PAPERS AND SHORT REPORTS

Relevance of osteoporosis in women with fracture of the femoral neck

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Abstract

A prospective study of fractures of the femoral neck was conducted over 12 months in order to ascertain the relevance of generalised osteoporosis as determined by metacarpal morphometry. A series of some 200 women sustaining a fracture of the femoral neck after minor trauma had bone mass measurements similar to those of a control population of normal women, and 16% were not osteoporotic. A history of previous fractures was documented in one third of the women, but this was unrelated to the presence or severity of osteoporosis, although over half of the fractures had occurred within the previous four years. Trochanteric fractures were seen more commonly in severely osteoporotic women ($p < 0.005$), whereas cervical fractures predominated in those who were not osteoporotic.

These findings support the hypothesis that postural instability is the major determinant for femoral neck fracture and that generalised osteoporosis, rather than being a prerequisite for fracture, merely determines the type of fracture sustained.

Introduction

Most studies of fracture of the femoral neck claim that generalised osteoporosis is the major aetiological factor, although none has established a densitometric fracture threshold above which such fractures would not occur.[1-4]

The relevance of osteoporosis in the aetiology of fracture of the femoral neck and the importance of establishing a fracture threshold are no longer matters of academic interest, since several therapeutic regimens are effective in preventing and treating osteoporosis,[5-7] highly reproducible methods for measuring bone mass are available,[8 9] and the ever increasing incidence of fracture of the femoral neck is generating escalating costs.[10 11]

Preventing osteoporosis would appear to be a logical way of preventing femoral neck fracture, but before embarking on such a programme it would be essential to know the proportion of patients who would not have sustained a fracture had their bone mass been normal. I therefore report a 12 month prospective study conducted in the Colchester District aimed at obtaining an estimate of the proportion of femoral neck fractures that are not related to generalised osteoporosis.

Patients and methods

From January 1982 to January 1983 women normally resident in the Colchester District who sustained a fracture of the proximal femur were considered for the study. Refractures of previously fractured femurs and fractures wholly below the lesser trochanter were excluded. Details of the circumstances immediately preceding the injury and any history of previous fractures were obtained within two weeks of admission to hospital. The history of other fractures was in most instances corroborated or supplemented by perusal of the patients' old hospital case notes.

The severity of the trauma experienced by each patient was classified as *severe* if the injury had occurred as a result of a road traffic accident, a fall while running, or a fall from a height equivalent to one or more steps (>10 cm) and as *minor* if the injury had occurred in any other way. The fractures were divided into *cervical*, which included subcapital and transcervical types, and *trochanteric*, which included basal cervical types.

A plain radiograph of both hands was obtained when the postoperative check radiographs were made.

The combined cortical thickness of the middle three metacarpals of both hands was derived from measurements of total and medullary width at the metacarpal midpoint[8] and the result expressed as a percentage of the combined metacarpal diameters at the same site; this gave a "six metacarpal hand score".[12] The mean percentage cortical thickness of the second metacarpals (mean hand score) was also calculated. The reproducibilities of the six metacarpal hand score and mean hand score were 3·0% and 4·5% respectively, as compared with 7·5% for measurements on the second metacarpal of one hand alone (hand score or metacarpal index).[13] The lower limit of normal for the hand score is 44%.[14-16]

The mean hand scores were plotted on a nomogram relating hand score to age, derived from 317 healthy Glaswegian women without

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biochemical evidence of metabolic bone disease, who had not sustained fractures of the femoral neck.[16 17]

The normal range for the six metacarpal hand score was established from measurements on 64 endocrinologically and biochemically normal premenopausal women aged 19-39 who were attending hospital with menstrual problems.

Data on the population at risk were obtained from the 1981 Census. Numerical results are expressed as means (and 1 SD). The χ^2 test with Yates's continuity correction was used for statistical analysis.

Results

Altogether 242 femoral neck fractures were recorded in 240 women. Seven fractures were pathological and were excluded from further assessment. Seven of the women were not interviewed, and radiographs of the hands were not obtained from 11 women, who died within three weeks of admission to hospital and had been considered too ill to justify further investigation.

