Volume 64 No. 2 **OCTOBER 1995**
ISSN 0041-6193

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THE ULSTER MEDICAL JOURNAL

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THE
ULSTER MEDICAL SOCIETY

The Ulster Medical Journal, Volume 64, No. 2
October 1995

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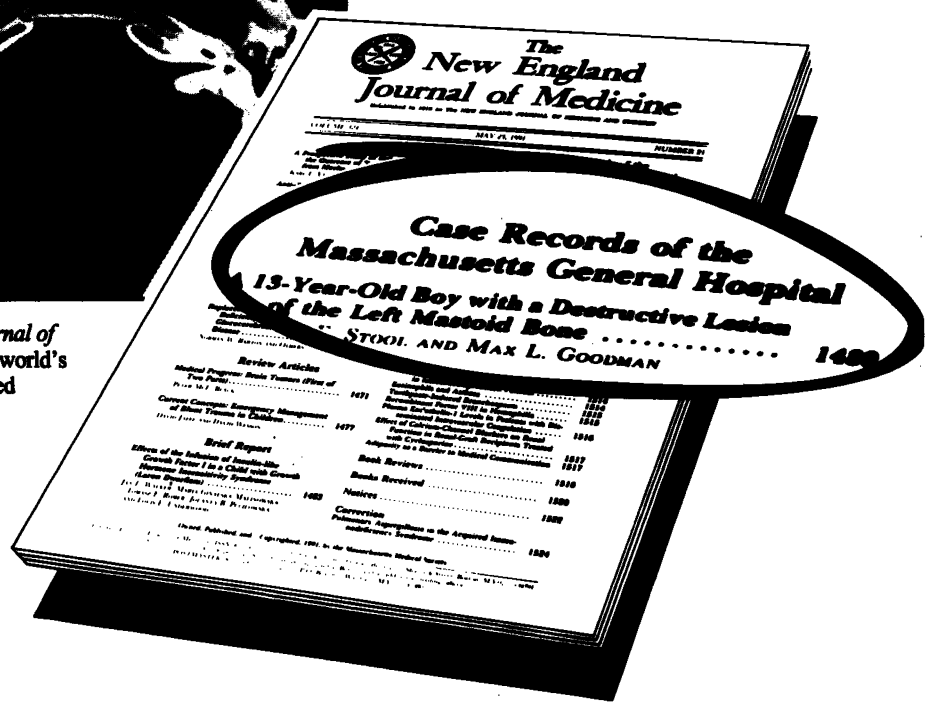

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The Ulster Medical Journal, Volume 64, No. 2, October 1995.

The Ulster Medical Journal

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THE ULSTER MEDICAL JOURNAL

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The Ulster Medical Journal

VOLUME 64

PUBLISHED BY

THE ULSTER MEDICAL SOCIETY

1995

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The Ulster Medical Journal, Volume 64, No. 2, October 1995.

THE ULSTER MEDICAL SOCIETY

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The Ulster Medical Journal, Volume 64, No. 2, October 1995.

David R Hadden MD, FRCPEd, FRCP
Honorary Editor
Ulster Medical Journal 1984-1995

For almost twelve years, David Hadden has with care and considerable patience edited The Ulster Medical Journal. During that period over four hundred papers have arrived on his desk in their various shapes and states ranging from the highly polished, nearly ready for the printer, to those in 'kit' form (minus a plan) requiring him to assemble them into a coherent whole.

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The Ulster Medical Journal

The Journal of the Ulster Medical Society

Volume 64 No. 2 October 1995

Editorial

A new hand at the helm

Editors, like navigators, are a sturdy breed. There have only been four in the 63 years since the Ulster Medical Journal was founded – refounded, because we like to trace our beginnings to 1806 and the Belfast Medical Society, or perhaps more accurately to 1854 and the short lived Transactions of the Belfast Clinical and Pathological Society. But enough of history . . . this journal is forward looking and will sail into the next millennium with alacrity!

Just how it will look in five years time will depend both on our contributors and our readers. The CD-ROM will allow most extensive literature surveys, and the word-processor will facilitate the more keyboard-dextrous in the production of a sophisticated looking paper. The content of the article, and its relevance in the world medical literature will still depend on the intelligence and understanding of the author. But the style and layout, which are essential features of good medical publishing, will depend on the editor.

Evidenced based medicine is a current fashion, and has much to commend it. The role of a general medical journal is to produce such evidence, and to facilitate publication of both the randomized clinical trials and the subsequent meta-analyses on which the concept depends. Peer review should minimise the chances of error, or even fraud: statistical counsel will verify complex mathematical concepts. But the common-sense of the paper will still depend on the editor.

Medical literacy may be broadened by the latest voice-activated forms of word-processors: spelling, never a medical high point, is said to be totally correct if you use the right word. But the similarity in sound between 'euthanasia' and 'youth in Asia' means that the editor must still be able to read the written word before it is printed. To say nothing of the problems of local vernacular language and the modern trend to wilfully split the much maligned infinitive.

So the appointment of a new editor is an important beacon for the future course of the journal. Keep sending Dr Gibson your good papers.

D R HADDEN

The Ulster Medical Journal, Volume 64, No. 2, pp. 118 – 125, October 1995.

The effect of minimal exercise on fitness in elderly women after hip surgery

A J Patterson, N M Murphy, A-M Nugent, O E Finlay, D P Nicholls, C A G Boreham, I Steele, S A Henderson, T R O Beringer

Accepted 4 August 1995

SUMMARY

To determine the effect of minimal exercise on functional fitness following total hip replacement in elderly women, 20 women (13 exercisers, 7 controls) who had undergone unilateral or bilateral hip replacement surgery for primary osteoarthritis were studied. An exercise treadmill test with respiratory gas and blood lactate analyses, and a field test of walking speed on a measured course, were administered before and after a twice weekly exercise programme of three months' duration. Markers of cardiorespiratory fitness, including peak achieved oxygen uptake (VO_2) and ventilatory and lactate thresholds were measured. Maximum self-selected walking speed was also measured over a flat course.

Peak VO_2 increased in the exercise group when compared to baseline ($P < 0.05$) but did not differ from the control group. The exercise group significantly improved their walking speed by 10.1% compared with non-exercising controls (1.41 vs 1.20 m/sec, $P < 0.05$), and increased VO_2 at lactate threshold. The improvements occurred despite the twice weekly exercise sessions being below the recommended frequency of exercise for improving cardiorespiratory fitness. Minimal exercise in elderly women after hip surgery can substantially improve submaximal exercise capacity, as well as walking speed.

INTRODUCTION

The number of elderly women requiring hip surgery is increasing.[1] Several studies have indicated that total hip replacement can improve quality of life,[2] including important functional parameters such as walking speed.[3] However, low walking speeds observed a year after hip surgery suggest that present post-operative rehabilitation may not promote

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maximal recovery.[4] Failure to achieve maximal recovery following hip surgery, compounded by age associated reductions in functional capacity, may seriously jeopardise capability of independent living.[5] The consequence of such an avoidable loss of independence is important both for the individual and as a general public health issue relating to effective use of health resources.[6]

The American College of Sports Medicine (ACSM) recommends that in order to improve cardiorespiratory fitness appropriate exercise should take place at least 3 days per week for 20 minutes at an intensity of 60% of maximum heart rate or 50% of maximum oxygen uptake.[7] It is likely that such guidelines are inappropriate for elderly subjects after hip surgery. The nature of the training response in such older individuals is poorly understood and requires clarification if suitable exercise regimes are to be developed. This study sought to establish whether the cardiorespiratory fitness of elderly hip replacement patients could be improved using a minimal amount of exercise, below that recommended by ACSM.

SUBJECTS AND METHODS

Elderly female subjects, aged 61-80 years of age, who had previously undergone hip replacement surgery for primary osteoarthritis at least six months previously and who were living independently in the community without assistance in self-care, were recruited by telephone from hospital medical records. A six month interval between surgery and inclusion in the study was adopted to limit the confounding influence of surgery on changes in cardiorespiratory fitness. Subjects underwent a full physical examination, including resting ECG and spirometry, to exclude significant respiratory or cardiac disease. Subjects were excluded if evidence of these was found or if they were using medication likely to affect cardiorespiratory or neuromuscular efficiency, such as beta-blockade. All subjects gave informed written consent to the procedures which were approved by the Medical Ethical Committee, The Queen's University of Belfast. Subjects were assigned either to an exercise group who took part in a twice weekly exercise programme for three months, or a control group who continued their normal activities (Table 1).

Subjects were assigned to exercise and control groups randomly on the basis of geographic location. Subjects living within a taxi drive from the Royal Victoria hospital, where the exercise classes took place, were assigned to the exercise group. Control subjects did not receive either sham exercise or specific advice on exercise. Provision of transport was essential to ensure that good attendance rates were achieved. There were no significant concurrent illnesses or changes in medication throughout the test period.

EXERCISE PROGRAMME

The exercise programme was developed by chartered physiotherapists skilled in the care of the elderly and took place in the physiotherapy department of the Royal Victoria hospital over a three month period. The emphasis was on enjoyable weight bearing activities. After an initial warm up period of 5-10 minutes (supervised walking, flexibility) the intensity of exercise increased and subjects took part in aerobic-type dance routines accompanied by music (15-20 minutes). This was followed by a cool-down period which involved stretching and balance exercises (10 minutes). Between each routine a short relaxation period was permitted, the duration of which decreased as fitness improved.

In order to gauge exercise intensity, heart-rate responses to a typical exercise class were measured for all exercisers using a miniaturised heart-rate monitor (Sportstester 3000, Polar Electro, Finland).

TABLE I

Physical characteristics of subjects

	Exercisers mean (range)	*Controls Mean (range)*	*All mean (SD)*
	n = 13	n = 7	n = 20
Age (Years)	70.8 (61-80)	71.0 (63-80)	70.9 (5.3)
Time since surgery (months)	13.3 (8-17)	15.6 (9-20)	14.1 (3.5)
Height (cm)	155.4 (143-172)	163.6 (162-165)	158.2 (6.9)
Weight (kg)	61.1 (50-74)	75.6 (64-95) *	66.2 (10.8)
Body fat (%)	31.2 (25-38)	33.6 (28-38)	31.8 (3.9)

* Significant difference ($p < 0.05$)

EXERCISE TESTING

All subjects performed maximal treadmill tests on three occasions. The treadmill tests were conducted by investigators (A-M N, I S) who were blinded to the allocation of subjects to the exercise or control group. An initial familiarisation test, as previously described[8] was followed by two further tests to establish peak oxygen uptake (Peak VO_2) which were undertaken at the start and at the completion of the intervention period (Test 1 and Test 2). During testing, subjects walked on a standard motorised non-programmable treadmill (Power-Jog). They were asked to use the handrails only for balance and encouraged during the test to exercise for as long as possible. The modified Naughton protocol was used for the familiarisation test.[9] Those subjects who performed less than 14 minutes remained on this protocol for further tests, whereas those who exceeded 14 minutes were tested using the Bruce protocol modified by an initial 3 minute stage at 5% incline and 2.7 km per hour.[10]

Mixed expired air was collected at rest over a two minute period, and at three minute intervals during the exercise test, and for five minutes into recovery following exercise. At the end of each 3 minute stage of exercise, blood pressure, heart rate, ST segment displacement and end tidal CO_2 (via Engstrom Eliza CO_2 Analyser) were recorded. Minute ventilation was measured using a vane turbine placed on the inspiratory side of a non-rebreathing respiratory valve circuit (Hans-Rudolph, Kansas City, KS, USA) in conjunction with a ventilometer (P K Morgan, Chatham Kent, UK). Interruptions of a light beam by the vane were counted to measure inspired flow volume, which was then converted to expired ventilation by using the Haldane correction and standard formulae.[11]

Expired air was directed from the subject via a large-bore flexible tube to a mixing chamber. Expired air was sampled continuously from the chamber from a point well away from the outlet, and expired 0_2 and CO_2 concentrations were measured by paramagnetic and infrared analysers respectively (P K Morgan). The outputs from the ventilometer and gas analysers were fed via an analogue–to–digital converter to an Amstrad PC 1640 microcomputer for on-line calculation of VO_2, minute CO_2 production (VCO_2) and expired ventilation (VE). The results were recorded at 15 second intervals. Anaerobic threshold was defined by retrospective (blinded) visual analysis of the VE/VO_2 curves.[12] Heart rate was measured

from an ECG signal (Delmar Avionics, Los Angeles, CA, USA) and was averaged for the period of stable respiration. Patients were invited to rate their perceived exertion on a non-linear scale of 10 points, known as the Borg scale.[13]

Prior to the test a teflon cannula was inserted into an antecubital vein and attached via a normal bore extension set (volume 1.5 ml) to a three-way tap for sampling. Samples of blood (2 mls) were taken at rest, at the end of each stage of exercise, at peak exercise and at three and six minutes into recovery after discarding the dead space volume. The samples were immediately deproteinised with 8% perchloric acid to inhibit glucose metabolism and stored for a short period in ice before being analysed for whole blood lactate concentrations. Lactate threshold was defined by visual inspection of the inflection point representing a non-linear rise of lactate concentration with reference to VO_2.

Walking speed was measured on commencing the exercise programme and again at completion. Subjects were instructed to walk at a comfortable walking speed and timed using a hand held stop watch. Stature was measured, without shoes, using a portable stadiometer and measurements were taken to the nearest centimetre. Body mass, measured to an accuracy of 0.1 kg was taken using portable scales (Seca, Germany). Shoes and heavy clothing were removed. Skinfolds were measured using Harpenden skinfold caliper (John Bull & Co, UK) at the biceps, triceps, subscapular and suprailiac sites on the right side of the body using Eurofit protocols.[14] Body fat was calculated according to Durnin and Rahaman.[15]

STATISTICAL METHODS

Within group changes were measured using paired t-tests. Independent sample t-tests were used to test between-group differences. Results are expressed as means with 95% confidence intervals, and values of $P < 0.05$ regarded as significant.

RESULTS

The physical characteristics of subjects are shown in Table 1. The mean body weight of the control group was significantly higher than the exercise group although there were no significant differences in age, height, body fat (%) or time since surgery.

The exercise programme lasted for 12 weeks and attendance rates were good (89%). During the aerobic section of the class, which lasted for 15-20 minutes, the mean heart rate ranged between 50% and 81% of age-predicted maximal heart rate [group mean 102 beats/min, or 67% of age predicted maximal heart rate (220-age)]. Expressed as a percentage of maximum achieved during the initial treadmill test, mean heart rates represented between 30% and 70% (group mean 52%).

All subjects completed Test 1 and Test 2 protocols successfully. Hip pain was cited as a reason for stopping in only one subject. Fatigue was the most common reason for stopping. Table II shows the peak VO_2, peak heart rate, respiratory exchange ratio, peak lactate, duration of exercise, anaerobic threshold, lactate threshold, walking speed, and Borg scores for the exercise and control groups in the pre- and post-intervention treadmill test. Thirteen of the 20 subjects reached a heart rate greater than or equal to their age-predicted maximum in Test 1 and test 2. Although a significant improvement in peak VO_2 occurred in the exercise group when compared to baseline ($P < 0.05$) with no change observed for the control group, the difference between exercise and control groups was not significant. A biphasic VE/VO_2 graph was recorded in 75% of patients enabling an anaerobic threshold to be identified (the point of increase in gradient of the VE/VO_2 graph). No significant difference was observed within or between active and control groups. No change occurred in perceived exertion (Borg Scale) between Tests 1 and 2.

The lactate threshold was identified in 17 subjects in Test 1 and 15 subjects in Test 2. Low concentrations of blood lactate during the last phase of the exercise test was the reason for non-identification of lactate threshold in some subjects. A significant improvement in lactate threshold was found in the exercise group. The lactate threshold occurred at 83% of peak oxygen uptake in Test 1 and 90% of peak oxygen uptake in Test 2 ($P < 0.05$). In contrast, no significant change was found for non-exercising controls. Changes in absolute heart rate at lactate threshold, or heart rates at lactate threshold expressed as a percentage of age-predicted maximum heart rate between Test 1 and Test 2 were not significant in either the exercise or control group. Improvements occurred in walking speed for exercisers (1.28 to 1.41 m/sec) but not in non-exercising controls and this post-training difference between exercise and control groups was significant ($P< 0.05$).

TABLE II

Values for physiological parameters measured during the initial treadmill test 1 and the post-intervention treadmill test 2 for exercisers and controls. Values are means (95% Confidence Intervals).

AT = Anaerobic Threshold LT = Lactate Threshold
RER = Respiratory Exchange Ratio VO_2 = Oxygen Uptake

	Exercisers n = 13		*Controls n = 7*	
	Test 1	*Test 2*	*Test 1*	*Test 2*
Peak VO_2 (ml/kg/min)	19.3 (17.0, 21.6)	21.9* (18.7, 25.1)	21.5 (17.4, 25.6)	21.4 (17.6, 25.2)
Peak heart rate (beats/min)	152 (143, 161)	153 (146, 160)	156 (138, 174)	154 (141, 167)
Peak RER	1.15+ (1.10, 1.20)	1.05 (0.98, 1.12)	1.08 (1.02, 1.14)	1.07 (1.02, 1.12)
Exercise duration (mins)	15.4 (13.3, 17.5)	16.5 (14.0, 19.0)	16.3 (13.5, 19.1)	16.7 (14.0, 19.4)
VO_2 at AT (ml/kg/min)	14.1 (12.1, 16.1)	15.5 (12.8, 18.2)	15.9 (11.4, 20.4)	15.8 (12.3, 19.3)
Peak Lactate (mmol/l)	4.2 (3.2, 5.2)	4.5 (3.5, 5.5)	4.7 (3.3, 6.1)	4.5 (3.1, 5.9)
VO2 at LT (ml/kg/min)	16.5 (14.6, 18.4)	20.7* + (18.4, 23.0)	17.0 (13.2, 20.8)	16.9 (14.0, 19.8)
Walking Speed (m/sec)	1.28 (1.18, 1.38)	1.41* + (1.31, 1.51)	1.25 (1.14, 1.36)	1.20 (1.04, 1.36)
Borg Score	3.9 (3.1, 4.7)	3.9 (3.4, 4.4)	3.1 (2.5, 3.7)	3.6 (2.8, 4.4)

* $P < 0.05$ compared to baseline

\+ $P < 0.05$ compared to controls

DISCUSSION

This study found that lactate threshold and walking speed could be significantly improved with a minimal exercise programme in elderly women following hip replacement. The ACSM [7] recommend that training takes place 3-5 days per week, for 20-60 minutes, at an intensity of 60-90% of maximum heart rate or 50-85% of maximum oxygen uptake. The exercisers in this study spent a maximum of 20 minutes at a training intensity which was close to the minimum guidelines recommended by ACSM of 60% maximum heart rate (50% of maximum oxygen uptake). However exercise took place only twice per week. Using lactate threshold as an indicator of training intensity[16, 17] it is clear that the experimental group in this study exercised below their anaerobic threshold.

In agreement with Foster et al[18] this study also demonstrated that peak VO_2 can be readily measured in elderly women. Conventional criteria for the attainment of maximum oxygen uptake i.e. a plateau in oxygen consumption with increasing work, respiratory exchange ratio value of greater than 1.15 heart rate at age-predicted maximum, and a lactate concentration greater than or equal to 8 mmol/l cannot be achieved by older subjects, probably due to lack of motivation or unfamiliarity with intense exercise hence the use of the term 'peak' oxygen uptake in this investigation. In this study, subjects achieved a mean peak lactate of 4.2 and 4.5 mmol/l in the first and second treadmill tests respectively. A plateau in oxygen uptake was observed in Test 1 and Test 2 for 17 subjects, and the mean peak respiratory exchange ratio was 1.05 or higher in Test 1 and Test 2. Age-predicted maximum heart rate was achieved in 13 of the 20 subjects.

The value of peak VO_2 for the whole group measured at the start of the study (mean = 20.0 ml/kg/min) was slightly higher than the value of 18.7 ml/kg/min recorded previously for both sedentary 74 year old women[19] and women aged 60-75 years.[20] Post-operative mean peak VO_2 for 18 female and 7 male hip replacement patients was 18.1 ml/kg/min in another study.[2] Initial walking speed for the subjects in this study (1.27 m/sec) was higher than the mean speed of 1.16 m/sec of a group of elderly women living independently with a similar mean age of 72 years.[21] It was also higher than pre-training walking speed in a group of women following hip surgery in Belfast[4] (0.82 m/sec), but lower than post-training values in this group (1.49 m/sec). Hence the hypothesis that significant fitness gains were a function of low initial fitness can be discounted. The stringent criteria applied at the screening stage to ensure safety during the treadmill testing may be responsible for these high initial values and this group of subjects may not be typical of elderly women after hip replacement. Even less vigorous exercise regimes may be sufficient for improving fitness in hip replacement patients whose aerobic capacity is lower than the subjects tested here.

Previous studies have produced inconclusive results regarding the influence of exercise intensity on training adaptation in the elderly. Some have shown that high intensity training elicits greater increases in aerobic capacity than low intensity training [22] while others found that low intensity training provided comparable increases in maximum oxygen uptake and lactate threshold to high intensity training.[23]

The improvement in peak VO_2 in our subjects after training (13%) was smaller than that reported in some other studies.[22, 23] The short duration of the exercise programme (12 weeks) was deliberately chosen as a feasible rehabilitation time for hip surgery patients, and may contribute to the relatively small changes. The improvement in lactate threshold by our subjects (4.2 ml/kg/min) is however greater than improvements reported previously.[24] The upper limit for improvement in peak VO_2 as a result of training may be reached sooner than the upper limit for lactate threshold, which may explain the greater increase in lactate threshold relative to peak oxygen uptake. Studies in younger subjects have shown that the

factors controlling the adaptation in oxygen consumption are different from those controlling the change in lactate threshold[25] and although the mechanisms are unclear, the central cardiovascular, peripheral circulation and local muscular adaptations have been cited as influences.

The principal limitations of this study included the small numbers and the lack of true randomisation to exercise and control groups which were determined by geographical location. However, the results obtained suggest that minimal exercise can improve functional fitness in elderly women who have undergone a hip replacement operation. The exercise group found the exercise programme manageable and enjoyable. Minimal exercise is thus a positive intervention following hip surgery for osteoarthritic patients.

Acknowledgements

We wish to acknowledge the considerable assistance of the elderly volunteers as well as the physiotherapy department and day hospital staff at the Royal Victoria Hospital. In particular we wish to thank physiotherapists Jacqueline Crosby and Hilary Preston for their enthusiasm and contribution to the exercise class.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 126 – 130, October 1995.

Laser lithotripsy for ureteric calculi: Results in 250 patients.

