

intervention. The frequency of overt heart failure and shock was four times higher in these patients and since left-ventricular function is the major determinant of hospital mortality in myocardial infarction, it is hardly surprising they fared less well. This difference between the groups might have disappeared had the study not been stopped prematurely and this would then have allowed a meaningful interpretation of the data. The decision of the data monitoring and ethical committee to stop this study seems to have been an error of judgment.

PTCA was undertaken in 92% of the group allocated to invasive intervention. Although the extent of coronary artery disease is not reported we can assume that a large number of patients with severe three-vessel disease underwent PTCA. The benefits of single-vessel PTCA in patients of this type are uncertain but are likely to be less favourable than in patients with single-vessel disease. Had coronary bypass grafting been offered to this high-risk group a better outcome might have been expected.

It may well be that immediate angiography and PTCA is not desirable following rTPA treatment in acute myocardial infarction. Unfortunately, in stopping their study prematurely, the European Cooperative Study Group has missed an important opportunity to prove the point.

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RESTENOSIS AFTER ANGIOPLASTY

SIR,—Your Dec 19 editorial discusses restenosis after a previously successful coronary angioplasty. Restenosis remains a challenging problem, particularly since Essed et al¹ reported that fibrocellular tissue proliferation is the underlying cause. Your editorial also focuses on attempts to prevent this tissue response by use of drugs that interfere with platelet adherence and with the release of platelet-derived growth factor.

The question remains why most patients experience a longlasting beneficial effect of angioplasty, whereas some do not. We suggested¹ that plaque composition may be an important factor in this respect. Our observations² in four patients who died after repeated percutaneous transluminal coronary angioplasty and in whom the coronary arteries were extensively studied support this suggestion. The fibrocellular tissue response in these arteries showed different stages of maturation. The older the reparative response, the more collagen and elastin fibres had formed, while the more recent reparative response showed a looser texture containing an abundance of glycosaminoglycans and readily identifiable cells. This process of maturation from an initial cellular tissue response to an almost acellular fibrous scar may explain why, in most patients who have restenosis after a first angioplasty, repeated angioplasty has a longlasting success. Basically, this concept is similar to our reasoning why most patients who undergo a first coronary angioplasty will not develop restenosis. On the basis of this concept we should try to identify patients with "favourable lesions", which might thus improve the long-term benefit of coronary angioplasty.

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1. Essed CE, van den Brand M, Becker AE. Transluminal coronary angioplasty and early restenosis: Fibrocellular occlusion after wall laceration. *Br Heart J* 1983; **49**: 393-46.

2. Ueda M, Becker AE, Fujimoto T. Pathology induced by repeated percutaneous transluminal coronary angioplasty. *Br Heart J* 1987; **58**: 635-43

HOME TREATMENT OF DEEP-VEIN THROMBOSIS

SIR,—Your Feb 6 editorial is a timely reminder that there is no consensus management for deep-vein thrombosis or pulmonary thromboembolism. You state that British practice¹ permits a short hospital stay but you do not question whether hospital admission is really needed for uncomplicated deep-vein thrombosis of the calf.

At our weekly postgraduate meeting on Nov 27, 1987, before an audience of primary care, hospital, and community practitioners, we debated the motion "This house believes that hospital treatment

of deep vein thrombosis is unnecessary". The proposers (G. R. Y. and J. G. B.) emphasised the benign prognosis of deep vein thrombosis confined to the calf, that heparin may be as effective subcutaneously as intravenously,² and that home treatment would save 250 hospital inpatient days per year in an average sized health district of 250 000 people. The opposers (I. L. H. and J. V. C.) were worried about the medical and legal implications of home treatment and especially the risk, albeit a small one, of pulmonary embolism. Urgent venography, domiciliary heparin, and follow-up in the anticoagulant clinic would all be difficult to organise, especially over weekends and holidays.

The motion was lost by 28 votes to 35.

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1. Anon. *Br Nat Formul* 1987; no 14. 102.

2. Walker MG, Shaw JW, Thomson GJL, Cumming JGR, Lea Thomas M. Subcutaneous calcium heparin versus intravenous sodium heparin in treatment of established acute deep vein thrombosis of the legs. a multicentre prospective randomised trial. *Br Med J* 1987; **294**: 1189-92

KHAT-CHEWING IN THE NEAR EAST

SIR,—Dr Weir and Dr Thuriaux (Feb 20, p 414) suggest that chewing of khat may not be as dangerous as Dr Goudie indicates (Dec 5, p 1340). However, case-reports of khat-induced psychosis have previously been discussed in *The Lancet*.^{1,2}

The leaves of khat, the *Catha edulis* plant, have for centuries been chewed for their stimulant properties by people living around the southern shores of the Red Sea. The plant resembles privet and grows to 3-5 m at an altitude of 900-1800 m. It is very hardy, being seedless and drought resistant. Some of the growing areas have winter frosts and even snow, so the plant could flourish in temperate zones. Potency is lost on drying, so the leaves must be chewed fresh. But potency is retained for forty-eight hours and if the leaves are deep-frozen it can be prolonged for months, which permits use of khat by immigrant communities in Europe and North America.