Figure 1 shows the age distribution of the women (excluding those with pathological fractures), and fig 2 shows the age specific fracture rates. There were 27 women who had experienced severe trauma and 206 women (mean age 81·2 (1 SD 9·1) years) minor trauma. The latter were subdivided into good historians

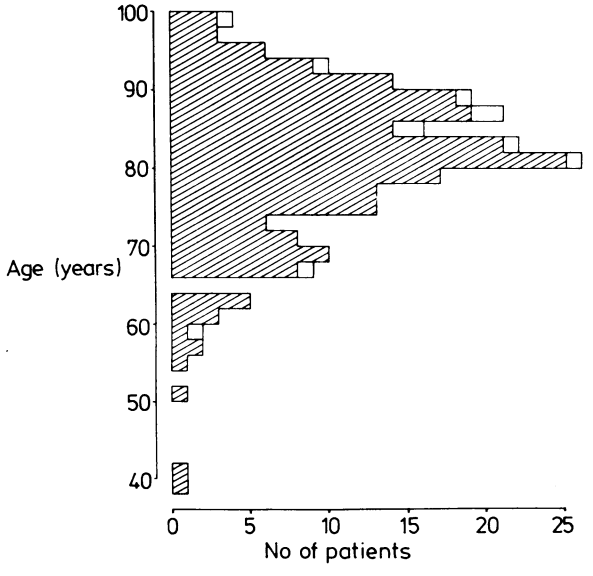

FIG 1—Distribution of ages of women studied (women with pathological fractures excluded). Open boxes represent women not examined by radiography.

(152), poor historians (32), and psychiatric (22) according to the veracity of the fracture history obtained. The psychiatric group were residents of the local mental hospital and were unable to give any meaningful account of themselves. The mean six metacarpal hand scores in these three groups of women were 37·9 (1 SD 6·8)%, 35·6 (6·0)%, and 36·9 (7·8)% respectively.

Figure 3 gives the mean hand score values from 195 of the women who had experienced minor trauma. Of these women, 159 (82%) were osteoporotic (mean hand score <44%), although the values were within the range found in healthy women of similar age but without femoral neck fractures.

The mean six metacarpal hand score of the 64 premenopausal controls was 59·7 (1 SD 7·8)%, giving a lower limit of normal (2 SD below the mean) of 44·1%. Values below 44% were therefore defined as osteoporotic and those below 34% arbitrarily defined as severely osteoporotic.

Figure 4 shows the six metacarpal hand score values of the women who had experienced minor trauma. Thirty one of the women (16%) were not osteoporotic (six metacarpal hand score >44%), 104 (53%) were moderately osteoporotic (score <44% but >34%), and 60 (31%) were severely osteoporotic (score <34%).

There were 66 women who had experienced minor trauma and also gave a history of previous fractures, excluding undocumented vertebral fractures (fig 5). Altogether 64 of these women were examined by radiography, of whom nine (14%) were not osteoporotic, 37 (58%) were moderately osteoporotic, and 18 (28%) were severely osteoporotic.

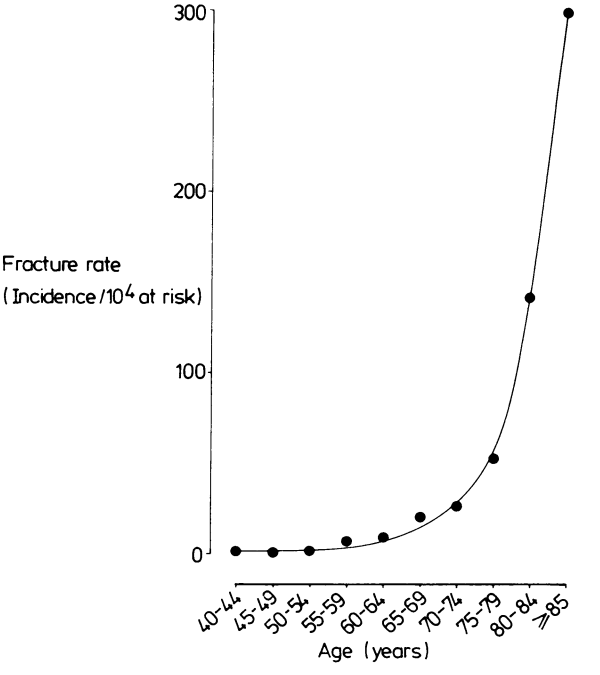

FIG 2—Age specific rate of fracture of femoral neck for all women except those with pathological fractures.