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Accepted 5 September 1995

SUMMARY

Two hundred and fifty patients with 290 stones presenting to the Department of Urology were treated with the Candela MDL 2000™ Laser Lithotripter. Overall stone clearance rate was 95%. The more proximal the calculus the lower the success rate. Ninety eight percent of stones in the lower ureter, 95% of mid ureteric and 91% of upper ureteric stones were cleared. The major complication was perforation which occurred in 6% of cases. This procedure is a safe and effective treatment for ureteric calculi and is associated with a low complication rate and a high clearance rate. Laser lithotripsy is the optimum ureteroscopic method of treating ureteric calculi and is complimentary to extra corporeal shock wave lithotripsy.

INTRODUCTION

The surgical management of both renal and ureteric calculi has undergone radical change in the past decade and open surgery is now rare with only one or two cases being operated on in this unit each year. Both extracorporeal shock wave lithotripsy,[1,2] and pulsed dye laser lithotripsy through small calibre instruments have revolutionised the management of ureteric calculi.[3-5] In units without access to a lithotriptor with radiographic screening facilities the management of ureteric calculi remains a significant part of the workload. Thus, endourological techniques will remain an important primary or adjunctive procedure in the management of ureteric calculi.[6] Blind manipulation of stones within the ureter is hazardous and in situ lithotripsy using ultrasound or electrohydraulic probes generates large amounts of heat which may damage the ureter. Ureteroscopy itself, has become safer with the advent of smaller calibre instruments. Pulsed dye laser lithotripsy has a wider safety margin than other methods of stone destruction within the ureter because energy generated in stone fragmentation is dissipated as photoacoustic energy rather than heat.

We report a consecutive series of 250 patients treated in three years at the Department of Urology in the Belfast City Hospital.

PATIENTS AND METHODS

All patients who underwent laser lithotripsy for ureteric calculi between April 1991 and July 1994 were studied. They were treated on a dedicated Uroskop™ screening table with the Candela MDL 2000™ pulsed dye laser. The stone size and position was measured in

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two planes, and the radiological investigations and the presence of ureteric obstruction was recorded (Tables I and II).

Ureteroscopy was performed using the 7.2 Ch miniscope (Candela™) which has two working channels and a fibreoptic illumination system with an outer semirigid casing. The current miniscope has been improved, to incorporate a larger flow channel and it is not necessary to use a pressure infusor device to maintain adequate vision. The larger irrigation channel also allows the passage of ureteric guide wires for insertion of double 'J' ureteric stents. Laser energy was delivered through a 320μm fibre at 10 MHz frequency. A range of energy settings (30-140 mJoules) may be used. In all cases lithotripsy was commenced at a power setting of 30 mJoules and increased slowly to achieve optimum effect. The power settings and the pulse count were recorded in each patient. A 3 Ch dormia basket is available for entrapment of stones to facilitate laser lithotripsy or for extraction of fragments. If there was any suspicion of ureteric injury an 'on table' ureterogram was performed.

Every patient was given gentamicin 80 mg intravenously peroperatively. The postoperative analgesic requirements of 20 patients were also recorded. All patients were reviewed, and the results of lithotripsy at three months are reported.

TABLE I

The anatomical position of 290 stones

position of calculi	*No.*	*%*
Upper ureteric	93	(32%)
Middle ureteric	58	(20%)
Lower ureteric	139	(48%)

TABLE II

size of calculi (mm)	*No.*	*%*
<10	154	(53%)
10-20	11-	(38%)
20+	23	(8%)
Stein strasse	3	(1%)

RESULTS

Two hundred and fifty patients, age range 12-87 years, with a total of 290 stones were treated. Seventeen patients had multiple calculi. Seven had bilateral stones and ten had multiple, unilateral stones. The overall stone clearance rate was 95%. The more proximal the stone the lower the success rate; 98% of lower ureteric stones were cleared compared with 95% and 91% of middle and upper ureteric stones.

Fifty eight patients (23%) had significant obstruction at the time of treatment. Twenty (8%) had 'J' ureteric stent insertion prior to laser lithotripsy and in thirty six (14%) stenting was carried out at the time of the procedure. In two it was not possible to pass a guide wire and a percutaneous nephrostomy was inserted.

In all 74 patients (29%) required adjunctive procedures during treatment (55 insertion of J stent, 15 dormia basket extraction, an 2 each had balloon entrapment or nephrostomy).

The complications associated with laser lithotripsy are listed in Table III. There were no deaths. The major complication was perforation which occurred in 15 cases (6%); in most instances the perforations were minor, and all but one (who required a nephrostomy) were treated by immediate ureteric stenting.

TABLE III

Complications associated with laser lithotripsy

complications/failures	*No.*	*%*
Failed access	17	(7%)
Perforation	15	(6%)
Retrograde stone migration	17	(7%)
Septicaemia	4	(1.6%)
Acute renal failure	1	(0.4%)
Retention	2	(0.8%)

In 17 patients (7%) the stone or a significant fragment floated back into the kidney. Only one of these patients has subsequently failed to clear the stone spontaneously or following retreatment of the fragments. Laser lithotripsy failed to fragment the stone in one patient who was subsequently found to have cystinuria. Retreatment for the same calculus was required in 17 patients, 15 patients had two treatments, and two required four treatment sessions.

Four patients (1.6%) developed septicaemia and required intravenous antibiotics; they have all recovered and are stone free. One patient with bilateral ureteric calculi and bilateral obstruction had both stones treated at a single session. He subsequently developed bilateral 'stein strasse' and went into acute renal failure with a total hospital stay of 55 days.

Overall hospital stay ranged from 0-55 days (median of 3 days). Seventy three percent of all patients were discharged within five days of admission. The number of day cases is steadily increasing, from 8% in 1991, to 10% in 1992 and 23% in 1993. Of 20 patients in whom it was recorded,13 required no postoperative analgesia, six required diclofenac and only one required an opiate analgesic.

DISCUSSION

This study confirms that laser lithotripsy is a safe and effective treatment for ureteric calculi. Using the Candela 7.2 miniscope no patient in our series required ureteric dilatation. The overall clearance rate in this study was 95% and only one patient required

a ureterolithotomy. These results are comparable to other series using lasertripsy,[7,8,9,10,11] in which clearance rates of 85-97% are quoted. Our results also compare favourably with those of extra corporeal shock wave lithotripsy for ureteric calculi,[2,12,13,14,15] where clearance rates are in the order of 80-85%.

We believe that laser lithotripsy should begin at the lowest power setting as this gives a feel for the stone and the rate of fragmentation. The power settings can then be adjusted to fragment the stone with maximum efficiency and the least risk of propelling the stone back into the kidney. Small smooth stones are most likely to float, and all but one of the stones that floated were smaller than 10 mm in diameter. Previous surgery, obesity and prostatic enlargement were significant factors contributing to failure of ureteroscopy. Passage of a ureteric guide wire into the kidney before lithotripsy commences is useful in patients where difficulty may be anticipated. If a stone cannot be seen or there is instrumental trauma to the ureter, it is then easy to place a ureteric stent. Patients with bilateral stones are best treated at separate sessions and should have the ureter stented following treatment if there is a large stone burden. Patients with solitary kidneys should have all stone fragments removed and if this is not possible a stent should be placed.

The major complication of laser lithotripsy was perforation in 6% of patients, varying from minimal extravasation of dye to more extensive trauma. The perforations were caused either from instrument or fibre trauma to the ureter or by blasting of stone fragments through the wall of a friable ureter during fragmentation. Initially we felt that the presence of a double J stent at the time of laser lithotripsy might make the ureteric wall friable and more liable to perforation, but we have now shown that there is no increased risk of perforation in such patients. Impacted stones with obstruction and signs of infection where there is also oedema and hyperaemia of the ureteric wall are more difficult to treat and bleeding often obscures the view. Such cases are best stented initially and left to settle for four to six weeks. Instrumental perforations will be impossible to eliminate from any extensive series of ureteroscopic lithotripsy; all but one of these patients were treated by immediate stenting and only one required a nephrostomy. Because of the risk of perforation we believe laser lithotripsy should be carried out on a screening table with the facility to perform retrograde studies and stenting if necessary. A single dose of gentamicin is a cheap and effective prophylactic antibiotic for this procedure, but despite its use, septicaemia was documented in four patients.

The management of ureteric calculi continues to evolve.[16,17,18] Extracorporeal shock wave lithotripsy machines with x-ray imaging can treat ureteric calculi with reported success rates in the order of 80-85%. The results of ureteroscopic laser lithotripsy are similar, but this is an invasive procedure and carries with it the risk of ureteric injury. Laser lithotripsy is complementary to extracorporeal shock wave lithotripsy and may be used to treat 'stein strasse' and stones refractory to shock wave lithotripsy both in the ureter and kidney.

Laser lithotripsy is a more efficient method of dealing with ureteric calculi than the 'push bang' technique which is often used in lithotriptor centres using ultrasound imaging.[6,19] Extracorporeal shock wave lithotripsy for upper ureteric stones is the ideal treatment, as these stones may be difficult to reach with a ureteroscope, but this is only practical with machines that have x-ray localisation. Extracorporeal shock wave lithotripsy for lower ureteric calculi necessitates placing the patient in the prone position and imaging may be difficult. Extracorporeal shock wave therapy with the added risk of ovarian irradiation is less attractive for lower ureteric calculi in females of reproductive age. There has been at least one reported miscarriage following this procedure.[20]

We have cleared all accessible lower ureteric stones, and we can clear 94% of stones overlying the bony pelvis, which compare favourably with any series in the world literature. Many urologists in the United Kingdom, including this centre do not have access to a fixed site extracorporeal shock wave lithotriptor and use mobile lithotripsy instead.[21, 22] Ureteric stones often require urgent treatment and in this setting laser lithotripsy is an ideal and safe technique.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 131 – 136, October 1995.

Diagnostic regimes for urinary tract infection – are research results applied to practice?

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Accepted 27 August 1995

SUMMARY

A clinical audit of ward practice for diagnosing and treating urinary tract infection was carried out to assess the impact on clinical practice four years after publicaton of a working protocol. Data were collected from all medical, surgical, gynaecology and geriatric wards in 25 hospitals in Northern Ireland. All wards made use of urinary dipsticks for ward testing, as recommended by the protocol. However many negative samples were still forwarded for laboratory analysis. The potential financial savings which would result from effective ward screening were not being realised and the publication appeared to have minimal impact on clinical practice. Advice on an improved diagnostic protocol for urinary tract infection may not have been disseminated to the nursing staff whose role was pivotal in the screening process.

INTRODUCTION

Urinary tract infections are among the most common infections.[1] They account for more than seven million doctor visits and necessitate or complicate more than one million hospital admissions in the United States annually.[2,3] In the United Kingdom this would correspond to about 1.5 million visits and 200,000 admissions. A rate of 14 hospital-acquired urinary tract infections per 1,000 admissions has been calculated for persons under 15 years,[4] while the average prevalence of asymptomatic bacteriuria during pregnancy is 6%.[5] In addition, urinary tract infections occur more commonly in elderly people,[6,7] with a prevalence of asymptomatic bacteriuria of 12% in elderly men, increasing with age.[8] Symptomatic and asymptomatic bacteriuria presents a risk factor for bacteraemia, sepsis and an increase in mortality, especially for elderly females.[9]

Urinary tract infection (UTI) is therefore responsible for a significant amount of morbidity in both young and elderly populations, and consequently a major part of the workload of bacteriology laboratories involves the processing of urine samples. There is a need for cost-effective testing at ward level to screen out negative samples.[10] Such screening tests are available and have been assessed by a number of investigators.[11-14] In 1989, an evaluation of four UTI screening tests in an elderly population produced a working protocol based on both visual appearance and dipstick testing at ward level.[13] In this system, the visual appearance of the urine sample is first tested, and only if it is cloudy is dipstick testing for nitrites and leucocytes performed. The dipstick test is positive if either the nitrite is positive

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or if the leucocyte esterase shows more than a trace positive. Only if a positive result is obtained from dipstick testing is the sample forwarded to the laboratory for bacteriological testing. This protocol has a sensitivity of 96.1% and a specificity of 50.6%. These recommendations were published and presented at national and local meetings. The current investigation aims to assess ward practice for diagnosing and treating urinary tract infections and in particular, to monitor the effective use of urinary dipsticks, four years after publication of the working protocol. Although information on practice before publication of these recommendations is not available, the current study provides information on how clinical practice relates to the recommendations.

METHODS

The study was carried out in 25 hospitals throughout Northern Ireland. Permission was obtained discreetly from the management of the hospitals involved so that the audit itself would not alter clinical practice. A questionnaire was designed to record current ward practice for diagnosing and treating urinary tract infections together with details relating to sample collection, number of samples, action on test results, staff involvement, and protocols. The hospital, ward and ward type were recorded. An audit form was also designed to record all sample details over a period of one week. Each time a urine sample was handled, a tick was placed in the appropriate box on the form which was to be displayed in the sluice room on each ward studied.

All medical, surgical, gynaecology and geriatric wards in the 25 participating hospitals were visited by a research nurse (BMcP). The questionnaire was administered and the audit form was left behind to be returned in the sae provided at the end of the one week audit period. Wards not returning their form were sent a second if three or more weeks had elapsed from the time of visit.

Statistical analysis was by SPSS.[15] Descriptive statistics were employed and the Pearson Chi-square (X^2) test for analysis of categorical data.

RESULTS

A total of 25 hospitals (194 wards) were visited throughout Northern Ireland. These comprised 67 geriatric (35%), 58 surgical (30%), 53 medical (27%) and 16 gynaecology wards (8%).

Questionnaire

The visual appearance test was used by 40 wards and always in combination with dipstick (Table I). A significantly greater proportion of the geriatric wards utilised visual appearance as a ward test (geriatric 46%; gynaecology 12%; surgical 7%; medical 6%; $p < 0.0001$). All wards used dipstick to test for UTI. 181 wards used Multistix 10 (132 exclusively; 31 in combination with visual test, 11 with other dipstick and 7 with both visual and other dipstick). Thirty-one wards utilised other dipsticks such as BM7 (22 wards), BM5 (5 wards), Nephur-Test & Leuco (2 wards), and Leuco/Nitrate Test Stix (2 wards) (11 exclusively, 2 in combination with visual test, 11 with Multistix 10 and 7 with both Multistix 10 and visual). (Details of the most commonly used dipsticks are shown in Table II).

6% of wards had no instructions or protocol. A protocol is defined as written instructions displayed visibly on the ward while 'other' instructions may be verbal. A total of 46 wards tested urine as a routine procedure on admission and 193 wards tested when symptoms were present. 97% of wards used the 'clean catch' method to obtain urine for testing. A significant difference was found in the number of samples collected by each speciality

($p < 0.0001$; Table II). 69% of geriatric wards collected < 10 samples per week while 66% of surgical wards collected > 20 samples per week.

In 66% of wards the UTI ward test was always performed by nursing staff. In one ward a nursing auxiliary performed the task, with the duty being carried out either by nurse or nursing auxiliary in 33% of wards. The decision on whether or not to request laboratory analysis when a positive result was obtained by ward test was taken by nursing staff in 143 wards (74%). Nursing or medical staff made the decision in 48 wards (25%) and in only three wards (1%) was the action decided exclusively by medical staff.

TABLE I
Questionnaire Results

	Medical	*Surgical*	*Gynae*	*Geriatric*	*Total*
Number of wards	53	58	16	67	194
Ward tests					
Dipstick only	50	54	14	36	154
Visual + Dipstick *	3	4	2	31	40
Instructions					
Protocol only	37	36	13	46	132
Other instructions only	8	14	3	12	37
Protocol + instructions	4	5	0	4	13
None	4	3	0	5	12
Action					
Treat all positives	30	42	11	34	117
Repeat all positives	6	5	1	11	23
Treat repeat all positives	17	9	3	19	48
No action on positive	0	2	1	3	6
Test as routine	8	16	3	19	46
Test if symptoms present	53	58	16	66	193
Use clean catch method	53	58	16	62	189

* $p < 0.001$ for difference between different types of wards.

TABLE II

Details of urinary dipsticks

Multistix 10SG 100 sticks £21.	Tests for specific gravity, pH, protein, glucose, ketones, bilirubin, blood, nitrite, urobilinogen, leucocytes.
BM test 5L 100 strips £12.	Tests for pH, protein, glucose, kentones, blood, bilirubin, urobilinogen.
BM test 7 100 strips £15.	Tests for pH, protein, glucose, ketones, blood, bilirubin, urobilinogen.
Nephur-test & Leucocytes 100 strips £20.	Tests for pH, protein, glucose, blood, nitrite, leucocytes.

TABLE III
Details of Weekly Sampling and Testing

	Medical			*Surgical*			*Gynae*			*Geriatric*			*Total*		
Number of Wards	53			58			16			67			194		
Number of Samples	<10	10-20	>20	<10	10-20	>20	<10	10-20	>20	<10	10-20	>20	<10	10-20	>20
Wards Collecting Samples*	4	18	31	5	16	38	0	3	13	46	16	5	54	53	87
Wards Using Ward Testa	6	16	31	5	17	36	0	4	12	47	15	5	58	52	84
Wards Sending MSU's	38	12	3	29	23	6	11	2	3	64	3	0	142	40	12

* $p < 0.0001$ for difference between types of wards.

Audit forms

156 audit forms were returned from the 194 wards tested. A total of 1957 urine samples were ward tested during an audit period of one week, of which 48% were negative (Table IV). The same 156 wards forwarded 740 samples for laboratory testing of which 44% were negative. It is not clear if all these samples were ward tested positive and sent for confirmation, or if they were not tested at ward level. Both possibilities would in fact be present in the wards returning audit details. Treatment was initiated in 184 patients; that is, 9.4% of samples tested led to treatment.

TABLE IV
Audit Results

	Medical	*Surgical*	*Gynae*	*Geriatric*	*Total*
Number of Wards	38	49	11	58	156
Ward tests positive	277	406	83	257	1023
Ward tests negative	305	379	135	115	934
Laboratory tested	177	49	62	183	740
Not laboratory tested	240	222	39	118	619
Returned positive	37	72	14	115	238
Returned negative	74	170	25	54	323
Treated	27	60	12	85	184
Not treated	74	141	19	81	315

DISCUSSION

The current investigation documents and quantifies the diagnostic testing regimes for urinary tract infection in 25 hospitals in Northern Ireland. The results of the study indicate universal usage of dipsticks as a ward test for the detection of UTI, irrespective of hospital or ward classification. Our results show that geriatric wards more frequently used dipstick screening in combination with the visual appearance test. This may suggest that the recommendations made by Flanagan,[13] who carried out his research in elderly patients, may have been adopted by geriatric wards. However not one of the 194 wards had a copy of Flanagan's protocol. The recommendation of screening with urinary dipsticks is supported by further studies in geriatric medicine [16] and in other specialties such as paediatrics [17] and surgical/medical units.[18] Most of the dipsticks used are also screening tests for renal disease and diabetes and this might partially explain why they are in such common use.

Diagnosis of the presence of UTI was sought either as routine or where symptoms indicated possible infection. The number of samples collected for diagnosis was related to the type of ward. This result is not surprising since the number of samples is dependent upon a

number of factors, for example, throughput of patients, and whether or not admissions are tested routinely. Our results show that geriatric wards performed the lowest number of weekly tests despite the fact that these patients are most at risk from UTI.[19] This discrepancy may be largely explained by the lower throughput in geriatric beds. In contrast, surgical wards, where a high throughput is expected, carried out the highest number of weekly tests. Screening for hospital – acquired infections may also have contributed to the increased number of samples. Interestingly, the rate of routine testing of all admissions varied little between ward categories.

Some form of protocol or other instructions were widely available and yet when the MSU results are examined, the instructions appear to have been ineffective. The audit returns showed two important findings. First, that 48% of ward tests were negative and should therefore have been 'screened out'; and second, that 44% of MSU tests were also negative suggesting ineffective screening. Although these figures include routine samples, where negative results would be expected, the potential to make significant financial savings by adopting the use of an effective protocol as a screening test remains. A typical hospital bacteriology laboratory may process on average 300 samples each day, at an annual cost of approximately £109,200 (assuming a cost of £10 per test). By following a protocol of visual appearance and dipstick testing, 96% of infected urine samples would be detected at ward level and the number of samples requiring processing by the laboratory reduced by 30%.[13] Using these estimates, a hospital could save approximately £327,600 per year, with the cost of dipsticks being negligible (£2,340 per annum). Levy et al [14] calculated a potential reduction of 60% in laboratory urinalysis in their hospital suggesting even greater potential savings. Tuel et al [18] suggest the use of a protocol advising laboratory culture only when dipstick test is positive; this is estimated to reduce the number of cultures by 83%. They add that use of dipstick screening methods by nursing staff can reduce the cost of weekly urine screening by 73%.

Where ward or MSU tests returned a positive result, only 8% of wards did not initiate treatment. This 'treat if positive' policy requires further investigation. If we examine the literature, Breitenbucher [20] suggests that even with a positive culture, elderly patients should not generally be treated unless other evidence supports a diagnosis of symptomatic UTI. Zhanel et al,[21] advocate treatment of asymptomatic bacteriuria only for neonates and pre-school children, pregnant women and men under 60 years.

The current results indicate that both testing and action on the test result were almost always performed by nursing staff. This is an important finding in terms of targeting education. Recommendations for altering clinical practice presented at medical meetings or published in the medical literature may be noted by doctors, but unless such information is disseminated to nursing staff there will be little change in clinical management. In the case of UTI, such changes are essential for the realisation of the potential financial savings associated with UTI diagnosis.

In conclusion, this investigation has shown that while dipstick testing at ward level is commonly used, its use as a screening tool has not been effectively implemented, resulting in unnecessary laboratory testing and financial expenditure. Nursing staff are pivotal in the clinical management of UTI and a possible flaw in the dissemination of the information recorded in medical publications from medical personnel to nursing staff has been identified. This study indicates the need for change in practice with respect to UTI diagnosis, both in terms of targeting information together with more effective screening at ward level. It also illustrates the difficulty of introducing research findings into clinical practice.

ACKNOWLEDGEMENT

This study was carried out with the support of funding from the DHSS (Northern Ireland). The authors would like to thank the participating hospitals and nursing staff.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 137 – 141, October 1995.

Comparison of nursing home residents admitted from home or hospital

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Accepted 4 August 1995

SUMMARY

A growing elderly population coupled with a reduction in hospital long term care has led to an increase in the independent nursing home sector. This is an expensive resource. Proper placement is therefore essential to ensure its efficient use. Prior to the introduction of care management there was no standard assessment procedure for admission to nursing home care from different sources. A nursing home population (n=624) in North and West Belfast was studied and mental scores, levels of disability, and the source of admission to the nursing home recorded. Residents admitted from geriatric medical units (n=132) were compared with those from general medical and surgical wards (n=168) and those from home (n=243). Residents who were admitted from a geriatric unit were the most disabled, those admitted from home were the least and those from general wards had intermediate levels of disability ($p<0.005$). This is likely to be the result of different assessment procedures for prospective nursing home residents. With the introduction of care management, it is hoped that standardised assessment will follow. The roles of different medical specialists in this process is not yet clear. Further study is needed to assess the appropriateness of placement in nursing homes under care management.

