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Editorial

Promoting physical activity in primary care: How to get over the hurdles?

PHYSICAL ACTIVITY AND HEALTH

Public health promotion policies have recognised the role of physical activity as a key determinant of good health. Activity is associated with reduced mortality, with the prevention of many conditions including cardiovascular disease, diabetes, osteoporosis, depression, colon cancer and obesity, and with improved levels of physical functioning and independent living.[1] However, there is a serious shortfall in the actual numbers of people who engage in sufficient levels of activity to confer health benefits.[1,2] This contributes significantly to ill health and risk of coronary heart disease, on a par with smoking, excessive alcohol consumption, elevated blood pressure, obesity and poor diet.

Primary care has been recognised as a potentially important site for promoting physical activity.[1]

PHYSICAL ACTIVITY PROMOTION IN PRIMARY CARE

Background

In 1995, the American College of Sports Medicine, in conjunction with the Centre for Disease Control recommended that "Every U.S. adult should accumulate at least 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week'.[3] In Northern Ireland 78% of people do not perform the recommended level of physical activity.[2]

Methods of delivery

Primary health care professionals may promote exercise by giving opportunistic advice during routine consultations or by referring patients to activity promoting programmes. These include exercise referral schemes (whereby the patient is given a prescription for exercise sessions at the local leisure centre) or supervised training sessions (such as an organised walk led by a health care professional).

Difficulties

Barriers to promoting physical activity which have been identified include a lack of health professionals' time, specialist knowledge and their own levels of interest in exercise.[4] Opportunistic, non-specific advice is applicable to all but has not been shown to lead to significant long-term changes in activity levels. Of the UK population, less than 1% are referred to specific exercise schemes. Most of those who are referred are white, middle-class, middle-aged, healthy women.

People also report a lack of time as a barrier to increasing their levels of activity and they find difficulty in sustaining interest in participation in activity programmes.

OVERCOMING THE DIFFICULTIES

Lack of health professionals' time

Using motivational interviewing techniques the doctor may assess the patient's desire to change their lifestyle and begin an exercise programme. This may avoid wasting health professionals' effort and time on those who are not serious about investing their effort and time in exercise.

When a patient clearly shows an intention to increase their activity, the General Practitioner GP may refer them to a local leisure centre to receive appropriate exercise testing by trained professionals. They may then embark on an activity programme[1] which uses specialist services to tailor exercise to the individual and offers a potential saving of time for the GP by reducing the necessity for follow up. Such programmes should address the needs of individual adults and local communities.[1] Patient selection should be medically led, targeting those who are sedentary, therefore allowing maximal potential for health gain, and those with specific medical conditions.[1]

Lack of specialist knowledge

Concern has been expressed regarding the suitability of GPs to prescribe exercise given their limited training in this area.[6] Some medical defence organisations advise that, if the GP is unsure of their own level of knowledge, rather than prescribing exercise, recommending it is appropriate.[1] There are some simple tools available to GPs to help patients reach their activity goals. These include brief motivational

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interviewing techniques which may be used to encourage patients to consider a positive change in their lifestyle, and pedometers.

Pedometers are small electronic devices that fit to the belt and are used to count numbers of steps taken. They are relatively cheap, easy to operate and can be used to assess compliance with an exercise programme by determining distance walked (stride length multiplied by number of steps) and speed of walking (distance over time). Such information can be used as a measure of the intensity of activity and to estimate total energy expenditure.

Patients may set themselves targets to reach in terms of number of steps. In a pilot study of a primary care based walking programme, not yet published, we found that pedometers provided a useful method of external monitoring, providing both a record of changing performance and a motivational tool. It has been proposed that younger adults should aim for between 7,000 and 13,000 steps per day of general activity and older adults between 6,000 and 8,500. To achieve this may mean an increase in daily routine activity (e.g. starting to walk to another department at work instead of phoning).

Lack of the professional's own interest in exercise

Primary care professionals' levels of personal activity or desire to change their own exercise habits tend to be directly related to their levels of exercise recommendation to patients. In one study[4] GPs who were already exercising or contemplating exercise were three times more likely to recommend exercise to their patients. This trend quadrupled with practice nurses. MacAuley & Jaques liken the sedentary physician recommending exercise with the doctor who smokes but tells their patient to stop; "although the advice is sound, will the message be heard?".[5]

Difficulties in recruiting patients to schemes

Difficulties in recruiting patients to physical activity schemes have been reported. In a pilot study in Swansea, only 38 patients were recruited from seven general practices over four months: the scheme was abandoned due to lack of interest. The Stockport 'Exercise on Prescription' scheme recruited 60% of patients invited to take part by GPs but after 10 weeks there was a high percentage of non-attendance. The problem of poor recruitment requires further study.

Patients report a lack of time as a barrier to increasing their activity levels and participating in schemes. Most people (health care professionals included) find life is getting busier and spare time shorter. Recent research suggests that health benefits can be accumulated over the course of a day by dividing 30 minutes' exercise into shorter bouts. Parking some distance from the workplace and walking briskly to and from it for 10-15 minutes could accomplish the recommended amount of daily activity.

Sustaining levels of adherence

A review of randomised controlled trials [6] revealed characteristics of programmes which were most effective at sustaining participation in physical activity:

- Activity performed at home, rather than in leisure facilities
- Unsupervised, informal exercise, at a time suitable to the individual
- Frequent professional contact, usually by telephone
- Moderate intensity exercise, with walking as the most common form

GPs could translate this knowledge by recommending patients undertake a programme of brisk walking for 30 minutes a day, on most days of the week. To empower the patient to maintain this activity GPs may suggest that they keep a simple diary, recording the exercise that has been performed. Accountability is a helpful thing, and these diaries could be returned to the practice nurse for evaluation.

Risks associated with regular physical activity

The risks associated with a more active lifestyle are relatively low with moderate levels of activity, but increase with intensity. Before beginning an exercise programme, a cardiac risk assessment should be made. Guidelines of professional organisations such as the American College of Sports Medicine can be used. For relatively healthy patients, risk assessment involves a brief medial history and physical examination to exclude risk factors for heart disease. In less healthy patients, more rigorous pre-exercise assessment may include a maximal stress test.[1] Patients with coronary heart disease have the most to gain from moderate intensity exercise, as long as care is taken to avoid performing exercise in sudden bursts and not ignore symptoms such as chest pain or dizziness.

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Conclusions for physical activity in primary care

Physical activity advice is firmly on the agenda for health promotion. Primary health care workers have been advised that they should always recommend or advise patients to increase levels of physical activity with the same priority as they give to dietary advice or smoking cessation.[1] Difficulties exist, but steps can be taken to minimize these. More study is needed on the promotion of exercise in primary care.

M.A. Tully*, M. E. Cupples*, I.S. Young†

*Department of General Practice, The Queen's University of Belfast, Dunluce Health Centre, 1 Dunluce Avenue, Belfast BT9 7HR.

†Department of Medicine, The Queen's University of Belfast, Institite of Clinical Science, Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA.

Correspondence to Mr Tully.

E-mail: m.tully@qub.ac.uk

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Accuracy of the clinical diagnosis of Down Syndrome

L Devlin, P J Morrison

Accepted 3 March 2004

SUMMARY

Objectives – to determine the accuracy of clinical diagnosis of Down syndrome, identify problems in reaching a diagnosis, to provide recommendations for improvement and estimate a minimum prevalence for all types of Down syndrome.

***Design* – A retrospective observational study was carried out over a five-year period. Genesis, a database located in the Department of Medical genetics, was used to identify the number of Down syndrome karyotypes including trisomy, translocation, and mosaic sample variants. Age of diagnosis was determined using date of receipt. Karyotyping requests for a clinical diagnosis of Down syndrome were also identified. Patient notes and cytogenetic laboratory reports were used to identify clinical indication for karyotyping.**

***Setting* – Regional Genetics Centre, covering all cytogenetic analyses for referrals within the entire Northern Ireland population.**

***Results* – 208 postnatal cases of Down syndrome were identified, 197 (94.7%) trisomy, 3 (1.45%) translocation, and 8 (3.85%) mosaic variants. 112 (54.8%) were male and 96 (46.2%) female. 268 samples were taken to confirm or exclude a clinical diagnosis of Down syndrome. 185 of these had Down syndrome, 77 were normal, and 6 had another abnormality. 90% and 100% of trisomy and translocation Down syndrome respectively were diagnosed on the basis of clinical features. This fell to 37.5% of mosaic Down syndrome patients being diagnosed clinically ($p<0.001$). Simian crease, sandal gap, epicanthic folds, hypotonia, upslanting palpebral fissures, and protruding tongue are the most frequent characteristic features seen. Similarly epicanthic folds, protruding tongue, simian crease and sandal gap, hypotonia, and upslanting palpebral fissures are also described in a significant proportion of karyotypically normal individuals, thus arousing a suspicion of Down syndrome. 89.4% of patients were diagnosed between day 1 and 7 of life. Of 10.6% patients diagnosed after day 7 of life, 7.6% were adults and 3% children. The minimum prevalence was estimated at 167.9 per 100,000, or 1 in 595 births.**

***Conclusion* – In a defined population, with a prevalence of around 1 in 600 births, accurate clinical diagnosis occurred in 90%, 100%, and 37.5% of trisomy, translocation, and mosaic patients. 49.5% of patients had one or more of the following phenotypic findings: Simian crease, sandal gap, epicanthic folds, hypotonia, upslanting palpebral fissures, and protruding tongue. However, the same six features aroused a suspicion of Down syndrome in individuals with normal karyotyping, thus causing undue stress and worry to parents.**

Mosaic cases may be more common than previously recognised, and often do not have dysmorphic features. It is therefore a diagnosis that should always be considered in those who are educationally subnormal without a definitive diagnosis.

INTRODUCTION

Down syndrome is one of the most common and the best known of all malformation syndromes,[1] with an estimated prevalence of 1/600 - 1/800.[2] Numerous clinical features have been recognised the accurate prevalence of the condition. Chromosomal analysis is time consuming, and delay leads to anxiety amongst parents whilst the diagnosis is unsure. Undue worry is caused to parents of karyotypically normal children being

Department of Medical Genetics, Belfast City Hospital Trust, Lisburn Road, Belfast BT9 7AB.

L Devlin, MB, BCh, Specialist Registrar Clinical Genetics.

P J Morrison, MD, FRCPCH, FFPHMI, Professor of Human Genetics.

Correspondence to Professor Morrison.

E-mail: patrick.morrison@bch.n-i.nhs.uk

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investigated for Down syndrome on the basis of a few clinical features.

Earlier clinical diagnosis allows parents to begin to accept the diagnosis at an earlier stage, and in some instances, make medical decisions about life threatening events.[4]

The objectives of this study were to determine accuracy of, and time taken to reach a clinical diagnosis, to identify problems in reaching a clinical diagnosis and provide some recommendations for improvement, whilst estimating the prevalence of the condition in a well defined population.

METHODS/STUDY DESIGN

A retrospective observational study was carried out over a five-year period from 01/01/97 – 31/12/01. Genesis, a genetic clinical and laboratory records database in the Department of Medical Genetics that covers the entire Northern Ireland population of 1.7 million, was used to collect data on the following: number of Down syndrome patients, including trisomy, translocation and mosaic variants, the clinical indication for karyotyping request, the ratio of male to female Down syndrome patients, age at diagnosis (using date of receipt), and number of karyotyping requests for a clinical suspicion of Down syndrome. A separate card index of all chromosome disorders from 1971 was also utilised, along with a search of the clinical records from the Northern Ireland genetics service (dating back to 1969), and cross checking these with the genesis records to achieve as complete an ascertainment as possible within the defined population of 1.7 million.

Patient notes and cytogenetic laboratory records were then used to identify clinical features of those who had undergone karyotyping for a clinical suspicion of Down syndrome, and reason for late diagnosis.

RESULTS

We identified 210 cases of Down syndrome. Two samples were from (prenatal) cordocentesis and therefore excluded from further analysis.

Of 208 cases included in our study 197 (94.7%) had full trisomy 21, three (1.45%) were translocation, and 8 (3.85%) were mosaic Down syndrome (Fig. 1). 112 (54.8%) were male and 96 (46.2%) female.

268 samples underwent karyotyping to confirm or exclude a clinical diagnosis of Down syndrome. 185 of these had Down syndrome, 77 were normal and 6 had another abnormality (Fig. 2.).

Clinical indication for karyotyping of 208 Down syndrome samples was recorded, including the breakdown for trisomy, translocation, and mosaic patients – Table I, 90% of trisomy Down syndrome and 100% of translocation Down syndrome were diagnosed on the basis of clinical features. This fell to 37.5% in mosaic Down syndrome patients. Statistical analysis using Fishers exact test showed a highly significant difference between mosaic group and the other two groups combined, in that mosaic Down syndrome is more difficult to detect clinically ($p<0.001$).

