A panel of histochemical stains (periodic acid-Schiff technique (PAS)), Grimelius silver stain, oil red O in sections of unprocessed tissue, Alcian blue (AB) pH 2·5, and high iron diamine (HID) reactions, as well as immunohistochemical reactions (monoclonal mouse anti-human carcinoembryonic antigen clone A5B7 DAKO = CEA), tissue polypeptide antigen = TPA, rabbit anti-TPA: B1AB), were done. Immunohistochemical analysis on formalin prefixed paraffin wax embedded tissues showed no cross reactivity of CEA A5B7 to polymorphonuclear neutrophils or erythrocytes. The antibody reacted with colorectal adenocarcinomas (more intense in necrotic debris). PAS was negative, except for small cytoplasmic globules present in occasional tumour cells.

Oil red O, Alcian blue pH 2·5, HID, and Grimelius stains were non-reactive. Immunohistochemical studies showed strong positivity for CEA and TPA. TPA was strongly positive in all tumour cells, particularly in cytoplasm surrounding some of the vacuoles.

A sample from the tumour was prepared for transmission electromicroscopy (TEM). The occurrence of multiple, apparently empty vacuoles was confirmed at the TEM level.

A panel of histochemical and immunohistochemical reactions (see above) was applied to sections from three cases of clear cell adenocarcinoma of the kidney. A PAS positive reaction within the vacuoles was recorded in about 50% of the tumour cells; CEA was positive only in the Golgi area in a few cells in some areas, whereas the vacuoles remained unstained. The cell membrane as well as the cytoplasm (but not the vacuoles) were stained in a few tumour cells (<1%) in sections challenged with TPA.

Necropsy microscopical examination

Material taken from tumours in the liver, lungs, and omentum at necropsy showed identical structures to those found in the surgical specimen. The kidneys, prostate, and thyroid were normal.

Discussion

This case is the sixth clear cell adenocarcinoma of the colon reported. Jewell *et al*[2] described two cases of clear cell adenoma as well as two cases of clear cell adenocarcinoma of the colon. These investigators concluded that the adenoma–carcinoma sequence, valid for other histological types of colorectal tumours, may also be valid for the clear cell adenocarcinoma of the large intestine.

The strong positivity for TPA present in our case indicates that tumour cells contain a marker that has been found in other adenocarcinomas of the digestive tract.[6]

At histology the colonic tumour was similar with another clear cell adenocarcinoma: clear cell adenocarcinoma of the kidney. The three kidney adenocarcinomas tested here showed a positive reaction for mucopolysaccarides (PAS) and lipids (oil red O), whereas our case of clear cell adenocarcinoma of the colon showed occasional small globules with a PAS positive cytoplasmic substance.

This appears to be the first reported case of clear cell adenocarcinoma of the colon with follow up. The patient had massive metastatic growth at necropsy examination. While no conclusion can be drawn from one case report, it would seem that clear cell adenocarcinoma may be at least as aggressive as other large bowel tumour phenotypes.

1 Hellstrom HR, Fischer ER. Physaliferous variant of carcinoma of colon. *Cancer* 1964;17:260–3.
2 Jewell LD, Barr JR, Elliott McCaughey WTE, Nguyen G-K, Owen DA. Clear-cell epithelial neoplasms of the large intestine. *Arch Pathol Lab Med* 1988;112:197–9.
3 Reed RJ, Love GL, Harkin JC. Consultation case. *Am J Surg Pathol* 1983;7:597–601.
4 Watson P, BChir MB. Clear-cell carcinoma of the anal canal: a variant of anal transitional zone carcinoma. Case studies. *Hum Pathol* 1990;21:350–2.
5 Rubio CA, Kato Y, Kitagawa T. Frequency of atypical mitosis in intestinal metaplasia of the gastric mucosa in Japanese patients. *Jpn J Cancer Res* 1994;85:284–9.
6 DAKO Specification Sheet. Monoclonal mouse anti-human carcinoembryonic antigen, 1994.

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Introduction of computer assisted control of oral anticoagulation in general practice

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Abstract

The number of patients referred to hospital clinics for monitoring of oral anticoagulation continues to rise rapidly. Introduction of computer programs for the control of oral anticoagulation improves the quality of anticoagulant control in hospital clinics. This approach has now been extended to include patients managed in general practice. Results confirm that the quality of anticoagulation can also be improved in these patients. A standard ap-

proach to anticoagulation for hospital and community based patients has also facilitated the transfer of patients on warfarin from the hospital anticoagulant clinics to the community with no deterioration in the quality of anticoagulant control. As a result, the workload in the hospital anticoagulant clinic has fallen for the first time.