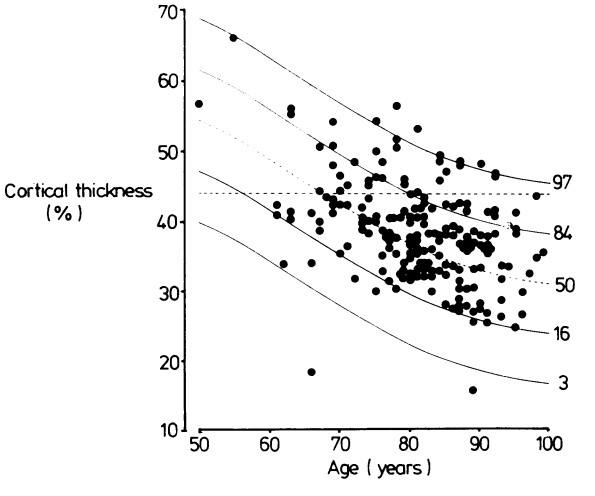

FIG 3—Relation between mean hand score values of 195 women who had experienced minor trauma and percentile values (curved lines) drawn through data from normal women without fractures of femoral neck. Values below horizontal interrupted line are osteoporotic.

Figure 6 shows the radiographic results of those women whose previous fractures had occurred within the past 24 years. Twenty nine of the women (51%) had sustained their previous fracture(s) within four years of their current femoral neck fracture, and six of these women were not osteoporotic.

Altogether 117 trochanteric and 118 cervical fractures had been sustained by the women with non-pathological fractures. Severe trauma was more commonly associated with trochanteric fractures. Figure 7 shows the relation between bone mass and the type of fracture sustained after minor trauma. Women who were not osteoporotic had sustained cervical fractures almost twice as commonly as trochanteric fractures, whereas women who were severely osteoporotic had sustained trochanteric fractures twice as often as cervical fractures ($\chi^2 = 10·1$; $p < 0·005$).

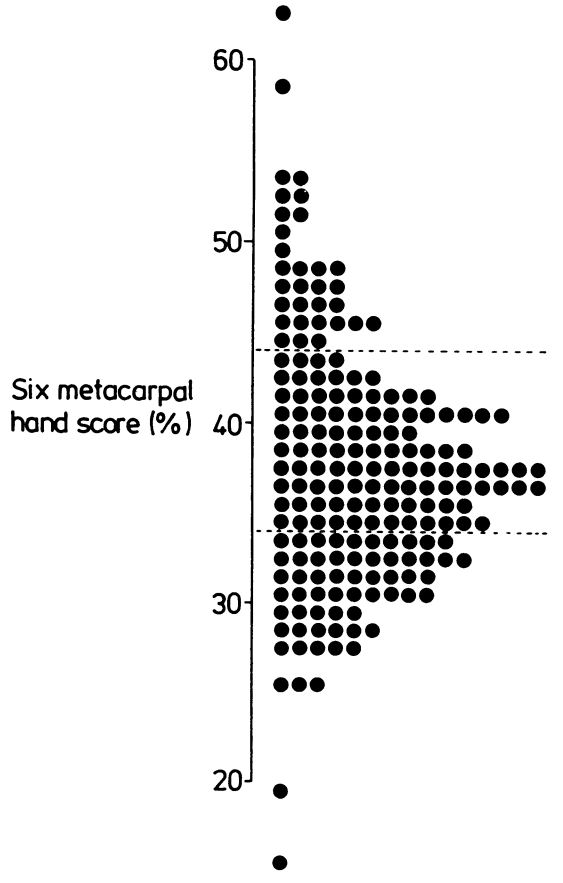

FIG 4—Distribution of six metacarpal hand score values among 195 women who had experienced minor trauma. Values above upper interrupted line (n=31) are not osteoporotic. Values below lower interrupted line (n=60) are severely osteoporotic.

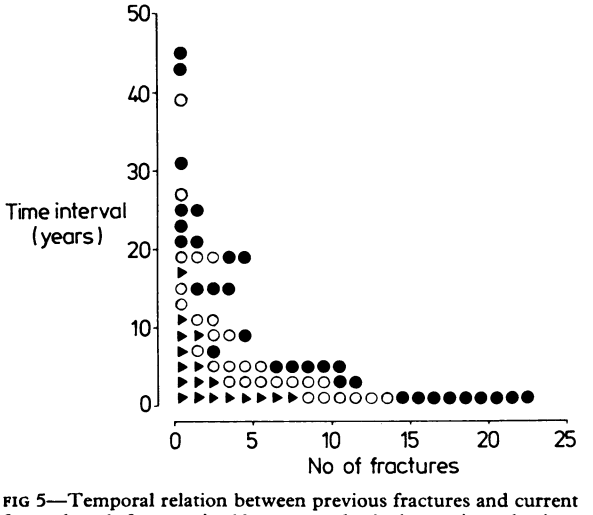

FIG 5—Temporal relation between previous fractures and current femoral neck fracture in 66 women who had experienced minor trauma and gave history of previous fractures. ▶ = Femoral neck fracture. ○ = Colles' fracture. ● = Other fracture.

