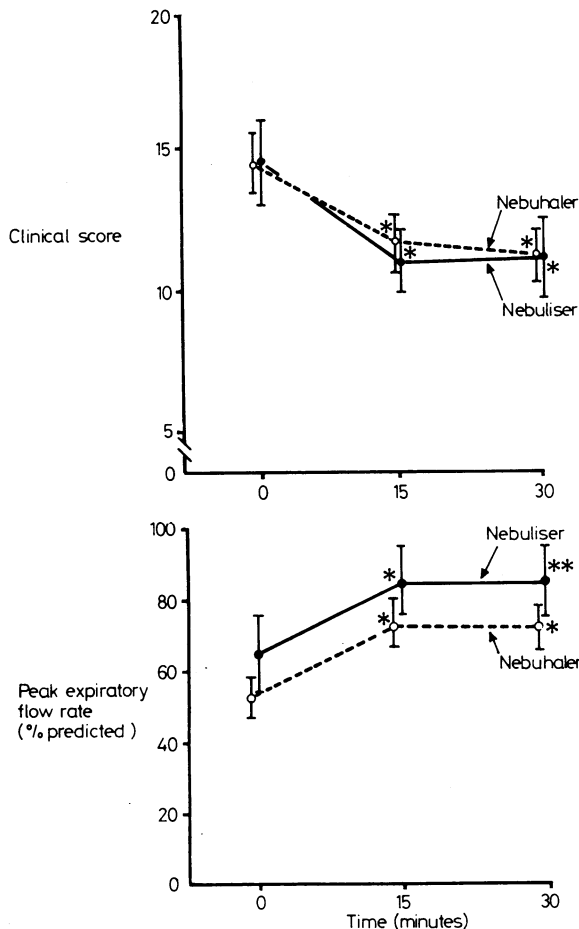


pulsus paradoxus. Variables were assessed on a scale of 0-4 and a total score obtained. Peak expiratory flow rate was measured with Wright's mini peak flow meter in children able to cooperate (six in the nebuliser and 11 in the Nebuhaler groups). The best of three attempts was recorded and expressed as a percentage of the value predicted for sex and height.

Results were analysed using Wilcoxon's signed rank test and paired or unpaired *t* tests when appropriate.

The sex distribution in the two groups were the same, but mean ages were 6.1 years in the nebuliser and 9.1 years in the Nebuhaler group ( $p < 0.005$ ). The figure shows the mean clinical scores and peak expiratory flow rates. There were no significant differences between the groups at any time but both groups showed appreciable improvements at 15 and 30 minutes.



Mean (SE) clinical scores and peak expiratory flow rates in groups using a nebuliser and Nebuhaler. There was a significant reduction in clinical scores ( $*p < 0.01$ ) and improvement in peak expiratory flow rates ( $*p < 0.01$ ,  $**p < 0.02$ ) in both groups but no significant differences between groups.

One child from the Nebuhaler group and three from the nebuliser group required admission to hospital despite initial treatment. Four children who used the Nebuhaler, including the one admitted, had difficulty triggering the valve, which was related to a greater degree of airways obstruction. On the other hand, four patients who had repeatedly used aerosols at home with little improvement responded well to the Nebuhaler.

## Comment

The results indicate that in children with acute asthma equal bronchodilatation can be achieved with Nebuhalers and nebulisers. Younger children and patients with severe airways obstruction, however, had problems with the Nebuhaler, probably because they could not produce sufficient flow rates to trigger the valve. The manufacturers are now investigating this. We conclude that, apart from this limitation, the Nebuhaler is an acceptable and cheaper alternative to wet nebuliser treatment of acute asthma in childhood.

We thank Astra Pharmaceuticals for providing the Nebuhaler and terbutaline and for financial support, and Mrs Gwen Maharaj for secretarial help.

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(Accepted 16 February 1984)

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## Tuberculosis of the breast

Tuberculosis of the breast is rare, presenting as either a breast lump or an abscess and often associated with evidence of active tuberculosis elsewhere in the body, particularly cervical lymphadenopathy or active pulmonary tuberculosis.<sup>1 2</sup> We report on five Asian women seen at this hospital over six months who were found to have tuberculosis of the breast.

### Case reports

**Case 1**—A 48 year old woman from Bangladesh presented with a four month history of a painful red lump in the right breast. At operation an abscess was drained and breast tissue biopsied. The pus grew *Mycobacterium tuberculosis*; histological examination showed caseating granulomas with giant cells.

**Case 2**—A 43 year old Malaysian nurse presented with a three week history of a painless lump in the right breast. Clinically this was thought to be a fibroadenoma, but histological examination showed an enlarged lymph node with areas of caseating necrosis and Langhans' giant cells.