As well as indication for karyotyping, individual clinical features of each child with Down syndrome were identified using karyotyping request forms and patient notes. In 29% of patients it was only stated that the patient had Down syndrome and individual clinical features were not noted. Of the remaining 71% who had clinical features described, the frequency of each feature was recorded and these were expressed as a percentage. The majority of patients had numerous features described. The results are therefore cumulative (Fig. 3).

Trisomy, Translocation and Mosaic Down syndrome

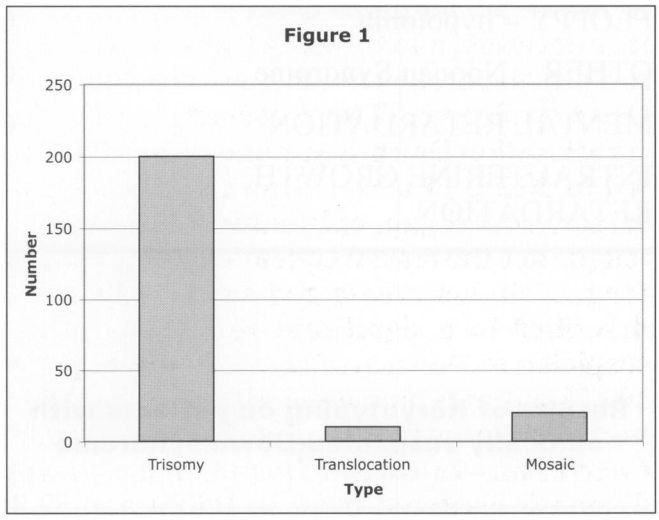

Fig 1. Number and type of Down syndrome

We analysed the 77 patients with a normal karyotyping result to see if we could identify clinical features that may have been suggestive of Down syndrome. In 13% no clinical features were described and Down syndrome only was

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TABLE I

Trisomy, Translocation, and Mosaic Down Syndrome - Clinical Indication for Karyotyping

Clinical Indication for Karyotyping	*Total (208)*		*Trisomy (197)*		*Translocation (3)*		*Mosaic (8)*	
	%	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*
DOWN SYNDROME – clinical suspicion of Down Syndrome	88	183	90	177	100	3	37.5	3
DYSMORPHIC/MCA – two or more dysmorphic features or multiple congenital abnormalities	7	15	7	14	0	0	12.5	1
DEVELOPMENTAL DELAY	0.5	1	0	0	0	0	12.5	1
CHECK – repeat sample. Previous sample identified Down Syndrome	1.5	3	1	2	0	0	12.5	1
CABNFH – chromosomal abnormality, family history of	0.5	1	0.5	1	0	0	0	0
FLOPPY – hypotonia	0.5	1	0.5	1	0	0	0	0
OTHER – Noonan Syndrome	0.5	1	0	0	0	0	12.5	1
MENTAL RETARDATION	0.5	1	0	0	0	0	12.5	1
INTRAUTERINE GROWTH RETARDATION	1	2	1	2	0	0	0	0

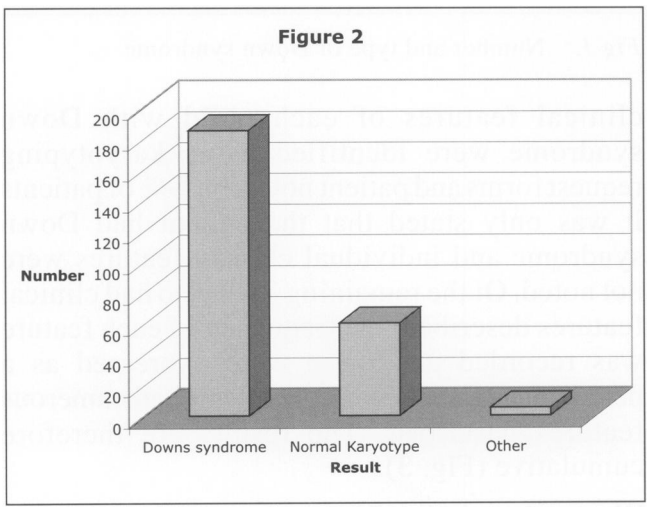

Fig 2. Results of karyotyping on patients with clinically suspected Down syndrome.

stated. In the remaining 86% the clinical features described were recorded and expressed as a percentage of frequency (Fig. 4).

Age at diagnosis was calculated using date of receipt of sample to the Cytogenetic Laboratory. 186 patients were diagnosed between day 1 and 7

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Frequency of Clinical Features found in patients with Down syndrome – expressed as a percentage

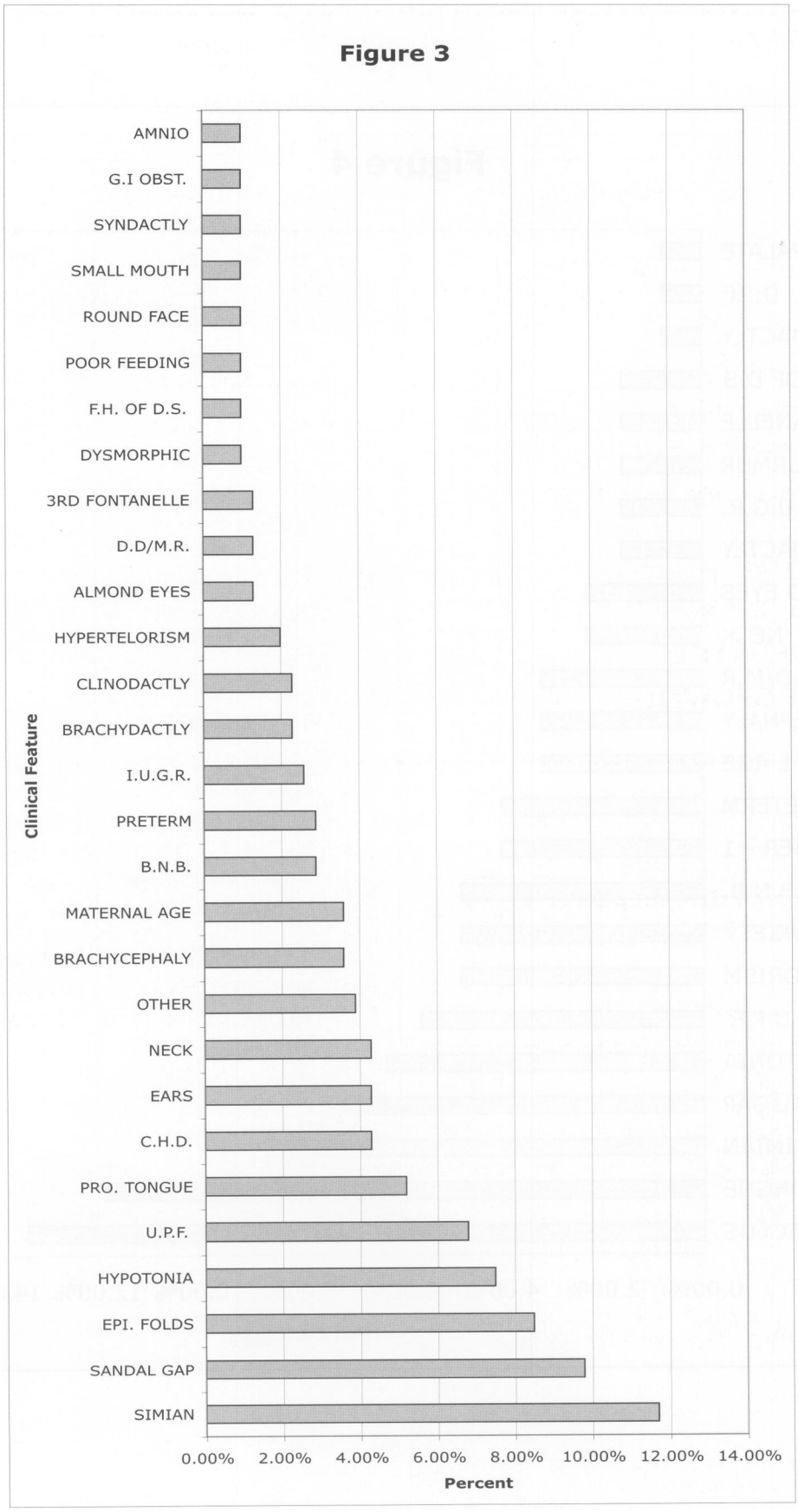

Fig 3. Frequency of clinical features found from records of patients with Down syndrome – expressed as a percentage

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Frequency of Clinical Features suggestive of Down syndrome in patients with normal Karyotyping – expressed as a percentage

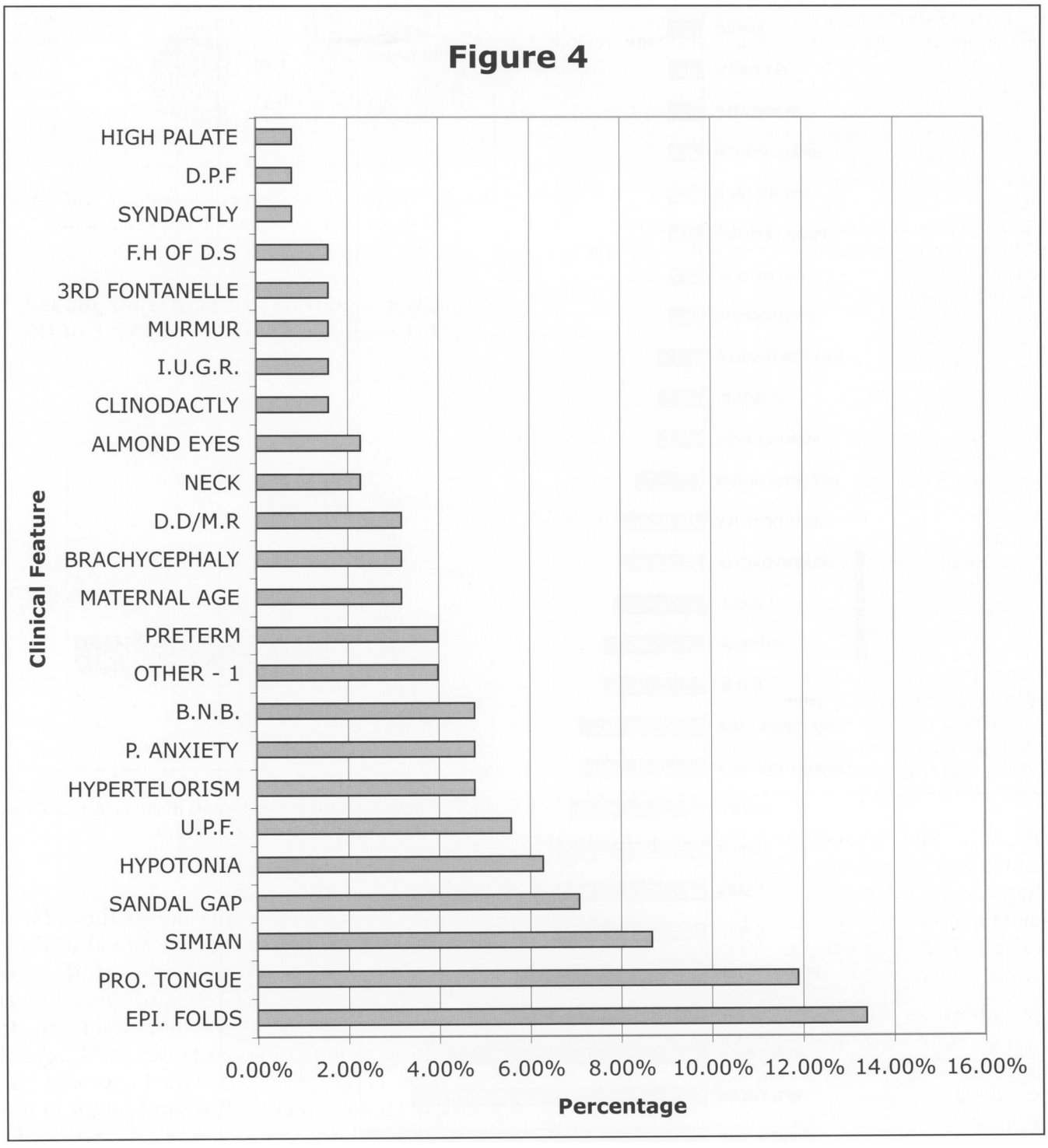

Fig 4. Frequency of clinical features suggestive of Down syndrome from records of patients with normal karyotyping – expressed as a percentage.