Discussion

It is widely believed that fractures in elderly people occur mainly as the result of generalised osteoporosis, which is a common accompaniment of aging. This dogma presupposes that the forces concerned in such traumatic events would not have caused a fracture in the absence of osteoporosis. There is little evidence, however, that these forces would be insufficient to fracture the femoral neck in the presence of a normal bone mass. By contrast, spontaneous fractures of the femoral neck, occurring during normal physical activity, are uncommon. Alffram found seven out of 1124 (0·6%)[18] and Melton *et al* 26 out of 1355 (1·9%)[19] spontaneous non-pathological fractures

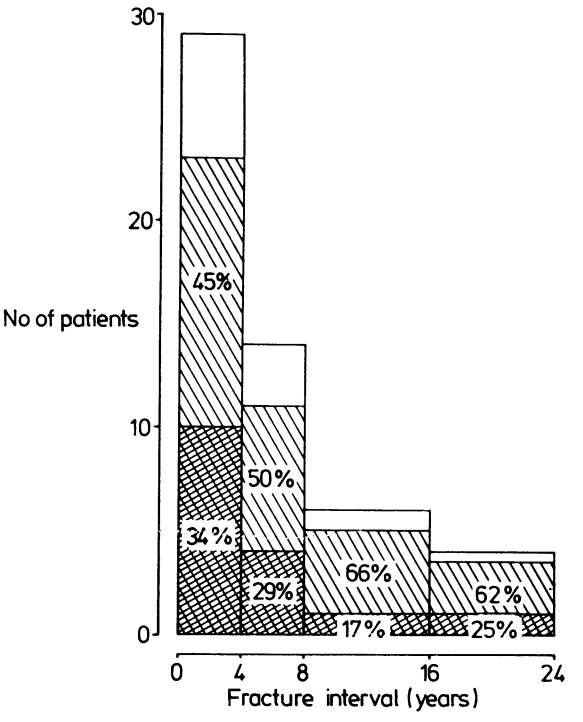

FIG 6—Relation between bone mineral state and time interval since last fracture in women who had experienced minor trauma. Single hatched area indicates moderate osteoporosis (six metacarpal hand score <44% but >34%); double hatched area indicates severe osteoporosis (six metacarpal hand score <34%).

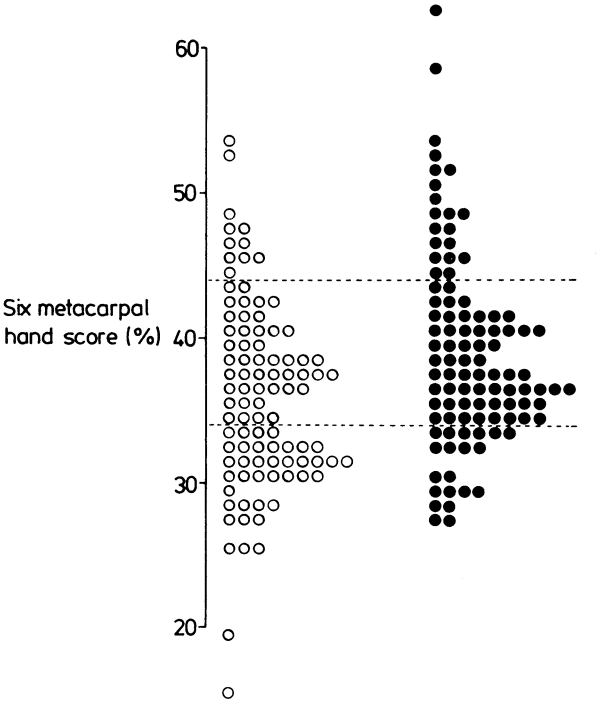

FIG 7—Distribution of six metacarpal hand score values in women who had experienced minor trauma resulting in trochanteric (○) and cervical (●) fractures. Values above upper interrupted line are not osteoporotic; values below lower interrupted line are severely osteoporotic.

in their retrospective studies. No spontaneous fractures were recorded in this study despite one third of the women being severely osteoporotic. Although the fracture history obtainable was inadequate in a quarter of the women, it seems unlikely that many of them had sustained a spontaneous fracture, since the six metacarpal hand score values were closely similar in the three groups of women who had experienced minor trauma.