**Case 3**—A 27 year old Indian woman presented with a one week history of fever and a painful swelling of the right breast. The right breast was tender, red, and indurated. An abscess was incised and pus drained, which was sterile on culture. The pus was not cultured for tuberculosis as this was not suspected. The abscess recurred despite treatment with ampicillin and flucloxacillin. She became feverish again and developed erythema nodosum. Two further drainage procedures were required. Histological examination showed chronic inflammatory tissue with epithelioid granulomas and Langhans' giant cells. The induration improved slowly with antituberculous chemotherapy.

**Case 4**—A 65 year old Indian woman presented with a one month history of a painful swelling overlying the upper part of the left breast; she was found in addition to have an enlarged left supraclavicular lymph node. At operation an abscess was drained; *M tuberculosis* was cultured from the pus, and histological findings were typical of tuberculosis.

**Case 5**—A 53 year old Indian woman presented with a three week history of a painful lump in the left breast. A thick walled abscess was drained. Histological findings were typical of tuberculosis, with caseating granulomas and giant cells. The pus was not cultured for tuberculosis.

### Comment

Previous reports have suggested that active tuberculosis is present in other sites in the body in 25-84% of patients with tuberculosis of the breast<sup>3 4</sup> but that evidence of previous tuberculosis elsewhere is

#### Findings in five women with unsuspected tuberculosis of the breast

Case No	Age (years)	Clinical finding	Result of:		
			Tuberculin test	Microbiological examination	Chest x ray examination
1	48	Abscess	Strongly positive	Culture positive	Hilar calcification
2	43	Lymph node	Not done	Not done	Hilar calcification
3	27	Abscess	Strongly positive	Not done	Normal
4	65	Abscess	Not done	Culture positive	Hilar calcification
5	53	Abscess	Not done	Not done	Hilar calcification

present in all.<sup>5</sup> In our patients there was evidence of previous tuberculosis, with calcified hilar nodes and peripheral foci, but no evidence of cavitation or active disease in the chest (table). One of our five patients had a single enlarged supraclavicular node, but there was no evidence of any other site being affected. All the patients were Asian, and in none was tuberculosis suspected as a possible diagnosis; in only two was either pus or a biopsy specimen cultured for tuberculosis, and in only two was a tuberculin test done. Our experience suggests that tuberculosis should be considered as a possible diagnosis in Asian patients presenting with a breast lump or abscess, with or without evidence of tuberculosis elsewhere. We suggest that in these patients pus and biopsy specimens from the breast should always be cultured for tuberculosis and that tuberculin testing and chest x ray examination should be used as part of the preoperative assessment.

We thank Mr R J Earlam and Mr A W Goode for permission to report on patients under their care.

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(Accepted 23 February 1984)

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## Smoking and insulin absorption from subcutaneous tissue

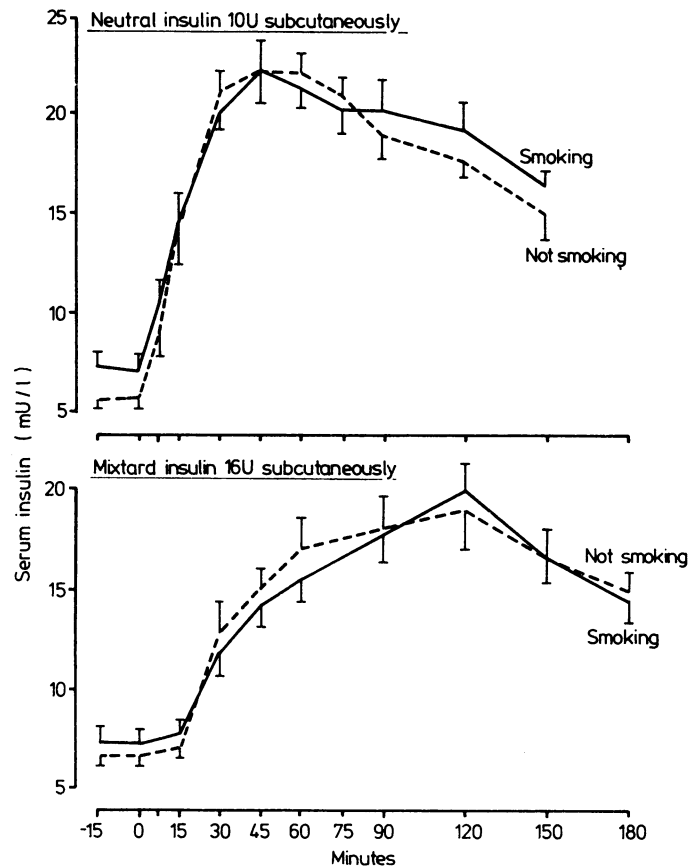
Klemp *et al* presented data suggesting decreased absorption of subcutaneously injected short acting insulin during and after smoking a cigarette.<sup>1</sup> They used an indirect method measuring the decay of radiation over the injection site of radioiodinated insulin, which—among other hypotheses—assumes that insulin is not degraded at the injection site.<sup>2</sup> Ample evidence has been presented that a significant amount of exogenous insulin is degraded at the site of injection.<sup>3</sup> Thus the indirect method used by Klemp *et al* is not suitable for assessing circulating concentrations of exogenous insulin after subcutaneous injection. Simple direct methods are available to investigate the absorption kinetics of subcutaneously injected insulin in normal people as well as in diabetic patients.<sup>3,4</sup> Furthermore, these methods do not require the injection of iodinated material to obtain results.