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ABBREVIATIONS

AMNIO – Previously diagnosed with Down syndrome on amniocentesis
B.N.B – Broad nasal bridge
CH.D – Congenital heart disease
D.D/M.R – Developmental delay / Mental retardation
D.P.F – Down slanting palpebral fissures
Dysmorphic – Dysmorphic features noted, not described individually
EARS – Low set or dysmorphic ears
EPI. FOLDS – Epicanthic folds
F.H of D.S – Family history of Down syndrome (1st degree)
G.I OBST. – Gastrointestinal obstruction
I.U.G.R – Intrauterine growth retardation
MATERNAL AGE – Maternal age >30
MURMUR – Undiagnosed cardiac murmur
NECK – Short neck / increased nuchal skin thickness
OTHER – Other abnormality / diagnosis in the Down syndrome group including:
- Macrocephaly
- Microcephaly
- Noonan Syndrome
- Renal abnormalities
- Short stature
- Swollen feet
- Talipes
- Umbilical hernia
- Wide spaced nipples

OTHER 1 – Other abnormality in group with normal karyotype including:
- Atrioventricular septal defect
- Duodenal Atresia
- Hydrops Fetalis
- Talipes
- Tracheoesophageal fistula

P. ANXIETY – Parental Anxiety
PRETERM – < 37 weeks gestation
PRO. TONGUE – Protruding tongue
SIMIAN – Simian crease, unilateral/bilateral.
U.P.F – Upslanting palpebral fissures

(89.4%). The breakdown of these patients is shown as a percentage (Fig. 5). Of the 7 patients diagnosed on day 6, two of these samples were taken over a holiday period, thus accounting for a slight delay in diagnosis. One sample on day 7 was also taken over a holiday period.

22 patients were diagnosed after day 7 of life. 16 (7.6%) adults and 6 (3%) children. These were further sub-divided into trisomy (15), translocation (1) and mosaic (6) Down Syndrome (Fig. 6).

Three patients in the mosaic group were diagnosed in childhood. One was diagnosed at 6 months of life and was clinically felt to be Noonan Syndrome. A second child in this group was diagnosed at 19 months and presented with developmental delay. The third child had a sample sent at 7.5 years of

Percentage of patients diagnosed with Down syndrome between day 1 and day 7 of life

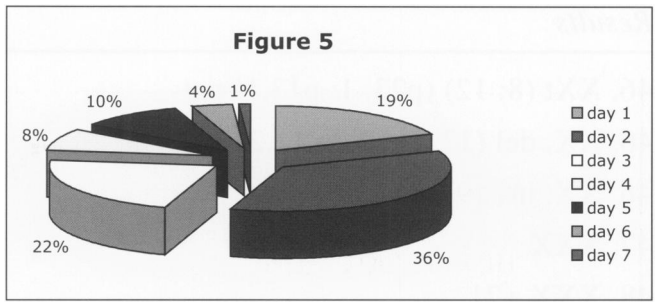

Fig 5. Percentage of patients diagnosed with Down syndrome between day 1 and day 7 of life.

Infants, children and adults diagnosed with Down syndrome after day 7 of life

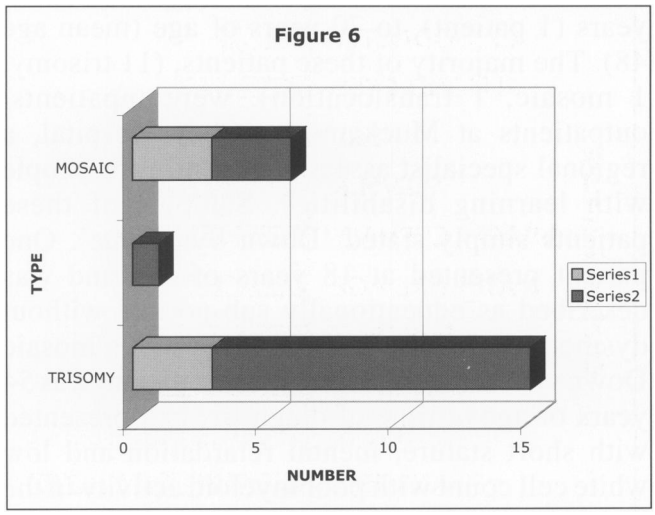

Fig 6. Infants, children and adults diagnosed with Down syndrome after day 7 of life.

age. This was a check sample and not time of first diagnosis. In the trisomy group a total of three children were diagnosed after day 7 of life. One infant was diagnosed at 23 days of life. Clinical indication for karyotyping was intrauterine growth retardation. Another diagnosis was at 31 days of life. This child presented with hypotonia and bilateral simian creases. The third infant in this group was a check sample sent at 37 days of life. All six children with a diagnosis later than day 7 of life were from different hospitals around the Northern Ireland region, including the regional neonatal centre. Baby checks are carried out by different specialities and different grades of staff in various hospitals.

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TABLE II

Abnormal results and their clinical interpretation

Results	*Clinical Interpretation*
46, XXt (8; 12) (p23, 1; p13.1) pat	Balanced translocation
46, XX, del (12) (p12.2p 11.23)	Partial deletion of chromosome 12
46, XX, inv (9) (p11q13)	Normal female with variant
47, XXX	Triple X
48, XXX +21	Triple X and trisomy 21
47, XX, +mar.ish	Small bisatellited dicentric derivative 15

Of those diagnosed as adults, there were 12 trisomies, 3 mosaics, and 1 translocation Down syndrome. Age in this group ranged from 18 years (1 patient), to 70 years of age (mean age 48). The majority of these patients, (11 trisomy, 1 mosaic, 1 translocation), were inpatients/ outpatients at Muckamore Abbey Hospital, a regional specialist assessment centre for people with learning disabilities. Samples of these patients simply stated 'Down Syndrome'. One patient presented at 18 years of life and was described as educationally sub-normal without dysmorphic features. This patient was a mosaic Down syndrome. A further mosaic patient was 54 years of age at time of diagnosis and presented with short stature, mental retardation and low white cell count with poor myeloid activity in the bone marrow. One trisomy patient was diagnosed at 54 years of age. Notes were unavailable. History on the request form stated that there was a family history of translocation.

Six karyotyping samples were found to be abnormal but not Down syndrome Table 2. In the sample group that was felt to be clinically Down syndrome, two samples were unsuccessfully karyotyped. One sample was in the wrong bottle and the second was an unbanded analysis from poor growth.

DISCUSSION

Based on the 5-year period having identified 192 births in the neonatal period, in a population total of 114,307 live births, a minimum prevalence of 167.9 per 100,000 (or 1 in 595 births) was calculated. This compares closely to previous (lower) estimates of the prevalence of Down syndrome and is an accurate minimum prevalence figure, taking into account the number of mosaic Down syndrome cases which are difficult to calculate in the population which may not be reflected in other less accurate prevalence figures. If we include the cases diagnosed in adulthood as a proxy for missed cases of mosaic Down syndrome yet to be recognised, (208), the figure increases to 181.9 per 100,000 (or approximately 1 in 550 births).

Over the study period, 208 postnatal cases of Down syndrome were identified. 94.7% trisomy, 1.45% translocation, and 3.85% mosaic variants. Expected ratios are 94% trisomy, 5% translocation, and 1% mosaic variants.[2] The detection rate of mosaic variants is higher than the standard quoted rates of 1-3%. Our study includes a complete population, and newly diagnosed adult cases, which may account for this. Often mosaic variants do not have dysmorphic features, and it is therefore worthwhile to carry out a chromosomal analysis on those who are educationally sub-normal without dysmorphic features.

46% of our Down syndrome cases were female and 54% male. The diagnosis was suspected clinically in 88% of patients – 90% of trisomy Down syndrome, 100% of translocation Down syndrome, and only 37.5% of mosaic Down syndrome. Using Fishers exact test this is a highly significant result ($p < 0.001$) proving that mosaic Down syndrome is more difficult to detect leading to a late diagnosis.

In patients with Down syndrome, simian crease, sandal gap, epicanthic folds, hypotonia, upslanting palpebral fissures, and protruding tongue are the most frequent characteristics seen

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and one or more are found in 49.5% of patients in our study. Hall [5] described ten cardinal features of trisomy 21 in the newborn. These included hypotonia, poor Moro reflex, hyper extensibility of joints, excess skin on back of neck, slanted palpebral fissures, and a flat facial profile. Hall looked at trisomy 21 only, without including mosaic or translocation Down syndrome. Our study includes translocation and mosaic Down syndrome and this may have accounted for the difference in results. Interestingly, epicanthic folds, protruding tongue, simian crease, sandal gap, hypotonia, and upslanting palpebral fissures are also described in 53% of karyotypically normal individuals thus arousing a suspicion of Down syndrome, and 28.7% of all karyotyping requests for clinically suspected Down syndrome were normal.

The prevalence of Down syndrome in this study compares well with other figures published previously and is higher. Two reasons are firstly, that this study figure is consistent with a more accurate figure inclusive of mosaic Down syndrome rates and consistent with the higher reported incidence of mosaic Down syndrome of around 4% in this study, when compared to older studies where rates are around 1-2%, and secondly, a reflection of the trend for increasing prevalence of Down syndrome over the last 10 years due to the tendency for couples to have their babies later in life.[6]

Recently, Hindley and Medakkar [7] looked at which criteria are being used to reach a diagnostic suspicion of Down syndrome in neonates using a questionnaire to cytogenetics laboratories in the United Kingdom. They found poor recording of characteristics of Down syndrome and almost one third of possible diagnoses were negative on karyotype.

Karyotyping request forms are not a completely accurate method of ascertaining the clinical features identified, or indeed present and not identified, on the patient. Many forms simply stated 'Down Syndrome' or 'clinical features of Down Syndrome'. Some requests may have only stated a few features elicited on the patient. The forms however give an indication of the reasons why samples are sent in or why the diagnosis of Down syndrome may be suspected and allow accuracy and referral reasons to be compared.

Age at diagnosis was determined using date of receipt of sample to the laboratory. We considered early diagnosis to be within 7 days and felt that this was sufficient to account for delay in sample to arrive in the laboratory due to weekends or holiday periods. After day 7 the earliest diagnosis was 23 days of life. A more accurate method may have been to use date of sampling. 89.4% of patients were diagnosed in the early period. Of those diagnosed after day seven, 7.6% were adults and only 3% children. Two children in this group were check samples meaning that only 6 children were diagnosed after day 7 of life. All 6 children were from different hospitals, thus baby checks were being carried out by different grades of staff. Numbers are not large enough to see any difference in outcome of time to diagnosis depending on who is carrying out the baby check.

The details in the patient notes held in the regional genetics centre, and request forms of the majority of those diagnosed as adults 13 were insufficient to determine whether they were a check sample or a first diagnosis. They may well have had a clinical diagnosis, but chromosomal analysis was not readily available at the time of first diagnosis.

CONCLUSION

49.5% of patients had one or more of six phenotypic findings: simian crease, sandal gap, epicanthic folds, hypotonia, upslanting palpebral fissures, and protruding tongue. Checking for these six features will heighten suspicion of a diagnosis of Down syndrome and the chances of abnormal karyotype. The overall minimum prevalence in the population is around 1 in 600 births. Mosaic cases are more common than previously recognised, and often do not have dysmorphic features, resulting in a later diagnosis Mosaic Down syndrome should always be considered in those who are educationally subnormal but have no definitive diagnosis

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Teaching PRHO prescribing

I Mainie, B Little, L Scott, J Leggett

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SUMMARY

Changes have occurred recently in the teaching syllabus in medical schools across the United Kingdom. These changes have taken the format of modular teaching with group participation and the grouping of topics such as anatomy, physiology and clinical medicine being combined. A short study was designed to assess if students of the new curriculum were competent at answering clinical questions that occur frequently, and common prescribing requests.

PARTICIPANTS

A study was carried out with 151 final year medical students, one week before their finals in May 2002. These students have experienced the new changes to the medical programme. All of the medical students were from Queen's University medical school. The study group was recruited from a cohort of medical students attending an all-day revision lecture in medicine and surgery. The faculty of medicine was consulted prior to setting up the revision lecture and this study. The participants in this study incurred no costs.

METHODS

Medical students were shown twelve questions (ward and pharmacology based) and asked to document their questions on the paper provided. One minute was allowed per question. These were collected at the end and marked by one examiner. Five Specialist Registrars in medicine had previously agreed on the answers. Some specific points were made to the final year students regarding the answers, prior to commencing the questions. For the questions regarding drug prescription (i.e. except question 1) it was specified that both dosage and frequency must be stated. Answers were regarded as incorrect if a dose was not stated, the drug prescribed in a sub-therapeutic dosage, or if a dangerously high dose was prescribed, e.g. Diazepam 100mg. Answers were correct if given in either the generic name or any trade name, e.g. both Maxalon and metaclopramide for question 8.

