

concentrations <100 µg/l before treatment with erythropoietin.

Transferrin saturation is a good indicator of the current balance of supply and demand of plasma iron, although it is an inadequate indicator of the amount of iron stored.^{2,3} In addition, Bainton and Finch showed that once the transferrin saturation falls below 16% iron supply for erythropoiesis may be inadequate.⁴ Our data also suggest that, during treatment with erythropoietin, monitoring of transferrin saturation is more reliable for detecting functional iron deficiency than is monitoring of serum ferritin concentration.

We believe that functional iron deficiency will become an increasing problem as treatment with erythropoietin is used more widely unless prophylactic iron is given parenterally when indicated—that is, when transferrin saturation falls below 20%. This iron

supplementation should also optimise the cost effectiveness of the drug.

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Randomised trial of two strategies offering women mobile screening for breast cancer

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High compliance is an important prerequisite for effective population screening.¹ Responses to breast cancer screening of 85% and over have been achieved in Sweden² and The Netherlands,³ but in the United Kingdom responses have been more modest: 60% in Guildford and 72% in Edinburgh.⁴ These responses resulted from active invitation to participate, though the precise methods used have not been reported.

We determined whether compliance would improve if a letter of invitation contained a definite appointment for screening rather than an open ended request to make an appointment.

Subjects, methods, and results

A sample of 450 women aged 45-64 was identified from the age-sex registers of two general practitioners from one practice in Aylesbury and randomly allocated to receive either a letter with an appointment (group 1) or an open ended letter of invitation (group 2) for breast cancer screening. The letters were signed by the general practitioner and had, as far as possible, identical texts. At the screening office alternate appointments were allocated to the two groups.

Women in group 1 were asked to contact the screening service to cancel or alter appointments but not to confirm them. Women in group 2 were invited to return a form indicating convenient times; an appointment was then sent. Non-responders were sent a reminder after three weeks. Non-attenders from both groups were sent another appointment.

Both groups were comparable for age, previous screening (56 (30%) and 69 (34%) respectively had been screened before as volunteers), and where they lived.

Three invitations were accidentally sent to men. These and women who had moved, were duplicated on the register, and were known to have been screened recently were excluded. Nine women were inadvertently sent invitations instead of appointments, and one was sent an appointment instead of an invitation; they were also excluded. This left 188 women in group 1 and 204 women in group 2.

The table gives the main results. Women in group 1

had a significantly higher rate of response than women in group 2. Significant differences remained when the 10 women inadvertently sent the wrong letter were included according to both the received and the intended strategies. Compliance was improved in group 1 after every contact, though individual differences were not significant, and was higher than that in group 2 for all age groups, for previously screened women, and for previously unscreened women ($p < 0.05$).

Response to invitation to breast cancer screening by appointment (group 1) or open ended invitation (group 2). Figures are numbers (percentages) unless stated otherwise

	Group 1 (n=188)	Group 2 (n=204)
Mean age (years)	55.4	56.1
Screened at:		
First contact	131 (69.7)	131 (64.2)
Second contact	26* (13.8)	19† (9.3)
All other contacts	5‡ (2.7)	4§ (2.0)
Total	162 (86.2)	154 (75.5)

*After cancellation (13) or non-attendance (13).

†After reminder.

‡After both cancellation and non-attendance.

§After cancellation (2) or non-attendance (2).

||Continuity adjusted $\chi^2 = 6.47$; $df = 1$; $p = 0.01$.

From a total of 273 appointments issued to women in group 1, 45 (24%) were unused through non-attendance; 32 (17%) became available for reuse—15 (80%) after cancellation and 17 (90%) after refusal or when letters were returned unopened. Unfilled and cancelled appointments in group 2 each accounted for under 2% (4) of the total.

Comment

This study shows that including an appointment in the invitation significantly enhances compliance with screening compared with an open ended invitation, confirming earlier findings reported for cervical screening.⁵ The improvement persisted across all contacts and age bands and remained regardless of screening history. This improvement may have arisen because a definite appointment may place more onus on women to attend.

The postage for group 1 cost about half that for group 2. Also, clerical staff reported that they found the appointment strategy more straightforward than the invitation strategy, though the work entailed was different. Non-responders are never given appointments with a system of open ended invitations. With pre-allocated appointments several remain vacant unless overbooking is allowed. Overbooking of pre-allocated appointments, however, remains to be tried,

particularly in a mobile service in which flexibility is limited. Furthermore, its use may affect acceptability.

In conclusion, higher compliance is achievable with preallocated appointments, though the method described requires further evaluation especially for use in mobile screening.

We thank the staff of the Aylesbury Vale breast screening service for their help and Drs E Rose and M Orton for allowing us to study patients under their care.

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Reversible toxicity in poisoning with colloidal bismuth subcitrate

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Blood urea, creatinine, and bismuth concentrations during 96 days after overdose with colloidal bismuth subcitrate

Days after ingestion	Before or after dialysis	Urea (mmol/l)	Creatinine (μ mol/l)	Blood bismuth* (μ g/l)
0		<2.5	97	
11		69.9	2804	260
12	{ Before	69.4	2952	185
	{ After	45.7	1693	84
13	{ Before	46.3	1938	165
	{ After	27.8	1165	160
14	{ Before			200
	{ After	16.7	760	160
15	{ Before			165
	{ After	9.4	460	150
16	{ Before	10.3	475	
	{ After	<2.5	140	150
20		7.7	185	200
60		3.8	98	19
96		2.7	88	8

*Measured by atomic absorption spectrometry.¹

and humans, with tissue binding in animal kidneys especially but also in the spleen, liver, brain, heart, and skeletal muscle.^{3,4} Bismuth may cause decreased glomerular filtration, reduced renal blood flow, and defects of proximal tubular reabsorption.⁵ In rats given high doses colloidal bismuth crosses the blood-brain barrier.

The absence of bismuth in cerebrospinal fluid may explain why the patient was not encephalopathic, and his transient neurological signs may have reflected his uraemia, itself a result of bismuth toxicity. The initial fall in blood bismuth concentration occurred after simple rehydration and purging. Reductions in blood bismuth concentration after haemodialysis were transient, the bismuth presumably being re-established from tissue stores but never reaching symptomatic concentrations.

The optimal treatment of overdose with colloidal bismuth is unknown. Within the first few hours absorption should be minimised by early hydration, gastric lavage (refused by this patient), and purging, even if the patient presents late as bismuth may well be absorbed from the colon. Chelating agents, such as penicillamine, may be effective in the early stages before tissue binding has occurred. Haemodialysis may be necessary, but whether this hastens tissue clearance of bismuth is uncertain. Even after large overdoses, as in this patient, the prognosis is good.

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Encephalopathy after long term treatment with some bismuth salts has been widely reported, but toxicity from colloidal bismuth has not been recognised. We report the results of an overdose of colloidal bismuth.

Case report

A 27 year old man was admitted four hours after an overdose of 100 De-Nol (colloidal bismuth) tablets (12 g), paracetamol (blood concentration 30 mg/l), and alcohol (blood concentration 162 mg/l). Blood bismuth concentration was not measured. The next day he felt well and was discharged. Ten days later he was admitted to our unit complaining of anorexia, nausea, vomiting, general malaise, weakness of his legs, blurring of vision, thirst, and poor urinary output. He was dehydrated and unwell but had no fever or tachycardia. He had proximal leg muscle weakness with hyperreflexia and ankle clonus. His plantar reflexes, all senses, and both fundi were normal. He was lucid with no signs of encephalopathy.

Biochemical investigations yielded the following results: serum sodium 130 mmol/l, serum potassium 4.3 mmol/l, plasma bicarbonate 30 mmol/l, plasma urea 69.9 mmol/l, and plasma creatinine 2804 μ mol/l. Bismuth was detectable in his blood (260 μ g/l), urine (120 μ g/l), and stools (26.9 mg/g) but not in cerebrospinal fluid. Standard tests of liver function yielded normal results. An abdominal x ray film showed opacification of the colon by ingested bismuth. An electroencephalogram showed non-specific slow wave changes over both hemispheres.

Renal failure and neurotoxicity induced by bismuth were diagnosed. After initial purgation with magnesium sulphate and rehydration with 0.9% saline haemodialysis was started. Five days later renal function had returned to normal and neurological signs resolved. The patient felt well. The table gives the blood urea, creatinine, and bismuth concentrations 96 days after ingestion.

Comment

Toxicity after ingestion of bismuth subgallate, subcitrate, and subsalicylate may result in tremors, confusion, myoclonus,² encephalopathy with characteristic electroencephalographic changes, and fits.³ The mechanisms are not clear. Although colloidal bismuth subcitrate is much less easily absorbed, small quantities of it do enter the blood of animals

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