

experience with 424 cancer patients receiving morphine alone, morphine plus haloperidol in daily doses up to 5 mg (used as an antiemetic), and morphine plus larger doses of haloperidol (up to 20–30 mg/day). The figure shows that there is clearly no left shift in the dose histograms (and plots of cumulative distributions confirm this). Patients receiving haloperidol were in fact generally being treated with *higher* doses of morphine, and the distributions for the morphine only patients and morphine plus low dose haloperidol are significantly different at the 5% level (Kolmogorov Smirnov test).

There are limitations to this sort of retrospective review. The data may reflect the bias of the prescribing physicians whose threshold for using haloperidol as an antiemetic is generally lower if patients are receiving high doses of morphine. However, the data do show that there is not even a suggestion of any opioid-sparing effect in our patients. Haloperidol remains our antiemetic of choice for narcotic or radiation induced nausea and emesis¹⁰ but the evidence that it is analgesic or that it has a specific opioid-potentiating effect is unconvincing.

We thank Dr R. G. Twycross for allowing us to study his patients.

Royal Marsden Hospital,
London SW36JJ

Department of Mathematics, Statistics,
and Computing, Oxford Polytechnic

Sir Michael Sobell House,
Churchill Hospital, Oxford

G. W. HANKS

P. J. THOMAS

T. TRUEMAN

E. WEEKS

THREE CASES OF ALLERGIC REACTION TO HUMAN INSULIN

SIR,—Parr et al¹ consider that the only indication for transferring a patient to human insulin (HI) is the rarely encountered generalised allergic response to insulins of animal origin. However, Carveth-Johnson et al² have reported an allergic reaction to HI in a patient known to be sensitive to highly purified beef insulins. Frankland³ questioned this observation, which was ascribed by Blandford et al⁴ to the "haptens" characteristics of immunogenic porcine or bovine insulin in relation to the "haptenic" role of HI in the induction of the generalised allergic response observed. Three recent observations shed some light on this issue.

A 47-year-old man with a history of asthma had a swelling at the injection site followed by acute dyspnoea 8 months after starting treatment with a highly purified beef insulin (PBI). Highly purified porcine insulin (PPI, Novo and Nordisk) caused the same reaction, as did HI (Novo). A standard 3-week desensitisation protocol with PPI and hydrocortisone injections led to a progressive disappearance of the local reaction, and treatment was continued with PPI.

A 35-year-old pregnant woman with a history of asthma and penicillin allergy, and two previous uncomplicated pregnancies, required insulin for gestational diabetes from 19 weeks to delivery. After 2 months of treatment with PPI, she had a strong and immediate reaction at the injection site. Intracutaneous tests using one unit of PPI (Organon, Novo, Nordisk) resulted in wheal-and-flare of more than 5 mm and up to 15 mm in less than 5 min. Tests showed a milder reaction to HI, which could be administered up to the time of delivery with only a slight local reaction for 60 min after each injection.

A 29-year-old woman with a history of penicillin allergy received PBI without allergic reaction in the last 10 weeks of her first pregnancy. She was treated with PPI 23 months later, at the 32nd

week of a second pregnancy. Swelling of hands, feet, and ears developed immediately accompanied by nausea and dizziness, and a persistent rash. Shift to HI led to the same reaction. Insulin was stopped and the patient remained mildly diabetic (fasting blood glucose 7 mmol/l) until 37 weeks, when she delivered a normal baby. The generalised skin reaction lasted for several days after insulin withdrawal. Intracutaneous tests were positive with all forms of insulin, including HI at high dilutions (1/400).

We conclude that primary allergy to HI has not yet been demonstrated. The hapten-carrier theory, advanced in a case where the generalised allergic response disappeared 18 months after withdrawal of insulin, may or may not account for a demonstrated reaction 23 months after a short period of treatment with PBI. Desensitisation protocols with PPI have generally proved effective. In patients with insulin allergy, a record of intermittent insulin treatment, or allergic manifestations, transfer to HI is unlikely to be the answer, although it may be of use if used from the outset in patients with a history of allergic disease.

J. J. ALTMAN

M. PEHUET

G. SLAMA

C. TCHOBROUTSKY

Diabetology Service,
Hôtel Dieu,
75181 Paris, France

SKELETAL LEAD BURDEN IN ABORIGINE PETROL SNIFFERS

SIR,—An X-ray fluorescence (XRF) system similar to that of Ahlgren and Mattsson¹ has been developed in Australia. Previously used on isolated occupationally lead-exposed subjects, the low-cost apparatus (£8000) was flown to an Aboriginal settlement 300 km east of Darwin, where one of us detected moderately raised blood lead levels 2.4–3.1 $\mu\text{mol/l}$ (1 $\mu\text{mol/l}$ = 20.7 $\mu\text{g/dl}$) in fourteen habitual petrol-inhaling teenagers.² Four years later "sniffing" continued unabated and measurements of lead were made in bone, blood, and hair. Petrol inhaling is endemic in other remote native populations, such as the Canadian Arctic.³ The inhaled organic lead is converted to inorganic lead which competes with calcium for deposition in bone.