RESULTS

The questions and outcomes are shown in the table overleaf. Most answers are self-evident, but with some specifics: For question 2, any benzodiazepine was accepted as correct, if prescribed in an appropriate dose. For question 5, a dose of either morphine 5-10mg or diamorphine 2.5-5mg was accepted, and for question 12, hydrocortisone 100mg IV, or adrenaline 1ml 1:1,000 IM or 1ml 1:10,000 IV were accepted. Answers containing solely the drug name were regarded as incorrect, as dosage and frequency were also required. For question 7, it was specified that the elevated potassium level had been checked twice, and the question related to medical treatment of the elevated potassium rather than confirming that it was not a spurious result. The answers to the remaining questions were as follows. Question 1: Heparin (no dose required). Question 3: Normal saline or saline 0.9%. Question 4: Paracetamol lg or two tablets, 4-6 hrly or 6 hourly. Rectal administration was also accepted. Question 6: Clexane or Enoxaparin

Belfast City Hospital, Lisburn Road, Belfast BT9 7AB.

I Maine, MB, BCh, MRCP, Specialist Registrar, Gastroenterology

J Leggett, MB, BCh, MRCP, Specialist Registrar, Respiratory Medicine

Gartnaval Hospital, Great Western Road, Glasgow G12 0XH

B Little, MB, BCh, MRCS, Specialist Registrar, Urology

Beatson Oncology Centre, Glasgow G11 6NT

L Scott, MB, BCh, MRCP, Specialist Registrar, Oncology

Correspondence to Dr Mainie, 127 Brantwood Gardens, Greystone Road, Antrim BT41 1HS.

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TABLE I
Percentage of correct response for each question

	Question	*Percentage correct*
1.	With what drug must an arterial blood gas sample be treated before analysis?	85
2.	Prescribe an oral sedative used in alcohol withdrawal	67
3.	What IV fluid would you use for someone with a head injury?	67
4.	What is the correct dose and frequency and route options for administration of paracetamol?	65
5.	What drug would you use for pain from a myocardial infarct, and what initial dose?	61
6.	What is the usual prophylactic dose of Clexane, and what is the route of administration?	43
7.	Prescribe the treatment for an elevated potassium of 7mmol/l	42
8.	Please prescribe an anti-emetic.	36
9.	When would you check Digoxin levels?	32
10.	Please prescribe night sedation for a fit 65-year-old man.	28
11.	Prescribe an antibiotic for a chest infection?	25
12.	Name two drugs used in the initial management of an acute anaphylactic reaction to an antibiotic, the dose used, and the route of administration.	14

20mg subcut. daily. 40mg dose was also accepted. Question 7: 50mls of 50% dextrose with 10-15 IU actrapid insulin. Answers to this question were not scored as incorrect if prior calcium gluconate treatment was omitted. Question 8: Cyclizine 50 mg 8hrly, Metaclopramide 10mg 8hrly or other anti-emetic with correct dose and frequency. Question 9: Any time between 6 and 12 hours after the last dose was accepted. Question 10: Any sedative in appropriate dose, e.g. Temazepam 10mg nocte. Question 11: Antibiotics for either community or hospital acquired infection were accepted, in either oral or intravenous dosage. E.g. Co-amoxyclav 375mg t.d.s (oral), or 1.2g t.d.s (intravenous)

COMMENT

The above results suggest difficulties in prescribing drug treatment of some common hospital conditions. The question on the treatment of anaphylaxis scored the worst, with most of the medical students prescribing the wrong dose of adrenaline via the wrong route. Difficulties in prescribing the other drugs ranged from the wrong dose to the wrong frequency. It is reassuring, however, that despite the fact that drug dosage and frequency are not part of final MB, the mean rate of correct prescribing was 42% when questions relating specifically to pharmacology are analysed, and questions 1, 3 and 9 are excluded.

Ideally, this study could have been used to compare the effect of the new curriculum on the correct response rate for this group of questions, compared to a previous cohort of final year students from the old curriculum. However, this could only have been done in a prospective study over two year groups, as a retrospective study cannot be used to acquire this kind of data.

Medical students are increasingly encouraged to attend ward rounds and be involved in the admission of medical patients. Universities across the U.K. have allocated periods during the academic year where final year medical students are ward based and are supervised by junior medical staff and consultants. In the United States, medical students are responsible for organising in-patient investigations, and must know all the

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patients of the consultant for whom they are working. It may be feasible for medical schools in the U.K. to give more responsibilities (under direct supervision) to final year medical students and get them more actively involved in the care of patients. Prescribing at medical school is poorly taught and more time should be taken to institute organised lectures in common drug prescribing, closer to the start of the houseman year. A useful development has been the production of pocket formularies, which are now given to all PRHOs at the start of the year. This could be supplemented by the provision of a quick-reference card containing the doses and frequency of administration for drugs that are either commonly prescribed or used in an acute medical emergency [1-3].

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Requests for emergency contraception at an accident and emergency department – assessing the impact of a change in legislation

S Mawhinney, O Dornan

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SUMMARY

The aim of this study was to examine the pattern of attendance of patients requesting Emergency Hormonal Contraception (EHC) at an accident and emergency department before and after a government driven change in legislation, which allowed EHC to be sold over-the-counter by trained pharmacists, to women aged 16 years and above.

We employed retrospective comparative study using computer records of all accident and emergency attendances coded as requests for emergency contraception for the years 2000 and 2001.

The number of patients requesting emergency contraception at the A&E department decreased after over-the-counter sales were introduced, from 196 in the year 2000 to 164 in 2001 (p=0.037).

Despite this, the number of teenagers requesting emergency contraception at the A&E department increased in 2001 – from 63 in 2000 to 74 in 2001 (p=0.0115).

Most requests are received outside local pharmacy opening hours – 63.77% in 2000 and 62.2% in 2001.

This study raises concerns that the government initiative allowing emergency hormonal contraception to be sold in pharmacies is having little impact on teenagers most in need of this service.

A&E departments can expect to continue to receive a significant number of requests for emergency contraception.

Further measures will be required to reduce the U.K.'s high rate of unplanned pregnancies.

INTRODUCTION

In 1995 the Royal College of Obstetricians and Gynaecologists and the Faculty of Family Planning and Reproductive Health Care issued a joint statement requesting that emergency hormonal contraception be reclassified from prescription-only to pharmacy status.[1] This came into effect on the 1st January 2001 after the introduction of a well tolerated, effective, single hormone treatment (0.75mg Levonorgestrel) and a change in legislation.

Levonorgestrel 0.75mg is an effective method of preventing unwanted pregnancy after unprotected intercourse or condom accident.[2] The first dose is given orally within 72 hours of the first act of unprotected intercourse and repeated 12 hours later. The efficacy of this treatment decreases markedly with time (95% of pregnancies prevented if given within the first 24 hours, falling to 58% by 72 hours – overall effectiveness 86%.)

The change in legislation, effective from 1st January 2001, made it possible for women aged 16 years and over to purchase emergency hormonal contraception from suitably trained

Antrim Area Hospital, 45 Bush Road, Antrim, BT41 2RL.

S Mawhinney, MRCOG, MRCGP, Specialist Registrar, Obstetrics and Gynaecology.

O Dornan, FRCP, FRCS, Consultant in Accident and Emergency Medicine.

Correspondence to Dr Mawhinney

E-mail: sandramawhinney@dsl.pipex.com

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pharmacists at a cost of £19.99 without a prescription. This change was introduced by the Government in the hope that improved access to emergency contraception would help to reduce the U.K's unacceptably high rate of unintended pregnancies amongst all age groups.[3] More specific government targets aim to halve the conception rate in those less than 18 years old by 2010, with a 15% reduction by 2004.[4]

Although it is hoped that direct sale through pharmacies will make access to emergency contraception easier for many women, it is acknowledged that current NHS routes of provision will still exist and remain important.[5]

Many women attend A&E departments each year to obtain emergency contraception, particularly at times when other outlets are not available e.g. GP surgeries and Family planning clinics.

This study examines the pattern of attendance of patients requesting emergency contraception at a busy A&E Department in a district general hospital in Northern Ireland before and after this change in legislation. We wanted to identify any change in: the number of emergency contraception requests made to the A&E department, the age profile of the patients who use this service and the day and time that these requests were made, in the light of local pharmacy opening hours.

METHOD

The setting for the study was an Accident and Emergency department in a district general hospital that serves a semi-urban population of around 300,000. The provision of emergency contraception in the department has recently been audited against standards drawn from the most up-to-date guidance note on emergency contraception produced by the Faculty of Family Planning and Reproductive Health Care.[6]

Computer records are kept for every patient attendance at the accident and emergency department. Our study groups were identified by examining data stored on the NIRAES computer system (Northern Ireland Regional Accident and Emergency System). NIRAES is a clinical and administrative database for A&E attendees. Demographic data, including the patient's date of birth, is entered into the system by A&E reception staff when the patient first attends the department. The nature of the patient's complaint is subsequently entered in free text form by the triage nurse. The system automatically records the date and time of attendance and each case is assigned a unique number; "the A&E number". Cases for this study were identified by searching the NIRAES database for any of the following free-text entries: "Morning after pill", "post-coital contraception", "unprotected intercourse", "MAP" and "PCC". Having obtained the list of A&E numbers for all cases containing any of these terms in the triage entry during the study period, the written A&E clinical records were retrieved and examined.

Group A consisted of all those who attended requesting emergency contraception from the 1st January 2000 to 31st December 2000 (i.e. the year prior to the change in legislation). Group B consisted of all patients requesting emergency contraception from 1st January 2001 to 31st December 2001 (i.e. the first year following the change in legislation.) The number of patients, the day and hour of their arrival and their ages were recorded. The two groups were compared using the X^2 test.

RESULTS

In the year 2000 (i.e. Group A) 196 women aged 13-55 years attended requesting emergency contraception. This figure decreased to 164 women in 2001 (Group B) (p=0.037). (The total number of women in this age group attending the A&E Department for any reason was 11,360 in 2000 and 11,827 in 2001.)

Despite the overall decrease in the number of patients requesting emergency contraception at the A&E Department in 2001 there was a statistically significant increase in the number of teenagers attending; from 63 in group A to 74 in group B (p=0.0115).

In 2000, 63.77% and in 2001, 62.2% of requests were outside local pharmacy opening hours (Monday-Saturday 0900-1800 hours.) The commonest day of attendance was Sunday in both year groups.

DISCUSSION

There is debate among accident and emergency staff as to whether a request for emergency hormonal contraception constitutes a true emergency. However, 96% of A&E departments have been shown to receive requests for emergency contraception.[7] The reduction in efficacy of emergency hormonal contraception with increased time since unprotected sexual intercourse could be used to justify attending

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A&E departments, particularly in Northern Ireland where the 1967 Abortion Act is not applicable.

This study was designed to examine the early impact of a change in legislation on patient demand for emergency hormonal contraception at hospital. Our results have shown an overall reduction in the number of requests received by this A&E Department in the one-year period following the introduction of over-the-counter sales of emergency contraception. Despite this, there is an increase in the numbers of teenagers requesting this service.

As this was an observational study that only looked at A&E-based demand, it is not possible to be certain why this was so and a number of potential variables should be considered. One explanation is that teenagers most in need of this service cannot afford the cost of the over-the-counter product and so for them accessibility has not actually increased. There is also concern that although adolescents know about emergency contraception, they had previously been uncertain how to obtain the pills and how to use them.[8,9] The publicity surrounding the legislative change and the launch of the over-the-counter product may have increased patient's awareness and knowledge of the different sources available.

Teenagers find A&E departments convenient, accessible and feel more assured of confidentiality here so perhaps they actively chose this route even if other options were available.[10]

Although the overall numbers of women attending requesting emergency contraception were small relative to the total number attending the accident and emergency department for any reason during the study period (196 out of 11,360 in 2000 and 164 out of a total of 11,827 in 2001), we are confident that all of those requesting emergency contraception were captured and therefore our results are accurate.

Most requests for emergency contraception at the A&E department still occur at times when local chemists are closed (63.77% in 2000 and 62.2% in 2001). Sunday remains the busiest day. Most traditional routes for obtaining contraceptives (i.e. GP surgeries and family planning clinics) are not available at these times of highest patient demand.

CONCLUSION

This study raises concern that the government initiative allowing emergency hormonal contraception to be sold in pharmacies is having little impact on the teenagers most in need of this service. If Government targets are to be realised, further measures will be required to ensure that a range of contraceptive services is available at the times of greatest demand (mainly weekends and evenings).

The pattern of patient attendance, predominantly outside pharmacy opening hours, suggests that A&E Departments will continue to receive a significant number of requests for emergency contraception. This is important to allow the appropriate allocation of resources to these departments.

It remains to be seen whether over-the-counter sales of emergency hormonal contraception will have any impact on the rate of unplanned pregnancy in the UK.

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MR staging in carcinoma of the endometrium and carcinoma of the cervix

M V Pakkal, V Rudralingam, W G McCluggage, B E Kelly

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SUMMARY

This study aimed to evaluate MR as an imaging modality for the assessment of myometrial and cervical invasion in endometrial carcinoma and for the assessment of parametrial and lymph node involvement in cervical carcinoma.

