1990 reached a high level of significance ($p < 0.0001$) for both types of specimens. The number of laboratory requests increased from 1446 in 1940 to 14 794 in 1990.

Discussion
This study shows that there has been a large increase in the number of words (337%) and items of information (273%) in reports of mastectomy and colectomy specimens. It is not clear whether this increase is due to demand from clinicians or a spontaneous reporting of more information by pathologists. The increases do not seem to have any temporal relation with the publication of pathological grading or staging systems. The largest increases in the number of words for both types of specimen occurred from 1940–1950 and 1980–90, with the main increase in the number of items occurring between 1980–1990. Dukes' staging of rectal carcinomas was first reported in 1932 with a follow up study in 1958; Jass described another system of staging in 1987, but this was not used in the department of this study in 1990. Bloom and Richardson's method of grading breast carcinoma was published in 1957; breast screening did not start in the centre until late 1990 and these specimens were not included in the study.

During the study period the workload of the laboratory (as measured by number of request forms) has increased by over 10 times. Although the number of staff has also increased, there has not been a reduction in the workload of an individual so the increase in report length cannot be related to this. The increase in number of words is not related to the mode of reporting because the reports have always been handwritten by the pathologists before typing. The ratio of words per item of information varies over the study period, but the figure in 1990 is only 1.3 words more than in 1940, so there has only been a slight increase in verbosity. There has been an increase in the number of trainee pathologists in the department and they may have been writing longer reports in preparation for examinations; it would be interesting to see if the same increases have occurred in district general hospitals.

With the wide availability of word-processing equipment a long report may not take as much secretarial time to produce as a long typed report created on a typewriter. An increase in efficiency using this technology is facilitated by the development of standardised reports for certain types of specimens. In the departments included in this study word-processors were not used to prepare surgical pathology reports so any increase in report length would increase the amount of secretarial work. The Welcan system has been described only in the past decade and it was not possible to apply it retrospectively to the specimens in this study to ascertain whether the increase in words and information was reflected in an increase in Welcan units. The results of this study indicate the need to review the length and informational content of histopathological reports when assessing total laboratory workload.

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Increased PIVKA-II concentrations in patients with cystic fibrosis

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Abstract
Serum vitamin K concentrations and prothrombin induced by absence of vitamin K (PIVKA-II) concentrations were assayed in 43 patients with cystic fibrosis. Twenty nine showed normal PIVKA-II and vitamin K concentrations; 14 showed an increased PIVKA-II concentration, in one of whom serum vitamin K was decreased. Although their vitamin K concentrations were normal, some patients with cystic fibrosis still had an increase. Trial [A-II]. To reduce as a significant correlation between PIVKA-II concentrations and the administration of antibiotics, a factor which has not previously been considered responsible for an increase in PIVKA-II.
Increased PIVKA-II concentrations in patients with cystic fibrosis

Children with cystic fibrosis tend to have malabsorption and are therefore at risk of vitamin K deficiency. The findings of a recent study, however, showed that median values of plasma vitamin K concentrations in such patients were in the same ranges as those of healthy controls. To assess vitamin K concentration among our patients with cystic fibrosis, we assayed plasma PIVKA-II (prothrombin induced by absence of vitamin K), which is an indicator of early vitamin K deficiency. Indeed, certain coagulation factors (II, VII, IX and X) must be processed in liver endoplasmic reticulum by vitamin K dependent enzymes, a process that is absent in vitamin K deficiency or in patients receiving oral anticoagulants: the plasma concentrations of PIVKA-II are then increased.

Methods
Forty three patients with cystic fibrosis were studied (mean age 10; range three months to 23 years). Four had liver damage. All but two received daily oral vitamin K (5–10 mg/day). All received oral prophylaxis with vitamin E (α-tocopherol) (100–1000 mg/day). Using a previously described method, involving staphylocoagulase and adsorbed undiluted citrated plasma, we assayed the plasma PIVKA-II concentrations in our patients. The thrombin-coagulase formed was measured on a chromogenic substrate, and the results were expressed in mU/ml. The upper limit of normal PIVKA-II is 15 mU/ml. Serum for vitamin K concentration was determined using a previously described high performance liquid chromatography assay. Normal values for vitamin K were established at 0.20–0.80 µg/l. Serum vitamin E concentration was determined using a high performance liquid chromatography assay (normal values 8–12 mg/l).

Results
Mean values of serum vitamin K and vitamin E concentrations of the 43 patients were as follows: 9.21 (range 0.24–23.74) µg/l and 8.2 (range 1.3–16.0) mg/l, respectively. Twenty nine of the 43 (67%) patients showed normal coagulation factor and PIVKA-II concentrations. Serum vitamin K concentration was normal in these 29 patients, including the four with liver damage. Fourteen of the 43 (33%) showed an increased PIVKA-II concentration above 15 mU/ml (the two patients who had not received prophylactic oral vitamin K were among them). Serum vitamin K concentration was decreased in one (0.16 µg/l). PIVKA-II concentration, assayed in this patient some days after vitamin K supplementation, was normal. Coagulation factor (II, VII, IX, X, V) concentrations were normal in all patients. Fourteen of the 29 patients with normal PIVKA-II concentrations and 12 of the 14 with increased PIVKA-II concentrations had been taking antibiotics (ceftazidime, cefalosporin, thienamycin, ticaricline), at the time the sample was collected. The difference between these two groups was significant: χ² test, p < 0.05. The difference between the mean (SD) PIVKA-II concentrations of patients who were not taking antibiotics (7.8 (12.4) mU/ml) and those who were (18.9 (14.8) mU/ml) was significant (p < 0.001; Mann-Whitney U test).

Discussion
Serum vitamin K concentration was not decreased in all our patients, only one, who had not received prophylactic treatment. We can therefore conclude that the vitamin K prophylaxis used was sufficient. But, although their vitamin K concentration was normal, some patients also had an increased PIVKA-II concentration: this was therefore not associated with vitamin K deficiency.

Increased PIVKA-II concentrations may be observed in contexts other than vitamin K deficiency: during oral anticoagulant treatment, hepatocellular carcinomas and the use of certain cephalosporins (moxalactam, cefamandole, cefoperazone). None of our patients had taken such drugs. We observed, however, a significant correlation between PIVKA-II concentrations and the administration of antibiotics. These have not previously been described as inhibiting gamma-carboxylation of PIVKA-II. Certain antibiotics seem to inhibit the carboxylation of the prothrombin and increase the plasma PIVKA-II concentration. The biochemical mechanism of this phenomenon is not described, however, and the phenomenon of vitamin K deficiency noted in patients with cystic fibrosis, vitamin E might also inhibit gamma-carboxylation of the vitamin K dependent enzymes, and this might explain the increased PIVKA-II concentrations in patients with cystic fibrosis. But we found no correlation between PIVKA-II and vitamin E concentrations.

5 Lipsky JJ. N-methyl thetirazoyle inhibition of the gamma-carboxylation of glutamic acid: possible mechanism for antibiotic associated hypoprothrombinemia. Lancet 1983;i:92-3.