and Herman in a smaller series from New York did not confirm that age is of prognostic importance,[20] nor did van Voorhis in a series of 762 patients from Iowa.[21] An early series in which radium alone was used failed to find any prognostic value in age.[19]

Series in which both surgery and radiotherapy have been given have not found age a significant factor in prognosis,[17 22-24] and indeed Gynning *et al* noted a different effect of age when two different treatment techniques were used for stage IB tumours (radical radiotherapy alone, both intracavity and external beam, or radical radiotherapy followed by elective hysterectomy).[29] Other radiotherapy series have found that the effect of age on survival varies with stage.[30 31]

These divergent and potentially confusing findings must result, at least in part, from the effect of other prognostic factors. Age alone does not adequately indicate prognosis even when the effect of stage is also considered. In this study there was no evidence that young patients with cervical cancer treated by radical radiotherapy during the 1970s had a more aggressive form of malignancy. In most stages of disease their prognosis was similar to that of older patients, and in stage IB it was considerably better. We therefore conclude that younger age alone is not an indication for adjuvant treatment for cervical cancer.

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References

1 Office of Population Censuses and Surveys. *Cancer statistics: registrations. England and Wales 1971*. London: HMSO, 1979.
2 Office of Population Censuses and Surveys. *Cancer statistics: registrations. England and Wales 1981*. London: HMSO, 1985.
3 Lindell A. Carcinoma of the uterine cervix; incidence and influence of age. *Acta Radiol* 1952;suppl 92:1-102.
4 Kottmeier H-L. Surgical and radiation treatment of carcinoma of the uterine cervix. *Acta Obstet Gynecol Scand* 1964;**43**(suppl 2):1-48.
5 Sidhu GS, Koss LG, Barber HRK. Relation of histologic factors to the response of stage I epidermoid carcinoma of the cervix to surgical treatment. *Obstet Gynecol* 1970;**35**:329-38.
6 Stanhope CR, Smith JP, Wharton JT, Rutledge FN, Fletcher GH, Gallager HS. Carcinoma of the cervix: the effect of age on survival. *Gynecol Oncol* 1980;**10**:188-93.
7 Prempree T, Patanaphan V, Sewchand W, Scott RM. The influence of patients' age and tumor grade on the prognosis of carcinoma of the cervix. *Cancer* 1983;**51**:1764-71.
8 Mendenhall WM, Thar TL, Bova FJ, Marcus RB, Morgan LS, Million RR. Prognostic and treatment factors affecting pelvic control of stage IB and IIA-B carcinoma of the intact uterine cervix treated with radiation therapy alone. *Cancer* 1984;**53**:2649-54.
9 International Federation of Gynaecology and Obstetrics. Classification and staging of malignant tumours in the female pelvis. *Acta Obstet Gynecol Scand* 1971;**50**:1-7.
10 Cole MP, Hunter RD. Cancer of the cervix uteri. In: Easson EC, Pointon RCS, eds. *The radiotherapy of malignant disease*. Berlin, Heidelberg: Springer-Verlag, 1985:281-301.
11 Kaplan EL, Meier P. Non-parametric estimation from incomplete observations. *Journal of the American Statistical Association* 1958;**53**:457-81.
12 Peto R, Pike MC, Armitage P, *et al*. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. II. Analysis and examples. *Br J Cancer* 1977;**35**:1-39.
13 Cox DR. Regression models and life tables. *Journal of the Royal Statistical Society, Series B* 1972;**34**:187-220.
14 Ashley DJB. Evidence for the existence of two forms of cervical carcinoma. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1966;**73**:382-9.
15 Cancer Registry of Norway. *Survival of cancer patients: cases diagnosed in Norway 1953-1967*. Oslo: Norwegian Cancer Society, 1975:93-6.
16 Futoran RJ, Nolan JF. Stage I carcinoma of the uterine cervix in patients under 40 years of age. *Am J Obstet Gynecol* 1976;**125**:790-7.
17 Decker DG, Fricke RE, Pratt JH. Invasive carcinoma of the cervix in young women. *JAMA* 1955;**158**:1417-20.
18 Brack CB, Townsend L, Haines BW, Dickson RJ. Cervical cancer: factors influencing prognosis in intraepithelial and clinical carcinoma of the cervix uteri. *Obstet Gynecol* 1956;**8**:728-35.
19 Maliphant RG. Variations in the malignancy of cancers of the uterine cervix. *Journal of Obstetrics and Gynaecology of the British Empire* 1960;**67**:420-8.
20 Gusberg SB, Herman GG. Radiosensitivity and virulence factors in cervical cancer. *Am J Obstet Gynecol* 1968;**100**:627-39.
21 Van Voorhis LW. Carcinoma of the cervix. I. Therapeutic and patient factors affecting survival. *Am J Obstet Gynecol* 1970;**108**:105-14.
22 Kyriakos M, Kempson RL, Perez CA. Carcinoma of the cervix in young women. I. Invasive carcinoma. *Obstet Gynecol* 1971;**38**:930-44.
23 Rampone JF, Klem V, Kolstad P. Combined treatment of stage IB carcinoma of the cervix. *Obstet Gynecol* 1973;**41**:163-7.
24 Kjorstad KE. Carcinoma of the cervix in the young patient. *Obstet Gynecol* 1977;**50**:28-30.
25 Berkowitz RS, Ehrmann RL, Lavizzo-Mourey R, Knapp RC. Invasive cervical carcinoma in young women. *Gynecol Oncol* 1979;**8**:311-6.
26 Hammond JA, Herson J, Freedman RS, *et al*. The impact of lymph node status on survival in cervical carcinoma. *Int J Radiat Oncol Biol Phys* 1981;**7**:1713-8.
27 Baltzer J, Koepcke W, Lohe KJ, Ober KG, Zander J. Age and 5-year survival rates in patients with operated carcinoma of the cervix. *Gynecol Oncol* 1982;**14**:220-4.
28 Turunen A, Vara P. Results of the surgical and radiological treatment of carcinoma of the cervix at the Women's Clinic, University of Helsinki, in 1953-1958. *Acta Obstet Gynecol Scand* 1964;**43**(suppl 7):62-7.
29 Gynning I, Johnsson J-E, Alm P, Tropé C. Age and prognosis in stage IB squamous cell carcinoma of the uterine cervix. *Gynecol Oncol* 1983;**15**:18-26.
30 Blomfield GW, Cherry CP, Glucksmann A. Biological factors influencing the radiotherapeutic results in carcinoma of the cervix. *Br J Radiol* 1965;**38**:241-54.
31 Walter L, Glucksmann A, Cherry CP. Biological and physical factors in the radiotherapy of carcinoma of the cervix. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1965;**72**:575-85.