Khat is cultivated from the Sudan in the north to the slopes of Mount Kenya in the south. The most khat-oriented society is the Yemen, where it is one of the main crops. However, khat is banned in Saudi Arabia and Somalia. The socioeconomic consequences of cultivation are considerable. Valuable agricultural land is used for the plant but the worst waste is that the plant requires much water to produce young leaves.

The leaves are chewed into a large quid inside the cheek. Usually chewing only lasts for a few hours, but if prolonged for days the results can be profound. Tannins in khat thicken the mucosa of the oropharynx and oesophagus, followed in some cases by malignancy, and also stain the teeth and cause caries. The higher the tannin content, the lower the alkaloid content, and incidentally the lower the price. The most expensive khat is young and has reddish tints to the leaves and shoots. The general effects are a feeling of well-being, talkativeness, excitement, and dryness of the mouth. This produces thirst and much water is swallowed, which reduces the oral effects and helps excretion because alkaloids in khat are excreted in the urine virtually unchanged. Then the appetite disappears, the pupils dilate, and there is tachycardia, tachypnoea, and constipation. Sexual effects vary from an increase in desire during the chewing time to a decrease after chewing when somnolence occurs. Prolonged chewing can produce mania, insomnia, hypertension, and running amok, which in an area where guns are plentiful can be horrendous. Yemenis deny that khat is addictive but withdrawal produces lethargy and nightmares.

Wolfes,³ probably working on dried leaves, isolated an alkaloid, cathine, which had a slight sympathomimetic action. A more potent alkaloid, cathione, which is similar to amphetamine, has also been isolated.⁴ Tannins may cause decay of cathione to cathine. Khat-chewing produces sympathetic stimulations: the mechanism at catecholamine neurotransmitter sites is increased liberation of noradrenaline and inhibition of its uptake. The receptors are initially stimulated but eventually not only become less sensitive but also may decrease in number, so that finally tolerance occurs from

lack of sensitivity and depletion of noradrenaline stocks. A long-term effect may be to reduce dopamine action on the pituitary, so that lactation and spermatogenesis are inhibited. Most gynaecologists who work in khat areas think that khat decreases the sperm count, which often recovers when khat-chewing ceases.

The clinical picture and outcome of many conditions can be modified by khat. I first noticed this with the dramatic increase of blood pressure in hypertensive disease of pregnancy. The systolic reading sometimes went over the top of the sphygmomanometer and the diastolic reading was sometimes 140 mm Hg. Pyrexia may be worsened by vasoconstriction and may proceed to heat-stroke. Cardiac disease is aggravated by inotropic and chronotropic effects. Reactions to anaesthetics and injury may be bizarre, depending upon the quantity of cathione in the blood and the state of the receptors at the appropriate synapses. As movement of populations increases, it is inevitable that clinicians outside the Red Sea area will soon encounter the clinical oddities produced by khat.

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1. Kalix P. Amphetamine psychosis due to khat leaves. *Lancet* 1984; i: 46.
2. Gough SP, Cookson IB. Khat-induced schizophreniform psychosis in UK. *Lancet* 1984; i: 455.
3. Wolfes O. Ulber dos Verhormen von d-nor-iso-ephedrin in Catha Edulis. *Arch Pharm* 1930; 268: 81-83.
4. United Nations. Etudes sur la composition clinique du khat: Recherches sur la fraction phenylalkylanine. UN document MNAR/11/1975.

MANIPULATING BROKEN NOSES

SIR,—Your Jan 30 editorial (p 221) points out the benefits of simple manipulation of fractured nasal bones and emphasises considerations of cost-effectiveness and acceptability. Crowther and O'Donoghue¹ discuss manipulation of the nasal bones under general anaesthetic, a technique that is risky for the patient and costly since admission as a day case is required. An alternative is correction of the deformity under local anaesthetic.

As soon as the decision to manipulate a recent nasal bony fracture is taken, the patient's nose is sprayed internally with 10% cocaine. After 15 min the external nose is anaesthetised by injection of 2% lignocaine and 1:80 000 adrenaline at the roots of the nasal bones and around the infraorbital nerve. The nose may then be manipulated, causing the patient no more than mild discomfort. This technique can be done by junior medical staff and avoids the need for hospital admission and general anaesthesia.