Twenty-eight patients with a preoperative histological diagnosis of endometrial carcinoma/ cervical carcinoma were included in the study. The findings were compared with the surgical staging and the histopathological report of the hysterectomy specimen.

Accuracy in detecting myometrial and cervical involvement in patients with endometrial carcinoma was 78% for both.

Accuracy in detecting parametrial and lymph node involvement in patients with cervical carcinoma was 71% and 86% respectively.

MR is a reliable method for preoperative assessment of endometrial and cervical carcinoma. It helps decide operability, the type of operation and aids in the selection of patients who need to be considered for specialist referral to a gynaecologist oncologist.

INTRODUCTION

Endometrial and cervical carcinoma represent the first and third most common cancers of the female genital tract in UK. In Northern Ireland there were 97 new cases of invasive cervical and 146 new cases of endometrial carcinoma in 2000.[1] The peak age at presentation for endometrial carcinoma is approximately sixty years. Ninety percent of these women present with abnormal vaginal bleeding and seventy-five percent present with stage 1 disease.

The peak age at presentation for cervical carcinoma is between thirty-five and fifty years. Invasive cervical carcinoma may be asymptomatic. If not detected at screening it can present as intermenstual, postcoital or postmenopausal bleeding. It is imperative to have a high index of suspicion for both these cancers. The tissue diagnosis is achieved by traditional means of hysteroscopy and dilatation and curettage or endometrial biopsy for endometrial cancer, and by cervical biopsy for cervical cancer.

One of the most important aspects of successful patient management with endometrial and cervical cancer is to accurately stage the disease at the time of diagnosis, thus initiating the right treatment plan without causing any unnecessary patient morbidity. Prognostic factors, which influence the treatment algorithm in endometrial carcinoma, include grade of tumour, histological type of tumour, depth of myometrial invasion, cervical involvement and lymphadenopathy. The prognostic factors for cervical carcinoma include disease staging, volume of the primary tumour and presence of lymph node metastases.

Spread of tumour to adjacent tissues is assessed by a combination of clinical and imaging

Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA.

Department of Radiology.
M V Pakkal, MRCOG, Specialist Registrar.
B E Kelly, MD, FRCS, FRCR, FFRRCSI, Consultant Radiologist.

Department of Surgery.
V Rudralingam, FRCS, Senior House Officer.

Department of Pathology.
W G McCluggage, FRCP(Path), Consultant Pathologist.

Correspondence to Dr Kelly.

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modalities. Cross sectional imaging such as computed tomography (CT) and magnetic resonance imaging (MR) are not officially part of the FIGO staging. Pelvic MR, however has the advantage of multiplanar data acquisition and is reported to be superior to CT and ultrasound because of inherent excellent soft tissue contrast.[2] In our retrospective study we compared the accuracy of MR in

a) determining myometrial invasion and cervical involvement in endometrial carcinoma and

b) determining parametrial and lymph node involvement in cervical carcinoma.

The MR staging was compared with the surgical and histopathological findings.

MATERIALS AND METHODS

Twenty-eight patients with a histological diagnosis of endometrial cancer/cervical carcinoma underwent preoperative MR at the Royal Victoria Hospital, Belfast from January 1998 - December 2001 (Figure 1). The MR was performed using a General Electric (Milwaukee, W.I., USA), Signa 1.5 Tesla super-conducting magnet using a body coil. Gadolinium (Magnevist, Schering, Germany) was used as intravenous contrast in a dose of 0.1ml/kg. All images were reported by a single consultant radiologist (BK). The imaging protocols used were

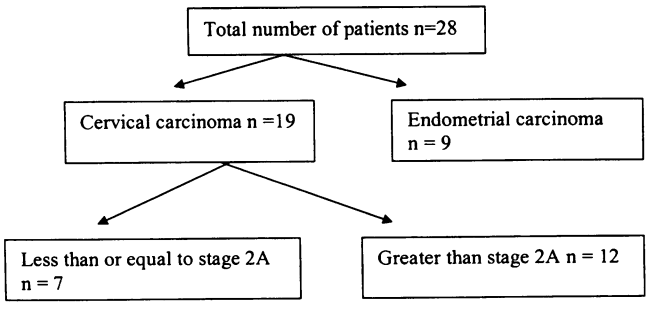
a) Cervical carcinoma: axial T1W, axial T2W, sagittal T2W and axial fat suppression.

b) Endometrial carcinoma: axial T1W, axial T2W, sagittal T2 and sagittal T1W post-contrast.

Carcinoma endometrium:

The parameters assessed were

Figure 1



1. Widening/heterogeneity of signal intensity within the endometrial canal with an intact junctional zone on the T2 weighted images = stage 1A.
2. Myometrial invasion was diagnosed if the normal low signal intensity of the junctional zone was lost in T2 weighted images. The depth of myometrial invasion was considered to be deep (1C) if more than 50% of the myometrium was involved and superficial (1B) if less than 50% was involved.
3. Cervical involvement was diagnosed if there was abnormal signal intensity in the cervical canal/disruption of the normal low signal intensity of the junctional zone in the cervix on T2-weighted images.

Cervical carcinoma:

1. On T2 weighted sequences tumour was identified as a hyperintense mass replacing part or all of the cervical tissue.
2. Parametrial invasion was diagnosed by the high intensity signal in the parametria with loss of the normal low signal intensity of the exocervical stroma on the axial STIR images and T2 weighted images.
3. Vaginal/bladder/rectal involvement was diagnosed by the disruption of the low intensity signal in the bladder/rectal walls on T2 weighted images.

Lymph node involvement was diagnosed if the largest nodal diameter was 1 cm irrespective of the signal intensity.

The MR staging was based on the FIGO 1989 staging of carcinoma of the endometrium and the FIGO 1995 staging for cervical cancer.

All the histology was reviewed by a gynaecological pathologist (WGM).

RESULTS

There were 19 patients with cervical and 9 patients with endometrial cancer (Fig. 1). Twelve patients had advanced cervical carcinoma (FIGO staging greater than 2A) and were excluded as they had primary treatment with radiotherapy or chemoradiation and therefore surgical correlation was not possible. These comprised seven patients with clinical stage 2B, three patients with stage 3 and two patients with stage 4 disease. Endometrial carcinoma: We studied nine patients with

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TABLE I

Comparison of MR staging and surgical staging of patients with endometrial carcinoma (n=9)

No.	*MR staging*	*Surgical/Histological staging*	*Coexistent pathology*
1	1C	1C	adenomyosis
2	1A	2B	Leiomyomata
3	1C	1C	
4	1B	1B	
5	1B	1B	
6	1B	1B	
7	2A	1B	Leiomyomata
8	1B	1B	
9	1A	3A	

endometrial carcinoma (Table I). We understaged two patients with endometrial carcinoma, one of whom had coexistent leiomyomata. The second patient had tumour in the fallopian tube, which was not picked up on MR (Table 1). One patient with leiomyomata was overstaged as having stage 2A. Histology revealed that the tumour extended into the isthmus but not into the cervical canal. Our accuracy in assessing myometrial and cervical involvement in patients with endometrial carcinoma was 78% for both (Table II).

Cervical carcinoma:

We understaged one patient in whom the tumour had just breached into the parametrium. One of the patients was overstaged as stage 2A whereas histology revealed the tumour to be restricted to the cervix (Table III). Our accuracy in assessing parametrial and lymph node involvement in patients with cervical carcinoma was 71% and 86% respectively (Table IV).

TABLE II

Accuracy of MR in endometrial staging

	Accuracy	*Literature*
Myometrial invasion	78%	74%-85%
Cervical invasion	78%	80%

TABLE III

Comparison of MR staging and surgical staging in patients with cervical carcinoma (n=7)

No.	*MR staging*	*Surgical/ histological staging*
1	1B	1B
2	2A	1B
3	1B	1B
4	1B	2B
5	1B	1B
6	1B	1B
7	1B	1B

TABLE IV

Accuracy of MR in staging cervical carcinoma

	Accuracy	*Literature*
Lymph node insolvement	86%	72%-90%
Parametrial invasion	71%	67%-94%

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DISCUSSION

Endometrial carcinoma

Prior to 1988 endometrial carcinoma was staged by examination under anaesthesia, hysteroscopy and dilatation and curettage. This resulted in understaging of 13-22% of cases.[3] Routine surgical staging (total abdominal hysterectomy and bilateral salpingo-oophorectomy with peritoneal washes with or without pelvic and para-aortic lymphadenopathy) was recommended by FIGO in 1988.

Deep myometrial invasion to the outer half of the myometrium (FIGO stage IC) is a poor prognostic factor, which is associated with an increased risk of pelvic, and para-aortic lymph node metastases.[4]

MR permits accurate assessment of myometrial involvement preoperatively. This is useful in selecting patients who require pelvic lymphadenectomy and hence referral to specialised centralised gynaecological oncology centres.[5] Large polypoidal tumours, leiomyomata, adenomyosis, congenital anomalies, small uteri, indistinct zonal anatomy and other factors may make it difficult to assess myometrial invasion at MR imaging.[6] Two of our patients who were inaccurately staged had coexistent leiomyomata. The use of the whole body coil and the coexistent pathology in two of our patients may have affected our accuracy in assessing myometrial invasion.

The accuracy rates for estimating extent of myometrial invasion in the literature are 74%-84%.[7,8] Our accuracy in predicting myometrial invasion was 78% (Table II). Cervical involvement is seen in approximately 10% -15% of endometrial carcinoma.[9] The presence of cervical stromal invasion would be an indication for radical hysterectomy.[10] MR, although relatively insensitive in diagnosing superficial cervical involvement, is accurate in detecting cervical stromal invasion.[11] Some would argue that superficial cervical involvement is not a prognostic factor.[12] In our series the accuracy in assessing cervical invasion was 78%, which compares favourably with studies from the literature.[11]

Cervical carcinoma

Radical surgery for cervical cancer confined to the cervix (stage 1) shows a 5-year survival rate of up to 90%. Surgical cure can be realistically achieved if tumour free excision margins are at least one centimetre and there is no lymph node involvement. Surgical treatment for tumours stage 2A or greater involves extensive radical surgery. i.e. pelvic exenteration. Most units in UK would prefer to use radiotherapy or chemoradiation as the first line of management. Traditionally, the staging of this disease has involved examination under anaesthesia, cystoscopy and intravenous urography/ultrasonography (to rule out hydronephrosis). Clinical staging has been shown to be inaccurate and often results in understaging.[13] The overall accuracy of MR in the evaluation of parametrial involvement is 67%-94%.[14,15,16] Our accuracy in assessing parametrial invasion compares favourably with studies from literature. False negatives can be due to microscopic tumour spread into the parametrium and false positives due to cervical stromal and adjacent parametrial tissue oedema.

The presence of lymph node metastases does not change the FIGO staging. However, it affects the adjuvant treatment (patients with positive lymph nodes would require radiotherapy or chemoradiation) and prognosis. Lymph node metastases are present in approximately 18.6% of cervical carcinoma lesser than or equal to stage 2A and in 44.3% greater than stage 2B.[17] The reported accuracy rates for lymph node evaluation is 72-90%.[16,18] In our series, the accuracy for lymph node assessment was 86%.

In conclusion, MR is a reliable method for determining the depth of myometrial invasion and cervical extension in patients with endometrial carcinoma. Presurgical knowledge of these factors helps select patients likely to benefit from pelvic lymphadenectomy and hence to be considered for specialist referral.

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Early experience with chronic hepatitis C in Northern Ireland: epidemiology and response to monotherapy

N I McDougall, W G McCluggage, P V Coyle, J M Sloan, M E Callender

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SUMMARY

Chronic hepatitis C virus (HCV) infection has become a major health problem affecting an estimated 170 million people worldwide. The epidemiology of HCV and its response to treatment in Northern Ireland has not been described before.

Our aims were to determine the epidemiology, histological stage, suitability for treatment and response to treatment in patients with hepatitis C presenting to one clinic in Northern Ireland. All patients were prospectively recruited with hepatitis C attending the Liver Clinic, Royal Victoria Hospital during the period December 1992 to June 1997.

Sixty patients (33 male, mean age 44 years, range 19-84 years) who tested anti-HCV antibody positive were identified. The predominant genotypes were 1b (33%), 3a (28%) and 1a (26%). Most patients (78%) were asymptomatic at the time of detection and only four (7%) gave a history of jaundice. The most common modes of transmission were i.v. drug use in 30 (50%) and blood products in 20 (33%) patients. Forty-eight (86%) of the 56 patients tested were PCR positive for HCV RNA. Fifty-one patients (85%) underwent liver biopsy of whom 13 had cirrhosis (22% of original group). Twenty-nine patients were suitable for treatment, but three declined treatment and only 26 (43%) started interferon-alpha. During treatment 17 (65%) patients became PCR negative and eight (31%) remained PCR negative 12 months after completion of therapy. Liver histology was assessed before and after interferon treatment in 17 patients and showed no change in total necroinflammatory scores (p=0.1) or staging of architectural change (p=0.55).