INTRODUCTION

Demographic changes have led to an increased number of frail, and very elderly people, and in turn to an increase in the demand for long term nursing care. The decrease in the number of hospital long stay beds in the NHS has meant that most of these patients are now cared for by the independent nursing home sector.[1]

A nursing home place costs in excess of £300 per week, and since the great majority of residents are not self-financing,[2] this represents a considerable financial demand on health resources.

Before the introduction of Care in the Community[3] in April 1993, there was no standardised assessment procedure for nursing home admission,[4] and there has been

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evidence of inappropriate placement.[5] Even after the introduction of care management, medical assessments may not conform to a uniform standard. We studied a population of elderly people resident in nursing homes prior to the introduction of care management in April 1993. We aimed to record levels of disability in residents and to relate these to sources of admission.

MATERIALS AND METHODS

This study was carried out between December 1992 and March 1993. All residents of private and voluntary nursing homes in North and West Belfast were studied as previously described.[2]

The nursing homes were visited by a trained nurse assessor, and a standard proforma was completed. This recorded age, sex, domicile and address from where each resident was admitted. A Barthel activities of daily living score [6] (range 0-20) and an abbreviated mental test questionnaire [7] (range 0-10) were completed. A Clifton Assessment Procedure for the Elderly (CAPE),[8] which is an instrument for assessment of general disability, was also performed. The results were recorded as disability grades from A to E (A equals no impairment, B equals mild impairment with low dependency, C equals moderate impairment and dependency, D equals marked impairment with high dependency and E severe impairment and maximum dependency).

Residents were divided by source of admission from geriatric medical units, general medical or surgical wards, and home. The characteristics of these various groups with different sources of admission were compared.

The results were analysed using the Statistical Package for Social Sciences (SPSS).[9] Differences between continuous and ordinal sets of data were analysed by analysis of variance (ANOVA). Differences between groups in different institutions were compared using Chi-squared analysis. Differences between skewed data were estimated by non-parametric methods.

TABLE I

Mean age, Barthel Index and mental test score of residents in nursing homes who originated from home, general medical and surgical wards and from geriatric medical units. 95% confidence intervals are in brackets.

	Home to nursing home	*General ward to nursing home*	*Geriatric ward to nursing home*
Number	243	168	132
Age in years	83.1 (81.9 - 84.2)	81.8 (80.4 - 83.1)	83.5 (81.7 - 84.4)
Barthel Index	11.2[a] (10.4 - 11.9)	9.6[b] (8.6 - 10.5)	7.5[c] (6.5 - 8.4)
Mental test score	5.3[d] (4.8 - 5.8)	4.6[e] (4.0 - 5.2)	3.6[f] (2.9 - 4.2)

ANOVA intergroup comparison:
ab(p=0.002), ac(p=<0.001), bc(p=0.006)
df(p<0.001), ef(p=0.05)

RESULTS

A total of 624 persons, 485 (78%) female and 139 (22%) male were entered into the study. They were recruited from 14 private and voluntary nursing homes throughout North and West Belfast. Of these, 243 (38.9%) were admitted from home, or from the homes of relatives. Three hundred were admitted directly from hospital, 168 (26.9%) from general medical and surgical wards (general group), and 132 (21.2%) from geriatric medical units (geriatric group). Of the remaining 81, 33 (5.1%) came from residential accommodation, 1 (0.2%) from a home for the elderly mentally infirm, and 41 (6.6%) from other nursing homes. These last three groups were not studied further. Accurate source of admission could not be determined in the remaining 6 individuals.

The group admitted from hospital comprised 74 males and 226 females (Table 1). There was no significant age difference between the "geriatric" (mean 83.1 years) and the "general" group (mean 81.8 years). There was also no significant difference in the lengths of stay in the nursing home of the two groups though the median length of stay in the group from geriatric units at 14 months was longer than the 10 months for the group from the general wards. The mean Barthel index score of activities of daily living of 7.5 in the geriatric group was significantly lower than the mean score of 9.6 in the group admitted from general wards. The general group had 23 (13%) of its number with a Barthel score of 17 or greater, compared with 11 (8.3%) in the geriatric group. Mental test scores were significantly higher in the group from general wards indicating that the group from geriatric units was more confused than the general ward group.

When compared to the groups admitted from home, both the geriatric and general groups had a significantly lower Barthel index and a lower mental test score (Table I). There was no significant difference in mean age between the group from home and either of the groups from hospital.

TABLE II

Numbers of nursing home residents in different CAPE (Clifton assessment procedure for the elderly) groups, classified by source of admission to the nursing home, with percentages of each source in brackets.

	Admitted from home	*Admitted from general ward*	*Admitted from geriatric unit*
CAPE grouping			
A	33(13.6)	11(6.5)	5(3.8)
B	43(17.7)	32(19.0)	15(11.4)
C	42(17.3)	22(13.1)	14(10.6)
D	45(18.5)	36(21.4)	29(22.0)
E	80(32.9)	67(39.9)	69(52.3)

Significantly more disabled residents in the geriatric group and significantly less disabled residents in the group admitted from home

Chi-squared = 25.4, df = 8, $p<0.005$

CAPE dependency groupings were available on all the individuals in the study. Groups A and B, which suggests no or little dependency, and would probably be assessed as not requiring nursing care, were recorded in all three groups. Twenty individuals in the geriatric group (15.1%), 43 in the general group (25.6%) and 76 from the group admitted from home (31.3%), were assessed as belonging in these two groups. However, these differences did not reach statistical significance (Chi-squared = 4.91, df = 3. $0.1>p>0.05$). Groups D and E which represent the most severely disabled individuals, and would be thought to be appropriate for nursing home care, were recorded in 98 (74.2%) of the geriatric group, 103 (61.3%) of the general group, and 125 (51.1%) of the group admitted from home. Overall, the distribution of disability between the three groups was significantly different (Chi-squared = 25.4, df = 8, $p<0.005$, Table II).

DISCUSSION

This study has shown a two-fold increase in the number of nursing home residents in North and West Belfast since the survey of 1989.[2] There has been a decrease in the numbers of residents who are functionally independent from 26% to 22%.

The population resident in these nursing homes is not homogeneous. Although the mean level of dependency is high, and mental score is low, there are a considerable number of residents in nursing homes who appear to be independent, and who may therefore be inappropriately placed and the majority of whom were admitted from the home and general groups. Such apparent inappropriate placement has been observed before, [4, 10] but has not previously been related to the source of admission of the residents. Those admitted from a home environment had the greatest degree of independence, those admitted from geriatric medical wards had the least independence and those from general medical and surgical wards had an intermediate level.

Since the ages in the different groups are similar, it is unlikely that this is a factor contributing to the observed differences in dependency between the groups. Similarly, the median length of stay in the nursing home [5] is equivalent in both the general and geriatric groups, (though it was longer in the group admitted from home) and is therefore unlikely to influence the differences between the groups, as any difference between the groups would be expected to decrease with time as they lived in the nursing home environment together. Lastly, while the Barthel ADL and CAPE assessment scores may be more insensitive at the upper (less disabled) end of the scales, they are widely validated in the assessment of elderly people[12] and any deficiencies are unlikely to account for the differences observed between the groups.

Currently elderly patients admitted to general medical wards tend to be younger, to have single pathology and be less frail than those admitted to geriatric wards.[11] This should not in itself account for the higher numbers of independent patients transferred to private nursing home, as it would be expected that persons with uncomplicated illness would return home. The availability of assessment procedures in hospital, and ease of access to the services of physiotherapy, occupational therapy and social work, should make it easier to have a successful discharge home. This is likely to be a significant factor in the higher threshold of dependency in those referred to nursing home care from geriatric wards, indicating that if all dependent elderly had access to skilled inter-disciplinary assessment and rehabilitation the need for nursing home admission might be significantly reduced. Despite this, the proportion of patients who appeared to be independent and who were admitted from geriatric units to nursing homes (at least 15%) is still significant. The persons admitted from their own home need not have been assessed by their general practitioner and

are likely to have been assessed only by the nursing home staff. It may be in the interest of the home to have a wide variation in levels of dependency among the residents.

This work was carried out before community care was implemented in Northern Ireland in April 1993. This process is intended to institute a more rigorous assessment of patients' care needs. Since the introduction of care management all applicants for nursing home should have multi-disciplinary assessments carried out by a doctor and other members of the health care team. It has been suggested that a doctor (either general practitioner or hospital consultant) should be involved in assessments on patients over the age of 65. There is evidence that this is not being achieved in Northern Ireland.[13]

These results would suggest that a greater involvement by practitioners trained in care of the elderly may lead to an increase in the appropriateness of transfer to nursing home. Further study of admission to private nursing homes after the implementation of care management is planned to assess the efficacy of inter-disciplinary assessment, and the effect, if any, of care management on the level of dependency in nursing home care. It is anticipated that if medical assessment in care management is carried out by practitioners without expertise in care of the elderly, significant differences will remain between those seeking institutional care from home, general and geriatric wards.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 142 – 146, October 1995.

The epidemiology of major trauma in Northern Ireland

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Accepted 28 August 1995

SUMMARY

In a one year population based study of major trauma (Injury Severity Score greater than 15) reaching hospitals in Northern Ireland in 1990/91 the incidence was 23.2 per 100,000 of the population or 20.5 per 100,000 excluding terrorist activities.

The expected number of patients with major trauma for the province, (population 1.54 million) is 359 patients per annum. Road accidents and falls accounted for 71% of all trauma. Ninetynine patients per annum are expected to require immediate surgery, a laparotomy in 59 instances and neurosurgical procedures in 26. These data facilitate resource allocation and help predict the effects of future changes in the trauma system.

INTRODUCTION

Planning services for major trauma and plotting yearly trends in morbidity and mortality require population based data. With these objectives in mind we conducted a one year survey of major trauma in Northern Ireland.

METHODS

Twelve of the 19 hospitals that receive major trauma in Northern Ireland were chosen on a random basis to include both small, (less than 20,000 new patients per annum attending their Accident and Emergency departments) and large hospitals, and also rural and urban hospitals serving a population of approximately 1 million people. From 1/8/90 data were collected prospectively for one year on all injured patients with an Injury Severity Score (ISS) greater than 15 who reached the chosen hospitals alive. All trauma patients are brought to the nearest hospital in Northern Ireland by a free ambulance service with the universal access telephone number 999.

Recorded details included mechanism of injury, pre-hospital care and times, patient details, revised Trauma Score on arrival[1], Injury Severity Score (ISS),[2] personnel in A&E, time of arrival, time to operating theatre, resuscitative and operative management and follow-up. TRISS (the Trauma score ISS, age combination index)[3] and ASCOT (A Severity Characterization of Trauma)[4] probabilities of survival and Injury Severity Score combined, were calculated, as was the estimated annual volume and rate per 100,000 (EAV; rate) for many variables. Glasgow Outcome scores[5] at one year post injury were recorded by one of the authors (B McN) through contact with patients and general practitioners.

Annual estimates for volumes of trauma with and without terrorist activities were extrapolated from known population estimates and forensic data.

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RESULTS

Two hundred and thirty nine patients were included. The Estimated Annual Volume and rate per 100,000 of the population (EAV; rate) were 359; 23.2 whilst excluding terrorist activities the EAV; rate was 316; 20.5.

Patient demographics and mechanisms of injury are shown in tables I and II.

The reasons for emergency surgery and predicted annual volumes are shown in table III. Emergency surgery was defined as surgery for haemorrhage from an organ or vessel scoring ISS 9 or more, surgery for acute intracranial bleeding or a perforation of the gastrointestinal tract. (Examples of an ISS 9 injury include; fractured femur, small splenic tear, popliteal artery laceration). Eighteen patients died in the emergency departments including one who had surgery there.

TABLE I

Patient demographics

	number		*EAV; rate*
Age > 64	38	(16%)	57; 3.9
Age < 15	30	(13%)	45; 2.9
Age 15-64	171	(71%)	257; 16.4
Total	239	(100%)	359; 23.2

male 194 (81%) (EAV; rate 291; 18.9), female 45 (19%)
(EAV; rate 68; 4.4) m : f ratio 4.3 : 1

TABLE II

Mechanism of Injury

Mechanism of injury			*EAV; rate*	*Deaths (mortality rate %)*		*EAV; rate*
Road Traffic Accident	110	(46%)	165; 10.7	33	(30%)	50; 3.3
Falls	60	(25%)	90; 5.7	20	(33%)	30; 1.8
Gunshot	23	(10%)	35; 2.3	12	(52%)	18; 1.2
Explosions	8	(3%)	12; 0.8	2	(25%)	3; 0.2
Burns	8	(3%)	12; 0.8	1	(13%)	2; 0.1
Crush	6	(2.5%)	9; 0.6	2	(33%)	3; 0.2
Stabbing	4	(1.6%)	6; 0.4	1	(25%)	2; 0.1
Assaults	3	(1.3%)	5; 0.3	0		2; 0.1
Others	17	(8%)	26; 1.7	3	(18%)	5; 0.3
Total	239	(100%)	359; 23.2	74		114; 4.8

TABLE III

Reasons for emergency surgery

Procedure	*no. of cases*
Laparotomy	38 (EAV 59; 3.7)
Neurosurgical	17 (EAV 26; 1.5)
Thoracotomy	6 (EAV 9; 0.6)
Vascular	3 (EAV 5; 0.3)
Total	64 (EAV 99; 6.2)

TABLE IV

Some Commoner Injuries *

Diagnosis	*number (isolated*	*EAV; rate (patients)*	*Evacuated*
Extradural haematoma	15 (12)	23; 1.5	5
Acute sub-dural haematoma	18 (14)	28; 1.7	12
Intracerebral haematoma	18 (14)	28; 1.7	12
Splenic injury	11	17; 1.0	
Liver injury	7	8; 0.05	
Penetrating cardiac injury	4	6; 0.4	
Aortic injury	4	6; 0.4	
Tension pneumothorax	3	5; 0.3	

* An abbreviated list.

Haemothorax and pneumothorax are not included as many score ISS < 16 and estimates would be misleading based on ISS > 15 alone.

Some commoner injuries are shown in table IV. Eighteen patients with head injuries were not seen at tertiary referral units and 13 of them died in outlying hospitals. One hundred and thirty two patients (51%) were not transferred to the tertiary referral units, and sixty of these died. Glasgow outcome scores at one year for patients AIS >3 are shown in table V.

TABLE V

Glasgow Outcome Scores at one year post injury for 113 head injuries ISS > 9.

Outcome	*Number (per cent)*	*EAV; rate*
Death	49 (45)	75; 5
Persistent vegetative state	0 (0)	0; 0
Severe disability	1 (.9)	2; 0.1
Moderate disability	11 (10)	17; 1.1
Good recovery	50 (45)	75; 1.1
Total *	111 (100)	

* two patients lost to follow-up

DISCUSSION

The epidemiology of major trauma reaching hospital has been mapped in Northern Ireland. This study provides a basis for quality assurance in the future, plots the first point on the hospital mortality graph and provides data for accurate planning of trauma services. It may also be used for inter-regional and international comparisons.

The data may be used for quality assurance by being able to differentiate a change in hospital mortality due to better medical care from a change due to variation in the volume and pattern of injury. For example if compliance with seat-belt and drink-driving laws were to deteriorate, a rise in hospital and pre-hospital deaths would be expected. This might be wrongly attributed to a fall in standards of hospital care. Analysis of the hospital deaths by ISS however, should then show that the volume and severity of major trauma had increased, whilst no change, or even a fall in the relative mortality rates might have occurred.

This method of analysis will also permit evaluation of the effects of better paramedical care (where a rise in the volume and severity of trauma reaching hospital could be expected), or better injury prevention (a fall in total volume and severity of injury).

Figures for blunt trauma published here while specific to Northern Ireland should approximate to those expected in the remainder of the United Kingdom, as figures for the Merseyside study[6] and for the North Staffordshire region[7] are similar. The mortality rates for injury in Northern Ireland are in the higher range for the United Kingdom.[8] Details of preventable deaths and resuscitation are published elsewhere.[9]

This study does not provide data on the large numbers of disabling, mainly orthopaedic injuries, as these often score less than 16 on the ISS. (The ISS is designed more to measure threat to life than disability). It does however include almost all potentially life-threatening injuries.

There is less major trauma than predicted by the American College of Surgeons estimates,[10] and based on annual mortality statistics[8] this number of injured patients will continue to fall. We predict that it will become increasingly difficult for any one surgeon to see the fifty major trauma cases per annum recommended to attain or maintain their skills.[10]

ACKNOWLEDGEMENTS

Our thanks to the Department of Health for funding, and the Forensic Pathologists for their assistance. All the participating hospitals (who wish to remain anonymous) gave their assistance voluntarily and to them we are most grateful. Our sincere thanks to all who helped us in the departments of Accident and Emergency, Surgery and Intensive Care.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 147 – 150, October 1995.

A critical evaluation of the use of the Schiller test in selecting blocks from the uterine cervix in suspected intraepithelial neoplasia

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Accepted 28 August 1995

SUMMARY

The value of dipping cervical cone biopsy specimens in iodine (the Schiller test) as a method of deciding which areas should be selected for histological examination was assessed. Schiller positive and negative areas were recorded in macroscopic specimen images from fifty specimens of cervix. The results were compared with the histological presence or absence of cervical intraepithelial neoplasia (CIN) or invasive malignancy. In 84% of cases the test was a reliable means of predicting the presence or absence of squamous CIN; in two cases it was positive in association with endocervical adenocarcinoma in situ. A false positive and false negative Schiller's test was present in three cases (6%) each.

Had this method been adopted as the sole means of selecting blocks for histological examination the areas of CIN would have been missed in 6% of cases. Therefore it is not a sound alternative to the submission of all tissue for histological examination.

INTRODUCTION

Since cervical dysplasia does not display any macroscopic abnormality,[1] it is mandatory to submit any cone biopsy specimen excised from a patient with suspected or established intraepithelial neoplasia of the uterine cervix (CIN) in its entirety for histological examination. Whether the specimen is opened at the twelve o'clock position and divided into longitudinal strips as recommended by some authors[2,3,4] or is sliced sagitally beginning from one lateral edge of the specimen[1,5] either yield multiple histological blocks. Even if more than one block is placed in each processing capsule[3] the processing of cervical tissue represents a significant proportion of the workload of any routine diagnostic histopathology laboratory, as cone biopsy is a commonly performed outpatient and inpatient operation. Consequently any procedure which would allow the pathologist to select those blocks which contained the most significant pathological lesion would allow a reduction in both workload and in the cost of processing cone biopsies.

The Schiller test[6] may be used as part of the colposcopic examination of the vagina and cervix.[7,8] This test consists of the application of aqueous iodine to the cervix: normal squamous epithelium stains a deep brown (Schiller negative) whilst areas of ectropion, metaplastic or dysplastic squamous epithelium do not take up the stain (Schiller positive).

In this study the suitability of this technique as a means of selecting blocks containing areas of squamous CIN was assessed. Since it can be applied to formalin fixed tissue the test can be easily accommodated to use in a routine histopathology laboratory.

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MATERIAL AND METHODS

Fifty consecutive cone biopsies submitted to the pathology department at this institution were dipped in a 5% solution of aqueous iodine and a colour print of the macroscopic specimen image was made using a Sony UP2200 video printer system.[9] The specimen was serially sectioned[1,3] and each block of tissue was placed in a processing cassette which was labelled with a unique identifying letter. The position from which each block originated was marked on the colour print and the presence of a positive or negative Schiller reaction was recorded. An average of six blocks were examined in each case.

The blocks were processed on a Miles Scientific Tissue Tek Vacuum Impregnation Processor 1000 using a standard processing schedule, embedded in high quality paraffin wax, and haematoxylin and eosin stained sections were cut at 5 μm intervals on a Leitz 1512 microtome. These were examined by the same pathologist. The presence of squamous CIN, infiltrative squamous carcinoma or other pathological abnormality in each of the histological sections was recorded and the results compared with the macroscopic findings. The presence of an ectropion or squamous metaplasia on histology was also noted.

RESULTS

In 84% of the 50 cases the use of the Schiller test was a reliable means of predicting the presence or absence of invasive and intraepithelial neoplasia in the ectocervical squamous and endocervical glandular epithelium. The Schiller test was also positive in cases of adenocarcinoma *in situ* and in benign conditions.

However in three cases in which no abnormality of the Schiller test was present, high grade CIN III was detected histologically. This was confined to the endocervical canal. In two cases CIN was present in association with squamous metaplasia. (See table)

TABLE

The type of lesion associated with a positive or negative Schiller's test in fifty consecutive cone biopsies of cervix.

Type of lesion	*Schiller positive*	*Schiller negative*
Ectocervical squamous dysplasia	39	3
Infiltrating squamous carcinoma	1	0
Adenocarcinoma *in situ*	2	0
Squamous metaplasia	2	0
Ectropion	1	0
No pathological lesion identified	0	2

Examination of the midline blocks taken from the 12 and 6 o'clock positions from the anterior and posterior lips provided an accurate assessment of the histological findings in the cervical epithelium in 49 cases. The exception was a case of a small focus of squamous CIN I which was located at the 1 o'clock position. By contrast all three cases of squamous CIN III which were Schiller negative were represented in the midline blocks of cervix.

DISCUSSION

This study indicates that the routine application of aqueous iodine as the sole method of selecting blocks for histology in cone biopsy specimens is of doubtful value due to its occasional failure to detect squamous CIN. Failures were due to dysplasia, confined to the endocervical canal, which could not be detected by visualisation of the ectocervical surface. This represents a significant limitation to the use of this technique as the exclusive means of selecting blocks for histological examination. In two of three cases squamous metaplasia correlating to the Schiller positive areas was identified elsewhere in the specimen. Had this method been used to select blocks for histology, the metaplasia might have been thought to account for the Schiller positive area and a high grade CIN lesion would have been missed. These findings are perhaps not surprising since gynaecologists have identified a high percentage of false positive and false negative cases when this test has been used in clinical practice.[10]

In addition to the identification of CIN lesions the histological examination of all submitted tissue from cone biopsy specimens of the cervix is justifiable since it allows assessment of resection limits and exclusion of invasive malignancy.

Hysterectomy specimens of uterus and cervix are also commonly encountered in most histopathology laboratories and account for 600 specimens in our department annually. Might the Schiller test have a role as a screening test for the detection of unsuspected CIN in hysterectomy specimens where the uterus and cervix were removed for conditions unrelated to cervical disease? The current practice of taking histological blocks from the anterior and posterior lips of the cervix[11] would have generated 100 histological blocks and would have allowed the detection of 98% of the cases of established cervical intraepithelial neoplasia in this series. By contrast, sectioning Schiller positive areas identified by this technique would have generated 161 additional blocks but would have resulted in fewer (94%) cases of CIN being detected. Since the Schiller test is also positive in the presence of squamous metaplasia and ectropion which are frequently identified on hysterectomy specimens, the routine application of the technique would result in the submission of unnecessary additional blocks for histology. Furthermore since it is recognised that Schiller's test may be negative in the presence of an infiltrating carcinoma[6] confining histological sampling to Schiller positive areas could result in invasive carcinomas being missed.