The fore or middle finger is lightly clamped and bilaterally exposed for 1000 s from two ^{57}Co sources collimated to irradiate 1 ml of the second phalanx. Characteristic K X-rays emitted by lead are measured with a solid state detector-spectrometer. The count rate is related to lead concentration by comparison with measurements on "phantoms" containing a known concentration of lead. The absorbed dose is about 500 mrad (5 mGy) to the 1 ml of irradiated finger, representing a mean active bone marrow dose of less than 0.2 mrad averaged over the total body bone marrow.⁴ The lower level of detection is 20 ppm bone mineral mass (ppm). The standard deviation of repeated measurements on eight subjects was ± 14 ppm.

Blood lead levels of 70 sniffers and 40 non-sniffers were measured by atomic absorption spectrometry. For hair analysis large samples were taken, including hair 3–4 cm from the hair-ends, prepared, and analysed,⁵ the hair being soaked in 2% EDTA to remove external contamination. For hair readings 67 sniffers are compared with 51 non-sniffers. Blood and hair leads correlated ($p < 0.005$) but there was no significant correlation between hair lead and bone lead.

In all cases with detectable bone lead (≥ 20 ppm), blood lead was also raised—ie, thus there were no false positives using XRF—and all XRF positive cases had blood lead above 1.7 $\mu\text{mol/l}$ (table). Sniffing is a childhood and teenage group activity and the members of a group can be ascertained. There were two groups of regular sniffers, each with about 30 members of whom about 6 were females. "Retired" sniffers are included in the sniffer cohort. Among the 60 sniffers tested by XRF, values for bone lead of 20 ppm or over were found in 23 (table). XRF was used in 18 non-sniffer controls and bone lead was not detected in any.

BONE (ppm), BL

Blood

Bone Pb 50–59

4.44

3.10

Bone Pb 40–49

4.50

4.20

Bone Pb 30–39

3.20

3.20

3.00

3.00

3.00

2.50

2.20

The mean blood lead level ($p < 0.001$) in sniffers had bone lead not detectable levels. and non-sniffers (ppm), respectively

The present study of these young sniffers likely to lower blood lead levels have refused to be unfit for inhalation

We thank Dr R. G. Twycross for allowing us to study his patients.

University Department
Clinical Sciences I
Royal Brisbane Hospital
Queensland 4029,

Department of Psychiatry
Queensland Institute of Mental Health

ENLARGED SCHLITZ WITHO

SIR,—A patient with a large ventricular septal defect (VSD) and other than bicuspid aortic valve.

The existence of well established roughly 70 discordant findings and environmental MZ twins and twins³ we represent members of their health predisposition disorder or evidence of

We tested co-twins with schizophrenia pairs. All

10. Hanks GW. Antiemetics for terminal cancer patients. *Lancet* 1982; i: 1410.

1. Parr JH, Abraham RR, Davie MWJ, Dornhorst A, Wynn V. Whither the latest insulin? *Lancet* 1982; ii: 831.

2. Carveth-Johnson AO, Mylvagama K, Child DF. Generalised allergic reaction with synthetic human insulin. *Lancet* 1982; ii: 1287.

3. Frankland AW. Generalised allergic reaction with synthetic human insulin. *Lancet* 1982; ii: 1468.

4. Blandford RL, Sewell H, Sharp P, Hearnshaw JR. Generalised allergic reaction with synthetic human insulin. *Lancet* 1982; ii: 1468.

1. Ahlgren L, Mattsson S. An X-ray fluorescence technique for the in-vivo determination of lead concentration in bone matrix. *Phys Med Biol* 1979; 25: 136–45.

2. Eastwell HD. Petrol inhalation in aboriginal towns: its remedy: the homeland movement. *Med J Aust* 1979; ii: 221–24.

3. Boeckx RL, Postl B, Coodin PJ. Gasoline sniffing and tetraethyl lead poisoning in children. *Pediatrics* 1977; 60: 140–45.

4. Ahlgren L, Haeger-Aronson B, Mattsson S, Schutz A. In-vivo determination of lead in the skeleton after occupational exposure to lead. *Br J Indust Med* 1980; 37: 109–13.

5. Reilly C. A comparison of zinc in scalp hair of residents of Oxford UK and Brisbane Qld. *Proc Nutr Soc Aust* 1981; 6: 141–43.

1. Editorial.

2. Gottesman

Univer

3. Reveley A

twins c

4. Spitzer R

York: