Community Clinics in Clinical Pharmacology

Refractory angina pectoris

ANDREW SMITH, M D RAWLINS

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Problem

A 61-year-old woodwork teacher who has been under the care of this practice all his life had had no major illnesses until three months ago, when he noticed chest pain radiating down his arms during relatively mild physical exercise. He had no symptoms of cardiac failure, and examination showed no abnormal cardiovascular signs. His blood pressure was 150/90 mm Hg. An electrocardiogram showed flattened T waves over the precordium (V4-6), but a chest radiograph was normal.

I gave him a supply of glyceryl trinitrate to relieve acute attacks of angina and started him on propranolol, 40 mg thrice daily, for prophylaxis. Although the glyceryl trinitrate has been effective, the propranolol has had no prophylactic effect and he can now walk only 40 to 50 yards. In view of his poor response to beta-blockade, is any other drug likely to be effective.

Advice

This man gave a classic history of angina pectoris when I saw him this morning. His symptoms disappear rapidly with sublingual glyceryl trinitrate but, as you say, propranolol has not influenced his exercise tolerance. He is a non-smoker and has no symptoms suggesting heart failure. Examination showed no cardiac abnormality, and his pulse rate was 74/min. He has no clinical signs of hyperlipidaemia.

I think you should eliminate the known "risk factors" for coronary artery disease. Since he is a non-smoker, and is not hypertensive, this is made somewhat easier, but I would recommend that you measure his fasting cholesterol and triglyceride concentrations, as well as examine his electrophoretic

lipoprotein "strip." Only if these are abnormal is it reasonable to attempt to manipulate his serum lipid concentrations by diet or drugs.

I agree that he should continue glyceryl trinitrate for acute exacerbations. This is a volatile substance that evaporates from tablets fairly rapidly—particularly if the container is not tightly closed or if cotton-wool packing (which absorbs glyceryl trinitrate) is used to stop the tablets rattling around. "Out-of-date" glyceryl trinitrate is a common cause for apparent therapeutic failure, and patients should replenish their supplies at least every three months. Nitrates are metabolised to nitrites in body tissues. The pharmacological and therapeutic effects are produced by the nitrite, and patients occasionally become "tolerant" to nitrates because of depletion of essential co-factors (sulphydryl groups) for their metabolism. This problem arises when patients have overdosed themselves, and they should therefore be warned against this.

Prophylaxis against anginal attacks is best achieved by beta-blockade, and in patients who do not have chronic bronchitis or asthma I invariably use the "non-selective" drug propranolol. Beta-blockers act by preventing the increase in cardiac work that normally accompanies exercise, but the dose that a particular patient needs is unpredictable. Much of this variability is because most of an oral dose of a beta-blocker, such as propranolol or oxprenolol, is removed by the liver before it reaches the general circulation. The extent of this so-called "first-pass" elimination varies greatly among individuals, so that the only satisfactory way to use the drug is to start with a small dose and increase it in the light of the clinical response. This can be assessed in three ways: firstly, by the patient's description of his exercise tolerance; secondly, from his resting pulse rate; and thirdly, from his heart rate during exercise. The last of these is probably the most sensitive but the least easy to perform in general practice.

I suspect that the man's apparent resistance to propranolol is simply because he is having too small a dose, and this is supported by his relatively fast resting pulse rate. I would recommend, therefore, that you increase his propranolol dose to 80 mg twice daily, and then to 160 mg twice daily if necessary. Obviously, if he develops symptoms or signs of overdosage (bradycardia and hypotension) during the titration period, you must reduce his dose.

Giving beta-blockers to patients with ischaemic heart disease

Whickham Health Centre, Whickham, Newcastle upon Tyne
ANDREW SMITH, MB, FRCP, general practitioner and lecturer in family medicine

Department of Pharmacological Sciences (Clinical Pharmacology), Newcastle upon Tyne NE1 7RU

M D RAWLINS, MD, FRCP, professor of clinical pharmacology

has the inherent danger of precipitating cardiac failure—because of the negative inotropic actions of these drugs. Indeed, some doctors recommend that all patients with angina starting treatment with beta-blockers should take digitalis—irrespective of whether they have symptoms of cardiac failure or not. While I don't recommend such a rigid approach, it is obviously important to look closely for symptoms and signs of cardiac disease before starting beta-blockers.

Long-acting nitrates are of doubtful value in the prophylaxis of angina, and they may cause tolerance of sublingual glyceryl trinitrate.

Two newer agents are available for the prophylaxis of angina. Perhexiline reduces the frequency and severity of anginal attacks, without altering the heart rate at rest. Dizziness, headaches, nausea, and anxiety occur commonly—especially

at the start of treatment—and a few patients develop hepatocellular damage or peripheral neuropathy. Nifedipine also reduces the frequency of angina: it reduces myocardial work and oxygen consumption, and is a vasodilator. Headache, fainting, and lethargy occur commonly at the start of treatment but reputedly disappear with time. The exact role of both these drugs is still questioned, and I would not advise their use unless beta-blockade has failed.

Postscript

The patient's exercise tolerance altered little on propranolol, 80 mg twice daily, but a further increase to 160 mg twice daily resulted in a definite and sustained improvement.