We have done a prospective study of manipulation of noses under local anaesthetic. 40 patients were randomly allocated to treatment under general or local anaesthetic. Before manipulation, the appearance and function of the nose were assessed by questionnaire and examination, and anterior rhinomanometry was done to measure nasal airflow. Patients were reassessed 4 weeks after manipulation.

The two groups were similar in terms of age and mode of injury. 17 in the local anaesthetic group and 12 in the general anaesthetic group completed the study. At follow-up 1 of the local anaesthetic and 5 of the general anaesthetic group were dissatisfied with their appearance and 3 from each group complained about their airway. Objective assessment showed that 12 of the local anaesthetic group and 6 of the general anaesthetic group were cosmetically improved. Total decongested nasal resistance was unaltered by either manipulation technique. Only 1 of the local anaesthetic group was so distressed by the procedure that he would demand a general anaesthetic in future.

Manipulation of noses under local anaesthetic is thus acceptable to most patients. It yields results no worse than those of general anaesthetic manipulation and is highly cost-effective.

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1. Crowther JA, O'Donoghue GM. The broken nose: does familiarity breed neglect? *Ann Roy Coll Surg Engl* 1987; 69: 259-60.

IMPACT OF SURGERY IN LOCALLY ADVANCED BREAST CANCER

SIR,—Professor Rainer (Feb 6, p 295) reports 19 patients with locally advanced breast cancer who refused modified radical mastectomy and, if anything, fared better than those who were operated upon. With such a small number of patients and without detailed data, it is impossible to judge whether or not the improved survival was the result of self-selection of intrinsically more favourable tumours or other bias. Assuming, however, that the observation is real, could it be that surgery is not merely unhelpful but harmful? This notion has much evidence in support.

Almost certainly these patients have latent disseminated disease and anything that might decrease systemic resistance to their tumours (eg, immunosuppression of surgery or of radiotherapy to the internal mammary lymphnodes) might shorten survival. In contrast, initial systemic treatment, which effectively debulks both systemic and loco-regional disease, is more promising.^{1,2} This was apparent in Rainer's study, where the two-year actuarial survival was 98% for patients who received initial systemic chemotherapy with subsequent mastectomy and only 53% for those who had loco-regional treatment only (radiotherapy plus surgery). Indeed, accumulating evidence strongly suggests that progressively intensive loco-regional treatment of breast cancer enhances recurrence. This adverse effect of loco-regional treatment on recurrence becomes more apparent as the disease advances and it was again evident in Rainer's study, where the local recurrence rate was 11% in the chemotherapy plus surgery group and 25% for the radiotherapy plus surgery group.

We are currently testing the hypothesis³ that aggressive, short-term systemic chemotherapy followed by as limited loco-regional treatment as possible (partial mastectomy without radiotherapy) may improve local disease control as well as survival. Results have been encouraging so far, but since we see progressively fewer patients in that stage, we have treated few patients up to now—hence the need for collaboration. A protocol for potential participants is available on request.

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1. Papaioannou AN, Kozonis AJ, Polychronis AA, et al. Preoperative chemotherapy: Advantages and clinical application in stage III breast cancer. In: Metzger U, Largadier F, Senn UJ, eds. Recent results in cancer research. Vol 98: Perioperative chemotherapy. Berlin: Springer-Verlag, 1985: 65-90.
2. Swain SM, Sorace RA, Bagley CS, et al. Neoadjuvant chemotherapy in the combined modality approach of locally advanced nonmetastatic breast cancer. *Cancer Res* 1987; 47: 3889-94.
3. Papaioannou AN. Hypothesis: Increasingly intensive locoregional treatment of breast cancer may promote recurrence. *J Surg Oncol* 1985; 30: 33-41.

UNUSUAL TREATMENT OF MASSIVE PHARYNGEAL POUCH

SIR,—The treatment of choice for pharyngo-oesophageal diverticula is one-stage diverticulectomy, usually combined with cricopharyngeal myotomy. We describe here treatment of a massive pharyngeal diverticulum by anastomosis of the lower end of the pouch to the distal oesophagus.

An 80-year-old man was admitted with a 1 year history of weight loss and dysphagia with regurgitation of undigested food. In the 3 weeks before admission he had had a productive cough with left-sided pleuritic chest pain. He had signs of consolidation anteriorly on the left side of his chest, associated with a pleural rub. Chest X-ray revealed a large mass in the upper mediastinum with an air-fluid level, and a barium swallow confirmed a large pharyngeal pouch containing food debris (fig 1). This pouch filled via a neck at the level of the thoracic inlet and the oesophagus was displaced anteriorly. A similar case, operated on by the late Sir Thomas Holmes-Sellers in 1960, was recalled by Mr R. A. Williams,¹ who recommended a similar approach (fig 2). The operation was done by Mr Tom Treasure.