These findings suggest that the routine application of iodine to hysterectomy specimens should not be adopted either as a means of selecting blocks for histological examination in cone biopsy specimens where CIN has already been established or as a screening procedure in hysterectomy specimens, given the possibility that iodine may induce artefactual changes which might be confused with CIN.[12]

Application of the Schiller test to cone biopsy specimens enables the macroscopic identification of dysplastic areas in a high proportion of cases. In a significant proportion of cases however such areas will be missed, so that application of the test would result in some high grade CIN lesions remaining unsampled. It is not therefore a valid alternative to histological examination of all the tissue submitted.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 151 – 156, October 1995.

An audit of therapeutic drug monitoring of anticonvulsants

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Accepted 14 August 1995

SUMMARY

An audit of therapeutic drug monitoring (TDM) of anticonvulsants was performed to assess both its use and misuse in the management of patients with epilepsy. Over a four week period all samples received for phenytoin, carbamazepine, sodium valproate and phenobarbitone assays were included in the audit. The aims were to establish the source of the specimens, the reasons for the requests and to ascertain what action, if any, would be taken when the result of the assay was provided. A total of 163 separate assays were performed over the four week period (43 phenytoin, 74 carbamazepine, 41 valproate, 5 phenobarbitone). Only 18.7% of all requests originated from the adult neurology department. The vast majority of tests had been ordered by junior medical staff (only 10% by consultants) and approximately 50% were 'routine' with no satisfactory clinical reason for the request offered. There was a tendency to manipulate prescribed doses on the basis of drug levels alone without taking the clinical picture into consideration. These results demonstrate a general ignorance, especially amongst junior medical staff, of the value of TDM of anticonvulsants, and reinforce the need for both an educative and interpretive service to be provided by the Chemical Pathology Department.

INTRODUCTION

Therapeutic drug monitoring (TDM) may be defined as the use of drug measurements in body fluids as an aid to the management of patients receiving drug therapy for the cure, alleviation or prevention of disease.[1] Several clinical studies have demonstrated benefit in utilising TDM to individualise dosing regimens in patients on anticonvulsant drugs where pharmacological response is not so easily established by clinical means or laboratory markers.[2-4] Although TDM assists in the optimisation of anticonvulsant therapy, clinical and other criteria are important and TDM should never be used as the sole basis for making dosage adjustments.[5] However there are few prospective studies showing any substantial long term benefit to patients from TDM of anticonvulsant, and some of the anticonvulsant drugs do not fulfil the criteria that are necessary for valid TDM. These criteria include:

a). a narrow therapeutic index.

b). a close concentration-effect relationship.

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c). absence of clinical markers of effect. (If the desired effect can be quantified by simple clinical measurements TDM are of little benefit.)

d). poor correlation between dose and plasma concentration or effect.

There is an impression of a general ignorance, especially among junior medical staff, with regard to the value and use of TDM of anticonvulsants and this has led to a large increase in demand for these tests and subsequent laboratory workload over the past 10-15 years. Indeed some reviews of TDM, in general, point to misuse and misapplication and a failure to apply the criteria for effective TDM.[6] In today's stringent financial climate there is also the issue of costs versus benefits to patients. Some reviews suggest that an education system, with help in interpretation of results to the prescribing doctor should be a high priority in centres performing these assays.[7] The concept of normal therapeutic ranges is controversial as frequently patients with epilepsy will have satisfactory control of seizures at levels below the normally accepted therapeutic range [8] while others require concentrations in excess of the normal therapeutic range without displaying toxic effects.[9,10] In view of these factors there is the potential for misuse and misinterpretation of TDM of anticonvulsants. The monitoring of patients whose seizures are well controlled and who are free of toxic side effects is also questionable.

It is because of these factors that this audit was performed to assess TDM of anticonvulsants in a teaching hospital, to establish why the test was requested, to assess the impact of the result on patient management and whether to attempt to provide an educative and interpretive service.

PATIENTS AND METHODS

Over a four week period in June 1993, all samples received by the biochemistry laboratory of the Royal Group of Hospitals, Belfast, for TDM of phenytoin, carbamazepine, sodium valproate and phenobarbitone were audited. The Royal Group of Hospitals is a major teaching hospital, with amongst other disciplines, an Accident and Emergency department, a respiratory intensive care unit, a paediatric department and the regional neurology and neurosurgery service. The source of the samples was identified and the drug assays were all performed using the established FPIA (fluorescence polarisation immunoassay) method (Abbott Diagnostics, Maidenhead, Berkshire, UK). Anticonvulsant assays were performed in batches on a twice weekly basis and the need for emergency assays at other times (including those outside normal laboratory working hours) was assessed by the Chemical Pathology registrar.

When the assay results were available the ward, out-patient department or general practitioner was phoned by the registrar (PCS) and the doctor who had ordered the test was contacted (e.g. if a senior house officer had ordered a test on a consultant's instructions, the consultant was contacted). The reason for the request was ascertained and the result of the assay given with the 'normal' therapeutic range, and the doctor was asked in view of this, as to what action, if any, would be taken in the prescribed dose for the patient. Subsequently he was given information on the interpretation of the result. All requests were allocated to one of 7 groups on the basis of the stated reason for the request, thus:

1. No specific indication ('routine'). The patient's epilepsy was well controlled and there was no clinical suspicion of toxicity.

2. A recent increase in the number of seizures, before which control had been reasonable, or continuing seizures (? compliance problem or too low a prescribed dose).

3. Recent change in dose of the medication, or had recently been commenced on the medication.
4. Possible symptoms and signs of toxicity and a drug level requested to verify this.
5. Status epilepticus.
6. Patient on potentially interacting drugs.
7. Overdose of anticonvulsant.

RESULTS

Over the four week period a total of 139 samples were received. Four of these were emergency samples which were performed outside of normal laboratory hours by the on-call technician (two overdoses in adults, one child with probable toxicity and another with status epilepticus in the children's intensive care unit). One hundred and fifteen (115) patients were on monotherapy to control their epilepsy while the other 24 patients were on two medications requiring the analysis of two separate anticonvulsant drugs, making a grand total of 163 separate assays (43 phenytoin, 74 carbamazepine, 41 valproate and 5 phenobarbitone). The sources of the requests are given in Table I and the reasons for the requests in Table II. Ten percent of the total hospital requests had been ordered by consultants, 22% by senior registrars/registrars and 68% by senior house officers. 11.5% of patient requests originated from general practice.

Phenytoin (26.4% of all requests)

In 20 routine assays (47% of phenytoin requests) in patients who were clinically well with no signs of toxicity, 18 out of 20 (90%) lay in the normal therapeutic range (10-20 mg/l), one was lower (6.4 mg/l), but no change in dosage was made, and one was higher (28.3 mg/l):

TABLE I

Sources of requests for TDM of anticonvulsants

Source	*Number of Patients*
Medical Wards	21 (15%)
Surgical Wards	5 (3.6%)
Medical Outpatients	18 (12.9%)
Neurology Outpatients	15 (10.8%)
Neurology Inpatients	11 (7.9%)
Intensive Care Unit	5 (3.6%)
Childrens Hospital Inpatients	28 (20.1%)
Childrens Hospital Outpatients	12 (8.6%)
Accident and Emergency	4 (2.9%)
Other Hospitals	4 (2.9%)
General Practice	16 (11.5%)

in this case a dose reduction was made even though the patient had no toxic symptoms. In the seven assays performed due to recent increased episodes of seizures, six out of seven displayed levels lower than the therapeutic range in keeping with either a compliance problem or too low a prescribed dose (all six either confronted the patient with regard to compliance or increased the prescribed dose), the other result was in the therapeutic range. In six cases of suspected toxicity, four were in the toxic range and the other two were in the upper normal range: in all cases a dose reduction was made. Five out of the six assays for status epilepticus were in a single patient receiving intravenous phenytoin.

TABLE II

Reasons for requests for TDM of the different anticonvulsants

Reason for request	*Phenytoin*	*Carbamazepine*	*Valproate*	*Phenobarbitone*
1. Routine level	20 (46.5%)	36 (48.6%)	26 (63.4%)	2 (40%)
2. Continuing seizures	7 (16.3%)	19 (25.7%)	12 (29.3%)	3 (60%)
3. Recent dose change	2 (4.7%)	8 (10.8%)	1 (2.4%)	0
4. Possible toxicity	6 (14.0%)	9 (12.2%)	1 (2.4%)	0
5. Status Epilepticus	6 (14.0%)	0	0	0
6. Interacting Drugs	0	1 (1.4%)	0	0
7. Overdose	2 (4.7%)	1 (1.4%)	1 (2.4%)	0

Carbamazepine (45.3% of all requests)

In 36 routine assays (49% of carbamazepine requests), 29 were in the normal therapeutic range (8-12 mg/l), four were lower with no increase in dose being prescribed and three were above the normal range (two patients had their dose reduced even though they were well with no toxic symptoms). In 19 patients with recent seizures, 14 were below the therapeutic range and the dose was either increased or the patient challenged regarding compliance. In the nine suspected toxicities, seven out of nine were in the 'toxic' range with the other two at the upper limit of the normal range: all doses were reduced.

Sodium Valproate (25.2% of all requests)

Out of 26 routine assays (63% of valproate requests), 13 were in the normal range, ten were below the therapeutic range (eight of these patients were either challenged with regard to compliance or had their prescribed doses increased) and three patients had valproate concentrations higher than the therapeutic range (all had their prescribed dose reduced). In the 12 patients with recent increase in seizures, six had levels lower than the normal therapeutic range and the other six lay in the therapeutic range; the six with the low levels had their doses increased. The one patient with suspected toxicity had a level in the normal range and the dose was reduced. The one overdose patient had a level of 610 mg/l but remained perfectly well with apparently no side effects.

Phenobarbitone (3.1% of requests)

Two routine (40%) checks had normal therapeutic levels, and of the three patients with recent increasing seizures, two had levels below the therapeutic range and doses were increased: one had a normal therapeutic level but nonetheless the prescribed dose was also increased.

DISCUSSION

This audit illustrates that there is misunderstanding with regard to the concept and uses of TDM of anticonvulsant drugs. Of particular interest is the fact that the vast majority of tests were ordered by junior medical staff and a comparatively small number (18.7% of requests) came from the adult neurology in-patient and out-patient departments, despite the fact that this department manages most patients with epilepsy. This most probably reflects their greater understanding of the usefulness of TDM in different circumstances. Also of interest is the fact that for approximately half of requests there was no specific indication for drug level measurement. Only one of this type of request came from the neurology department. It appears that there is little potential benefit to the patient in this category as the majority of levels lie within the normal therapeutic range. Of more concern is that in patients with well controlled epilepsy, without toxic side effects, but with drug levels above the therapeutic range, there was a tendency to 'treat' the drug level and reduce the dose, despite the fact that some of these patients may require higher plasma concentrations to control their seizures. From this audit we can also see that most of those with either recent increasing incidence of seizures or with suspected toxicity displayed the appropriate low or high levels respectively and that clinical judgement was accurate. The notable exception to all of the above is sodium valproate. This drug displays a wide circadian variation with plasma concentrations varying by as much as 100% across the dosage interval. The normal therapeutic or target range is difficult to define, plasma concentrations are no better a guide to clinical response than is dose, and toxic effects show no clear relationship with level. These facts are borne out by our results and it is suggested that routine monitoring should not be practised and is, in fact, potentially misleading.[11, 12]

Monitoring of carbamazepine can be of use in some circumstances. The major problem with its measurement relates to its metabolism in the liver to carbamazepine–10, 11–epoxide, which is active but is not measured in most routine assays, including our own. However, the active metabolite can be measured using HPLC (high performance liquid chromatography), but this is not routinely available in most biochemistry laboratories and is expensive and time consuming to perform. Monitoring of carbamazepine is also complicated by individual pharmacodynamic variability; it induces its own metabolism and its metabolism can be altered by other anticonvulsants. The dosage of carbamazepine is a poor guide to plasma concentration and TDM is useful when seizure control is difficult.[13, 14]

Of all the anticonvulsants phenytoin appears to be the most useful to monitor.[15] It displays dose dependent pharmacokinetics and the hepatic system which metabolises it can become saturated, meaning that there is a non-linear relationship between dose and plasma concentration with the saturation levels varying between individuals. The normal therapeutic range has been designated 10-20 mg/l but some patients are controlled both at lower and higher levels and the prescribed dose of phenytoin should not be reduced on the basis of a high level if the patient is free from side effects.

With phenobarbitone, tolerance can develop on longer term therapy and there is a poor correlation between plasma concentration and adverse effects, and very low levels can have significant antiepileptic effects. There is a potential interaction with valproate which can lead to high phenobarbitone levels but in general TDM is not of much use except in children.

The results of this audit demonstrate an apparent lack of knowledge with regard to the value and use of TDM of anticonvulsants and a tendency to perform levels as a matter of routine. There is also a tendency to manipulate drug doses on the results of plasma levels alone,

aiming to establish the patient in the centre of the normal therapeutic range without taking the whole clinical picture into consideration. It is widely recognised that phenytoin is the most helpful drug to monitor because of its saturation kinetics, and that monitoring sodium valproate offers little reliable information and in fact can be misleading. The need to monitor patients whose seizures are well controlled is debatable and therapeutic decisions should never be based solely on drug concentrations. TDM can be useful in the assessment of non-compliance. For instance, repeatedly zero plasma concentrations in a patient who is 'well controlled' probably indicates misdiagnosis or that therapy is no longer required. The 'normal' therapeutic range should be used for guidance only with the knowledge that some patients may be well controlled at lower or higher levels and similarly patients can display toxicity in the normal therapeutic range. Patients on two or more medications merit more regular monitoring as there is potential for drug interactions and it can be difficult to tell which drug is causing possible toxic side effects or is not being prescribed in an appropriate dose. Education provided by the laboratory into the interpretation of results is essential and it is envisaged that guidelines will be drawn up to help medical staff. Cost effectiveness is of major importance in today's climate and the question should be asked "Is knowing a drug level going to help me in the management of this patient at this particular time?"

ACKNOWLEDGEMENT

We wish to thank Miss Elaine Gilmartin for her assistance with the manuscript.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 157 – 163, October 1995.

Alcohol intake in patients admitted acutely to a general medical unit

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Accepted 10 September 1995

SUMMARY

The role of alcohol in causing acute medical admissions is recognised but not well quantified. Using a questionnaire we have studied prospectively alcohol intake in patients aged 18-60 years admitted to a medical unit and have analysed the contribution of alcohol to their admission. One hundred and six patients (61 male : 45 female) who fulfilled our preset age criteria were studied. Alcohol intake (mean ± SEM) was 9 ± 1 and 12 ± 1 units on average and heavy drinking days respectively, and 38 ± 6 units during their last drinking week. Gamma glutamyl transferase (GGT) was >60 U/l (upper limit of normal) in 29 (n = 92). Eighteen (30%) men had drunk >50 units and seven (16%) women had taken >35 units in their last drinking week. In 25 (41%) men and 11 (24%) women alcohol intake was felt to contribute to their admission. In this subgroup, intake was 15 ± 2 and 20 ± 1 units on average and heavy drinking days respectively, and 87 ± 13 units in the last drinking week. GGT was available in 29 and was abnormal in 18. Admission diagnoses were drug overdose (n = 16), alcohol withdrawal symptoms (n = 7), liver disease (n = 6), haematemesis (n = 14) and others (n = 3). Fifteen (42%) felt they had a definite alcohol problem. The use and abuse of alcohol contributes significantly to the general medical workload in the age group studied.

INTRODUCTION

It is widely accepted that excessive alcohol consumption causes many different problems within our society.[1] It may contribute to physical and psychological ill health[2,3] as well as accidents.[4]

A number of previous studies have reported alcohol-related problems in general hospital patients.[2] There have been marked differences in prevalence depending on the definitions of alcohol- related illness used, and the respective patient populations studied.

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Previous studies have concentrated mainly on identifying those patients with alcohol dependence or problem drinking. In contrast there have been few reports examining alcohol intake in patients admitted to medical units.[6-7] Our aims were to record alcohol consumption in patients requiring acute medical admission and to assess the contribution of alcohol to the presenting illness. We also wished to study the value of serum gamma glutamyl transferase activity in identifying patients with potential alcohol problems, and to assess both dependence and the patients' perception of that dependence.

PATIENTS AND METHODS

Consecutive patients aged 18-60 years requiring emergency admission to a general medical unit in the Belfast City Hospital were identified over a six month period beginning in November 1990. Patients admitted to surgical or observation wards were not included. After informed verbal consent a questionnaire was used to obtain information about their use of alcohol. This was designed to assess patients' alcohol consumption, to study dependence and withdrawal symptoms and to ascertain their perception of the problem. Alcohol consumption on an average drinking day was quantified. Following this, consumption on a heavy drinking day was quantified and consumption during a week was estimated by asking them to say whether alcohol intake was 'light', 'average' or 'heavy' on each day during their last drinking week. The number of units of alcohol (equivalent to 8 g alcohol) during each of these periods was calculated.

Information on dependence and problem drinking was obtained using the 'CAGE' questionnaire.[8,9] For our study problem drinkers were defined as those giving a positive reply to one or more of the 'CAGE' questions. Symptoms after withdrawal of alcohol were sought and graded from no symptoms through mild symptoms (defined as mild shakiness, nausea, vomiting and loss of appetite at least once during the last month) and severe symptoms (mild symptoms plus hallucinations and seizures or continuous drinking for the last month without withdrawal). At the end of the questionnaire patients were asked directly if they considered themselves to have an alcohol problem. A sample questionnaire is available on request.

Venous blood was analysed for mean cell volume, asparate aminotransferase (AST) alaninine aminotransferase (ALT) and gamma glutamyl transferase (GGT).

At discharge, case notes were reviewed by J McK to establish the diagnosis, reason for admission and whether or not alcohol intake had contributed directly to that admission.

Alcohol consumption during the last drinking week was grouped according to risk groups as defined by the Royal College of Physicians.[10] They have suggested that weekly consumption <21 units in men and <14 units in women is "safe", 21-49 units in men and 14-35 in women is "hazardous" and >49 in men or >35 in women is "dangerous". A value of $p<0.01$ was required for significance.

RESULTS

Three hundred and seventy-two patients were admitted during the study period. One hundred and six (61 male : 45 female) fulfilled the age criteria. The mean age was 38 ± 1 years.

Alcohol intake is shown in Table 1. This varied from 0 to 250 units per week. A breakdown according to accepted risk groups is shown in Table II. Forty-eight per cent of male admissions and twenty-two percent of female admissions had been drinking more than is considered safe.[10]

TABLE I

Alcohol intake (units) in the study population (mean ± SEM).

	Men	*Women*	*Total*
Average day	12.6 ± 1.2	4.6 ± 0.7	9.2 ± 0.8
Heavy day	16.4 ± 1.3	5.5 ± 1.0	11.8 ± 1.0
Last drinking weel	53.9 ± 9.4	17.6 ± 5.3	38.5 ± 6.1
	n = 61	n = 45	n = 106

TABLE II

Alcohol consumption, CAGE questionnaire results, withdrawal symptoms and GGT accoding to recognised risk groups (n = 106).

	Men (n = 61) Units/ Week	*n*	*Women (n = 45 Units/ Week*	*n*	*CAGE +ve n*	*CAGE −ve n*	*Withdrawal Yes*	*Symptoms No*	*GGT (u/L)*	*GGT Normal (<60 u/L)*	*(n = 92) Abnormal (>60 u/L)*
Safe	< 21	32	< 14	35	6	61	2	65	52.8 ± 12.8	49	8
Hazardous	21-49	11	14-35	3	3	11	2	12	74.6 ± 17.3	5	7
Dangerous	> 49	18	> 35	7	20	5	20	5	194.0 ± 54.1	9	14

TABLE III

Alcohol consumption on average and heavy days and last drinking week compared to biochemical and haematological markers using Spearman rank correlation coefficients.

	Average		*Heavy*		*Week*	
	RS	*P*	*RS*	*P*	*RS*	*P*
Average	–	–	0.89	< 0.001	0.84	< 0.001
Heavy	0.89	< 0.001	—	—	0.79	< 0.001
Weekly	0.84	< 0.001	0.79	< 0.001	—	—
MCV	0.26	< 0.01	—	(NS)	0.26	< 0.01
AST	0.30	< 0.01	—	(NS)	—	(NS)
ALT	0.28	< 0.01	0.29	< 0.001	—	(NS)
GGT	0.29	< 0.01	—	(NS)	0.32	< 0.01
AST/ALT ratio	—	(NS)	—	(NS)	—	(NS)

(NS: p> 0.01)

The relationships between the biochemical and haematological parameters and alcohol consumption are shown in Table III. Alcohol consumption on average and heavy drinking days correlated significantly with each other. Alcohol consumption during the last drinking week correlated with both MCV and GGT but not with either AST or ALT. The relationship between GGT and risk categories of alcohol consumption is shown in Table II. Of 35 whose consumption was considered unsafe GGT was abnormal in 21 suggesting a sensitivity of 60%. Of 57 patients whose consumption was considered safe 49 had a normal GGT indicating a specificity of 86%.

Twenty-nine (21 male : 8 female) had a positive CAGE enquiry (Table II). The sensitivity and specificity of a single positive CAGE answer in detecting patients who drink more than is safe was 59% and 91% respectively. Sensitivity improved to 80% if only those with "dangerous" intake were included. Six patients with a positive CAGE did not report excessive intake in their last drinking week. Two of these had a previous history of alcoholism, one other had collapsed with a serum alcohol level of 295 mg/dl and two had been advised to reduce their intake, because of a duodenal ulcer and epilepsy respectively.

Twenty-four (17 male : 7 female) had withdrawal symptoms (Table II) and in six men symptoms were severe. Sensitivity and specificity of these symptoms in detecting those who drink more than is safe was 56% and 97%. Fifteen (11 male : 4 female) believed they had a definite alcohol problem. All but the previously mentioned two patients were in the 'at risk' categories of alcohol consumption.

In 36 of our 106 patients alcohol intake contributed directly to their admission (Table IV). In three of the 16 with an alcohol related overdose, serum alcohol was available on admission and was >200 mg/dl in all. Gastritis was confirmed by endoscopy in all patients presenting with haematemesis. Two patients had collapsed when intoxicated. The 34 year old man with gout drank 189 units of alcohol per week.

Alcohol consumption in those with an alcohol related admission is shown in Table V. GGT was abnormal in 62%. Twenty-two (61%) of these patients had a positive CAGE enquiry, 21 (58%) reported withdrawal symptoms and in six (17%) symptoms were severe. Only 15 (42%) felt they had a definite alcohol problem.

TABLE IV

Final admission diagnoses in those patients whose alcohol ingestion contributed to admission.

