works and does not cause adverse effects. One example of such an intervention might be calcium and vitamin D supplementation yet only recently has this been reported in a large clinical trial not to be effective for hip fracture prevention and was associated with an increased risk of renal calculi formation.³

While I agree that people with coeliac disease should have appropriate and rational guidance with respect to fracture risk, the safest approach might be simply to inform them of their low absolute excess risk with respect to the general population. Whether this is better or worse than DEXA scanning and intervening with prescribed medication, such as bisphosphonates, as suggested by others, remains uncertain.^{4,5} Walters writes that for people with coeliac disease "osteoporosis... ..should now be recognised as their most significant long-term medical concern". This for the vast majority of people with coeliac disease seems overstated. Most adults, regardless of whether or not they have coeliac disease, will die of either circulatory disease or cancer (fig 1). I would have thought those conditions were of more concern.

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Genetic polymorphisms of mannan binding lectin (MBL), serum levels of MBL, the MBL associated serine protease and H-ficolin in patients with Crohn's disease

The observation of mannan binding lectin (MBL) expression in the small intestine¹ suggests that MBL could be a component in the pathogenesis in Crohn's disease. Seibold *et al*² recently compared the frequencies of MBL polymorphisms in 74 patients with Crohn's disease with 32 healthy controls, and observed a significantly increased frequency of homozygous exon-1 variations. We evaluated the role of MBL polymorphisms, the MBL associated serine protease-2 (MASP-2) and H-ficolin in a cohort of Danish patients with Crohn's disease.

A total of 171 patients (73 males and 98 females) were evaluated. Age at onset of Crohn's disease, localisation and disease behaviour were classified according to the Vienna classification.³ Plasma levels of MBL were measured by a functional time resolved immunofluorometric assay.⁴ Genetic variations in exon-1 (at codons 52, 54 and 57) and polymorphisms in the promoter region (at positions –550 (H/L) and –221 (X/Y)) were determined by a real time polymerase chain reaction technique.⁵ Based on this genetic characterisation, patients were classified by structural genotype: A/A, A/O and O/O where O designates any exon-1 variation (B, C or D). A sandwich-type, time resolved immunofluorometric assay using a combination of two monoclonal anti-MASP-2 antibodies was used for quantification of MASP-2 in serum.⁶ Serum values of MBL and MASP-2 were compared with a control population of 350 healthy unrelated Danish individuals. Serum levels of H-ficolin were analysed in 135 patients.

As expected, a significant difference in levels of MBL was noted between the different

Figure 1 No differences observed in serum values of mannan binding lectin (MBL) or MBL associated serine protease-2 (MASP-2) between the different disease groups classified according to the Vienna classification.

genotypes. The distribution frequency of the exon-1 allele and resulting genotypes was not significantly different from a previously published control population of healthy unrelated Danish individuals (table 1).⁵ The median level of MBL in patients was 1279 mg/l (interquartile range (IQR) 358–2538) which was not significantly different from the median in the control population (1126 mg/l; IQR 319–2460). A significantly higher median level for MASP-2 of 468 ng/ml (IQR 352–601) was observed in patients compared with 415 ng/ml (IQR 332–514) in controls ($p=0.003$). There were no significant differences in MBL or MASP-2 levels in terms of age of disease onset, disease location or disease behaviour (fig 1). A significantly higher level of MBL was observed in male patients with Crohn's disease (1751 mg/l; IQR 1870–2994) compared with female patients (746 mg/l; IQR 135–2089) ($p=0.001$). This could be explained by a significantly larger proportion of female patients with a low MBL genotype (females 46 of 98 v males 19 of 73; $p=0.007$). The median level of H-ficolin at 23.0 ng/ml (IQR 17.2–29.4) was not different from that of a control group of 122 healthy blood donors (median 22.6 ng/ml; IQR 18.1–25.9). No significant differences in serum levels of H-ficolin were noted between the disease groups characterised according to the Vienna classification.

In conclusion, we were unable to confirm the increased frequency of MBL genotypes leading to reduced levels of MBL or MBL deficiency in Danish patients with Crohn's disease. In contrast, we found that the frequency of exon-1 variations and promoter polymorphisms was very similar to a control population of healthy unrelated individuals. No differences in MBL or H-ficolin serum levels were observed between disease groups characterised according to the Vienna classification. Interestingly, female patients with Crohn's disease showed significantly lower levels of MBL than male patients; this was explained by an increased female representation of exon-1 single nucleotide polymorphisms. To the best of our knowledge this difference between the sexes has not been observed previously in either patients with Crohn's disease or controls.⁷ Based on these findings, variations in MBL, MASP-2 and H-ficolin appear to be of limited importance in the pathogenesis of Crohn's disease.

Figure 1 Age standardised mortality rates for selected broad disease groups, 1911–2003, England and Wales. Source: Office for National Statistics.

Table 1 Frequency of exon-1 allele and genotype of mannan binding lectin

Exon 1 allele	Crohn's disease (n = 171)	Controls (n = 100)	Genotype	Crohn's disease (n = 171)	Controls (n = 100)
A	273 (79.8%)	152 (76%)	A/A	110 (64%)	56 (56%)
B	44 (12.8%)	27 (13.5%)	A/O	53 (31%)	40 (40%)
C	5 (1.5%)	4 (2%)	O/O	8 (5%)	4 (4%)
D	20 (5.8%)	17 (8.5%)			

No differences observed between patients with Crohn's disease and controls.

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