THE EAR LOBE CREASE: CHROMOSOMES, ACUPUNCTURE, AND ATHEROSCLEROSIS

Sir,—The ear lobe crease has been associated with coronary artery disease,1,2 and Dr Jarrett asks (March 3, p 513) whether the ear lobe crease and chromosome 11, which is associated with a propensity for atherosclerosis, have something in common. External ear malformations have been associated with trisomy 11.3 Familial ear lobe crease associated with hallux syndactyly and unilateral polydactyly has been reported.4 The shape of the pinnse results from the intrinsic folding of cartilaginous tubercles of branchial arches during embryogenesis; they are innervated by C3, C4, and cranial nerves V, VII, IX, and X.5 A map of the background surface and whisker on the auricle has been proposed to explain ear acupuncture.6 The ear lobe crease itself points to an area on the pinnse corresponding to the heart, according to the acupuncture somatotopic map.

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ABSENCE OF BRONCHODILATORY EFFECT FROM ETAMPHYLLINE

Sir,—In their report on the ineffectiveness of oral doses of etamphylline solution Dr Vazquez and colleagues (April 21, p 914) mention that no information is available about pharmacokinetics or pharmacodynamics of etamphylline. In 1981 I inquired of the manufacturers and they gave me all the information they had, which was the data on a study by Dr W. D. Linehan of Dublin, a double-blind, placebo-controlled trial of a standard dose of 100 mg etamphylline capsules in thirteen asthmatic patients. These data also contain no evidence of a bronchodilatory effect. No human pharmacokinetic data are available.

Etamphylline is therefore like all the other N-7 theophylline compounds most ably reviewed by Zuidema and Merkus in 1979. None of these derivatives yield theophylline in vivo, and their kinetic and dynamic properties are their own. They were introduced nearly forty years ago in attempts to avoid the gastric irritation from theophylline, and they seem to achieve this. As Zuidema and Merkus point out, the bronchodilator action of those that are absorbed is at best very weak compared with theophylline. Fleetham et al7 found no evidence of absorption or efficacy of acceptylvine. Furukawa and others8 confirmed that diprophyllyne has about one-fifth of the bronchodilating power of theophylline, and so is about equivalent to proxypophyllyne.9 These are the N-7 derivatives listed in the British National Formulary (7th edition), which comments on their doubtful efficacy and infrequent use.

Vazquez and colleagues are quite right when they say that theophylline is the only clinically useful xanthine. It should be used as one of the many highly effective slow-release formulations presently widely available. The evidence on this is mostly recently admirably reviewed by Weinberger's group10 which includes a brief similar comment on the uselessness of the N-7 derivatives.

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Medicine and the Law

Death of Patient Participating in Trial of Oral Morphine for Relief of Postoperative Pain

A woman of 69 was admitted to the Women's Hospital, Liverpool, for removal of a large ovarian cyst, total hysterectomy, and bilateral salpingo-oophorectomy. The afternoon before the operation she was persuaded, with some considerable reluctance, to take part in a trial to assess the efficacy of 'MST Continus' (morphine sulphate; Napp Laboratories) in the relief of postoperative pain. This preparation was also to be used for premedication and the trial required that subsequent doses and the time intervals needed to produce analgesia should be noted. This patient was the 70th participant in a trial scheme of 100. It was also the aim of the trial to assess whether nausea and/or vomiting would preclude the preparation's general use and whether there was any variation in analgesia with different techniques of anaesthesia.

Prescription of the morphine was not ad hoc but prearranged as follows for this patient:

April 14, 1983 6 am (preoperative) 60 mg
2 pm (postoperative) 60 mg
10 pm 60 mg
April 15 6 am 60 mg
Total 240 mg

She recovered normally from the anaesthetic but she passed a restless night and pulled the drip from her arm. In the morning she was fully conscious but complained of a full bladder; she went to the lavatory assisted by two nurses, but she could not pass urine; she was catheterised at 9.30 am and 800 ml was collected. She appeared fit and well for the rest of the morning. The hospital's evidence was that she was found around 2 pm deeply unconscious with pinpoint pupils and laboured respiration. A registrar in gynaecology, called to examine the patient, did not know of her participation in the trial. Although the nursing staff knew the patient was in the trial, this was not pointed out to the registrar, who diagnosed a cerebrovascular accident and ordered various investigations. A physician at the Royal Liverpool Hospital agreed that a doctor should be sent to see the patient, but no one came and the patient's family became increasingly alarmed. Her husband asked for a named consultant physician at the Royal Liverpool to be called and he arrived promptly. The patient was deeply comatose. On inquiry, the doctor realised that the patient had had four slow-release morphine tablets and postulated a morphine reaction. A single injection of naloxone produced rapid response. She regained consciousness and was able to speak.

A severe chest infection developed, and over the next few days her condition rapidly deteriorated. After transfer to intensive care she went into renal failure and died on May 3.

The first chest X-ray of April 15, taken while she was in coma, showed collapse at the right base and probable venous congestion. These findings were interpreted as indicating that aspiration of stomach contents might have taken place by then. The trial of the morphine preparation was discontinued after the patient's death.

OUTCOME OF INQUEST

On May 5 an inquest was opened, adjourned till Oct 19, and resumed on March 22, 1984. A verdict of accidental death was recorded. The questions and the evidence raised serious issues about the way in which this drug trial was carried out.

The cause of death was given by a pathologist as: bilateral pneumonia and renal cortical necrosis; inhalation of gastric contents; unconsciousness following oral morphine therapy. The necropsy findings did not suggest any cause for the patient going into coma.

Evidence of Clinical Pharmacologists

Prof Alasdair Breckenridge, in a written statement, found no need to implicate a similarity to morphine. Drug absorption tended to be slower in the elderly. Morphine delayed gastric emptying and absorption could be slow. The light lunch the patient had had might...