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Faecal blood loss in response to exercise

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Abstract

Recently qualitative tests have indicated that gastrointestinal bleeding during exercise may be an important contributory factor in sports anaemia. In six healthy men who walked 37 km on four consecutive days faecal haemoglobin content remained normal (reference range 0·10-2·53 mg/g faeces) with no significant differences between values. In 28 marathon runners who refrained from taking drugs or food containing blood the median faecal haemoglobin content increased by 0·42 mg/g faeces (95% confidence interval 0·12 to 0·83 mg/g) from 1·06 (0·86 to 1·31) mg/g before the race. In 13 runners who had taken drugs before the race the corresponding increase in the median faecal haemoglobin content was 0·87 (−0·03 to 2·20) mg/g from the value before the race of 0·93 (0·46 to 1·55) mg/g.

Prolonged walking had no effect on gastrointestinal blood loss. Intense endurance exercise in the form of marathon running induced a significant but clinically unimportant increase. This may be exaggerated by the ingestion of drugs and assume importance in causing iron deficiency and sports anaemia. The use of drugs, particularly analgesics, by marathon runners should be actively discouraged.

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Introduction

Sports or runners' anaemia is a well recognised complication of endurance exercise and has been variously attributed to plasma volume expansion, traumatic red cell haemolysis, and iron deficiency. This iron deficiency has been ascribed to haematuria, haemoglobinuria, iron loss through excessive sweating, impaired iron absorption, and, more recently, occult gastrointestinal blood

loss.[1] A pilot study reported that occult gastrointestinal blood loss was not unusual after a marathon race,[2] and an increased loss was subsequently observed in trained athletes after racing.[3]

Subjects and methods

Prolonged walking—Six healthy men (mean age 28, range 24-39) walked three laps of a flat 12·3 km course on four consecutive days. Their diet was unrestricted except that no caffeine, alcohol, or drugs were allowed. Total daily faecal collections were made and a small sample (about 1 g) taken from each bowel movement for subsequent analysis of blood content.

Marathon running—Forty six volunteers (three women, 43 men) who were taking part in marathons (42·2 km) run in Aberdeen and Fortrose were studied. They were diverse in terms of age (mean 37, range 20-61), running ability (race time 218 minutes, range 161-290), and training (weekly training distance 67 km, range 10-176). Each subject completed a questionnaire detailing dietary habits, drugs taken, gastrointestinal disturbances, and training programme and provided a faecal sample (about 1 g) sometime in the two days preceding the race and from the first and second bowel movements passed after the race.