Diagnosis	n	M/F
Drug overdose	16	9/7
Alcohol withdrawal	7	7/0
Liver disease	6	3/3
Haematemesis	4	4/0
Collapse	2	1/1
Gout	1	1/0

TABLE V

Alcohol consumption in those patients whose alcohol ingestion contributed to admission.

	Men	*Women*	*Total*
Safe	6	3	9
Hazardous	4	2	6
Dangerous	15	6	21

DISCUSSION

A questionnaire approach had been used extensively to assess alcohol dependence.[8, 9, 11, 12] Hesselbrock et al [11] obtained corroborative evidence from relatives of patients admitted to an alcoholism unit and suggested that the information obtained from patients was accurate. In a study of patients attending a liver clinic however a personal interview was found to be less reliable.[13] If some of our patients denied an alcohol problem they may have underestimated their consumption. Our results show that a large proportion of our medical patients drink more alcohol than is considered safe. In a random sample of the Belfast population 27% of men and 12% of women of a similar age group (n=4598) drink more than is safe (Prof. A E Evans, Belfast Monica project, personal communication). A higher proportion of heavy drinkers (48% of men, 22% of women) was found in our inpatient survey. This difference between hospital and general populations has been noted elsewhere[14] and may imply an aetiological role for alcohol in admission to hospital. It also may reflect differing alcohol intakes in groups more susceptible to medical illness because of socio-economic reasons for example.[6]

We found that alcohol ingestion contributed to 34% of admissions but was excessive in only 75% of this group during their last drinking week. We have used a cut-off of 21 units for men and 14 units for women during the last drinking week to predict potential alcohol problems.[10] This seems justified as 77% of the 35 patients in our total study who would drink more than this had an alcohol related admission. By contrast alcohol contributed to the admission of only 13% of patients drinking less. Other studies have reported alcohol related illness as causing 16-27% of admissions to different units. [6, 15, 16, 17, 18] The higher percentage of alcohol related illness in our study may be due in part to the large number of cases of overdose. We were careful to include only those patients whose admissions were alcohol related. Many other patients were admitted with drug overdose but alcohol was not felt to contribute to their admission. Other patients admitted to hospital with alcohol related overdose also may have been observed overnight in the accident and emergency department. The overall spectrum of alcohol related diagnoses reported here, however, is similar to that previous publications.[6,15]

Mean cell volume and GGT correlated with weekly alcohol consumption. This has been noted previously[19, 20] and might further support the accuracy of our questionnaire. The sensitivity of GGT in detecting alcoholism has been reported to range from 54-85%.[21] The sensitivity and specificity of GGT in our inpatient population, in which there is a high prevalence of excessive drinkers make it a useful test in this group, but it may be of less use in general population screening[21] where there is a lower prevalence of alcoholism.

It has been suggested that multiple discriminant analysis of a number of markers of alcohol ingestion might improve the specificity of biochemical testing.[22] The specificity of 86% is good and would be improved further if patients with other obvious causes of elevated GGT, eg obstructive jaundice had been excluded. We did not exclude any available GGT result from analysis.

The low sensitivity of GGT has led to the search for other markers for alcohol consumption such as carbohydrate deficient transferrin,[23] though technical problems with this assay must be overcome[19] before it is more widely available. The other major method for screening for alcohol problems is by questionnaire. Our CAGE enquiry and simple questions about withdrawal symptoms had a very similar sensitivity and specificity to GGT.

Screening tests are useful in alerting a doctor to potential alcohol abusers, and may stimulate further history-taking. There is however, no substitute for the alert doctor with a high degree of suspicion, and yet sufficient tact to be able to take a good drinking history without alienating the patient.[24]

In conclusions we have found a high prevalence of alcohol related problems in general medical inpatients. Some are aware of the problem while others, particularly the young, do not admit to any difficulty. A simple counselling session may benefit these patients,[25] but follow-up can be difficult.[26] Identification of the problem has important implications for health promotion. If effective therapy is to be achieved strong links must be developed between hospital and community services.

ACKNOWLEDGEMENTS

We wish to thank the junior medical staff of Level 6, and the Department of Clinical Chemistry, Belfast City Hospital for their help with this study. We are also grateful Mrs Marie Loughran, Miss Bronagh Shannon and Miss Cathy Gilmartin for secretarial and photographic assistance.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 164 – 171, October 1995.

The Visual Arts in Northern Ireland Hospitals

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Accepted 18 August 1995

SUMMARY

Since 1989 there has been a burgeoning of the visual arts in Northern Ireland hospitals. This paper compares the three organisational models for hospital arts currently operating within the Province and in an overview discusses ways to coordinate working practice for future development of the visual arts in local hospitals.

INTRODUCTION

Within the rapidly changing culture of the National Health Service there is a growing recognition that the visual arts have an effective contribution to make to the quality of both the physical and social health care environments.[1] Art projects have been established in many hospitals, and aesthetic considerations are increasingly being given to newbuild and refurbishment schemes.[2] Within Northern Ireland (NI) there are currently three organisational models for hospital arts: the Royal Hospitals' in-house Arts and Environment Project; the art programme at Antrim Hospital directed by Health Care Arts, Dundee; and ArtsCare, which acts as an umbrella group in the provision of arts for many NI hospitals. These three models represent, respectively, a local hospital group, a national organisation and a provincial organisation. This paper looks at the structures of the three models and their approaches to the visual arts within the hospital environment, and in an overview identifies common areas of interest and initiatives which could encourage a more innovative development of the visual arts within NI hospitals.

THE ARTS AND ENVIRONMENT PROJECT, THE ROYAL HOSPITALS, BELFAST, 1989-95

The Arts and Environment Project, which was established at the Royal Hospitals in 1989, has the stated objective of improving and enriching the total environment of the hospital. The Project is run by an Advisory Committee, consisting of members of staff and practising artists, and centres on an artist-in-residence. Since the inception of the Project there have been two artists-in-residence, each employed on a part-time basis (22 hours per week). The artist-in-residence has an extensive job description involving a wide range of artistic, administrative and managerial skills, including fund-raising. In addition to producing artwork, the artist-in-residence is also responsible for commissioning and co-ordinating the work of other artists and involving patients, staff and the local community in appropriate aspects of the Project.

The Arts and Environment Project at the Royal Hospitals represented an innovation for hospitals in NI and was viewed by the Department of Health and Social Services (DHSS) as a pilot study for other Health and Social Services Boards within the province. In its first

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four years, Michael Swallow, who was then Chair of the Advisory Committee, and Ruth Priestly, the first artist-in-residence, had the difficult task of establishing the groundwork for the Project. This included building up good working relationships with individuals and departments and establishing the credibility for contemporary art within a highly structured and well-established hospital organisation. The setting up of the Arts and Environment Project was documented in an evaluation of the Project carried out in 1991.[3]

A wide range of art activities, including the performing arts and creative writing, has been undertaken by the Arts and Environment Project. The visual artwork falls broadly into five categories:

— artwork produced by the artist-in-residence;

— commissioned artwork;

— patient workshops;

— artwork by students from the Faculty of Art and Design, University of Ulster (UU);

— a collection of original artwork for loan to departments within the hospital.

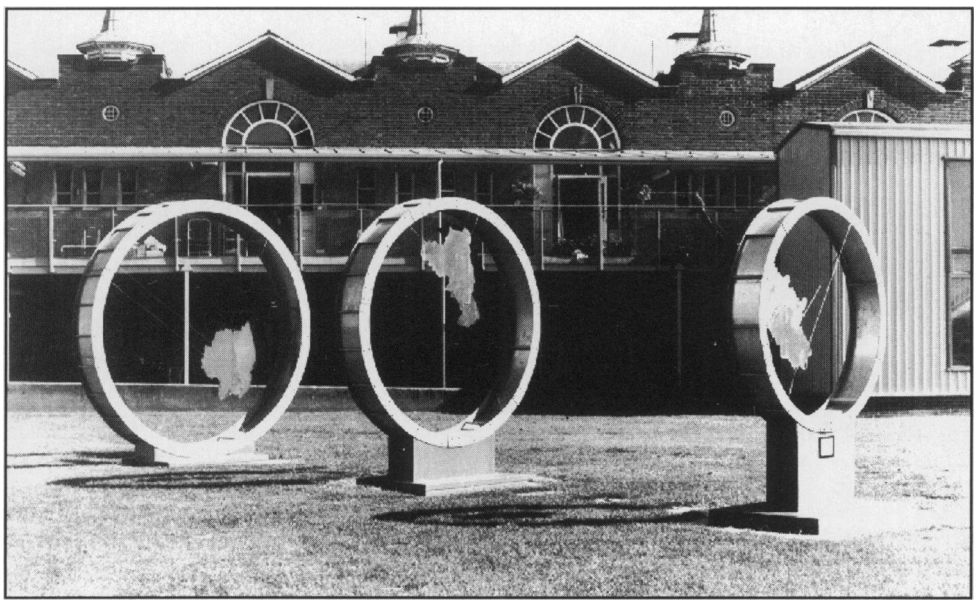

Fig 1. Lorna Flanagan, *Microscope* (1994) Royal Hospitals, Belfast.

Murals are a dominant feature of the artwork to date. They have been introduced into four prominent public sites: Ruth Priestly's aquarium and wave murals at 'A' Block (1990-92); Eileen Bannon's *Medicinal Herbs and Plants* mural (1993) in the link corridor; Brendan Ellis' *Four Seasons* mural (1993) at the entrance to the Outpatient Department; and a mural, untitled (1992), by Ben Allen in Chatters Restaurant. Two major site specific sculptures have also been commissioned: a sculpture in wood, untitled (1993) by Owen Crawford and a sculpture in aluminium and copper, *Microscope* (1994) by Lorna Flanagan (Fig 1).

As the Project has progressed, many staff feel that it is improving the hospital environment, and it has stimulated some staff throughout the site to consider the aesthetics of their own

working areas. During the course of research by the author for a case study on the Project a number of medical staff indicated that they find it hard to reconcile the Arts and Environment Project with financial cutbacks in clinical areas and remain cynical about the value of art within the hospital environment.[4] Despite the fact that the Project does not receive funding from any medical budget, there remains some resentment that an art project can go ahead while financial constraints in the clinical areas bear ever harder. Such comments would, of course, represent a common attitude among many staff – and public – towards art in hospitals and there would seem to be a need for those responsible for the provision of art in hospitals to highlight the value of creative thought and activity and its benefit to patients and visitors for whom the hospital environment can be both intimidating and threatening.[5] The vulnerability and stress often experienced by patients and visitors underline the need for supportive environments, and a discriminating use of the arts contributes significantly towards creating such environments, giving users a sense of self-identity and self-worth. The quality of the working environment can also have a major impact, for good or ill, upon staff performance, morale and self-worth, an important factor for the Royal Hospitals as a major employer.

The administration of the Project, including fund-raising, is undertaken by the Chair of the Advisory Committee, a full-time consultant physician, and the artist-in-residence.

Sources providing financial support for the Project include the Arts Council, the Gulbenkian Foundation, the NI Voluntary Trust and Hospital Trust Funds.

The commissioning of a new children's hospital and the appointment of local artist, Rita Duffy, as arts adviser to the design team presents an exciting opportunity for the visual arts to be given a major role in this newbuild, directly influencing the way users experience it. The rebuilding of the Royal Victoria Hospital represents a further opportunity for art involvement from the earliest stage of planning. As with all major capital projects the arts should be considered as an integral part of the planning process, necessitating the appointment of an arts adviser from the outset of planning to allow for co-ordination between all members of the design team including architects, designers, engineers and arts adviser.[6] Now that architects for the new building have been commissioned such an appointment is opportune.

The Arts and Environment Project has become an established feature of the Royal Hospitals. It has now established its credibility and the time is ripe for imaginative, high quality artwork which would be more challenging artistically.

ART PROGRAMME AT ANTRIM HOSPITAL DIRECTED BY HEALTH CARE ARTS, DUNDEE, 1991-95

An Artworks Group was formed in response to the commissioning of the Antrim Hospital, which was officially opened in July 1994, to initiate a programme of art for the new building. Several years into the project the Artworks Group recognised the need for specialist expertise and advice in organising and managing the art programme, and in 1991 Health Care Arts, Dundee were appointed as external art consultants to oversee the project.

Health Care Arts have considerable expertise in introducing and developing art programmes in hospitals throughout Scotland and have wide experience in the area of fund-raising. The Director of Health Care Arts, Elizabeth McFall, hails from County Antrim where her family still lives. She is a graduate of the Faculty of Art and Design, UU. McFall is therefore familiar with social and political factors within NI and has an awareness of the local art scene. The huge administrative workload in organising art in hospitals and the management of commissions is a crucial service which Health Care Arts undertake. Their initial

appointment was for one year, with their contract renewable annually; their current contract expires in October 1995.

Health Care Arts interests focus on the visual arts – they are not involved in the performing arts. They have a major input into the craft sector and are the biggest craft commissioners in Scotland.[7] According to McFall the crafts have a particularly wide appeal in that people are interested in and appreciate how things are made even if they cannot grasp the fuller artistic references or significance. Health Care Arts' aim is that artwork should be of the highest possible quality and should integrate with the surroundings.

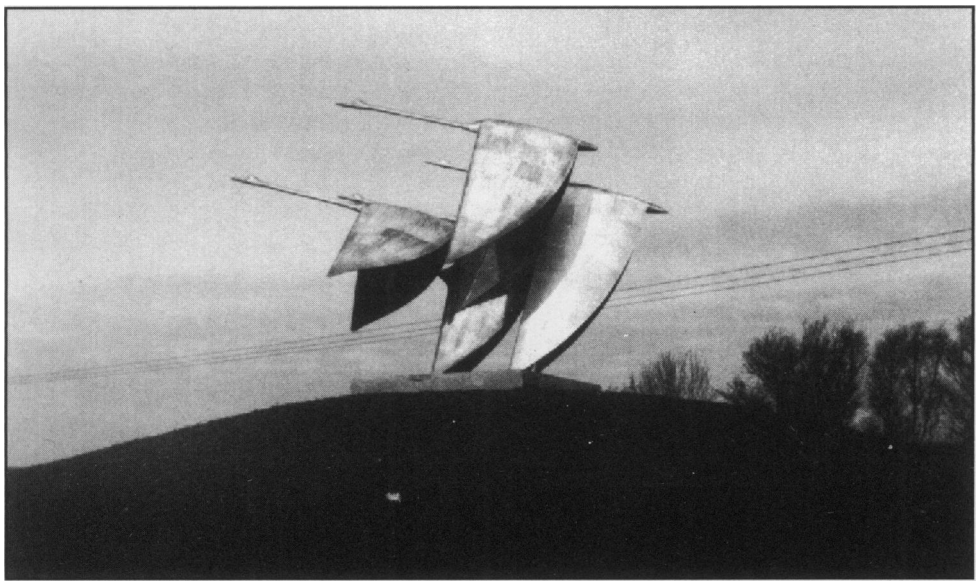

Fig 2. Eamon O'Doherty, *Swans in Flight* (1994) Antrim Hospital.

The Artworks Group, under the direction of Health Care Arts, have been selective in their approach, undertaking a staged introduction of artwork into the new building. A series of artworks was planned to be *in situ* for the official opening of the hospital and the main elements of this were:

— a ceramic commission for the Outpatient Department by Diane McCormick

— two sculpture commissions for the hospital grounds by Brian Connelly and Eamon O'Doherty (Fig 2)

— a schools project

— an exhibition space

The initial programme centres on three major commissions which have set a standard at the outset against which future artwork can be judged. The Artworks Group have resisted 'decorating' walls or covering large areas quickly, as is the aim with some large-scale murals, adopting instead a more considered approach.

While the Antrim Hospital is externally attractive – a low-level building with the emphasis upon natural materials, situated in a pleasant rural setting - the interior is, by contrast, predictable, bland and institutional. The main entrance to the hospital has few distinguishing

features and the entrance foyer is cold and unwelcoming. Internally the main corridors of the three levels have a common colour scheme, and conventional hospital signage has been used. At Antrim Hospital the function of the artwork is to humanise and personalise a sterile, institutional environment rather than to complement or enhance a stimulating architectural design. This may be partly due to the nucleus design of the building which precludes a total integration of art and architecture producing as it does a hospital design to a stereotype. Also, the appointment of Health Care Arts several years into the planning process ruled out close co-ordination and consultation with members of the design team from the outset.

While Health Care Arts give leadership and management to art projects, one of their main roles is that of facilitator, enabling local art committees to make their own choices and decisions. This is done through an educative process of presenting examples of good practice demonstrating the richness and scope of the visual arts. As part of this process the Artworks Group visited several art exhibitions, including final year degree shows at the Faculty of Art and Design, UU. This helped to acquaint the Group with a wide range of contemporary art, including some of the more innovative art, and also gave an opportunity to meet new artists.

Considerable time and energy have been expended by the Artworks Group in fund-raising. A 'percent for art' policy was not adopted at Antrim Hospital, and with foresight the ring-fencing of a proportion of the building costs to finance an arts programme would have freed the Artworks Group to utilise their energies in the commissioning and purchasing of a greater number of artworks. It is hoped that the experience with fund-raising at Antrim Hospital will encourage those involved in the commissioning of new health buildings to consider adopting a 'percent for art' policy.

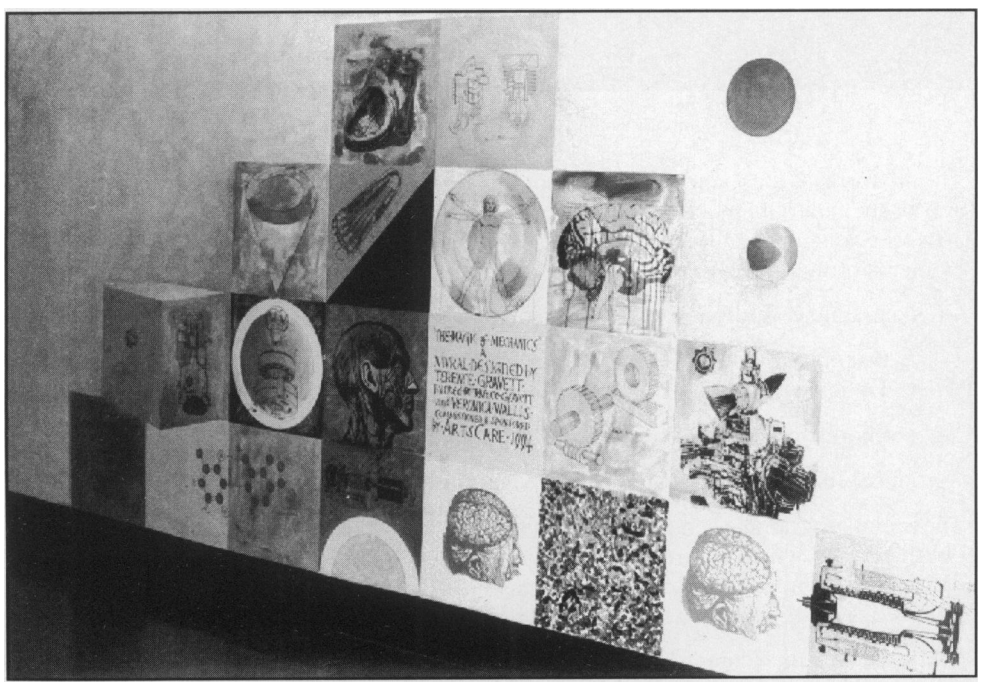

Fig 3. Terence Gravett, *The Magic of Mechanics* (1994) Ulster Hospital, Dundonald.

In March 1994 the Antrim Hospital became operational and, as many of the original Artworks Group are no longer directly involved with the hospital, a new art committee is being formed.

ARTSCARE, 1992-95

ArtsCare is a voluntary trust established in 1992 by the DHSS to promote and co-ordinate the development of the arts in health care environs throughout NI. ArtsCare was established in response to the Arts and Environment Projectat the Royal Hospitals which was viewed by the DHSS as a pilot project for a local arts organisation operating within the public health care sector. ArtsCare is run by a Board of Trustees who represent a broad spectrum of the arts and health care.

The role of ArtsCare is to work as activator and catalyst in conjunction with hospital and community trusts and district medical units in NI, and this is achieved through establishing a framework of ArtsCare groups in health care setting throughout the province. ArtsCare groups have a large measure of autonomy within each hospital and it is the responsibility of individual groups to identify the arts needs for their own environment. When an ArtsCare group is established, a member of the Board of Trustees is co-opted on to the committee and this allows for co-ordination and support with the core organisation. The groups which have been most successful are those with interested and enthusiastic committee members.

ArtsCare groups can apply to the Board of Trustees for funding for projects but are also encouraged to make their own efforts to secure funding.

ArtsCare is involved in promoting a broad spectrum of the arts including both visual and performing arts. The major input into the visual arts includes:

— (a) the appointment of part-time artists-in-residence at Green Park Healthcare Trust, Belfast, Knockbracken Healthcare Park, Belfast, and Belfast City Hospital

— (b) a commissioned mural at the Ulster Hospital, Dundonald, by Terence Gravett (Fig 3)

— (c) a series of patient workshops at Windsor House, Belfast City Hospital

— (d) a collection of original artwork for loan to individual ArtsCare groups

ArtsCare has developed a strong community arts base. Many of the visual arts projects have patient involvement and it is noteworthy that in the visual arts they have had a major input in the area of mental health, such as long-stay psychiatric hospitals, thus presenting greater opportunities for patient participation than in acute hospitals where the artistic emphasis is usually on environmental enhancement. The appointment of artists-in-residence at Knockbracken Healthcare Park, Green Park Healthcare Unit Trust and Belfast City Hospital has provided a firm base for the development of an arts provision on these three major hospital sites.

In its short history, ArtsCare has made a major contribution to the provision of art in health care environs in NI. ArtsCare groups have been established in units within all four Health and Social Services Boards, increasing awareness of the hospital environment and its potential for the arts. Support from the DHSS, who were instrumental in its establishment, gives it a firm credibility base from which to operate.

With ArtsCare groups growing in number, and the consequent growth in arts activities, the demand on the part-time voluntary Chair and Board of Trustees must be great and it is difficult to see how the organisation can be run on this basis in the long term. With more

people, services could be extended and enhanced to facilitate the growing number of ArtsCare groups and the development of art in hospitals and other health care units throughout the province.

OVERVIEW

The three organisational models presented here have been largely responsible for a rapid development of the visual arts in NI hospitals over six years. The innovative activity of the Arts and Environment Project at the Royal Hospitals, the educative and managerial expertise of Health Care Arts at Antrim Hospital and the strong community arts base of ArtsCare are all major factors in this development. It is the author's view that there is room for all three models within the province.

There are, however, common areas of interest and initiatives which could be developed for the benefit of all organising bodies in the province. These include:

— (a) the fostering of communication networks at committee level between all organising bodies.