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Previous studies have shown that the introduction of a computer program for determining the dose of oral anticoagulant can lead to an improvement in the quality of anticoagulant control in hospital anticoagulant clinics.[1 2] With the increasing indications for anticoagulation the number of referrals to hospital anticoagulant clinics continues to increase, particularly for patients with atrial fibrillation.[3] As a result of this increasing hospital workload there is pressure to refer patients back to their general practitioner for monitoring of their anticoagulation. For this to be satisfactorily undertaken, it is essential that the quality of anticoagulant control should not deteriorate. We have therefore used a previously reported computer program[1] to determine the dose of oral anticoagulant for patients managed in general practice.

Methods

The anticoagulant clinic at Bishop Auckland Hospitals NHS Trust is held on a weekly basis. Since 1990, all patients have had their warfarin dosage controlled using a computer program for determining the dose of oral anticoagulant. The clinic is run by a staff pharmacist and nurse acting under the direction of a consultant haematologist.[4] The same method for monitoring oral anticoagulation was therefore extended to include patients who did not attend the hospital anticoagulant clinic.

Ten general practices who use our laboratory were approached to see if they would agree to the laboratory taking over the management of their patients on oral anticoagulants. These practices were the most distant from the laboratory. All patients on warfarin were registered on the anticoagulant clinic computer and the reasons for anticoagulation were recorded. As part of the computer program, the target international normalised ratio (INR) range according to the British Society for Haematology guidelines was allocated.[5] All general practitioners had previously been circulated with these guidelines.

All general practitioners and practice nurses in these practices were visited prior to the start of the study. General practitioners were asked to send blood samples to the laboratory on the same day each week. This ensured that sufficient samples were analysed at the same time to produce adequate data for analysis. Each patient sample was accompanied by their anticoagulant book. Once the INR had been calculated, the dose generated by the computer was entered into each patient's anticoagulant book. These books were returned to the practice the next morning. All samples were analysed on the day of venepuncture. All high INR values were either telephoned or faxed to each general practice. During this study, all new patients in these practices who were started on warfarin were monitored by this system and were not seen at the hospital anticoagulant clinic. The quality of anticoagulant control in these patients was then compared with those patients who attended the hospital anticoagulant clinic. The significance of any improvement in anticoagulant control was determined by comparing the mean INR of each patient group at the beginning and the end of the study. The workload of the hospital anticoagulant clinic was also monitored.

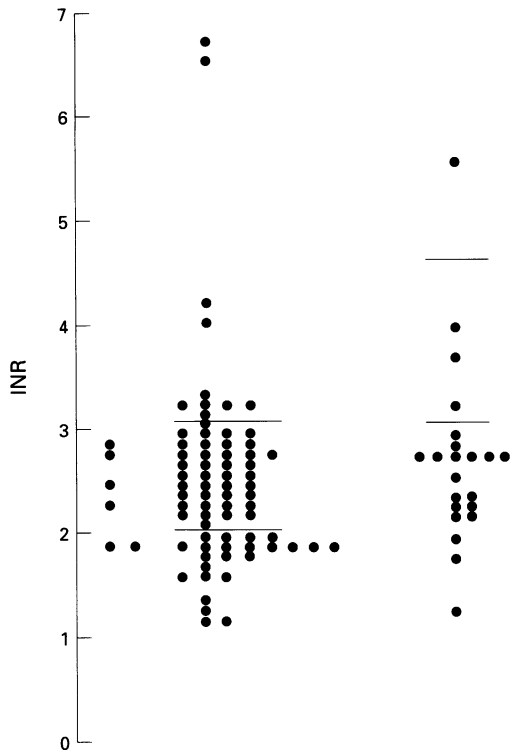
Results

Between September 1993 and January 1995, 210 general practice patients were enrolled into this programme. The INR values for the first 100 patients enrolled are shown in the figure. Overall, 46% of patients had INR results within the therapeutic range, this included 55% of patients whose target INR was 2·0–3·0 and 13% of patients whose target INR was 3·0–4·5 were in the therapeutic range. INR results have shown a consistent improvement since computer adjusted control of the warfarin dose has been instituted. The percentage of patients now in range for these two groups has increased to 72% and 57%, respectively. This improvement in anticoagulant control was only statistically significant for those patients whose target INR range was 3·0–4·5 (table).

