Progression and regression of atherosclerosis

SIR,—“The most important disease in man is that which produces intimal nodules in the larger arteries,” to quote Sir George Pickering speaking quite a long time ago. The subject is discussed in your leading article (28 February, p 481), which points out that the cause of this condition remains unknown and furthermore that evidence regarding progression or regression of the lesions is not available. Dietary manipulations in animals may produce interesting results but evidence of beneficial regression of the lesions in man is lacking. You go on to say that the only sure way to show that lesions regress in man is to watch them do so in a series of arteriograms.

Unfortunately one must agree with these statements with the exception of the view regarding arteriography. Firstly, from the scientific point of view arteriography is too inaccurate to be of quantitative value in assessing degrees of atherosclerosis unless very elaborate techniques are used and precautions taken. It is well recognised, for instance, that the arteriographic appearance of a vessel frequently relates poorly with the actual state of the vessel when it is exposed for surgical treatment. Furthermore, it is difficult to compare arteriographic appearances with the actual haemodynamic capability of the vasculature. As well as being expensive to perform, arteriography carries definite risks which must surely be expected to increase if repeated follow-up studies are to be carried out.¹

Recent advances in non-invasive techniques should be brought to the attention of those workers studying and writing about atherosclerosis. In particular the value of ultrasound scanning, both echo systems and especially Doppler systems.²⁻⁴ It is unfortunate that information about developments in these areas appears so infrequently in general medical journals, being confined mainly to specialty publications.

The problem of chronic degenerative arterial disease and acute arterial obstruction is so large in Western civilisation at this time that although the somewhat depressing facts described in your article cannot be denied, areas where even some progress is being made should not be overlooked if the general medical public are to be given a balanced view.

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¹ Carr, J. and FitzGerald, D E, World Congress of Radiology, Edinburgh, June 1975.

² Gosling, R G, et al, in *Cardiovascular Applications of Ultrasound*, ed R S Reneman. Amsterdam, Elsevier, 1974.

³ McCormack, P D, and FitzGerald, D E, *Journal of the Institute of Mathematics and its Applications*, 1975, 16, 361.

⁴ FitzGerald, D E, and Carr, J, *Angiology*, 1975, 26, 283.

SIR,—Your leading article (28 February, p 481) discusses an important topic which regrettably has received too little attention from clinicians and epidemiologists.

In examining the possibility of regression of atherosclerotic lesions in human arteries you refer to the clues provided by animal experiments and by pathological examination of wasted humans. There is one other clue which may provide circumstantial evidence consistent with the possibility of regression of atherosclerosis in humans. In our experience

an active and graduated long-term exercise programme combined with the assiduous elimination of coronary risk factors, and particularly the cessation of cigarette smoking, leads to a substantial improvement or resolution of symptoms in most patients with stable intermittent claudication. Also, in a large group of patients with postinfarction angina pectoris studied by us an improvement or resolution of symptoms occurred over a two-year period in 40% of cases with this form of intervention and without the routine use of drugs.

Improvement in angina of effort and intermittent claudication over the long term does not provide proof of resolution of the underlying atheroma. An improving collateral circulation, biochemical changes, and other factors may account for such results, but at least the benefits conferred by exercise programmes and by risk-factor intervention are consistent with the hypothesis that human atheroma can regress.

We believe that the experimental approach to human atherosclerosis and the treatment methods adopted by us should be based on such an optimistic concept. Arteriographic examination of the coronary and leg arteries in patients with angina and peripheral vascular disease before and after full risk-factor intervention combined with graduated exercise programmes would provide information about possible regression or non-progression of atheroma.

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Hazards of multilaxative mixtures

SIR,—In Dr G S Clayden's admirable article on “Constipation and soiling in childhood” (28 February, p 515) it is stated that “standardised senna (Senokot) is effective but should not be used with Dioctyl-Medo as there is some evidence that myenteric damage may occur if these are mixed.” However, no warning is given against the use of Dioctyl-Medo (dioctyl sodium sulphosuccinate (DSS)), which is a detergent, with other anthraquinone laxatives such as danthron or the polyphenolics such as bisacodyl. Also, the detergent itself could be the agent mainly responsible.