— (b) the dissemination of information, advice and examples of good practice. This could take place through conferences or seminars which encourage debate and dialogue. Both the Arts Council and the Faculty of Art and Design, UU, have played a significant part in encouraging art in hospitals and could have a role in stimulating debate. Such forums should also be of interest to architects and planners within the Estates Services Directorate of the DHSS who, through new hospitals buildings and refurbishment schemes, can influence and encourage a greater degree of integration between art and architecture. The publication of information packs, would also contribute towards improving art practice. The dissemination of information and models of good practice could also be useful in attracting sponsorship for projects.

— (c) education and training initiatives for artists and NHS staff interested in the role of the arts in health care environments. Understanding the processes of artistic thought and activity can be as alien to hospital staff as can the clinical environment for the artist. The marrying of art and hospital practice requires understanding on the part of both artists and NHS staff, and local co-ordination of resources could provide an effective network of training and education initiatives benefiting both hospital users and art practitioners.

— (d) issues of finance and fund-raising. Common sources of funding tapped by all three models include the Arts Council, the NI Voluntary Trust, Association for Business Sponsorship of the Arts, DHSS and commercial sponsorship. Considerable time and energy are expended by committees in raising funds and this is an area in which ArtsCare could take the lead and have a major role as a funding body. Opportunities to apply for funding could be extended to projects which do not come under the umbrella of ArtsCare and, as is good practice, the source of funding would be clearly acknowledged alongside the artwork.

A process of monitoring and evaluation of art projects in hospitals has much to commend it and has great value in maintaining overall standards, improving quality, encouraging innovation and providing reassurance of merit to fund-aiding bodies.[8] Important lessons can be learned which can influence future art practice and provide models of good practice. While evaluation is a major commitment in terms of time and resources, benefits could prove invaluable in the long term development of the arts in local hospitals.

With co-operation, debate and dissemination of information the firm base which has been established locally could be improved upon and developed, leading to a bolder and more stimulating approach to the visual arts in hospitals and contributing towards the many varied and distinct needs of those for whom hospitals exist.

ACKNOWLEDGEMENT

I wish to acknowledge the invaluable support and guidance of Dr. John Nixon, Lecturer, Faculty of Art and Design, University of Ulster.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 172, October 1995.

Book reviews

Basic Sciences for Obstetrics and Gynaecology. Fourth Edition. Tim Chard and Richard Lilford. Springer-Verlag. ISBN No. 3-540-19903-9. £19.50.

The authors of this book honestly and correctly admit, in their preface, that the underlying philosophy is to address only those facts which are neither speculative nor contentious. Surprisingly, in a subject which is full of speculation and contention there are 194 pages of fact. Over the years this book has provided an excellent starting point and end point for reading for Part I Membership of the Royal College of Obstetricians and Gynaecologists.

Having acknowledged the limitations of the book, it would be unreasonable of me to pick holes in specific sections. There are, however, glaring deficiencies in molecular biology, which is only explained extremely superficially, in sex steroid endocrinology where only the most major hormones earn a mention, in statistics which has increased by just over a 100% from one page to two pages from the first edition but is still woefully inadequate, and in the explanation of ultrasound and doppler.

I recommend this book to all Part I Membership candidates. However, there are no references in this text. It contains only the most superficial knowledge and can act only as an aid memoire for this subject.

NEIL McCLURE

Pelvic Floor Re-education, Principles and Practice: Schussler, Laycock, Norton and Stanton. Springer-Verlag. ISBN No. 0-387-19860-1. £65.00.

This is a beautiful book. It consists of 180 pages of extremely readable information on urogynaecology and the treatment of stress incontinence. There is barely one page devoted to pelvic surgery.

Despite the fact that there are twenty-seven authors in this short book, the editors have fulfilled their job magnificently: the terminology and thinking appear to be standardised throughout the entire text.

As a gynaecologist who enjoys vaginal surgery (and the challenge of a laparoscopic colposuspension) this book is itself a challenge to adopt a much less aggressive surgical and a much more physiotherapeutic approach to the correction of stress incontinence of urine. The arguments are meticulously reasoned.

The book is divided into four sections: (1) the anatomy and function of the pelvic floor musculature; (2) the evaluation of the pelvic floor; (3) childbirth and pelvic floor damage and (4) pelvic floor re-education. No section should be read without reading the preceding sections. Each section is short and written by an expert in its field. The standard of illustration is high, by and large. The concept of pelvic floor musculature and its relation to urethral function is something which has always perplexed me (as it is my firm belief, has it perplexed most of the authors that I have read before on this subject). However, in this book the gaps in knowledge are fully stated, but as far as is possible present day knowledge is logically and clearly explained.

As a clinician, though, the section on the pelvic floor re-education was the most enlightening. Like most gynaecologists, I know that patients spend a long time attending the physiotherapists and that pelvic floor exercises are done. However, the assessment of patients for the correct pelvic floor exercises and the importance of encouragement are emphasised. I feel, that having read this book I will be able to talk to the physiotherapists and understand what they are saying.

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NEIL McCLURE

The Ulster Medical Journal, Volume 64, No. 2, pp. 173 – 177, October 1995.

Case Report:

Intensive care management of the HELLP syndrome

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Accepted 24 July 1995

In 1982 Weinstein reported a syndrome in pregnancy characterized by haemolysis, elevated liver enzymes and low patelet count, the HELLP syndrome, and described it as a severe consequence of pre-eclampsia.[1] Patients may present with a wide variety of signs and symptoms but evidence of pre-eclampsia may not be present.[2] Multisystem failure may occur due to widespread microcirculatory dysfunction. This case demonstrates the range of supportive therapy required in the intensive care management of such patients.

CASE REPORT.

A 26 year old primigravid woman was admitted to the intensive care unit (ICU) following Pfannensteil laparotomy for suspected concealed post-partum haemorrhage 4 hours after Barnes Neville forceps delivery for fetal distress. No bleeding point was identified and the patient was transferred ventilated to the intensive care unit as she remained hypotensive and oliguric. A central venous line had been inserted in theatre and a dopamine infusion commenced at 5 μg/kg/min.

The only problem in pregnancy had been a mildly elevated diastolic blood pressure (90-95 mmHg) at 39 weeks with no proteinuria or oedema, but when spontaneous labour was established one week later the blood pressure had returned to normal (125/85 mmHg).

The patient had complained of epigastric pain two hours prior to delivery and this persisted intermittently into the post partum period. Blood pressure measurements were normal throughout labour but 30 minutes following delivery she developed hypotension which responded initially to the administration of intravenous fluids. Blood cultures were taken prior to the administration of intravenous antibiotics due to the development of a pyrexia of 38.4°C. Full blood count and coagulation profiles at that time showed haemoglobin 7.0 g/dl, white cell count 30 x 10^9 1, platelets 37 x 10^9 1, prothrombin time 28 seconds (normal 12-17 seconds), activated partial thromboplastin time 93 seconds (normal 29-40 seconds) fibrinogen 1.67 g/1 (normal 2-5 g/1) and fibrinogen degradation products >10<40 μg/ml (normal <10 μg/ml). Ultrasound scan of the abdomen revealed a small amount of intraperitoneal fluid and the decision was taken to proceed to laparotomy.

On arrival in ICU the patient was noted to be oozing a considerable amount of blood from the Pfannensteil incision. She had marked oedema of her face, hands and legs which, in addition to the history of epigastric pain associated with a low haemoglobin and platelet

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count and coagulopathy, suggested the diagnosis of HELLP syndrome. An urgent biochemistry assay showed AST 6234 U/L (normal 10-40 U/L), alkaline phosphatase 93 U/L (normal 35-120 U/L) and bilirubin 61 μmol/L (normal 3-18 μmol/L). As the patient was bleeding profusely from the abdominal incision and requiring large amounts of blood and clotting factors no evidence of haemolysis was sought.

The patient's problems in ICU can be summarized as follows:-

1. Coagulopathy and haemorrhage

During the first three days in ICU the patient continued to have major haemorrhage from the abdominal incision in the presence of a worsening coagulopathy that showed the initial features of disseminated intravascular coagulation. Her requirements for blood and blood products during that time and during the whole of her stay in ICU are shown in table I. Antifibrinolytic therapy with aprotonin and tranexamic acid was employed in an attempt to reverse the process but with no apparent success. On day three a repeat laparotomy was performed and, although no bleeding points were identified, heavy packs plus further administration of coagulation products resulted in cessation of the bleeding. Episodic vaginal bleeds of 500-1000 mls occurred repeatedly over the next three weeks despite normal coagulation profiles. On day 25 an abdominal hysterectomy with left salpingo-oophorectomy was performed with complete cessation of bleeding.

TABLE I

Blood and blood products received in the intensive care unit

	TOTALS	
	72 hours	*next 32 days*
red cell concentrate	42 units	33 units
fresh frozen plasma	38 units	17 units
cryoprecipitate	10 units	
platelets	50 donors	

2. Cardiovascular instability

A pulmonary artery floatation catheter was inserted on admission to ICU as the patient remained hypotensive despite what appeared to be adequate fluid replacement and a CVP reading of +10 mmHg. Subsequent measurements revealed pulmonary capillary wedge pressure 11 mmHg (normal 5-12 mmHg), systemic vascular resistance 550 dynes/cm^5 (normal 950-1300 dynes/cm^5) and cardiac output 9.01 min (normal 4-6 l/min). Infusions of noradrenaline and dobutamine were therefore commenced but it was possible to discontinue these within 48 hours while maintaining the dopamine at 3 μg/kg/min.

3. Acute renal failure

The patient rapidly became anuric despite adequate central and arterial blood pressures and the administration of frusemide and dopamine. Haemodialysis was initiated on day two, because of an elevated plasma potassium level of 6.8 mmol/L, and continued daily for the next three weeks. There was gradual recovery of renal function with subsequent polyuria and return to normal biochemistry.

4. Infection

The patient was initially commenced on broad spectrum antibiotics. However all blood and urine cultures were negative. Over the first 10 days there were two significant episodes of pyrexia and leucocytosis. A CT scan of the abdomen and pelvis on day nine showed a very large liver with areas of necrosis but no focal collections. A subsequent examination under anaesthesia revealed no palpable pelvic abscesses but it was possible to incise and drain a large right sided paravaginal haematoma which resulted in a reduction in temperature and leucocytosis.

5. Deranged liver function

Biochemical analysis showed hepatocellular dysfunction with hyperbilirubinaemia (peak 450-500 umol/L) which gradually subsided as the patient's condition improved. Hepatitis B and C serology were negative. An infusion of 50% dextrose was required initially to treat persistent hypoglycaemia but this gradually resolved. On discharge from ICU the patient's bilirubin, AST and alkaline phosphatase levels had all returned to within their normal ranges.

6. Ventilatory requirements

The patient remained ventilated for six days until there was control of her multisystem disorder. Her inspired oxygen requirements were never greater than 50%.

7. Nervous system

An isolated seizure occurred on day 30 and phenytoin therapy was commenced.

The patient was discharged to the ward on day 35 and returned home 10 days later with her baby who was successfully resuscitated at the time of delivery.

DISCUSSION

Intensive care physicians may be required to treat patients with HELLP syndrome when one or more organ system failure has occurred. These patients may present at any time in pregnancy with 30% occurring in the post-partum period.[3] Maternal mortality from the condition ranges from 0-24%.[4]

Weinstein proposed that the HELLP syndrome described a unique group of patients with severe pre-eclampsia.[1] However, a series of 6 cases has been reported with the features of HELLP syndrome in whom hypertension and proteinuria were absent.[2] The most common presenting symptoms in affected patients are right upper quadrant or epigastric pain (65%), nausea or vomiting (36%) and headache (31%).[3] Patients with HELLP syndrome may be mistakenly diagnosed as having various surgical and medical disorders.[4] In an attempt to improve diagnostic accuracy criteria for the condition have been proposed and are shown in table II.[4]

The pathophysiology of HELLP syndrome is thought to be similar to that of pre-eclampsia with vasospasm and endothelial lesions within multiple organ systems.[5] Platelet consumption occurs by adherence to the endothelial lesions within the microcirculation. The fibrin network produced results in occlusion of the small vessels, organ malperfusion and further activation of the coagulation system. In the liver, occlusion of vessels may result in congestion, ischaemia and necrosis, subcapsular haemorrhage or even rupture. Upper abdominal pain occurs as a result of liver distention. Renal failure may occur due to damaged microcirculation in the kidneys or as a result of intravascular volume depletion secondary to leakage of plasma from the damaged systemic microcirculation.

TABLE II

Criteria for HELLP syndrome

1. **Haemolysis**
   abnormal peripheral blood film
   total bilirubin > 1.2 mg/dl^{-1} (~ 14 μmol/l^{-1})
   lactate dehydrogenase > 600Ul^{-1}

2. **Elevated liver enzymes**
   aspartate aminotransferase > 70Ul^{-1}
   lactate dehydrogenase > 600Ul^{-1}

3. **Low platelets**
   platelet count < 100 000 mm^{-3}

The microangiopathic haemolytic anaemia that is the hallmark of HELLP syndrome is thought to result from the passage of red blood cells through small blood vessels with damaged intima and fibrin mesh deposits.[4] Disseminated intravascular coagulation (DIC) was suspected or manifest at delivery in all 18 patients with HELLP syndrome investigated by Van Dam et al.[6] The laboratory criteria of DIC were found to correspond with the degree of organ dysfunction.

The intensive care management of patients with HELLP syndrome producing multiple organ system failure consists of careful monitoring with active and supportive treatment of any complications, as demonstrated in this case. Coagulopathy and haemorrhage require aggressive replacement with blood and clotting factors. In patients in whom hypertension is predominant a high systemic vascular resistance (SVR) may be expected and intravenous vasodilators required. This patient had a low measured SVR with no hypertension and noradrenaline was initially required.

Intervention with renal dialysis may be required early in the presence of hyperkalaemia due to the massive intravascular haemolysis and accompanying renal failure. Even with prolonged renal support there was gradual return of urine production and eventual biochemical homeostasis by the kidneys in this patient.

Hepatobiliary complications secondary to the HELLP syndrome may require surgical intervention.[5] In particular, subcapsular liver haematomas may need to be evacuated and sudden collapse may occur due to hepatic rupture requiring urgent laparotomy. Areas of hepatic necrosis were noted on CT scan in this patient but surgical intervention was not required. The main problem related to hepatic failure was persistent hypoglycaemia which has previously been reported in association with the HELLP syndrome.[7,8]

Adult Respiratory Distress Syndrome has been reported to occur as a result of the HELLP syndrome.[3] Although this patient initially required ventilatory support the F_IO_2 was never greater than 0.5 and ARDS did not occur. One feature to note with these patients is that laryngeal oedema may be present and intubation may prove difficult. Two out of the four deaths in a review of 442 cases by Sibai were as a result of cerebral hypoxia secondary to failed intubation.[3] Difficult intubation must be predicted and the ability to provide an emergency surgical airway must be available.

It has been suggested that exchange plasmapheresis with fresh frozen plasma may be beneficial in patients with persistent thrombocytopenia.[9] The mechanism of action of such intervention is not clear and, as this is an invasive and expensive procedure, its use in such patients should await the results of a randomised trial.

Seizures may occur at any time due to associated eclampsia. The isolated generalised convulsive seizure in this patient occurred on day 30 and was probably unrelated to the presenting disorder and more likely due to uraemia or ciprofloxacin therapy.

This case highlights many of the problems encountered in the intensive care management of patients with the HELLP syndrome. Obstetricians and intensive care physicians must be aware of the condition and consider it in the differential diagnosis of critically ill patients during pregnancy and the peripartum period.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 178 – 180, October 1995.

Case Report:

Iatrogenic acute angle closure glaucoma masked by general anaesthesia and intensive care

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Accepted 24 July 1995

Acute angle closure glaucoma is a medical emergency which can result in blindness. As it is very painful patients are usually referred rapidly to an ophthalmologist. If it occurs following general anaesthesia however, the diagnosis may not be considered and symptoms such as pain and vomiting wrongly attributed. Delayed diagnosis puts the patient at risk both from the ocular complications of acute angle closure glaucoma, and also from inappropriate investigation and intervention. We report an illustrative case where bilateral acute angle closure glaucoma followed a general anaesthetic. The correct diagnosis was delayed for 11 days.

CASE REPORT. A 66 year old lady underwent abdominal hysterectomy. During her general anaesthetic she was preoxygenated. Her intubation with an endotracheal tube was moderately difficult. The intravenous anaesthetic agents administered (in order of use) were; atropine, thiopentone, suxamethonium, vecuronium, cyclizine, neostigmine, doxapram and glycopyrrolate. There were no intra-operative complications but extubation was difficult. Immediately post- operatively she became hypoxic, as assessed by her oxygen saturation, and was reintubated and transferred to the Intensive Care Unit. The clinical impression at that time was that she had aspirated during surgery and developed left ventricular failure. A chest radiograph confirmed pulmonary oedema. She was ventilated for two days and during this time developed a pneumothorax following the insertion of a central venous line. This was successfully treated with the insertion of a chest drain. In the Intensive Care Unit she received intravenous frusemide, digoxin, amoxycillin and subcutaneous heparin. Clinically at this time she appeared to have developed a chest infection with the development of coarse crepitations at the lung bases, and to aid respiration nebulised solutions of ipratropium bromide and salbutamol were commenced. A subsequent chest radiograph showed lung fields to be clear and her pneumothorax to have resolved.

She returned to the ward on the fourth postoperative day with nausea and vomiting. Her right eye was noted to be injected but she made no complaint of specific ocular discomfort. Her abdominal wound dehisced and was resutured under general anaesthetic. She made an uneventful recovery from this procedure. Over the following two days she received repeated doses of intramuscular pethidine and cyclizine for pain and nausea. She also continued to receive nebulised solutions of ipratropium bromide and salbutamol.

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On day six following her first operation she became increasingly confused and aggressive and appeared to have visual hallucinations. She was also noted to have markedly reduced vision with bilateral injected eyes. She complained of eye discomfort at that time. Her eye condition was treated with topical chloramphenicol eye drops and further intramuscular pethidine injections for pain relief. She was treated with oral thioridazine for confusion, but this worsened on day seven and intramuscular chlorpromazine hydrochloride was administered. A provisional diagnosis of cerebral infarction was made. However computerised tomography of brain was normal.

Subsequently her confusion lessened and her eyes although remaining injected became less painful. On day eleven following her first operation she was seen by an ophthalmologist. He noted visual acuity as hand movements in each eye, bilateral corneal oedema, shallow anterior chambers, non-reactive mid-dilated pupils and raised intraocular pressures. He also noted that the patient was hypermetropic (by spectacle measurement) and had bilateral lens opacities. A diagnosis of spontaneously resolving bilateral acute angle closure glaucoma was made and the patient treated with oral acetazolamide and pilocarpine, dexamethasone and betaxolol eye drops. The intra-ocular pressures after this treatment were 44 mmHg and 15 mmHg on right and left side respectively.

Her corneal oedema slowly resolved over the following month. No specific glaucomflecken were noted but sectorial iris atrophy was present in her right eye consistent with the previous acute rise in intra-ocular pressure. Gonioscopy revealed 270 degree permanent angle closure in her right eye and a 360 degree grade 1 angle in her left eye. She underwent bilateral laser iridotomies two months later. Persistent elevated intra-ocular pressures of 40 mmHg od and 17 mmHg os and cataract development necessitated subsequent combined right trabeculectomy, cataract extraction and intra-ocular lens implantation. Five months after this surgery she still requires pilocarpine eye drops in her left eye and betaxolol eye drops in both eyes to control intra-ocular pressures. Current visual acuity is 6/9 and 6/12 in her right and left eyes respectively and current intra-ocular pressures are 21 mmHg ou. Optic discs show minimal cupping with a 0.2 cup – disc ratio in each eye and intact neuroretinal rims, consistent with her hypermetropia. Visual fields show marginal field loss with a nasal arcuate scotoma in the right eye only

DISCUSSION

Acute angle closure glaucoma occurs in 0.1 % of the British population over the age of 40. It affects females four times more commonly than males and is more common in patients who are hypermetropic or who have an enlarged lens due to age or cataract. The acute rise in the intra-ocular pressure produces pain, vomiting, blurred vision and haloes (due to corneal oedema). Sequelae include iris atrophy, cataract, chronic angle closure glaucoma, chronic corneal oedema, glaucomatous visual field loss and anterior ischaemic optic neuropathy. Drugs which increase pupillary dilatation can precipitate acute angle closure glaucoma in a susceptible individual.[1,2,3] These drugs include anti-muscarinic agents such as ipratropium bromide, chlorpromazine bromide, thioridazine and cyclizine, all of which this patient received whilst suffering from acute angle closure glaucoma. In addition salbutamol, a β_2 adrenoreceptor agonist, can compound the problem as it increases aqueous humour production and thus acts in synergy with ipratropium bromide to increase intraocular pressure.[1]

It is likely that in this case the acute angle closure glaucoma was precipitated by the anti-muscarinic agents (intravenous cyclizine and nebulised ipratropium bromide) and nebulised salbutamol, which the patient received during and shortly after her first anaesthetic. Intravenous atropine administered in standard premedication doses has no effect on the

intra-ocular pressure in healthy[4] or glaucomatous eyes.[5] The postoperative vomiting which contributed to her wound dehiscence was probably caused by glaucoma as were the pain, nausea and visual hallucinations for which she received further inappropriate medication. The oral thioridazine and intramuscular chlorpromazine hydrochloride given for her confusion may have perpetuated and compounded the attack of glaucoma and also prevented the patient communicating her symptoms.

Cases of iatrogenic acute closed angle glaucoma have been described before.[1-3] What this case illustrates in particular is the need for a high index of suspicion in an intensive care situation where the classic signs of acute angle closure glaucoma can be masked by a patient's more obvious surgical or anaesthetic needs, and the diagnosis of underlying acute closed angle glaucoma can be delayed for several days. Failure to consider it in a patient with a red eye may result in drug therapy which can both further obscure the correct diagnosis and prolong the glaucomatous episode. Acute angle closure glaucoma is an important differential diagnosis in a patient with a painful red eye. If suspected, ophthalmic advice should be obtained urgently, so that further complications can be avoided. Early detection and treatment of acute angle closure glaucoma lead to a better visual outcome.[6]

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The Ulster Medical Journal, Volume 64, No. 2, pp. 181 – 184, October 1995.

Case Report

Metastatic biphasic pulmonary adencarcinoma mimicking malignant gastrointestinal stromal tumour

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Accepted 1 September 1995

It is well recognised that spindle cell change can occur in a variety of malignant neoplasms including squamous carcinoma of skin, oesophagus, lung and cervix, breast ductal carcinoma, renal carcinoma, transitional carcinoma of bladder, malignant melanoma and mesothelioma. Spindle cell change in lung adenocarcinoma has been less frequently reported [1-6] and raises a range of differential diagnoses. Extra-pulmonary metastatic deposits may occur in a number of sites, including the gastrointestinal tract, and be a source of diagnostic confusion.[3-5] We report the case of a 75 year old female with a peripheral lung adenocarcinoma containing a spindle cell component metastasising and mimicking malignant gastrointestinal stromal tumour.