Conclusions: **The epidemiology and response to therapy of HCV in Northern Ireland appear comparable to elsewhere in the UK. Only a minority of anti-HCV positive non-haemophiliac patients progress to have interferon therapy suggesting that the cost of treating chronic HCV may not be as great as initially thought.**

INTRODUCTION

The hepatitis C virus (HCV) results in chronic hepatitis C (CHC) in up to 85% of those acutely infected.[1] Chronic HCV infection has become a major health issue throughout the world affecting an estimated 170 million people.[2] Up to one third of those with CHC will develop cirrhosis, and end-stage liver disease due to CHC is now the leading indication for liver transplantation worldwide.[3] The goal of therapy is obviously to prevent progression to end-stage liver disease with its consequences. Monotherapy with interferon alpha was the mainstay of treatment for CHC from the virus was first identified in 1989 until the late 1990's. Given the scale of the

Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA.

The Liver Unit, 1st Floor, East Wing.

N I McDougall, MD, FRCP, Consultant Gastroenterologist and Hepatologist.

M E Callender, FRCP, Consultant Hepatologist.

Department of Histopathology.

W G McCluggage, FRCPath, Consultant Pathologist.

J M Sloan, MD, FRCPath, Consultant Pathologist.

Regional Virus Laboratory.

P V Coyle, MD, FRCPath.

Correspondence to Dr McDougall.

E-mail: neil.mcdougall@royalhospitals.n-i.nhs.uk

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HCV problem, the cost of treating most HCV patients is potentially enormous. However not all chronic HCV patients may be suitable for treatment and some have fairly indolent disease that does not require therapy.

Despite over a decade of experience with HCV, debate continues regarding whom to treat and how. Studies have shown that a number of factors can influence response to therapy such as viral load and viral genotype.[4] There are six main HCV genotypes and genotype 1 is associated with a worse response to interferon therapy. The prevalence of genotype 1 varies throughout the world and its prevalence in Northern Ireland is unknown. Northern Ireland is thought to have a lower incidence of i.v. drug abuse (one of the main risk factors for HCV) than elsewhere in the United Kingdom but the epidemiology of HCV in Northern Ireland has not previously been described. Variations in factors such as genotype prevalence could translate into different treatment response rates in Northern Ireland compared to elsewhere.

Chronic HCV patients were first treated with interferon in Northern Ireland in 1992 and patients were treated with the same monotherapy protocol until 1997 when the NIH Consensus Statement on Management of Hepatitis C was published leading to a change in treatment protocols.[6] The aims of this study were twofold: To prospectively recruit all non-haemophiliac chronic HCV patients presenting to the largest hepatology clinic in Northern Ireland from 1992 until 1997 and to describe their demographic details; and secondly, using clearly defined criteria, to determine the proportion of such patients who required treatment and to describe their histological and biochemical responses.

PATIENTS AND METHODS

All non-haemophiliac patients attending the Hepatology Clinic at the Royal Victoria Hospital, Belfast who were found to be anti-HCV positive during the period December 1992 to June 1997 were prospectively recruited. Preliminary assessment involved blood testing for liver biochemistry, anti-HCV antibody, HCV RNA testing by polymerase chain reaction (PCR) and HCV genotyping. Liver biopsy was offered to all patients who had a positive PCR for HCV-RNA or had abnormal LFTs. Patients who were PCR positive for HCV-RNA who had evidence of interface or intralobular hepatitis or cirrhosis on liver biopsy and were medically fit to undergo treatment were offered interferon alpha therapy. Those patients who had decompensated cirrhosis, human immunodeficiency virus (HIV) infection, severe co-morbidity, pregnancy, continued intravenous drug abuse, other causes of chronic liver disease or who were PCR negative were excluded from treatment.

Interferon alpha 2a was given as a starting dose of 3 million units (MU) subcutaneously thrice weekly for 1 month, then 4 MU thrice weekly for 1 month and finally up to 5 MU thrice weekly for 6 months with monthly monitoring of LFTs, FBP and HCV-RNA PCR. Patients who had difficulty with side-effects or a low platelet count due to interferon were maintained for 6 months on the maximum dose tolerated.

On completion of therapy, LFTs and PCR were monitored every 3 months in those who had become PCR negative during treatment and a repeat liver biopsy was offered. Biopsies were independently scored by two pathologists who were blinded to the timing of each biopsy with relation to treatment. Each biopsy was scored for necroinflammation (0-18) and fibrosis (0-6) in accordance with the previously published modified Knodell Histology Activity Index for grading and staging of chronic hepatitis (Ishak *et al*, J Hepatol, 1995).

Treatment response was defined as clearance of virus from the blood (PCR negative) and normalisation of ALT at completion of therapy and sustained viral response as the maintenance of this response at 6 months after completion of therapy.[7]

RESULTS

Sixty patients were recruited (33 male, mean age 44 years, age range 19-84 years). The most common genotypes were 1b (33%), 3a (28%) and 1a (26%). Most patients (47 (78%)) had minimal symptoms related to liver disease and were detected by screening (including 12 who attended a genitourinary clinic, 12 who had screening of abnormal LFTs, six detected by the Blood Transfusion service, three detected by the Blood Transfusion Lookback exercise, nine who were screened because they had previous risk factors and five who were tested by their GP on a routine visit). Only four (7%) patients gave a history of a previous illness with jaundice. The modes of transmission of HCV were i.v. drug use in 30

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Fig 1. Mode of transmission of HCV in 60 non-haemophiliac anti-HCV positive patients.

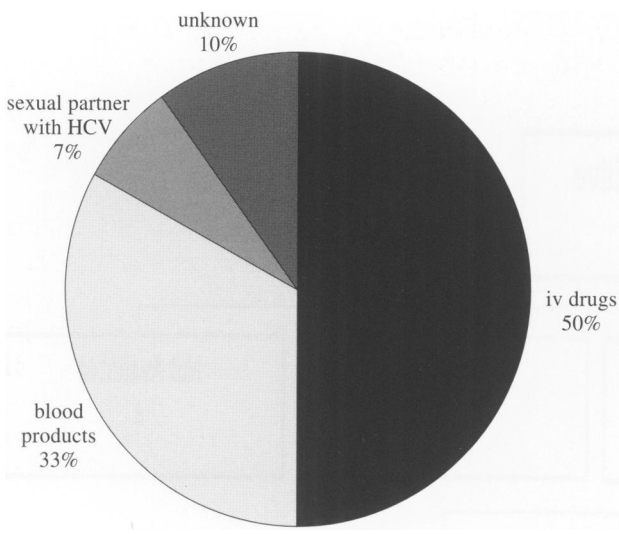
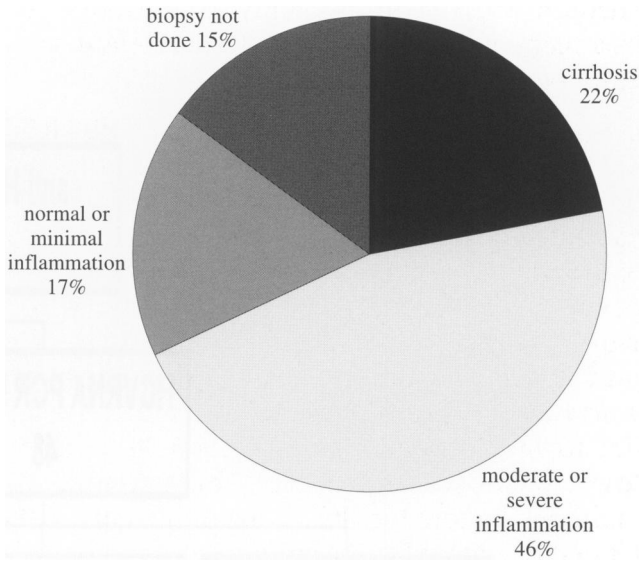


Fig 2. Results of liver histology for 60 non-haemophiliac anti-HCV positive patients.



(50%), blood products in 20 (33%), sexual contacts in four (7%) and unknown in six (10%) patients (Figure 1).

Forty-eight (86%) of the 56 patients tested by PCR were positive for HCVRNA (80% of the original group, with four patients failing to attend for PCR testing). Blood investigations revealed abnormal liver biochemistry (elevated AST, ALT or GGT) in 72% of the cohort. Liver biopsy was performed in 51 (85%) patients and revealed cirrhosis in 13 (22% of the original group, Figure 2). Alcohol may have been a factor in three of the 13 cirrhotic patients. Two patients (3%) developed a hepatoma during follow-up: one patient was cirrhotic at presentation, became PCR negative with interferon therapy but relapsed on stopping treatment and died four years after presentation (aged 48 yrs); the other patient was also cirrhotic at presentation, failed to respond to interferon therapy and died one year after presentation aged 72.

Figure 3 shows the outcome of the 60 patients studied with respect to whether or not they received interferon treatment. Twelve patients were excluded as they were PCR negative. Five patients who were HCV-RNA PCR positive failed to attend for follow-up assessment and a further three patients underwent full assessment but declined the offer of treatment. Fourteen patients who were HCV-RNA PCR positive were not offered treatment due to the fact that they were either not medically fit to undergo treatment (6) or were deemed to have minimal disease activity (8) based on LFTs and liver histology. This left 26 patients (43%) who were offered and accepted interferon therapy. Two patients (8%) developed thyroid dysfunction (one thyrotoxic, one hypothyroid) during interferon therapy.

Seventeen (65%) patients became HCV-RNA negative during therapy and nine remained positive (including one patient who only had 2 days of therapy, one who defaulted after just one month of interferon and four who were unable to achieve a satisfactory interferon dose or length of therapy due to side effects). Eight (31%) patients had a sustained response, remaining HCVRNA negative at least 12 months after stopping therapy, eight became HCVRNA positive again and one patient became HCVRNA negative but failed to attend for follow-up (Figure 3). Age, sex, genotype, presence of cirrhosis or mode of transmission did not significantly affect treatment success.

The Table shows the results of liver histology in 17 patients before and after interferon therapy (including three who failed to become PCR negative). The overall total scores showed no significant improvement with treatment for either grading of necroinflammatory scores ($p=0.1$) or staging of architectural change, fibrosis and cirrhosis ($p=0.55$). Assessment of the four separate components of grading showed that there was a significant improvement in the score for focal lytic necrosis, apoptosis and focal inflammation ($p=0.01$) but no significant change in the scores for piecemeal necrosis, confluent necrosis or portal inflammation.

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Fig 3. Outcome of 60 ant-HCV positive non-haemophiliac patients showing HCVRNA PCR status and outcome of interferon therapy.

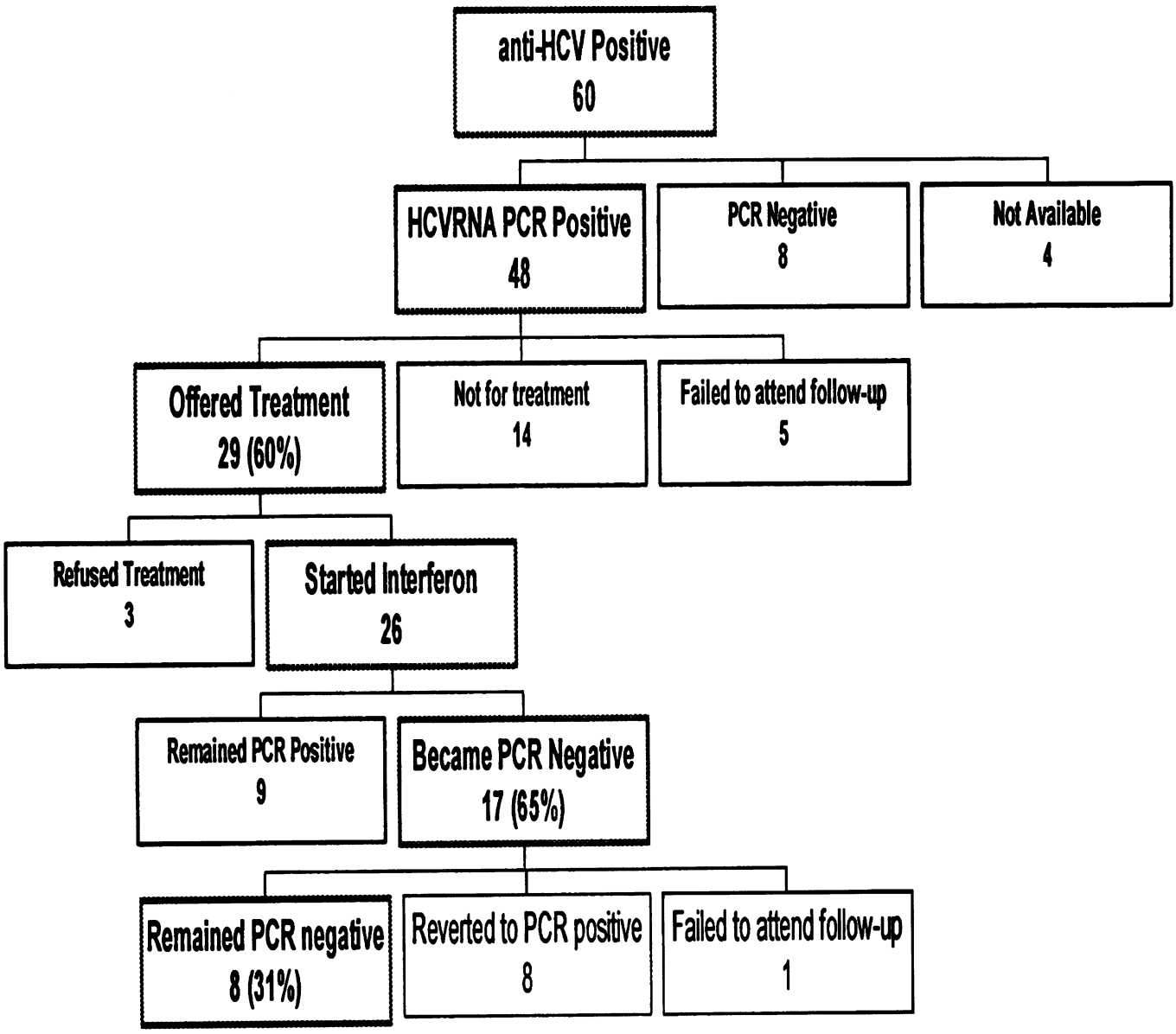

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TABLE

Histological scores for grading and staging of chronic hepatitis in 17 patients before and after treatment of chronic HCV with interferon alpha (Modified Knodell Histology Activity Index)