Since the suggested decrease of more than 100% in the rate of absorption of subcutaneously injected insulin during cigarette smoking<sup>1</sup> might be of considerable clinical importance for some diabetic patients, we have investigated the possible influence of smoking on insulin absorption using a direct method to monitor insulin pharmacokinetics.

### Subjects, methods, and results

Experiments were carried out on eight healthy male habitual smokers (age 20-30 years) of normal weight after a 12 hour overnight fast and abstinence from smoking. Throughout the experiments, which started at 0800, the subjects rested supine at a constant room temperature and abstained from food and drink. Blood was taken from a cubital vein for determinations of blood glucose (Beckman glucose analyser) and serum insulin and C peptide concentrations, as described.<sup>4</sup>

All eight subjects took part in the following four experiments, which were carried out in random order over 10 days; in each case insulin was injected subcutaneously into the front of the thigh: (1) 10 U neutral insulin (Velosulin; Nordisk) without smoking, (2) 10 U neutral insulin with smoking, (3) 16 U Mixtard insulin (Nordisk; a mixture of 30% neutral and 70% isophane insulin) without smoking, (4) 16 U Mixtard insulin with smoking.



Mean serum concentrations of insulin during each experiment (n=8). Bars are SEM.

In the smoking experiments each subject smoked two cigarettes (filter tipped, 0.9 mg nicotine each), beginning at time points zero and 7.5 minutes. Insulin was injected at 2.5 minutes using a 1 ml Plastipak syringe (Becton Dickinson). All injections were given by the same person (HJC), and great care was taken to keep the conditions of the injection technique constant. During the experiments with neutral insulin blood was taken at -15, 0, 7.5, 15, 30, 45, 60, 75, 90, 120, and 150 minutes, and during the experiments with Mixtard insulin blood was taken at -15, 0, 15, 30, 45, 60, 90, 120, 150, and 180 minutes.

Statistical evaluation of differences was by Student's *t* test for paired comparison. Results are given as means and SEM.

Throughout the study serum insulin, C peptide, and blood glucose concentrations showed virtually no difference with and without smoking. The figure shows the serum insulin concentrations. In the experiments with neutral insulin blood glucose values decreased from a basal 4.6 (SEM 0.2) mmol/l (82 (SEM 3) mg/100 ml) without smoking and 4.8 (0.1) mmol/l (86 (2) mg/100 ml) with smoking to a minimum of 3.1 (0.2) mmol/l (56 (4) mg/100 ml) without smoking and 3.3 (0.2) mmol/l (60 (3) mg/100 ml) with smoking at 90 minutes. Serum C peptide concentrations decreased from a basal 1.1 (SEM 0.1)  $\mu$ g/l without smoking and 1.2 (0.1)  $\mu$ g/l with smoking to a minimum of 0.2 (0.1)  $\mu$ g/l without smoking and 0.2 (0.1)  $\mu$ g/l with smoking at 150 minutes.

In the experiments with Mixtard insulin blood glucose values fell from 4.7 (0.1) mmol/l (85 (2) mg/100 ml) without smoking and 4.7 (0.1) mmol/l (85 (2) mg/100 ml) with smoking to a minimum of 3.3 (0.1) mmol/l (59 (2) mg/100 ml) without smoking and 3.2 (0.1) mmol/l (58 (2) mg/100 ml) with smoking at 150 minutes. C peptide concentrations decreased from 1.2 (0.2)  $\mu$ g/l without smoking and 1.0 (0.2)  $\mu$ g/l with smoking to a minimum of 0.2 (0.1)  $\mu$ g/l without smoking and 0.2 (0.1)  $\mu$ g/l with smoking at 180 minutes.

### Comment

These results show that in habitual smokers smoking has no acute effect on the absorption of subcutaneously injected insulin. By contrast with the study of Klemp *et al*<sup>1</sup> our subjects smoked one cigarette two and a half minutes before and one five minutes after the insulin injection, aiming at stable and high concentrations of nicotine in the circulation during the time of maximal insulin absorption from the subcutaneous tissue. As a consequence of our study, diabetic patients need not consider smoking a cigarette a relevant factor influencing insulin absorption from the subcutaneous tissue. Insulin absorption studies based on controversial indirect methods and using