CASE REPORT

A 75 year old lady presented with a one month history of fresh haemoptysis (2-3 episodes daily), loss of energy and increasing dyspnoea. She had smoked 15 cigarettes per day for many years and had a past medical history of partial gastrectomy for benign gastric ulceration. Chest x-ray and CT scans showed an irregular mass in the apical segment of the right lower lobe which was subsequently resected. There was no evidence of disease elsewhere on CT or ultra-sound imaging of brain, chest and abdomen. One year later she re-presented with symptoms and signs of small bowel obstruction. Laparotomy showed perforation of the proximal jejunum with an ulcerated pale tumour mass 50 centimetres from the duodeno-jejunal flexure which was thickening the bowel wall and impinging on the transverse colon. She had an uneventful post-operative recovery with no evidence of other tumour and remains reasonably well at twelve months review.

PATHOLOGY

The right lower lobectomy specimen contained a peripheral, irregular 2 centimetre diameter tumour which mostly had a moderately differentiated, tubulo-papillary adenocarcinomatous pattern. About 15% of the tumour showed transition to a malignant spindle cell component with nuclear pleomorphism, hyperchromasia, mitotic activity, elongate eosinophilic cytoplasm and focal necrosis (Figure 1). Both of the tumour elements were strongly positive with epithelial markers (CAM 5.2, AE1/AE3) and the tumour tubules reacted with anti-CEA antibody. The spindle cells were also weakly positive with

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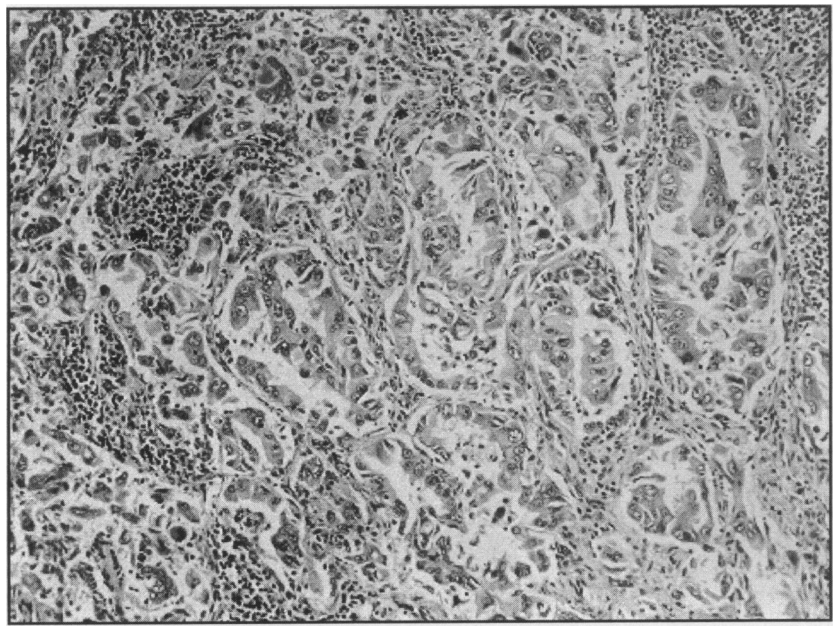

Fig 1a. Moderately differentiated pulmonary ademocarcinoma.

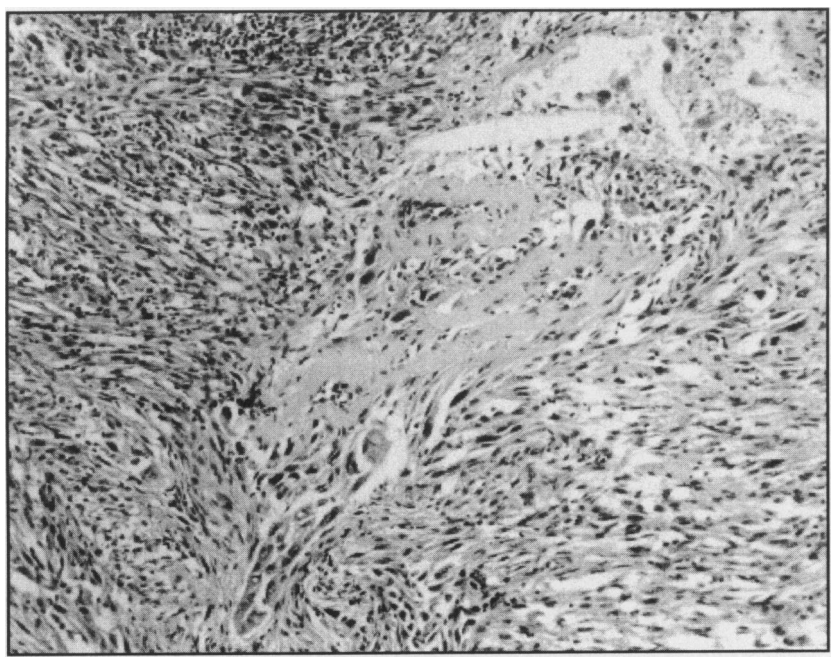

Fig 1b. Adenocarcinoma blending with the spindle cell component.

vimentin and smooth muscle actin antibodies. The bronchial resection limit and a small hilar lymph node were free from involvement. The subsequent small bowel resection contained an irregular, deficient and perforated tumour, pale in colour, ulcerating the mucosa and infiltrating the bowel wall, serosa and mesenteric fat. Histology showed a poorly differentiated malignant spindle cell tumour with features similar to those seen in the lung carcinoma. The immunohistochemical profile was identical with strong epithelial and weak vimentin/smooth muscle actin staining. Desmin and S100 protein antibodies were negative. It was concluded that this represented a metastatic deposit from the dedifferentiated component of the lung carcinoma but that its morphological appearance, on initial examination mimicked malignant gastrointestinal stromal tumour. This was made more problematic as the reporting pathologist was unaware of the previous lung resection which only became evident from the laboratory computer record, allowing correlation of both samples.

DISCUSSION

The blend of malignant epithelial and spindle cell elements in a lung neoplasm raises a wide range of differential diagnoses including carcinosarcoma, pulmonary blastoma, mesothelioma, sarcoma with entrapped native glands, carcinoma with pseudosarcomatous stroma, collision tumour and squamous or adenocarcinoma with metaplastic spindle cell change. Carcinosarcoma is composed of malignant epithelial and mesenchymal components (often including heterologous elements) with no zones of transition between them; the spindle cells express strongly for vimentin and only focally for cytokeratin intermediate filaments. Blastoma has a mixture of immature embryonal mesenchyme and epithelium while mesothelioma is pleura based rather than intrapulmonary and negative for CEA antigen. Sarcoma entrapping lung tissue may show specific features, eg smooth muscle or neural differentiation. Pseudosarcomatous stroma often has a desmoplastic appearance with a sharp interface rather than gradual blend with the carcinoma. Collision tumours should not show transition between the two elements and seem to be increasingly rare with the primitive stem cell theory of divergent differentiation now in favour. Malignant "metaplastic" spindle cell change is well recognised in various carcinomas and the present case represents another example of this less frequently reported occurrence in lung adenocarcinoma: this is underscored by the gradual transition between the two elements and the strong cytokeratin/weak vimentin staining indicating mesenchymal metaplasia from a malignant epithelial stem cell.[1, 4] This can be corroborated by demonstration of tonofilaments and desmosomes in the spindle cells on ultra-structural examination.[3, 4, 6] Biphasic lung adenocarcinoma has been noted to be bronchogenic in location[1] but is more often peripherally situated.[2-5] The glandular tissue usually shows a well to moderately differentiated tubulo-papillary pattern (with or without mucin secretion) and the spindle cells vary from sarcoma, NOS (Not Otherwise Specified), to a malignant fibrous histiocytoma picture. It has potential to form widespread metastatic deposits with a particular propensity for dissemination of the spindle cell component.[3-5] This can cause considerable diagnostic confusion especially if the history of previous lung carcinoma is not available. Drlicek *et al*[5] described an extradural deposit in the thoracic spine mimicking leiomyosarcoma on morphological and initial immunohistological study two years after the lung primary. Leiomyosarcoma was also the primary biopsy diagnosis in a 79 year old lady who presented with a submucosal tumour in the gastric fundus.[3] Post mortem one year later showed a right lower lobe carcinoma with cytokeratin positive mixed adenocarcinoma/pleomorphic spindle cell sarcoma and multiple gastric and visceral metastases. Hiroshima *et al*[4] reported a similar lung carcinoma, the glandular component of which spread to the kidney and the spindle cell element to chest wall, adrenal gland and gingiva.

Gastrointestinal tract is a well recognised site of spread for lung carcinoma. This report further highlights the possible occurrence of spindle cell change in primary and secondary carcinoma and its ability to mimic sarcoma either at the original or metastatic site. Differential diagnoses in the resection specimen with their relevant immunological profiles included primary malignant gastrointestinal stromal tumour (vimentin +, desmin ±, actin ±, S100 ±, epithelial marker –), malignant melanoma (S100 +) and disseminated pleural or peritoneal mesothelioma (CEA –). Importance is placed on knowing the full clinical history, studying morphological features closely and using a panel of immunoperoxidase markers. Caution in interpretation of the latter should be exercised as it is well recognised that some carcinomas (eg lung) and sarcomas (eg leiomyosarcoma) can show co-expression of epithelial and mesenchymal intermediate filament antibodies. Electron microscopy is also a useful adjunct.

ACKNOWLEDGEMENTS

The authors thank the following colleagues for their permission to publish details of the case: Mr J McGuigan, Mr R Spence, Dr R Lowry, Dr J Logan and Dr Heather Elliott.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 185 – 190, October 1995.

Case Report

Hepatic abscess formation following embolisation of a carcinoid metastasis

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Accepted 6 September 1995

Carcinoid tumours are rare with an annual incidence of 1.3 per 100,000 in the N. Ireland population.[1] Carcinoid tumours are unusual in that hepatic metastases are compatible with a 20 to 40% five year survival.[2] Nevertheless, most patients become symptomatic when hepatic metastasis occurs. The resulting local symptoms and those of the carcinoid syndrome (where hepatic metastasis can be found in more than 95% of cases) greatly reduce the quality of the patient's life.[3,4] It is therefore usual to treat such cases aggressively with somatostatin analogues and other anti-serotonin agents, chemotherapy, surgical debulking and hepatic artery occlusion (by ligation, temporary occlusion or embolisation).[5] The latter is effective as hepatic neoplasms are almost solely supplied by the hepatic artery.[6] The resultant selective tumour necrosis produces effective palliation of symptoms, which may be prolonged due to the slow growing nature of the carcinoid tumour.[7]

The following case report presents an unusual post-embolisation complication (hepatic abscess formation). The overall management of carcinoid hepatic metastases is briefly discussed.

CASE REPORT

A 61 year old man presented in 1987 with haemoptysis. A right lower lobe bronchial carcinoid tumour was discovered and subsequently resected. Over the next few months he developed diarrhoea, nocturnal wheeze and flushing. In 1989, investigation disclosed deranged liver function tests (LFTs), raised urinary 5-hydroxyindole acetic acid (5-HIAA) and raised plasma pancreatic polypeptide (PPP). An alcohol provocation test induced marked flushing which was greatly reduced by injection of a somatostatin analogue. There was no evidence of secretion of 5-hydroxytryptamine, prostaglandins, insulin, gastrin, vasoactive intestinal peptide, ACTH, parathormone or other active peptides, which may occur with carcinoid tumours of foregut embryonic origin. Four hepatic metastases were revealed on abdominal ultrasound (three in the right lobe and one in the left lobe). Intra-heptic arterial chemotherapy combined with somatostatin was used at this time with good symptomatic control.

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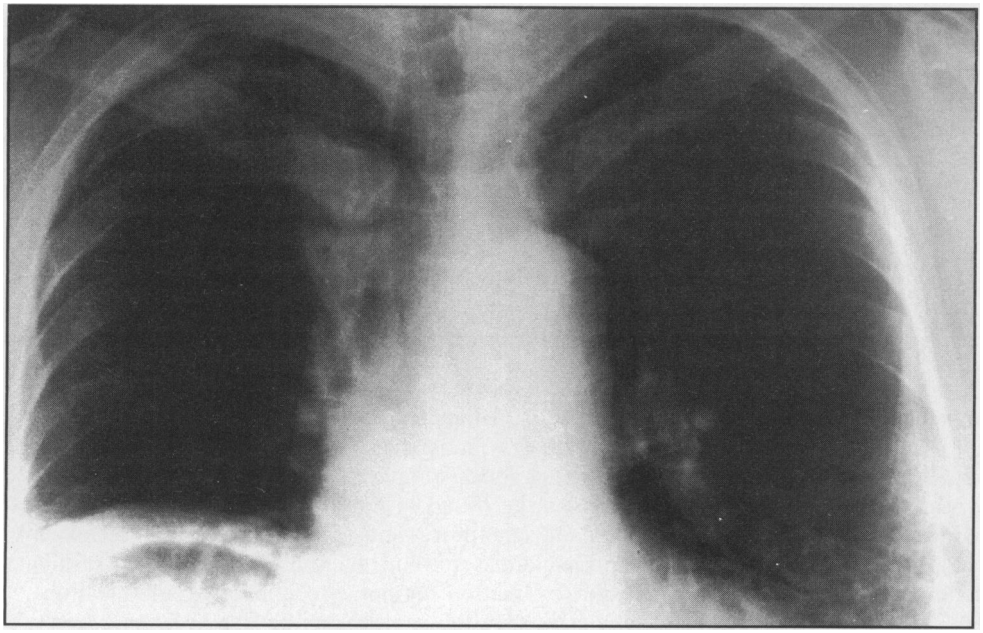

Fig 1. Chest X-ray showing hepatic abscess as gas-fluid level under right hemidiaphragm.

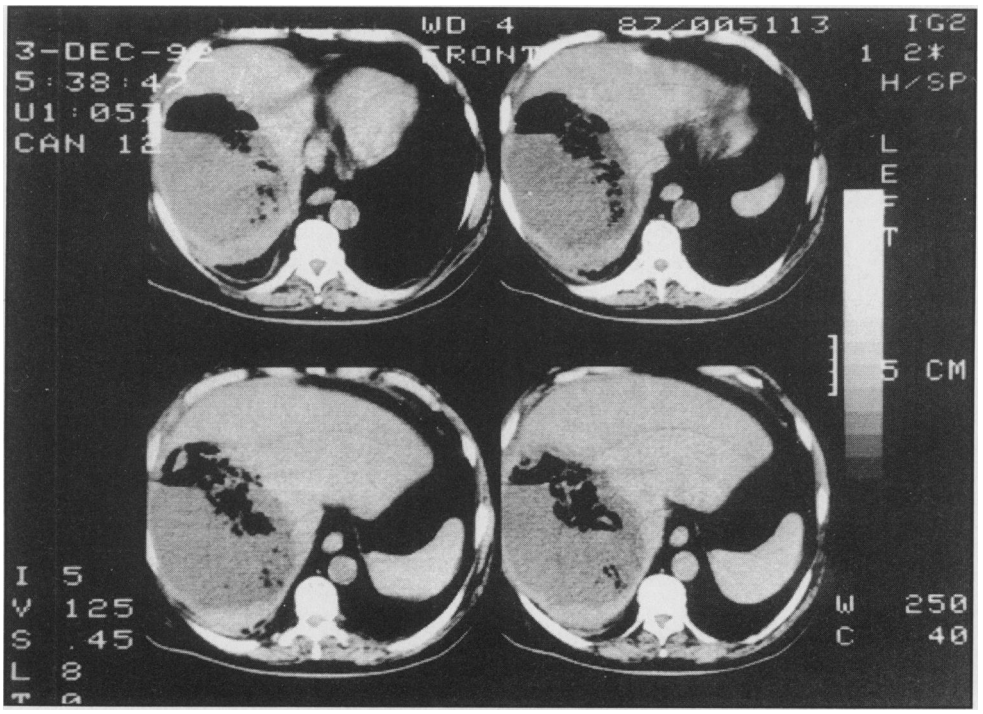

Fig 2. CT scan showing hepatic abscess with gas in liver substance.

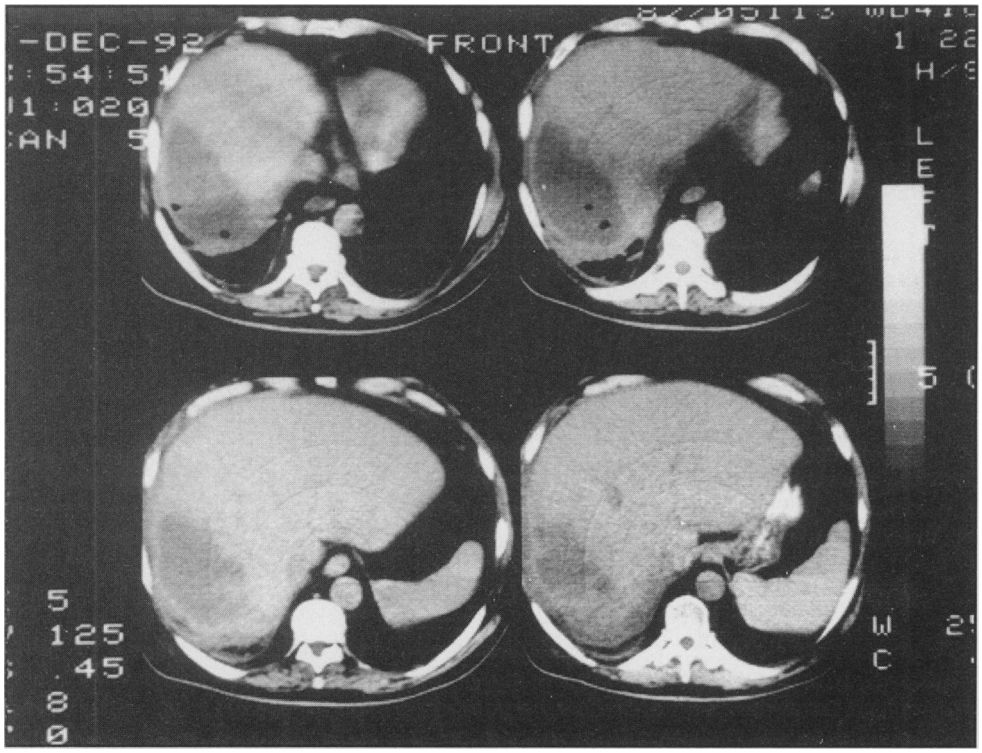

Fig 3. Post-operative CT scan after resection and drainage showing fluid-filled cavity in right hepatic lobe.

In early 1992 there was symptomatic deterioration combined with biochemical and radiological evidence of tumour recurrence. In October 1992 he was admitted to hospital with pain in the right upper quadrant (RUQ) of the abdomen and evidence of a right basal pneumonia. Following treatment of the pneumonia, hepatic artery embolisation using particulate polyvinylchloride (PVC) was carried out on a large right lobar metastasis. He subsequently developed a short lived episode of vomiting and abdominal pain which settled with symptomatic treatment. An abdominal ultrasound scan prior to discharge at ten days post-embolisation revealed an eight centimetre embolised lesion with no evidence of complications.

Fifteen days later he was re-admitted with malaise, RUQ pain and tenderness, and constipation. Chest X-ray (Figure 1) revealed an air-fluid level under the right hemidiaphragm and abdominal films showed hepatic mottling with gas shadows. These findings were consistent with the development of an aseptic abscess in the liver with gas formation. This was confirmed on computerised tomography (CT) which revealed that the embolised lesion was now liquid in attenuation values with areas of gas giving rise to a "soapbubble" appearance (Figure 2).

Based on worsening clinical and radiological findings, rupture of the abscess was thought to be imminent with the risk of carcinoid crisis or peritonitis. A formal drainage procedure was therefore carried out with resection of the necrotic right lobar metastasis under somatostatin and antibiotic cover. Post-operative recovery in the intensive care unit was uneventful.

A post-operative CT scan demonstrated multiple small hepatic metastases and a significantly improved fluid filled cavity in the right lobe of the liver (Figure 3). He was discharged on maintenance somatostatin and has remained well since, with flushing as his only complaint.

DISCUSSION

In Northern Ireland there is a central diagnostic laboratory and register collecting data on neuroendocrine tumours. There were 368 such tumours in the province between 1970 and 1985, of which 318 were carcinoids and 28 (9%) arose in the lung.[1] Carcinoid tumours are slow growing neuroendocrine tumours.[8] They occasionally produce local symptoms (e.g. haemoptysis with a pulmonary carcinoid, obstruction with an appendiceal carcinoid) but usually produce symptoms secondary to hormone secretion.[9] Eighty percent of carcinoid tumours are "midgut" in origin and secreted hormones are thus subject to hepatic first pass metabolism.[10] Such tumours are therefore usually asymptomatic until hepatic metastases have occurred when hormones can be secreted into the systemic circulation and produce the carcinoid syndrome. It is at this time that most cases are diagnosed.

Treatment firstly requires anatomical and functional characterisation.[9] Small primary tumours can be locally resected whereas larger ones may require formal "enbloc" resection or palliative debulking. Such operations can be very successful e.g. resection of bronchial primary carcinoids results in a 70% five year survival.

Since hepatic metastases produce the main symptoms but are not invariably fatal, they are treated aggressively with the following procedures:

1. Pharmacological hormonal manipulation. Somatostatin decreases both the synthesis and release of hormones by the tumour, as well as increasing the synthesis of inhibitory proteins. It may also prove to be anti-neoplastic and to slow tumour progression.

2. Chemotherapy with streptozotocin.

3. Surgical debulking – this is of particular use with unilobar hepatic metastases where a hepatic lobectomy can be performed.

4. Hepatic artery occlusion.[5,7,11,12,13] This can be achieved by ligation or embolisation. Formal ligation requires a laparotomy and is associated with an operative mortality and rapid collateral formation. It produces symptomatic relief lasting a mean of five months. Temporary occlusion can be carried out by vessel layer formation or by implanting a tourniquet. These options reduce perioperative mortality by separating tumour necrosis from the laparotomy. They can also be repeated, and reduce collateral formation as the hepatic artery occlusion is only temporary.