Faecal blood testing—Faecal blood content was evaluated by both qualitative and quantitative techniques. Firstly, three slide tests based on guaiacum resin commonly used in screening were used according to the manufacturer's instructions: Hemoccult (Smith Kline Instruments Inc, United States), Hema-Chek (Ames Division, Miles Laboratories Inc, United States), and Fecatwin S (Labsystems Oy, Finland). Secondly, a quantitative assay, HemoQuant, which is not yet commercially available, was performed as recommended.[4,5] This two stage procedure, specific for faecal haem, measures not only total faecal haemoglobin but also the fraction converted to porphyrin by gut flora (the intestinal converted fraction). Unlike haem, this does not exhibit any pseudoperoxidase activity and hence is not measured by tests based on guaiacum resin.

Statistical methods—An analysis of variance for repeated measurements, which used the BMDP statistical package, was used followed by the Duncan multiple range test for the data obtained after prolonged exercise. Non-parametric analysis with a Wilcoxon signed rank procedure (Minitab) was used on the marathon data to avoid the bias of outlying values. Unless otherwise stated the results given are medians and 95% confidence intervals. Correlation coefficients (r) were calculated by linear regression.

Results

PROLONGED WALKING

No significant change in daily faecal weight was recorded, and all slide tests for faecal occult blood gave negative results. Faecal haemoglobin content, corrected for intestinal degradation, on each of the four consecutive days was (mean (SD)) 1·17 (0·87), 0·93 (0·71), 0·86 (0·52), and 0·78 (0·53) mg haemoglobin/g faeces (reference range 0·10-2·53 mg/g). There was no significant difference between values.

MARATHON RUNNING

The 46 subjects were retrospectively classified into two groups depending on whether their faecal occult blood results were likely to have been complicated by ingestion of drugs (n=13) or not (n=28). Three subjects were eliminated from the study because of abnormally high values before the race not attributable to drugs or food containing blood; and two who reported that they regularly ate a food containing blood (black pudding or sausage) and showed falsely high results throughout (mean 5·7 mg haemoglobin/g before the race and 3·6 and 8·0 mg/g after the race) were also excluded.

The table shows the distribution of positive slide test results for both groups. According to the HemoQuant assay, all tests yielded a comparable number of false positive results: Hema-Chek 60%, Hemoccult 44%, and Fecatwin S 57%.

Subjects who had not taken drugs (n=28)—The quantitative values in samples obtained before the race showed no correlation with age (r=0·243, p>0·1) or the weekly distance run in training (r=0·181, p>0·1), but there was a significant correlation with race time (r=0·384, p<0·05). Twenty subjects showed an increase in blood loss after the race (five in excess of normal, range 3·0-4·35 mg haemoglobin/g), but this attained significance only for the peak values (table) and the increase did not correlate with age (r=0·148), weekly distance run in training (r=0·265), or race time (r=0·216).

Quantitative and qualitative results of tests for faecal occult blood in marathon runners

	Before race	After race: First bowel movement	After race: Second bowel movement	After race: Peak blood loss value
Subjects who did not report taking drugs (n=28)				
Mean Hb content by HemoQuant (mg/g) (95% confidence interval)	1·06 (0·86 to 1·31)	1·33 (1·01 to 1·77)	1·19 (0·91 to 1·49)	1·51** (1·17 to 2·02)
No positive by:				
Hema-Chek	3	6	4	
Hemoccult	2	5	0	
Fecatwin S	3	4	4	
Subjects who reported taking drugs				
Mean Hb content by HemoQuant (mg/g) (95% confidence interval)	0·93 (0·46 to 1·55)	1·42 (0·88 to 3·07)	1·58 (0·82 to 2·78)	1·88* (0·95 to 3·46)
No positive by:				
Hema-Chek	1	3	4	
Hemoccult	1	2	3	
Fecatwin S	1	3	4	

Hb=Haemoglobin.
*p<0·05, **p<0·01.

Subjects who had taken drugs (n=13)—These subjects reported taking a drug before the race: aspirin (three), paracetamol (three), naproxen and aspirin (one); and (one each) naproxen, pseudoephedrine, clavulanic acid, diphenhydramine, aluminium hydroxide, and thyroxine with nitrazepam. One subject had an increased faecal blood loss (7·34 mg haemoglobin/g) before the race but four had excessive peak losses (3·46, 3·62, 4·74, and 13·08 mg/g) after the race. The subject who took aspirin and naproxen before running had a normal value for faecal occult blood before the race but a highly significant loss (13·08 mg/g) in the sample taken immediately after the race.