The active constituents of standardised senna are rhein-dianthrone glycosides (sennosides A and B), while danthron is 1, 8-dihydroxyanthraquinone—that is, a free anthraquinone. The glycosides, “protected” by their glucose molecules, reach the colon unchanged where the active anthrones are released by interaction with bacterial enzymes, thus giving a virtually colon-specific action, whereas the smaller, “unprotected” danthron molecule is absorbed to an appreciable extent and a large part of the dose is metabolised in the liver and lost.¹⁻⁵

Danthron was found not to be lethal to rats in amounts up to 22 mg/kg, but when DSS was added only 9 mg/kg gave a 50% kill.⁶ With standardised senna, owing to its very low toxicity, LD₅₀ values cannot be obtained. The effect of adding DSS is unknown. The cumulative LD₅₀ values for DSS with danthron or oxphenisatin and for DSS alone suggest that the wetting agent might be the primary cause of toxicity of wetting agent/laxative mixtures.⁷ Patients given therapeutic doses of DSS excrete a considerable proportion in the bile and toxicity tests of DSS on cell cultures from human liver indicate that the wetting agent could be hepatotoxic.^{8,9} DSS alters the histological appearance of the surface absorptive cells of the rat colon and, in both animals and man, inhibits water absorption.¹⁰

Surfactants can also overcome the gastric mucosal barrier and facilitate the absorption of noxious substances.¹¹

Prolonged, excessive ingestion of chemical laxatives, producing persistent loose stools, must result in metabolic disturbances, especially loss of fluid and electrolytes, and over a sufficiently long period these disturbances give rise to structural damage of the gut neuromusculature. However, such adverse metabolic effects can be produced by many substances (for example, lactose in lactase-deficient patients) and there is no evidence that either the anthraquinone or polyphenolic laxatives have a direct damaging effect on the myenteric plexus.

Clearly we need to know much more about the pharmacology of all chemical laxatives. In the meantime, and as discussed more fully elsewhere,¹² it would seem wise to avoid the use of multilaxative mixtures, especially those containing detergents such as DSS.

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Totland, IW

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² Schmid, W, *Planta medica*, 1959, 7, 336.

³ Fairbairn, J W, and Moss, M J R, *Journal of Pharmacy and Pharmacology*, 1970, 22, 584.

⁴ Dobbs, H E, Lane, A C, and Macfarlane, I R, *Il Pharmacology*, 1975, 2, 147.

⁵ Hardcastle, J D, and Wilkins, J L, *Gut*, 1970, 11, 1038.

⁶ US Patent 2 851 394.

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⁸ Dujovne, C A, and Shoeman, D W, *Pharmacologist*, 1971, 13, 288.

⁹ Dujovne, C A, and Shoeman, D W, *Clinical Pharmacology and Therapeutics*, 1972, 13, 602.

¹⁰ Saunders, D R, Sillery, J, and Rachmilewitz, D, *Gastroenterology*, 1975, 69, 380.

¹¹ Correa, P, et al, *Lancet*, 1975, 2, 58.

¹² Jones, F A, and Godding, E W, *Management of Constipation*. Oxford, Blackwell Scientific, 1972.

Misdiagnosis of urinary tract infection in women

SIR,—Dr P E Gower and Dr P R W Tasker (20 March, p 684) are to be congratulated in their use of suprapubic aspiration of the bladder for the diagnosis and confirmation of urinary tract infection in women. A not infrequent finding for a venereologist is to see a male patient with gonococcal urethritis and to be told that the female contact has complained of dysuria and frequency which has been diagnosed elsewhere as a urinary tract infection without the same strict criteria as used by the authors, when in all probability it was in fact gonorrhoea.

I should like to point out that, especially in urban areas, the possibility of gonococcal infection should be considered when a young woman presents with dysuria and frequency.

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Conservative Policy Group on Mental Health

SIR,—Your readers may be interested to know that a committee to study the mental health service has been set up by Patrick Jenkin, MP, the Conservative spokesman on social services, who has appointed me as chairman of the committee and Dr Peter Sykes, a consultant psychiatrist, as director.