	Before Treatment		*After Treatment*	
	Grade (0 - 18)	*Stage (0 - 6)*	*Grade (0 - 18)*	*Stage (0 - 6)*
P1	7	3	3	3
P2	7	3	5	3
P3	10	5	9	6
P4	8	5	4	6
P5	7	5	11	5
P6	7	5	7	5
P7	6	3	5	2
P8	6	5	6	5
P9	5	4	3	2
P10	6	1	1	1
P11	4	3	4	3
P12	4	2	2	1
P13	6	3	3	3
P14	8	5	16	6
P15	6	3	4	2
P16	8	3	4	3
P17	5	3	5	3
Overall Median (IQR)	6(5.5-7.5)	3(3-5)	4(3-6.5) p = 0.1	3(2-5) p = 0.55

DISCUSSION

Estimates suggest that hepatitis C currently affects 200,000 to 400,000 people in the UK, the majority of whom have chronic HCV infection.[8] The most important route for transmission of HCV is parenteral and the majority of those infected give a history of either intravenous drug abuse or receipt of blood/blood products prior to 1991 when screening of blood for HCV was introduced. Much less commonly, infection can be due to sexual contact, vertical transmission or non-sexual household contact. A small proportion of patients have no identifiable risk factors.

Not all patients with chronic HCV infection develop severe liver disease but 20-30% go on to develop cirrhosis after a mean of 30 years and up to 4% of cirrhotic HCV patients per year develop a hepatoma.[6] Several factors are associated with increased risk of disease progression: age over 40 at time of infection, male sex, excess alcohol, high viral load, immune deficiency, coinfection with HIV or hepatitis B and genotype 1. Six genotypes and numerous subtypes of HCV have been identified. Genotypes 1a and 1b are by far the most common in the Western world, accounting for up to 70% of cases in the USA.[9] This figure is thought to be closer to 50% in the UK but there are no comprehensive data.

Perhaps not surprisingly, the epidemiology of chronic HCV in Northern Ireland (based on our study sample) is in keeping with the data described above. Allowances should be made for the fact that our study group excluded haemophiliac patients who mostly acquired HCV from blood products. Genotypes 1a and 1b accounted for 57% of those whose genotype was tested and iv drug abuse was the most common risk factor accounting for half of the study group. As expected

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from other data, 1 in 10 people had no identifiable risk factor for HCV. The fact that at least 22% of the study group had cirrhosis at the time of presentation is probably in keeping with the widely quoted figure of 20-30% of chronic HCV patients developing cirrhosis within 20 years.[1] This relatively high figure demonstrates the insidiously progressive nature of chronic HCV infection that can present many years after infection with advanced disease. Unfortunately we were unable to determine the length of time from initial HCV infection until presentation and therefore cannot comment on the mean time until development of cirrhosis.

The similarity between our study group demographics and other UK data [1] does not suggest that there should be any significant differences in response to treatment and the data bear this out. The initial response to interferon monotherapy treatment (61%) and subsequent sustained response rate (31%) both compare very favourably with the generally quoted initial response and sustained response rates of 47% and 20% respectively.[1] The slightly better figures we obtained should not be over-interpreted, because of the small sample size. However it could be suggested that the slightly higher response rate was due to higher doses of interferon used (5 million units thrice weekly rather than the more commonly used 3 million units thrice weekly). Liver histology data showed an improvement following therapy in some of the inflammatory parameters. Presumably if numbers had been larger it would have been possible to demonstrate a significant improvement in overall histology scores of necroinflanimation and liver architecture.

The treatment data for the Northern Ireland cohort helps to illustrate one very important point regarding the number of patients treated. Given the prevalence of chronic HCV infection worldwide and the cost of treatment with interferon, the potential cost of treating the problem might seem prohibitive. Yet this study has shown that a minority of non-haemophiliac patients with previous HCV infection who present to a hospital clinic actually proceed to have interferon therapy (Figure 3). A combination of factors such as minimal evidence of disease progression, unsuitability for interferon therapy and failure to comply with medical advice and follow-up resulted in only 43% of our group starting treatment. Failure to comply was one of the most important factors accounting for almost 1 in 5 of those who had chronic HCV. Anecdotal evidence from many centres confirms that poor compliance is often a problem with non-haemophiliac chronic HCV patients partly due to the large proportion who are previous or current i.v. drug abusers. One study showed that as many as 42% of patients who underwent investigation of chronic HCV infection did not want to proceed with treatment.[10]

In summary, based on a cohort of 60 non-haemophiliac patients the epidemiology of HCV infection in Northern Ireland appears to be very comparable to elsewhere in the UK. The most common risk factor is iv drug abuse followed by contact with blood products and over half of patients are genotype 1a or 1b. Only a minority of patients actually receives treatment and response rates with interferon monotherapy compare favourably with elsewhere.

The last patient was recruited to this study in 1997 and since then there have been dramatic advances in the treatment of chronic HCV infection. Combination therapy (interferon plus oral ribavirin) has been introduced and more recently the use of pegylated interferon has improved response rates. The length of treatment is now tailored to match the specific hepatitis C genotype. In January 2004, NICE produced updated guidelines stating that combination therapy with pegylated interferon alpha and oral ribavirin is now the treatment of choice for patients with chronic HCV infection.[11] Studies have demonstrated that sustained response rates of 76-82% are now achievable for genotypes two and three.[12, 13] The response rates in Northern Ireland to newer therapeutic strategies are yet to be determined.

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CT-guided fine-needle aspiration of lung nodules: effect on outcome of using coaxial technique and Immediate cytological evaluation

CP Mullan, BE Kelly, PK Ellis, S Hughes, N Anderson, WG McCluggage

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PURPOSE

To evaluate the risk of pneumothorax during CT-guided fine-needle aspiration (FNA) of lung nodules with single needle and coaxial needle techniques and to assess the effect on diagnostic accuracy of immediate cytological examination of lung FNA samples.

MATERIALS AND METHODS

This prospective study analysed 53 patients undergoing transthoracic FNA biopsy of lung. 36 cases were performed by a radiologist using a coaxial technique, with 17 cases performed by a radiologist using a direct single-needle method. Effect of technique on occurrence of pneumothorax was recorded. FNA samples from all the patients in the study were examined immediately on-site by a cytologist or MLSO to determine whether sufficient aspirate had been obtained. Provisional diagnosis at immediate examination was compared to final diagnosis following full pathological evaluation.

RESULTS

Coaxial and non-coaxial groups were comparable for age and gender. Number of pleural passes was significantly lower in coaxial group (P< 0.01). Pneumothorax occurred in six (17%) of the 36 patients biopsied by coaxial technique, compared to four (24%) of the 17 patients by non-coaxial method (P= 0.55). Chest tube placement was required in four patients (11%) in the co-axial group, and two patients (12%) in the non-coaxial group (P= 0.85).

A provisional cytological diagnosis was recorded for 74% of the patients in the study. 83% of the provisional reports were accurate on comparison with full pathology report. Specimen size was sufficient in 81% of cases.

CONCLUSIONS

The use of coaxial technique for CT-guided lung FNA biopsy reduced the number of pleural passes but did not significantly reduce the occurrence of pneumothorax. Immediate cytological examination of FNA specimens provided an accurate provisional diagnosis in the majority of cases, and should be routinely employed.

INTRODUCTION

CT-guided fine needle aspiration (FNA) biopsy is a well-established diagnostic procedure used in the investigation of pulmonary nodules. Equipment and expertise required to perform this procedure are available in many hospital radiology departments. Cytopathological examination of specimen obtained from lung nodules by CT-guided FNA biopsy is an accurate and sensitive way of diagnosing malignancy[2,3]. During the procedure, a needle is inserted percutaneously through the chest wall under CT guidance in

Royal Victoria Hospital, Grosvenor Road, Belfast, BT12 6BA. Department of Radiology

CP Mullan, MRCP, Specialist Registrar in Radiology

BE Kelly, MD, FRCS, FRCP, FFRRCSI, Consultant Radiologist

PF Ellis, MB, MRCP, FRCR, FFRRCSI, Consultant Radiologist

S Hughes, MRCP, FRCP, Consultant Radiologist

Department of Cytopathology

N Anderson, MD, MRCPath, Consultant Pathologist

WG McCluggage MB, MRCPath, Consultant Pathologist

Correspondance to Dr Kelly

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order to aspirate suitable specimen from the lung nodule for cytological analysis (Figure 1).

If a single needle technique is used, a pleural puncture must be performed each time FNA of the nodule is attempted. Coaxial biopsy systems enable multiple fine needle aspirates to be performed with a single pleural puncture. The purpose of this study was to examine the effect of coaxial needle technique on the occurrence of post-procedure pneumothorax. In many centres, immediate cytological examination is performed on-site in the radiology department by a cytopathologist or MLSO. The other purpose of this study was to assess the diagnostic accuracy of immediate cytological examination during CT-guided FNA lung biopsy.

MATERIAL AND METHODS

This prospective study involved 53 patients who had lung nodules suspicious of malignancy identified on CT imaging, and who were subsequently referred by consultant medical staff for CT-guided FNA biopsy. All procedures were performed at the Department of Radiology, Royal Victoria Hospital. The 53 patients presented sequentially over a period of 18 months. Written informed consent was obtained in all cases. 36 cases were performed by one consultant radiologist using a coaxial technique. The other 17 cases were performed by one consultant radiologist using a single needle technique.

A Greene (Cook, Bloomington, Ind) 22-gauge needle in a 19-gauge introducer needle was used by the radiologist performing FNA by coaxial technique. A Greene 22-gauge needle alone was used by the radiologist performing FNA by single needle technique. Local anaesthesia was administered by subcutaneous injection of 2% lignocaine. The procedure was performed with the patient in prone, supine or lateral decubitus position, depending on the location of the lesion.

Each patient had follow-up CT scan immediately after FNA biopsy to check for post-procedure pneumothorax. An erect chest radiograph was also obtained after FNA to detect pneumothorax. The number of patients developing post-procedure pneumothorax, and pneumothorax requiring pleural drainage was recorded.

A cytologist was present at 38 cases (72%), and a MLSO was present in the other 15 cases (28%). All specimens obtained were immediately smeared and stained. The adequacy of the sample for diagnosis was assessed by the cytologist or MLSO. Additional aspirates were obtained when original specimens were not considered sufficient for diagnosis. A provisional report was provided by the cytologist or MLSO, indicating the preliminary diagnosis when possible. The specimen was then taken to the cytopathology laboratory for full analysis. The accuracy of the provisional report in comparison to the final cytopathology report was recorded.

RESULTS

There was no statistically significant difference in age between patients in the two groups (Table 1), with a mean age of 61.9 years for patients undergoing FNA by coaxial technique and a mean age of 66.3 years for patients having FNA by single needle method. There was also no significant difference in gender ratio between patients in the two groups.

The mean duration of the procedure was 23.5 min for patients in the coaxial group and 19.9 min for patients in the single needle group, which was not significantly different. The number of pleural passes per case was significantly lower when the coaxial technique was employed. The median number of pleural passes per case was one in the coaxial group, and two in the single needle group. The median number of aspirates per case was lower when FNA biopsy was performed by the coaxial technique, but this was of borderline significance only ($p=0.05$).

