imeson J, Stirling Y. Effects of changes in smoking and other characteristics on clotting factors and the risk of ischaemic heart disease. *Lancet* 1987;ii:986-8.
- 19 Lowe GDO. Blood rheology in general medicine and surgery. *Clinical Haematology* 1987;1:827-61.

Spending some of the preregistration year in general practice

Needs incentives to make it happen

"Why is it," asked one of my students, "that in hospital I hear so much that's bad about the hospital?" That student is not alone in raising such a question.¹⁻⁴ When one group is critical of another the criticism may be deserved; the critic may be mad, sad, or bad; or neither side may understand the other. Though there are undoubted faults in both hospitals and general practice, the main cause of strain lies in misunderstanding—whereas all doctors have worked in hospital only a few hospital doctors have experience of general practice.

For this reason the Medical Health Act of 1978 allowed the possibility that experience of general practice could be provided in the preregistration year. The splitting of the first year after qualification into three periods of four months with two periods spent in traditional medical and surgical rotations allows a preregistration doctor to be attached to a general practice. This experience should be valuable in bridging the gap in understanding between the two main branches of the health service. The same idea has been attracting attention in New Zealand, and a recent report from Australia recommends a mandatory two year preregistration term including general practice.⁵

But the opportunity to do general practice before registration is rarely taken. There are a few reports of preregistration doctors working in general practice,⁶⁻⁹ and all emphasise the legal, administrative, and academic difficulties in such a programme. Only a few general practices are suitable and willing to undertake such teaching, which, unlike teaching vocational trainees or students, carries no financial inducement. The recurring presence of an inexperienced doctor in a practice every four months is disruptive and presents organisational problems in prescribing and continuity of care. On the other side, young doctors may be reluctant to depart from the usual pattern of preregistration posts and to appear

different when starting on a career already overpacked with "essential" experience. Against these negative aspects should be weighed the obvious enthusiasm reported by all those who have had experience of such a scheme; subsequently no harm has been done to a houseman's career, and the unusual experience has aroused great interest at interviews.⁶

Experience in general practice for the future specialist holds out the hope of bridging a schism which mars the health service. Yet little is done to encourage it, and the schemes that have been reported have struggled against considerable odds to achieve their success. New schemes are unlikely to develop unless rewards are offered to attract suitable applicants and general practices. Incentives for the practices might take the form of grants for special equipment as well as financial reward. It is less easy to see how young doctors might be encouraged to apply for preregistration posts in general practice, and a mandatory requirement as recommended in Australia is impossible for lack of suitable practices.

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- 1 Cartwright A, Anderson R. *General practice revisited*. London: Tavistock, 1981.
- 2 Dowie R. *General practitioners and consultants*. London: King Edward's Hospital Fund, 1983.
- 3 Hiatt HH. *America's health in the balance*. New York: Harper and Row, 1987.
- 4 Hull FM, Westerman RF. Referral to medical outpatients departments at teaching hospitals in Birmingham and Amsterdam. *Br Med J* 1986;293:311-4.
- 5 Doherty RL, Amos BJ, Hicks N, et al. *Report of the Committee of Enquiry into Medical Education and the Medical Workforce*. Canberra: Australian Government Publishing Service, 1988.
- 6 Harris CM, Dudley HAF, Jarman B, Kidner PH. Preregistration rotation including general practice at St Mary's Hospital Medical School. *Br Med J* 1985;290:1811-3.
- 7 Harris CM. Pre-registration posts in general practice. *Med Educ* 1986;20:136-9.
- 8 Freeman GK, Coles CR. The preregistration houseman in general practice. *Br Med J* 1982;284:1379-83.
- 9 McGuinness BW. A house officer attachment in general practice. *Practitioner* 1982;226:1216-8.