Hepatic artery embolisation is a palliative procedure used to control pain, haemorrhage, hormone secretion and tumour size. Any accessible tumour can be embolised but it is most effective when used for metastatic neuroendocrine tumours. The procedure is covered with antibiotics and somatostatin to reduce the risk of infection and a carcinoid crisis respectively.[14] Percutaneous selective angiography is used to identify the feeding vessels of the tumour. A shower of small particles embolises the smaller peripheral vessels, thus reducing collateral formation (analogous to surgical isolation), and is followed by embolisation of the main feeding vessels.[7,11] A choice of embolising materials can be used including iodized oil, Gelfoam, Oxycel, PVC (available in graded sizes) and coils (which exclude re-embolisation as well as concurrent intra-arterial chemotherapy). Re-embolisation can be carried out for tumour regrowth or to occlude subsequent collateral arteries. Re-embolisation was only required in under 10% of cases within 5 years in a Swedish trial.[15]

Palliation of symptoms occurs in almost every case and has a duration of 2-18 months (mean 7 months) and a further 3-18 months (mean 11 months) following reembolisation.[14] Hepatic artery embolisation was initially used for bilobar hepatic metastases, where resection is impossible, and for patients unfit for surgery. It is now more widely used as it has a lower morbidity and negligible mortality compared to the alternatives, and requires less than one week of hospitalisation. Earlier and repeated embolisation may also improve patient survival.[9] It also enables concurrent intra-arterial chemotherapy if a degradeable material is used. Such a combined chemoembolisation procedure improves tumour uptake of the chemotherapeutic agent while protecting the normal liver. This allows control of carcinoid symptoms as well as regression or stabilisation of the liver tumours in 80% of patients.[16]

As all embolised tumours undergo selective aseptic necrosis, the postembolisation syndrome (RUQ pain, nausea, pyrexia, leucocytosis and derangement of LFTs) is ubiquitous to a greater or lesser extent. Symptomatic treatment in the early stages with analgesia and anti-emetics is sufficient.[17] Prolonged symptoms lasting more than five days should be investigated to exclude rare complications. This would include abscesses which can be drained percutaneously or drained at laparotomy.[5, 12] Other complications of embolisation include septicaemia, carcinoid crisis, haemorrhage, gall-bladder ischaemia, pancreatic pseudocyst, hepatic artery aneurysm formation, and embolisation of unrelated arteries by release of the material into the general circulation.[3, 9, 13]

Embolisation is becoming increasingly popular since it produces effective clinical and biochemical suppression of carcinoid metastases; it is both safe and inexpensive. However, it remains a purely palliative procedure. The only real hope for cure lies with orthoptic liver transplantation (OLT). In a series of 1000 OLTs over 6 years in Pittsburgh, two cases were for carcinoid metastases.[19] Both patients died from causes unrelated to tumour recurrence and had no evidence of this at postmortem. This hopeful pointer to curative management should be examined prospectively in a trial of OLT against standard treatment. Early and repeated embolisation appears to be the current safest mode of management for patients with hepatic carcinoid metastases.

ACKNOWLEDGEMENT

We wish to thank Professor K D Buchanan for his help with this patient's management, and for permission to report this case.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 191 – 196, October 1995.

Case Report

Primary systemic amyloidosis and the gastrointestinal tract

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Accepted 1 September 1995

Clinical manifestations of primary amyloidosis can be subtle, particularly when the gastrointestinal tract is involved. We present two cases that illustrate the diversity of such involvement and the subsequent problems with diagnosis. Gastrointestinal effects of primary systemic amyloidosis are reviewed and clinical pointers towards diagnosis are discussed. In particular these cases illustrate the importance of providing all the clinical details to the pathologist and mentioning amyloidosis as a possible diagnosis.

CASE 1

A 47-year-old lady presented to surgical outpatients with a three month history of diarrhoea, mild steatorrhoea, central abdominal discomfort and 4 kg weight loss. She complained of nausea and fatty food intolerance over the preceding two years: oral cholecystogram at another hospital had revealed a solitary large gallstone. Routine biochemical and haematological tests were normal. Three day faecal fats were elevated at 76.1 mmol/l (normal<18mmol/l). Barium meal, follow through and barium enema were normal. Antigliadin antibody, auto-antibody screen and a gut hormone profile were normal. Incidental proteinuria was documented and later measured at 1 g/24 hrs. She underwent cholecystectomy which improved some symptoms, but steatorrhoea and weight loss persisted. A further small bowel series showed a coarse mucosal pattern in keeping with malabsorption. Jejunal biopsy was normal as was endoscopic retrograde cholecystopancreatography. Colonoscopy was performed to exclude colitis and biopsies were initially reported as normal.

A year later the patient complained of easy bruising, and areas of purpura and hepatomegaly were found on examination. Mild elevation of alkaline phosphatase and gamma glutamyl transferase were noted. The prothrombin time was prolonged and a mild normocytic, normochromic anaemia had developed. Ultrasound and isotope liver scans suggested metastatic disease in the liver. At laparotomy the liver and spleen were enlarged and firm and pale in appearance. A liver nodule was biopsied and Congo red staining demonstrated amyloid fibril deposition. The fibril type was not identified. No evidence of malignancy was seen. Restaining of the colonic biopsies previously reported as normal showed similar amyloid deposition. Electrophoresis of plasma and urine proteins were repeatedly normal and a bone marrow biopsy was normal with 4% plasma cells.

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Over the following year she developed cardiac failure and postural hypotension. An ECG showed small voltage complexes with a pseudoinfarction picture of septal Q waves. She subsequently developed vertebral collapse with isotope bone scan evidence of bony infiltration. She died in hospital three and a half years after presentation due to the combined effects of heart failure and cachexia.

CASE 2

A 57-year-old lady presented to the gastroenterology clinic with a two year history of crampy lower abdominal pain and a two month history of profuse watery diarrhoea. She described episodes of nocturnal diarrhoea and faecal incontinence but no blood loss. She had lost 4 kg in weight. A recent barium enema had been normal. Six years previously she had been diagnosed as having a cutaneous vasculitis, having presented with a diffuse bruising purpuric rash. Skin biopsy at that time demonstrated thickened dermal blood vessels with C1q deposition. There were no serological markers or other features of vasculitis. A year prior to this presentation, investigation for atrial fibrillation had revealed mild cardiomegaly, and echocardiographic evidence of early left ventricular hypertrophy.

On examination there was a purpuric rash over her upper chest, arms and peri-orbital area (figure 1a, b, c). Dipstick urinalysis showed proteinuria. Blood pressure was 90/60 mmHg. Flexible sigmoidoscopy revealed a diffusely abnormal mucosa with a glistening oedematous appearance. There were friable areas which bled easily on contact. Clinically her presentation was consistent with colitis, possibly vasculitic in origin. Rectal biopsy however showed only thick walled sub mucosal vessels. Full blood count, sedimentation rate, and biochemical investigations remained normal throughout. A small bowel series showed rapid transit but no mucosal abnormality. A therapeutic trial of prednisolone enemas and oral mesalazine produced no clinical benefit. She was later readmitted for further investigation of persisting

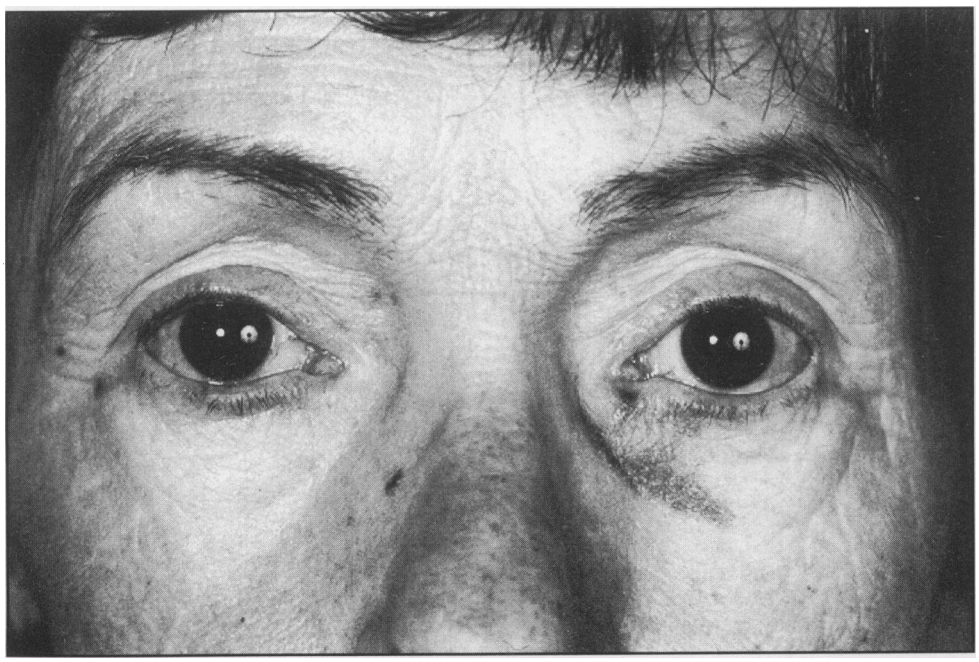

Fig 1a. Face.

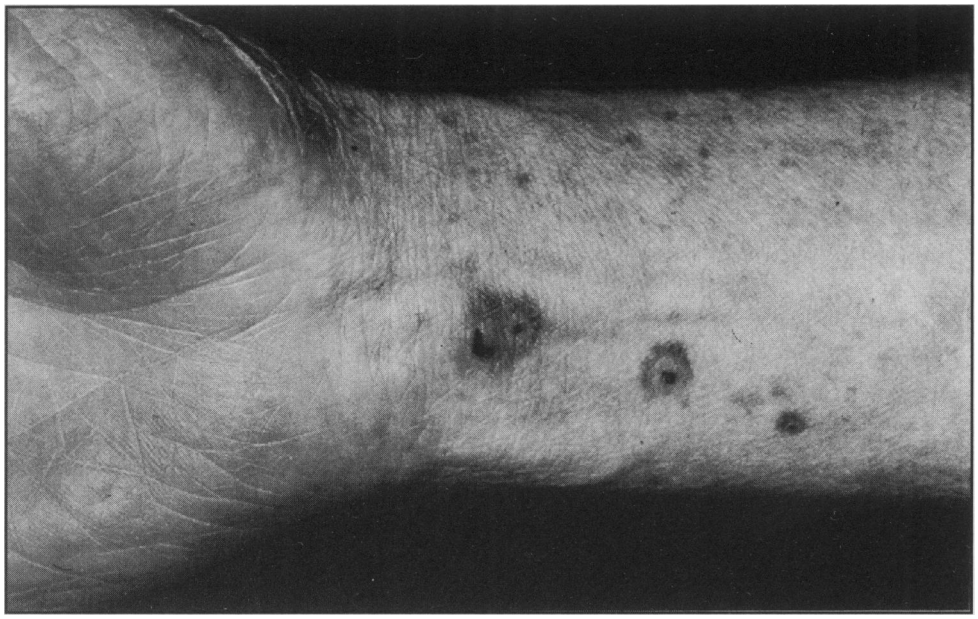

Fig 1b. Wrist

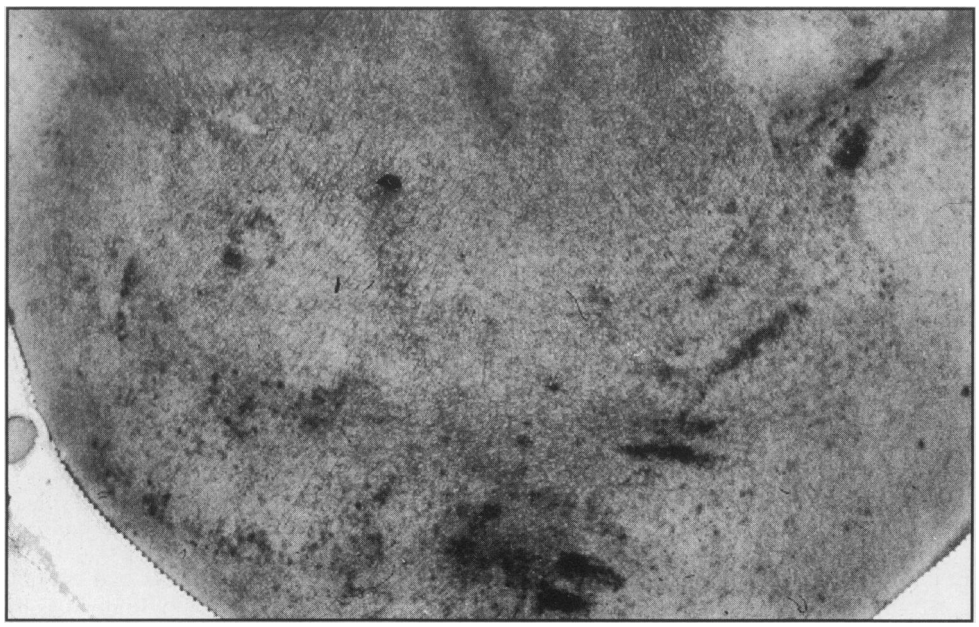

Fig 1c. Upper chest

diarrhoea and an episode of rectal bleeding. Repeat sigmoidoscopy showed the same mucosal appearance and further biopsies were taken though this time the possibility of amyloidosis was raised.

Light microscopy with Congo red staining revealed amyloid deposition in the submucosa, vessel walls and interstitium. There were no features of vasculitis or inflammatory bowel disease. Staining for AA amyloid fibrils was negative and the pathologist felt this probably represented AL amyloidosis. Congo red staining of the archival samples from skin and the recent rectal biopsy showed similar amyloid deposition. Plasma protein and urine electrophoresis which had been previously normal both now showed a small discrete IgA kappa light chain. Bone marrow aspirate and trephine showed a normal plasma cell population. Just prior to this admission she had presented elsewhere with an episode of atrial fibrillation and congestive cardiac failure. An echocardiogram showed left ventricular hypertrophy with a ground glass appearance typical of amyloid deposition. Impairment of ventricular function was noted. The patient was treated with an ACE inhibitor, digoxin and symptomatic anti-diarrhoeal therapy. Two years after diagnosis she died following a bowel perforation and peritonitis. Post-mortem revealed no evidence of myeloma or other source of amyloid.

DISCUSSION

The term amyloid, meaning "starchlike", refers to the first descriptions of its staining pattern with iodine in the 19th century (reviewed in ref. 1). Amyloidosis encompasses a group of diseases characterised by deposition of a fibrillar, proteinaceous material in various tissues. Pathological diagnosis today is still based largely on Congo red staining of the amyloid fibril subunit when the typical apple-green birefringence is seen under polarised light.[1] Classification of amyloidosis is now based on the biochemical characteristics of these protein fibrils.[2] At least fifteen normally non-fibrillary proteins have been identified as precursors of the pathogenic amyloid fibril. Despite differences in primary fibril structure the organisation of the fibrils into similar secondary structures with a beta-pleated sheet conformation probably favours deposition and appears to be a crucial step in amyloidogenesis. Congo-red staining can occasionally be absent and in such cases typical amyloid fibrillar change has been recognised by electron microscopy.[3] The amyloid-protein associated with plasma cell dyscrasias (AL- amyloid protein from light chain) is the same protein found in primary amyloidosis. This reflects a common pathogenesis between these plasma cell proliferative processes, and the separation of AL amyloidosis into patients with and without multiple myeloma is by no means clear cut.[3]

Using sensitive techniques a paraprotein band may be detected in serum or urine in 86% of patients with primary amyloidosis.[3] When no monoclonal protein is demonstrated the possibility of unrecognised familial amyloid polyneuropathy should be considered.[4]

In primary amyloidosis initial findings associated with multiple myeloma such as lytic bone lesions, hypercalcaemia and renal failure are usually absent. Clinical manifestations of the extracellular deposition of these relatively insoluble protein fibrils depend on the extent of amyloid deposition and the organ involved.

The clinical expression of amyloidosis in the gastrointestinal tract depends on the site of GI involvement and may be less obvious than cardiac, neural or renal involvement.

In a large series of patients with primary amyloidosis 8% of 769 patients had clinical gastrointestinal involvement.[5] However diagnosis of primary systemic amyloidosis is by rectal biopsy, where 80% are positive. This suggests either asymptomatic deposition or poor clinical recognition of the effects on the GI tract.

Any part of the gastrointestinal tract may be involved and can cause a range of features from obstruction, malabsorption, ulceration, haemorrhage, infarction to more non-specific features such as diarrhoea and constipation. Weight loss as seen in both cases here is almost universal. Given the range of clinical expression the clue to diagnosis lies in the duration of symptoms and the associated features of amyloid in other organs.

Case 1 illustrates malabsorption as a presenting feature. Malabsorption may be due to mucosal infiltration or autonomic neuropathy with bacterial overgrowth. Pancreatic involvement has been described and may account for the significant fat malabsorption seen in this case.[6] The diagnosis of primary amyloidosis was not made until hepatic involvement occurred eighteen months after presentation. Clues to hepatic amyloidosis include hepatomegaly out of proportion to the upset in liver function tests and Howell-Jolly bodies due to hyposplenism.[3] In such patients associated proteinuria and a monoclonal protein band can help with diagnosis. In this case the normal serum and urine electrophoresis raise the possibility of a sporadic form of familial amyloidosis. However hepatic disease causing hepatomegaly or cholestatic liver function tests occurs in 16% of patients with primary amyloidosis and rarely in patients with familial amyloidosis.[4] This feature plus the absence of peripheral neuropathy was not typical of familial amyloidosis. It is also likely that a small monoclonal protein band was not demonstrated during standard plasma and urine electrophoresis. Screening of serum and urine for the monoclonal protein peak is best done after direct communication with the biochemistry laboratory, where immunoelectrophoresis may be more sensitive. This patient later had evidence of cardiac and autonomic disease. Bony involvement with vertebral collapse has been described before in association with amyloidosis without overt myeloma.[7]

Case 2 demonstrates colonic amyloidosis with preceding skin and cardiac involvement. Amyloid deposition in the colon, although common on biopsy, is rarely clinically significant or radiologically obvious. CT scanning can demonstrate bowel wall thickening.[8] The cardiac and skin involvement were felt to be unrelated to her diarrhoea until after diagnosis. Left ventricular hypertrophy without hypertension or features of cardiomyopathy is another clue to diagnosis. This aspect of the disease is seen more commonly now with the advent of echocardiography. ECG changes such as the pseudoinfarction pattern seen in the first patient occur later. Cardiac failure is a poor prognostic feature in primary amyloidosis with a median survival of eight months.[3]

Both patients had early evidence of renal involvement with persistent proteinuria. This clinical clue was disregarded until after diagnosis. Nephrotic syndrome, seen in 44% of patients, is the commonest mode of presentation.[3] Progressive renal disease is seen usually in the presence of a raised creatinine or nephrotic range proteinuria at presentation, dialysis being required for 18% of a large series of patients with primary amyloidosis.[9]

Neither patient had macroglossia which occurs in only 10% of patients. Both patients had evidence of autonomic neuropathy with postural hypotension but no features of peripheral neuropathy. Both patients demonstrated skin involvement, the second patient having presented six years previously with the typical purpuric rash and capillary fragility. This is a classical example of cutaneous involvement by amyloidosis though only 5-16% of patients have purpura at presentation. The non-specific findings on skin biopsy were erroneously interpreted as vasculitis for which she was treated with immunosuppressive agents for a number of months. Immunosuppression has been tried unsuccessfully in primary amyloidosis and now chemotherapy with melphalan and prednisolone is reserved for some patients where response rates of only 20% are seen.[10] These patients who have less advanced disease show a median survival of 6-7 years.

These cases illustrate the subtlety of primary amyloidosis affecting the gastrointestinal tract. Earlier diagnosis can be achieved using the extragastrointestinal clues mentioned above in association with urine and plasma electrophoresis. Even at this stage the diagnosis can be missed if the pathologist is not alerted to the possibility of amyloidosis as a clinical differential diagnosis. This approach will avoid unnecessary investigation and subsequently inappropriate and potentially dangerous treatment.

ACKNOWLEDGEMENTS

We would like to thank Drs Claire Hill, Damian McManus and Maureen Walsh, Department of Pathology, Royal Victoria Hospital, for advice with the second case.

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The Ulster Medical Journal, Volume 64, No. 2, pp. 197 – 198, October 1995.

Case Report:

Dietary deficiency of iron – an extreme example

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Accepted 20 July 1995

Iron deficiency anaemia is still a problem in childhood, and even mild anaemia may interfere with psychomotor development. Occasionally, very severe anaemia is seen in paediatric wards. We present an extreme example of anaemia secondary to dietary deficiency of iron.

CASE REPORT: A three and a half year old girl was admitted with lethargy and extreme pallor. The history was of increasing lethargy for three weeks with nothing to suggest acute or chronic blood loss. She was not troubled with recurrent infections but her mother described her as a "picky" eater who had sustained herself almost exclusively on cow's milk for one year. On examination she was severely anaemic with signs of marked congestive heart failure. Temperature was normal. There was no bruising, koilonychia or glossitis. Weight which was on the tenth centile at birth had dropped to the third centile and height was on the tenth centile.

Chest radiography showed marked congestive heart failure, and an electrocardiograph demonstrated right ventricular strain. Prior to transfusion haemoglobin was 1.3 g/dl, MCV 56 fl, white cells 7.9 x 10^9/1, platelets 62 x 10^9/1. The blood film was consistent with iron deficiency anaemia with normal white cell morphology. Serum ferritin was 4.2 µg/litre, serum iron 1.3 µmol/litre, total iron-binding capacity 102.3 µmol/litre and the transferrin was 1.3% saturated. Other investigations were performed post transfusion. Serum B_{12}, folate, copper, zinc, urea, electrolytes, calcium, thyroid and liver function were normal. Anti-gliadin and anti-endomysial antibody screening was negative. Faecal occult bloods were negative and there was no haematuria.

She was slowly transfused with semi-packed cells with diuretic cover for 48 hours. Her heart failure resolved and she was commenced on oral folate and iron. Three days after commencing her oral therapy haemoglobin had risen to 9.0 g/dl, MCV to 77 fl and platelets to 630 x 10^9/1 with a reticulocytosis of 5%. One week after transfusion, echocardiography revealed a small pericardial effusion but good ventricular function. Two months later haemoglobin was 12.6 g/dl and oral iron was stopped with no recurrence of anaemia. Repeat echocardiography showed only a rim of pericardial fluid anteriorly and good left ventricular function. Over the following six months her weight gradually increased from the third to the fiftieth centile and her height from the tenth to the twenty-fifth centile.

DISCUSSION

This child had been breast fed for six months. Her mother did not require extra iron during the pregnancy but had a blood transfusion in the post partum period. Solids were introduced

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at the age of six months and at this stage a formula milk was substituted for the breast. By all accounts she thrived until she was two when her younger sister was born. It was at this time that the child began to refuse all food except cow's milk with occasional toast and breakfast cereal. She also took Abidec vitamin drops for six months after the age of two. She displayed pica and chewed her father's slippers and watch-strap.

Dietary analysis showed minimal iron sources in her diet. The small amount of iron in the cereal would not have been absorbed well because of the lack of vitamin C and the presence of phytates in the cereal.[1] The family had little contact with their general practitioner. When the child was last seen medically at two and a half years she was felt to be well, with weight on the fiftieth centile. On two occasions in the past year the health visitor had been concerned about the child's pallor but further help was not sought. Her younger sister had also developed an iron deficiency anaemia.

Iron deficiency is increasingly recognised as a systemic disease.[2,3] This child readily passed the fiftieth centiles in the Denver Developmental Screening test but this does not prove optimal psychomotor development as she might have achieved more had her iron stores been normal. The possibility of coeliac disease was considered but jejunal biopsy was not thought to be necessary when she responded so well to oral iron.

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