The results of this study suggest that the absence of generalised osteoporosis is no protection against a femoral neck fracture when an elderly woman has a simple fall. Furthermore, generalised skeletal wasting in such women is apparently similar in extent to that found in normal women of similar age but without fractures.

Other studies using trabecular bone volume measured in iliac crest biopsy samples showed that as many as two thirds of women aged 60-80 years with a femoral neck fracture were *not* osteoporotic,[3 4] although where radiographic methods were employed between 16%[3] and 27%[20] were found not to be osteoporotic. Those authors claimed that women with fractures of the femoral neck have thinner bones than age matched controls, although the controls used included men,[3] were few in number,[4] or were selected for non-osteoporotic characteristics.[20] Although osteoporosis may be more prevalent in middle aged women with such fractures than in age matched controls,[3] such women account for less than 2% of the yearly workload generated by minor trauma.

The method used to assess bone mass in this study was metacarpal morphometry, which might be considered to be inappropriate and unlikely to reflect bone mass at the femoral neck. Postmortem studies in women, however, show that bone mass/unit volume of whole bone at the metacarpal midshaft correlates well with bone mass at sites (including the femur) where either trabecular or cortical bone predominates.[21] Only where osteoporosis is strictly localised, either to the femoral neck or to the hands, would metacarpal morphometry be unhelpful, but this is an unlikely explanation for the apparent lack of osteoporosis in 16% of the women studied.

In this study the control population were Glaswegian women, who might be thought not to reflect the true prevalence of osteoporosis in Colchester. According to Nordin, however, the relation between the metacarpal index and age in white women in the United States is closely similar to that in Glaswegian women.[22]

Previous studies have highlighted the fact that as many as 30% of women with fracture of the femoral neck will have evidence of previous fractures and that the proportion may be as high as two thirds if previous fractures include radiographic evidence of vertebral deformity.[2] This observation has been interpreted to imply that these women have structurally weak bones secondary to osteoporosis. If this interpretation were correct, however, we should expect a history of fractures to be most common in those with the thinnest bones and least common in those who were not osteoporotic. The present study failed to confirm this.

The hyperbolic relation found in this study between the incidence of previous fractures and the time since the present fracture has also been shown in patients with two successive fractures of the femoral neck.[23] In that study the initial fracture was cervical in type in three quarters of the patients. The observation that cervical fractures occur in patients who are least osteoporotic,[3] which was confirmed in this study, would imply that patients do not sustain two successive fractures of the femoral neck primarily because they are osteoporotic.

Although osteoporosis may play some part in the aetiology of femoral neck fracture, it is important not to overlook the fact that over 98% of these fractures result from a fall. Sheldon found that, among patients aged over 50 women fell four times more often than men and that the incidence of falls rose exponentially with age up to 85 years.[24] These observations would readily explain both the lower fracture rate in elderly men and the exponential increase in fractures with age in women without implicating osteoporosis.[25] The comprehensive study of Iskrant and Smith also supports this hypothesis, in so far as they showed that women over the age of 65 who were *not* osteoporotic were as likely to sustain a fracture in a fall as women who were osteoporotic.[26] Furthermore, Solomon's[27] claim that elderly Bantu women in Johannesburg rarely sustain femoral neck fractures but are no less osteoporotic than elderly white women in Johannesburg[28] who readily sustain such fractures would not lend support to the hypothesis that osteoporosis and femoral neck fractures are causally related.

Although there are compelling logical reasons for assuming a cause and effect relation between osteoporosis and fractures of the femoral neck, the actual proportion of such fractures that are indeed causally related may be much smaller than assumed hitherto. Furthermore, the apparent absence of a true fracture threshold would make the goal for preventing osteoporosis difficult to define. It is clear that in the present investigation at least 36% of all women admitted with a fracture of the femoral neck (pathological fractures, severe trauma, absence of osteoporosis, and postural instability) would not have benefited from prophylaxis against osteoporosis, except in so far as thicker bones might have affected the type of fracture sustained and therefore simplified the operative procedure.