MATERIA NON MEDICA

Waiting for the postman

As my professional life draws erratically to its close I have elected to settle down in a quiet village where a mere four years' occupancy undistinguished by my poor attendance at the local inn have so far failed to gain me full recognition as an inhabitant. On my first retirement the unavoidable transfer from executive residence to pensioner's cottage led to some unexpected blank spaces in a previously busy daily routine and an inexplicable failure of literary communications with the outside world. In this social void the arrival of the postman became an occasion for mixed excitement and apprehension. Our mail man, a red-toupeed eccentric with a loathing for any article of uniform, took pity on my apparent ostracism and occasionally handed me a letter for a neighbour, addressing me cheerfully as the mood took him as "Squire," "General," or "Professor."

The pharmaceutical companies appeared to have relegated me to their obituary lists, although the Inland Revenue still took a tender interest in my welfare. Invitations to Service reunions and college or society meetings did not compensate for the absence of the factual attractions of *MIMS* and *Update* and the other quasimedical publications which I had once affected to patronise. Just as I was getting resigned to being permanently blacklisted by some influential back-room computer the tide began to turn. Flower catalogues from Holland, publishers' booklists from Germany and America, scientific tracts from Switzerland, even commissions from the odd friendly editor, all fell heavily into my letter-box together with wide-ranging questionnaires from esoteric research organisations.

The final accolade of resurrection was the receipt, to my slightly smug bewilderment, of two letters informing me that I had been awarded the Order of Community Merit and selected for special mention in the International Dictionary of Biography. The confirmation of these honours was, however, conditional on the immediate despatch of a voluntary nominal donation to defray administrative expenses.

The Royal Mail van now happily drawing up daily at my front gate is gradually creating the myth among my thawing but intrigued near neighbours that I am a person of some international but discreetly unspecified consequence. But the postman is not deceived. When he hands me my elastic-banded packets of letters, magazines, and books he does so with a theatrical flourish and the remark, "Here is some more rubbish, with the best of luck to you."—HARRY POZNER (general practitioner, Hampshire).

Skiing

I am on a skiing holiday in the Alps and I have been doing this every February for the past 14 years. Every year I notice, often to my surprise, a conscious feeling of healthiness, of positive wellbeing, of exhilaration of the spirits. I do not think it is purely subjective because my exercise tolerance goes up in leaps and bounds (almost literally). Whether, objectively, in the physiological sense, it actually "does me good" I do not know. Is it perhaps the altitude? Surely this should have the opposite effect: my resting pulse rate is in fact slower than at home. (Perhaps I ought to bring a sphygmomanometer and a spirometer next time.) Is it perhaps the "air"? A fellow guest tells me that

there is a theory about "negative ions" in mountain air, whatever that means. It cannot be the exercise per se that gives one the marvellous afterglow (for want of a better phrase). There are sedentary pursuits that have the same effect—you get it after an exciting day's sailing, for example, and presumably motor racing and hunting do it too. I remember it 40 years ago, after a hard game of hospital rugby—that marvellous feeling of relaxation in the hot bath and the thirst that only beer can quench. I think it is because of another ingredient, at least as far as downhill skiing is concerned. I am thinking of that indefinable thrill, not simply the thrill of speed but the added tiny tang of danger, of pitting one's skill against the forces of gravity. I believe it is not just the exercise but exercise plus adrenaline—a combination that does something for you that jogging can never do. And no doubt the air and the sunshine and the scenery all help too. But the point is I am a sexagenarian. What a recipe for rejuvenation. I am sure it is true, even though I know too that the feeling will not last long after I get back to earth with a bump next week, at Gatwick.—W NORMAN-TAYLOR (occupational medical adviser, Chorleywood, Herts).

Pastoral presentation

In 1966 my wife and I and a friend went on a motor caravan tour of Greece. We came near Olympia and camped on the edge of a wood beside a cooling stream. However isolated our camp sites we always found that, within half an hour, the nearest goatherd had grazed his goats and sheep closer and closer to us in order to inspect us more carefully. We had also found to our cost that a Volkswagen was still not welcome among the hill dwellers of Greece and we always had to establish our British nationality before we could hope for any friendly relationship.

On this occasion the handsome young goatherd could speak a few words of English and we were soon friends, finding him to be one of the many Greeks who had never forgotten that the British had seriously weakened their North African forces to come to their aid during the war, even though our help had not been successful. He held up two fingers in the V sign and pointing to one said "Breetish" then to the other "Greek," finally bringing the two fingers together he said "Brothers."

He then beckoned to me to follow him and we walked towards his mixed herd grazing in a clearing. After motioning to me to stand still, he handed me his beautifully carved crook and made me hold it in my two hands across my body. When satisfied that the crook was quite horizontal he uttered a low sibilant note and immediately the most magnificent billy goat I have ever seen raised his head from the centre of the herd and made his way towards us. Coming to a halt in front of me the goat looked me in the eye for a few moments then lowered his head to enable me to place one hand on his head between his huge curling horns. He then raised his head and slowly backed away a few paces. When I returned the crook to its owner the goat turned away and rejoined the herd.

I said goodbye to my friend and returned to camp with the feeling that I had been greatly privileged.—ROB OLVER (retired general practitioner, Crantock, Cornwall).