As a result of monitoring anticoagulant control in the community, the hospital anticoagulant clinic workload has decreased for the first time. The total number of patients seen in the anticoagulant clinic has been increasing at the rate of 16% per year in the last five years. Despite a further 6% increase in the number of new patients referred in the last 12 months, the total number of patients seen in the hospital anticoagulant clinic fell by 2% from 3475 to 3405.

Discussion

In this study 46% of patients had INR values within the therapeutic range prior to the introduction of computer adjusted dosage for anticoagulation. This is lower than one other study of anticoagulation in general practice where 52% of patients were reported as being within the therapeutic range.[6] This difference between the two studies appears to be due to better control of patients whose target INR was in the range 3·0–4·5. The reasons for this difference are not clear but may have been because of a lack of awareness by local general practitioners of the British Society for Haematology guidelines. However, these guidelines had been circulated prior to the start of this study.



INR results for the first 100 patients enrolled into the study.

INR values (mean (SD)) before and after the introducton of computer assisted control of oral anticoagulation

INR value	General practice patients	Hospital patients	p value
Target INR 3·4–4·5			
Before	2·68 (0·56)	3·37 (0·85)	p<0·001
After	3·37 (0·85)	3·5 (1·02)	NS
Target INR 2·0–3·0			
Before	2·64 (1·4)	2·46 (0·57)	NS
After	2·39 (0·53)	2·37 (0·7)	NS

Our study has shown that the introduction of a computer controlled dosage scheme for general practice patients taking warfarin can lead to an improvement in the quality of anticoagulation. This improvement is similar to that observed following the introduction of a computer assisted dosage scheme into a hospital anticoagulant clinic.[1 4] INR results for those patients monitored in the community are now equivalent to those monitored in the hospital anticoagulant clinic. The implication is that most patients can now have their warfarin treatment monitored satisfactorily in the community without the need for repeated attendance at the hospital anticoagulant clinic. The introduction of this system has allowed non-medical staff to take over the day to day management of patients on warfarin.

We used the existing laboratory transport system to return anticoagulant books to each general practice. One improvement to our service may be to post the anticoagulant book directly to the patient. In view of the number of patients now being monitored, this approach would require additional clerical staff.

In the future it may also be possible to decentralise anticoagulant control further with the introduction of near-patient testing. A number of small coagulometers are now available and are currently undergoing evaluation.[7] Before this approach is introduced, the performance of these coagulometers in general practice must be equivalent to those used in the laboratory, where quality control and quality assurance are closely monitored.

In view of the increasing number of patients referred for anticoagulation, the move towards community based care could have major financial implications. We have not included an economic evaluation in our study. One other study of community based anticoagulation described potential savings of between £8 and £38 per patient visit.[7] This study did not report the use of a computer program to control oral anticoagulant therapy of their patients.

Success in developing anticoagulant control in general practice relies on the co-operation of local general practitioners, practice nurses and patients. Each practice was visited to explain how the programme would operate. This ensured that the transfer of patients to a practice based approach was achieved smoothly. Most patients seem to be happy with the arrangements. We have only had an occasional patient who wished to return to the anticoagulant clinic. This was usually because the patient preferred to have venepuncture performed in the hospital.

We now plan to extend this service to all local general practitioners. We then hope to use the anticoagulant clinic only for initial stabilisation of warfarin dose, patient education and monitoring those patients whose anticoagulation is difficult to control. This approach is likely not only to improve patient care but also to reduce costs.

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1 Ryan PJ, Gilbert M, Rose PE. Computer control of anticoagulant dose for therapeutic management. *BMJ* 1989; **299**:1207–9.
2 Kubie A, James AH, Timms J, Pritt RP. Experience with a computer-assisted anticoagulant clinic. *Clin Lab Haematol* 1989;**11**:385–91.
3 Lowe GDO. Antithrombotic treatment and atrial fibrillation [editorial]. *BMJ* 1992;**305**:1445–6.
4 Kent L, Galloway MJ. Use of computers in anticoagulant clinics [letter]. *J Clin Pathol* 1992;**45**:549.
5 British Society for Haematology. Guidelines on oral anticoagulation: second edition. *J Clin Pathol* 1990;**43**:177–83.
6 Pell JP, McIver B, Stuart P, Malone DNS, Alcock J. Comparison of anticoagulant control among patients attending general practice and a hospital anticoagulant clinic. *Br J Gen Pract* 1993;**43**:152–4.
7 Baglin T. Decentralisation of anticoagulant control. Proceedings of the British Committee for Standards in Haematology. 30th Anniversary symposium; 1994 Apr 25; Harrogate. *Clin Lab Haematol* 1994;**16**:327–9.