87.1±52.2, P=0.0001). ROC analysis showed this bone collagen turnover ratio to be a good biochemical discriminant of osteoporosis in these men, indicating a possible deficiency of bone collagen synthesis and increased collagen resorption.
This ratio may have potential as a screening test for the early diagnosis of osteoporosis in men.

P58. Circulating levels of vitamin K in osteoporosis and skeletal lesions

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Circulating levels of vitamins K_1 and K_2 (VK1 and VK2) have been reported to be dramatically decreased in senile and post-menopausal osteoporotic fracture patients. It has also been reported that ambulatory elderly have a reduced circulating level of at least one VK2 congener and that the proportion of des-y-carboxylated osteocalcin is elevated in post-menopausal women (PMW). Supplementation with VK1 in PMW normalises urinary hydroxyproline and Ca^{2+} excretion, and serum osteocalcin. Young traumatic fracture patients hav been shown to have decreased circulating levels of VK1 on admission to hospital, which return to normal with healing Using reverse-phase HPLC coupled to electrochemical detection we have measured circulating VK1 levels in young healthy adults admitted for elective jaw surgery, prior to and after surgery These results have been compared to patients admitted for soft tissue surgery. The bone surgery patients show a precipitous decrease in circulating levels of VK1 on the day after surgery, which remain low for 4-6 weeks before returning to normal levels. In comparison, the soft tissue patients, who also experienced an immediate post surgery drop in VK1 levels, were found to return to normal levels within several days. These results suggest the need for further investigation into the vitamin K status of osteoporotic fracture patients.

P59. Disease severity as a determinant of rates of bone loss and bone turnover in early rheumatoid arthritis

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The earliest radiological change in rheumatoid arthritis (RA) is osteopenia affecting the juxta-articular regions of the hand. The aims of this study were to determine whether disease severity is a determinant of a) the rate of bone loss from the hand; and b) the rate of bone turnover in early RA. We studied 19 subjects with early RA (< 3 years). BMD of the right hand was measured by DXA (Hologic QDR 1000\W) at 0 and 6 months (precision error 1.0%). Excretion of pyridinoline (Pyd) and deoxypyridinoline (Dpd) were measured at baseline by HPLC in 2-hour second void urine samples. Disease activity was assessed at baseline from erythrocyte sedimentation rate (ESR) and serum C-reactive protein levels (CRP). Disability was determined from a health assessment questionnaire (HAQ) and grip strength of the right hand (GS). At six months there was significant decrease in hand BMD of 1.0% (SD 1.7, P<0.02). The table shows correlations with rates of bone loss and bone turnover.

	Hand bone loss, %/6 months	Pyd, nmol/mmol creatinine	Dpd, nmol/mmol creatinine
ESR, mm/hour	0.48*	0.55*	0.63**
CRP, mg/L	0.55*	0.35	0.51*
HAQ score	0.22	0.68**	0.34
GS, mmHg	-0.37	-0.58**	-0.45

*P<0.05, **P<0.01

We conclude that disease severity is a determinant of a) the rate of bone loss from the hand and b) the rate of bone turnover in early RA.

P60. Effect of calcium supplementation on the circadian rhythm of bone resorption

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Bone resorption shows a circadian rhythm. The determinants of this rhythm are unknown. We compared the circadian rhythm of bone resorption in 14 premenopausal women, before and after oral calcium supplementation (1000 mg calcium daily x 14 days). Subjects were randomised to receive calcium at either 08.00h (n=6) or 23.00h (n=8). We measured total deoxypyridinoline in urine by HPLC (Dpd), the cross-linked N-telopeptide of type I collagen by ELISA (NTX), galactosyl hydroxylysine by HPLC (GH), and immunoreactive free pyridinoline by ELISA (*i*FPyd). All markers showed significant circadian variability (ANOVA P<0.001) with peak flow rates in the early morning, and lower flow rates in the late afternoon. The mean amplitude (peak to trough) of the rhythm was similar for NTX, Dpd and GH (45%, 48%, 36% respectively), but lower for *i*FPyd (19%). The amplitude of the NTX and Dpd rhythms were significantly reduced by evening calcium supplementation P<0.01, Amplitudes decreased to 18% and 7% respectively). Morning calcium supplementation had no significant effect on the circadian variation of NTX or Dpd. We conclude that evening calcium supplementation alters the circadian rhythm of bone resorption, and that the daily rhythm of calcium intake is likely to be an important determinant of this rhythm.

P61. Skeletal fluoride uptake: A possible defence mechanism

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We performed 32 metabolic studies of calcium, phosphorus and fluoride balance in 17 osteoporotic patients (13 women and 4 men) at extended intervals during long term sodium fluoride therapy (20mg thrice daily). Each study consisted of 2 4-day collection periods. In 20 studies the timing of fluoride dosage alternated in the 2 periods between mealtimes,with calcium supplements, and at least 2 hours between meals.
Taking fluoride between meals increased its absorption from 74 to 87 percent (P <.001) and its retention to a lesser extent, 25 to 29 percent (P <.02). These changes correlated positively (r = 0.657 P <.01). Fluoride uptake varied as much with time in the same patient as it did between different individuals. However, at all times it correlated very significantly with the change from pre-treatment alkaline phosphatase, particularly when faecal variance was minimised by intake between meals (in women $r = 0.741$, $P < .001$).
Fluoride uptake is therefore closely predicted by changes in alkaline phosphatase during long-term therapy. This prompts the hypothesis that osteoblasts may respond to fluoride primarily to effect its sequestration, in defence against a widely-distributed ion that is toxic to many cellular activities.

P62. Low spinal bone mass in Asian women reflects their small skeleton size

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