I thank the orthopaedic personnel and radiographic staff at Black Notley Hospital, who made this study possible; Dr Deryk Smith, of the Bone Metabolism Research Unit, Glasgow, who kindly supplied the data from his normal population study; and Winnie Hatton, who provided the census data for the Colchester District.

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Effects of self poisoning with maprotiline

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Abstract

Self poisoning with maprotiline was studied in 41 patients (43 episodes) consecutively admitted to an intensive care unit. Thirty five patients had taken more than one drug or alcohol. Fifteen patients were in coma grade III or IV; 17 patients were still not conscious after 24 hours in the intensive care unit. Among six patients given ventilation the mean duration of ventilation in the five who recovered was 36 hours. Three patients had a cardiorespiratory arrest, and one patient died. Twenty eight patients had a QRS interval of 100 ms or more, and 15 patients had seizures. In six patients seizures were precipitated by physostigmine.

Cardiotoxicity after overdosage of maprotiline is equal to if not greater than that found after overdosage of conventional tricyclic antidepressants. Overdosage of maprotiline is more often associated with seizures than overdosage with tricyclic antidepressants. Physostigmine further increases the risk of seizures and should not be used in cases of overdosage of maprotiline.

Introduction

Self poisoning with antidepressant drugs is a common medical emergency requiring intensive care, although many patients die before admission to hospital.[1] Because of the risk of self poisoning by patients with depression many new antidepressants have been marketed, each claiming fewer side effects and reduced acute toxic effects compared with the others. Maprotiline was one of the first commercially available tetracyclic antidepressants and was launched as a rapidly acting antidepressant with relatively few anticholinergic and cardiovascular side effects.[2] Several case reports have recently been published of grand mal seizures during treatment with[3-9] and after overdose of [10-11] maprotiline in patients not known to be epileptics. Seizures are known to be a complication of overdosage of tricyclic antidepressants.[12] We carried out a study to assess the effects of self poisoning with maprotiline with particular reference to seizures.

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Patients and methods

Forty one patients with overdosage of maprotiline consecutively admitted to the intensive care units at Sahlgren's and East hospitals, Gothenburg, from January 1978 to May 1983 were included in the study. The diagnosis of overdosage of maprotiline was confirmed by the patient on recovery or by quantitative or qualitative toxicological analysis, or both. Coma grade was assessed using the scale of Matthew and Lawson,[13] the most severe grade being recorded for each patient (grade 0, fully conscious; grade I, drowsy but obeys commands; grade II, unresponsive to commands but responds well to pain; grade III, unresponsive to commands and minimally responsive to pain; grade IV, completely unresponsive). Hypotension was defined as a systolic blood pressure <90 mm Hg. Statistical analysis was made using the χ^2 test.

Results

Patients and drugs—The 41 patients were treated for 43 episodes of overdosage with maprotiline. The mean age of the patients was 34 (SD 11·2) years (range 20-66 years); overdosage was most common among patients aged 20-40. The 41 patients comprised 27 women and 14 men. Six patients had taken maprotiline alone; the remaining 35 patients had taken more than one drug (maprotiline plus a benzodiazepine, 18 patients; maprotiline plus alcohol, nine; maprotiline plus a tricyclic antidepressant, one; maprotiline plus a tricyclic antidepressant and alcohol, four; maprotiline plus a tricyclic antidepressant and a benzodiazepine, one; and maprotiline plus other drugs, four). The amount of maprotiline ingested could be estimated in 35 patients. The average ingested dose was 2·31 (1·47) g; five patients had taken more than 4 g and one patient more than 7 g.

Coma—The table shows the depth of coma as assessed with the Matthew-Lawson coma scale. Twenty four hours after admission 17 of the patients were still comatose; seven patients were still comatose after 48 hours and three patients after 72 hours.

Respiratory depression—An endotracheal tube was passed in nine of the 43 episodes. Six patients required assisted ventilation. Of these six, one received ventilation for 23 days because of brain damage after cardiac arrest. The five other patients, whose clinical course was not complicated, received ventilation for a mean of 36 hours.

Cardiovascular reactions—Eighteen patients were admitted with a heart rate of 100 beats/min or more. Characteristic electrocardiographic changes were first degree atrioventricular block (11 patients) and an increased QRS interval ($\geqslant$100 ms, 28 patients; $\geqslant$120 ms,