Of the 46 runners, 11 reported gastrointestinal disturbances during the race, particularly stomach cramp that was subjectively ascribed to low environmental temperature or intake of water before or during the race. Although these subjects had a significant increase (p<0·05) in blood loss after the race, this did not exceed that in the other subjects.

Discussion

Several recent studies suggesting that iron deficiency and the anaemia commonly found in endurance athletes may be due to gastrointestinal blood loss have been based on qualitative stool tests.[2,6,7] These depend on the peroxidase activity of haemoglobin and have, as substantiated in this study, variable sensitivity.[8] They are influenced not only by extraneous peroxidases derived from meat containing blood, certain vegetables, and the reducing activity of products containing vitamin C[9] but also by the loss of peroxidase activity after the degradation of haemoglobin during transit through the bowel. These major drawbacks do not apply to the HemoQuant

assay, which is quantitative, is not complicated by dietary factors other than ingestion of blood, and measures both intact haemoglobin and its degradation products.

When evaluating faecal occult blood loss during exercise variables other than analytical ones must also be considered; these include sampling methods,[10] gut transit time,[3 8] and the faecal mass and its water content.[11] The normal range of daily gastrointestinal blood loss has been established as 0·5-2·0 mg haemoglobin/g by radiochromium labelling methods[12 13]; by HemoQuant assay we found a similar range (0·10-2·53 mg/g). During prolonged walking we did not show any significant day to day variation in faecal blood loss, and clearly this form of low intensity exercise had no adverse effects on the gastrointestinal tract.

In previous studies of marathon runners tests for faecal occult blood gave positive results in 8% (n=39),[7] 13% (n=63),[6] and 22% (n=32)[2] of runners after the race, but only peroxidase based screening tests were used and none excluded possible interference by medicinal or dietary factors. In our study 13 out of 46 (28%) marathon runners reported taking some form of drug before the race, and in two runners dietary factors invalidated the test results.

In the only previous study that measured actual gastrointestinal blood loss before and after races of between 10 and 42·2 km faecal blood increased in 20 out of 24 (83%) runners, from a mean loss of 0·99 mg haemoglobin/g before the race to a mean peak value of 3·96 mg/g after the race, although this last figure seems to have been biased by the inclusion of one subject with a blood loss after the race of 43·2 mg/g.[3] Our study of a larger and more heterogeneous population who completed a marathon found only a minor median increase in blood loss after the race equivalent to 0·4 ml of whole blood a day after we had excluded results complicated by drug or dietary factors. Although this increase was significant, we regard it as having no clinical relevance in healthy athletes. More important, however, we showed that this increase was significantly exaggerated in those who took drugs, especially analgesics, before the race. We believe that the apparently common practice of taking analgesics before marathon running[2] should be strongly discouraged.

The mechanism of the gastrointestinal blood loss associated with marathon running has been recently reviewed[14] and variously attributed to gut ischaemia, mechanical factors including "caecal slap"[15] and volvulus,[16] and aggravation of pre-existing occult or overt gut lesions.

References

1 Hallberg L, Magnusson B. The etiology of 'sports anemia.' *Acta Med Scand* 1984;**216**:145-8.
2 McMahon LF, Ryan MJ, Larson D, Fisher RL. Occult gastrointestinal blood loss in marathon runners. *Ann Intern Med* 1984;**100**:846-7.
3 Stewart JG, Ahlquist DA, McGill DB, Ilstronys DM, Schwartz S, Owen RA. Gastrointestinal blood loss and anemia in runners. *Ann Intern Med* 1984;**100**:843-5.
4 Schwartz J, Dahl J, Ellefson M, Ahlquist D. HemoQuant test: a specific and quantitative determination of heme (hemoglobin) in feces and other materials. *Clin Chem* 1983;**29**:2061-7.
5 Alquist DA, McGill DB, Schwartz MD, Taylor WF, Ellefson M, Owen RA. HemoQuant, a new quantitative assay for fecal hemoglobin. *Ann Intern Med* 1984;**101**:297-302.
6 Halvorsen FA, Lyng J, Ritland S. Gastrointestinal bleeding in marathon runners. *Scand J Gastroenterol* 1986;**21**:493-7.
7 Porter AMW. Do some marathon runners bleed into the gut? *Br Med J* 1983;**287**:1427.
8 Ostrow JD, Mulvaney CA, Mansell JR, Rhodes RS. Sensitivity and reproducibility of chemical tests for fecal occult blood with emphasis on false-positive reactions. *American Journal of Digestive Diseases* 1973;**18**:930-40.
9 Irons GV, Kirsner JB. Routine chemical tests of the stools for occult blood: an evaluation. *Am J Med Sci* 1965;**249**:247-60.
10 Rosenfield RE, Kochwa S, Kaczera Z, Maimon J. Non-uniform distribution of occult blood in feces. *Am J Clin Pathol* 1979;**71**:204-9.
11 Sullivan SN. The gastrointestinal symptoms of running. *N Engl J Med* 1981;**304**:915.
12 Ebaugh FG, Clemens T, Rodnan G, Peterson RE. Quantitative measurement of gastrointestinal blood loss. *Am J Med* 1958;**25**:169-81.
13 Roche M, Perez-Gimenez ME, Layrisse M, di Prisco E. The study of urinary and fecal excretion of radioactive chromium Cr-51 in man. *J Clin Invest* 1957;**36**:1183-92.
14 Sullivan SN. Gastrointestinal bleeding in distance runners. *Sports Med* 1986;**3**:1-3.
15 Porter AMW. Marathon running and the caecal slap syndrome. *Br J Sports Med* 1981;**16**:178.
16 Pruett TL, Wilkins ME, Gamble WG. Cecal volvulus: a different twist for the serious runner. *N Engl J Med* 1985;**312**:1262-3.

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SHORT REPORTS

Echocardiography in ischaemic cerebrovascular disease

Despite several studies the indications for echocardiography in ischaemic cerebrovascular disease and its impact on treatment remain undefined. In randomly tested patients the yield has been poor and echocardiography has not been reported as a screening method.[1] On the other hand, liberal use of echocardiography has been encouraged in young patients with cardiac disease, especially when angiograms have been unhelpful.[2 3]

The purpose of this study was, firstly, to identify useful predictors that would detect patients with embolic cardiac disease and, secondly, to discover the prevalence and type of echocardiographic abnormalities in these patients.

Patients, methods, and results

During September 1983 to December 1985 we examined a total of 97 patients, most of whom were suffering from ischaemic infarction of the carotid territory. All patients were aged under 70 and the 55 patients aged 49 or less accounted for three quarters of all patients of that age in our own hospital's catchment area who suffered ischaemic strokes. Both two dimensional and M mode echocardiography was performed on all patients according to the recommendations of the American Society of Echocardiography.[4] The type of equipment used was an ATL Mk 300C with a 3·0 MHz transducer.

We chose the following as possible predictors of echocardiographic abnormalities: evidence of cardiac disease reported in the case notes, cardiac murmurs, electrocardiographic abnormalities, and increased size of the heart in radiographs. Carotid angiography of the affected artery was performed in 72 patients and the angiograms classified according to presence or absence of atheromatosis.

Fifty eight of the 97 patients had an abnormal echocardiogram, 11 showing left atrial or ventricular thrombi (table). The prevalence and type of abnormalities in patients under 50 were identical with those in the whole sample. The presence of one or more of the four predictors was associated with an increased risk of echocardiographic abnormalities ($\chi^2=23·4$; df=4; $p<0·0005$), 31 out of 35 patients positive for two or more of the predictors having an abnormal echocardiogram. On the other hand, 11 of the 34 patients without any of the predictors had an abnormal echocardiogram, in two cases showing left atrial or ventricular thrombi. Carotid angiograms had no predictive value; the echocardiogram was abnormal in 12 out of 20 patients with atheromatous changes in the angiogram and in 32 out of 50 patients whose angiograms either were completely normal or showed occlusions of some of the distal cerebral arteries only.

Echocardiographic findings in 97 patients with ischaemic cerebrovascular disease

	No of patients
Left atrial/ventricular thrombus associated with local hypokinesia (three cases) and hypertrophic obstructive cardiomyopathy, mitral valve prolapse, prosthetic valve, mitral stenosis/insufficiency, and aortic valve thickening (one case each)	11
Left atrial/ventricular dilatation	11
Mitral valve prolapse	9
Aortic cusp fibrosis/thickening	7
Local hypokinesia	5
Hypertrophic obstructive cardiomyopathy	3
Ventricular wall hypertrophy	3
Aortic stenosis/insufficiency	2
Mitral stenosis/insufficiency	1
Mitral insufficiency	2
Intramyocardial calcification, right ventricular hypertrophy, atrial septal defect, fibrous plaque of myocardium (one case each)	4
Normal	39
Total	97