Each patient was checked for post-procedure pneumothorax by CT-imaging and chest Xray. CT is more sensitive in the detection of small pneumothoraces. Table 2 shows that nine (25%) of the 36 cases performed by coaxial technique were complicated by post-procedure pneumothorax (identified on CT or chest Xray), compared to four (24%) of the 17 cases performed by single needle technique. This difference was not statistically significant. six (17%) of the 36 patients in the coaxial group developed pneumothorax sufficient to be detected on post-procedure chest xray, in comparison to four (24%) of patients in the single needle group. This difference was again not statistically significant. There was no significant difference in the number of patients with post-procedure pneumothorax requiring pleural drainage, with four cases (11%) in the coaxial group and two cases (12%) in the

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single needle group.

Immediate cytological evaluation of the FNA specimens was performed in all 53 cases to confirm adequacy of specimen cellularity. Table 3 shows that the cytologist was able to make a preliminary diagnosis in 39 (74%) of the 53 cases, but was unable to reach a preliminary diagnosis in 14 cases (26%). The final cytopatholgy report was available in 48 of the cases. The specimen subsequently received by the cytology laboratory was deemed to be adequate analysis in 39 (81%) of the 48 cases. It was possible to compare the preliminary diagnosis made at immediate cytology to the final laboratory report in 36 of the cases. The preliminary diagnosis was accurate in comparison to the final report in 31 (86%) of the 36 cases.

Table 4 shows the accuracy of immediate cytological evaluation of FNA specimens in the detection of malignancy. In comparison to the final laboratory report, the preliminary diagnosis had a sensitivity of 90.0% and a specificity of 83.3% in the detection of malignancy. There was a positive predictive value of 96.4% and a negative predictive value of 62.5%, in the detection of malignancy.

TABLE I

Comparison of Coaxial Group and Single Needle Group in Relation to Demographic and Procedure-related Variables

Parameter	Coaxial group	Single needle group	P Value
Mean age	61.9 ± 14.4	66.3 ± 11.6	0.75
Male/Female ratio	0.8	0.9	0.91
Procedure duration (min)	23.5 ± 8.3	19.9 ± 8.5	0.77
Number of pleural passes	1 ± 0.3	2 ± 0.7	<0.01
Number of aspirates	1 ± 1.0	2 ± 0.7	0.05

TABLE II

Occurrence of Pneumothorax Following CT-guided Lung FNA Biopsy

Pneumothorax	Coaxial group	Single needle group	P Value
Pneumothorax on CT or Chest Xray	9 (25%)	4 (24%)	0.92
Pneumothorax on Chest Xray	6 (17%)	4 (24%)	0.55
Pneumothorax requiring pleural drainage	4 (11%)	2 (12%)	0.85

TABLE III

Specimen Adequacy and Preliminary Diagnosis with Use of Immediate Cytological Evaluation

Immediate cytology	% of cases
Specimen adequate for full laboratory analysis (n=48)	81
Preliminary diagnosis made(n=53)	74
Preliminary diagnosis accurate(n=36)	86

TABLE IV

Detection of Malignancy by Immediate Cytological Evaluation

Immediate cytology: Detection of malignancy	% rate
Sensitivity	90.0
Specificity	83.3
Predictive value of positive result	96.4
Predictive value of negative result	62.5

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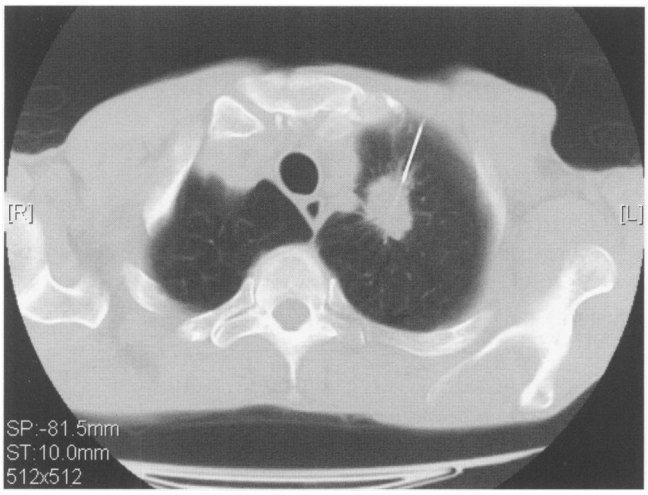

Fig 1. CT image obtained during FNA biopsy of a solitary left upper lobe lung nodule in a 53 year old male patient. This axial image shows percutaneous insertion of FNA biopsy needle through anterior chest wall, with patient in supine position.

DISCUSSION

CT-guided FNA lung biopsy is a procedure of low mortality and limited morbidity[5]. Pneumothorax is by far the most frequent complication of CT-guided lung FNA, followed by haemoptysis and pulmonary haemorrhage[1]. Rare complications include seeding of malignant cells into needle tract, lung torsion, empyema, systemic air embolism and pericardial tamponade[2]. The rate of pneumothorax after CT-guided lung FNA biopsy reported in medical literature ranges from 7.6% - 46%[1]. The recently published British Thoracic Society guidelines for radiologically guided lung biopsy recommend that operators should try to achieve the lowest quoted complication rates, ie pneumothorax in 20.5% of biopsies[7]. Pneumothorax is usually detected by CT imaging immediately after FNA, or on post-procedure chest Xray. Most patients developing pneumothorax are managed conservatively, but a proportion need pleural drainage. The percentage of patients requiring pleural drainage after biopsy in reported studies varies between 3.3% and 15 %[7]. Various articles have shown that patients with emphysema and other respiratory disease are more likely to develop pneumothorax after CT-guided lung FNA, and more frequently require pleural drainage[1,2]. Lesion size and location have also been reported to correlate with rate of post-procedure pneumothorax[1,2,3]. 13 of the 53 patients in this study developed post-procedure pneumothorax, giving an overall rate of 24.5%. This compares favourably to the range reported in medical literature from similar studies and the target level recommended in the British Thoracic Society guidelines[1,7]. The overall rate of post-procedure pneumothorax requiring pleural drainage was 11.3% (6 of 53 cases), which again lies within the range reported in other studies.

The influence of other procedure-related variables on development of pneumothorax has also been investigated. If a single needle technique is used, a pleural puncture must be performed each time FNA of the nodule is attempted. Coaxial biopsy systems enable multiple fine needle aspirates to be obtained via an introducer needle which remains within lung parenchyma for a variable time. Multiple FNA biopsies can therefore be performed with a single pleural puncture. As expected, the results of this study show that the number of pleural passes performed was significantly lower in cases using the coaxial technique compared to the single needle technique. Although use of coaxial technique reduces the number of pleural punctures, several studies have failed to show significant correlation between the number of pleural passes and the pneumothorax rate[2,3,6]. The results of our study further support this conclusion, as there was no significant difference in the total rate of pneumothorax or the rate of pneumothorax requiring pleural drainage between the coaxial and single needle groups.

Analysis of the results shows that patients undergoing CT-guided lung FNA by coaxial technique were comparable to patients in the single needle group in terms of age and gender. There was also no significant difference in procedure duration between the two groups. The number of aspirates per case was lower in patients having FNA lung biopsy by coaxial technique, but this was only of borderline significance. A number of potential confounding variables in development of post-procedure pneumothorax were not investigated in this study. These include the size of the lung nodule, the location and depth of the nodule, and coexistent respiratory disease such as emphysema. However, all patients undergoing CT-guided lung FNA biopsy by the two radiologists during the 18 month period were included in the study without exclusion. The potential confounding effect of other variables is therefore likely to be small.

The specimen obtained by CT-guided FNA lung

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biopsy undergoes cytological examination to establish if malignancy is present. The specimen must be of adequate cellularity for diagnostic assessment. Preparation and staining of the specimen is performed in the cytopathology laboratory prior to full assessment. In many centres, immediate cytological examination is performed on-site in the radiology department by a cytopathologist or MLSO. There are several perceived benefits of immediate cytology. Initial examination of the specimen can indicate whether it is of sufficient cellularity, so that FNA biopsy can be repeated immediately if specimen is inadequate[4,5]. The British Thoracic Society guidelines indicate it is likely that immediate microscopic examination reduces the number of biopsy samples required to achieve a diagnosis[7]. A provisional diagnosis can be made, helping to guide patient management more quickly. Immediate cytology may also indicate whether additional specimen is required for ancillary studies, such as cytogenetics.

In this study, a cytologist or MLSO was available to perform immediate cytological evaluation of the specimen obtained by CT-guided lung FNA in all 53 cases. This enabled FNA to be repeated at time of procedure if specimen was inadequate. The use of immediate cytology resulted in a specimen adequate for full laboratory analysis in a large majority (81%) of cases. The cytologist or MLSO was able to provide a preliminary diagnosis at immediate cytology in most cases (74%). When a preliminary diagnosis was made, this proved to be accurate in comparison to the final cytopathology report in 86% of cases. This study also demonstrates that immediate cytological examination of specimens during CT-guided lung FNA biopsy has relatively high sensitivity and specificity in the detection of malignancy. This highlights the potential role of immediate cytology in guiding patient diagnosis and management more rapidly.

In conclusion, our results indicate that the use of a coaxial technique during CT-guided lung FNA biopsy reduces the number of pleural passes per case, but does not significantly reduce the occurrence of pneumothorax. The overall rate of pneumothorax was within the range reported in other similar studies. Immediate cytological examination of FNA specimens provides an accurate provisional diagnosis in the majority of cases, and results in a high rate of specimens adequate for full laboratory analysis. Therefore, immediate cytology should be routinely employed during CT-guided FNA biopsy of lung, whenever available.

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Consent to medical treatment – does doctor know best?

A paper delivered to the Ulster Medical Society on 20th November 2003 by The Right Honourable Sir Robert Carswell, Lord Chief Justice of Northern Ireland *

One of the agreeable features about engaging in practice in the sphere of personal injuries litigation is the opportunity which it gives to lawyers to get to know a variety of medical practitioners. Over some 25 years I made a host of good friends in the medical profession, and I am glad to see so many here tonight, together with some legal stalwarts who are brave enough to put up with listening to me holding forth yet again. May I say what a pleasure it is to have the chance to address you and to renew old friendships.

The aspect of medical practice and its interface with the law which I want to discuss tonight is that of consent, the type of patient's consent which is required for medical and surgical procedures and the problems which can arise – and many of them have arisen in the past.

If one goes far enough back in time – and perhaps not beyond the professional lifetime of some of the audience tonight – consent did not pose much of a problem. You will of course remember that Hippocrates himself advised physicians to conceal most things from the patients, as when given information many patients have taken a turn for the worse. There is little doubt that there has historically been a paternalistic tinge to the practice of medicine, what one commentator called *"the oracular nature of early medicine, with heavy reliance on magical powers and ritual in preserving the mystique of the healer."* One also finds traces in some of the cases of the view, now perhaps regarded as old-fashioned, that patients prefer to put themselves in the hands of their doctors and are made more anxious by being given additional information. And think of the great surgeon Sir Lancelot Spratt in *Doctor in the House*: to the grandees of his day the idea that a patient might have a say in the operation to be carried out would have been outwith his contemplation. If the patient had had the temerity to pipe up and announce that he did not agree to it, Sir Lancelot (and many others of his time) would have regarded that as conclusive evidence of mental incapacity. And the mind boggles at the reaction he would have shown if the patient had attempted to sue him.

Modern legal and ethical requirements have made a big difference to the approach which doctors are obliged to adopt these days, and there is a discernible tendency to overload the information dumped on the patients about infinitesimal risks until the unhappy souls are either scared out of their wits or disregard the lot as incomprehensible mumbo-jumbo.

Consent as a concept is not a difficult thing, and any sensible person will ordinarily know quite easily when a patient consents to treatment. Lawyers love to break things down into components, however, and preferably to complicate them a bit, and so I can define for you three elements of a proper consent:

- capacity
- voluntariness
- sufficiency of information.

There is not really any magic in any of these. Obviously if a patient has not legal capacity, he or she cannot give consent. Equally obviously, if it is not voluntary no one could call it consent. The third part, information, overlaps to an extent with the second, because if you do not know what you are agreeing to, you can hardly give true consent. This part is a bit more difficult to apply in practice.

Perhaps I could say a word about each of these and how they affect the way that doctors have to go about their work and make their decisions. You will, I am sure, be aware that medico-legal text books contain a hefty chunk on the subject – 100 pages in Professor Michael Jones' tome on

* now Lord Carswell, Lord of Appeal in Ordinary, in the House of Lords.

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medical negligence – and you could write a book on that topic alone, as London barrister Andrew Hockton has recently done. Indeed, a glance through the contents table of his book will show the breadth of issues on which the question of consent bears – children, incompetent adults, information and the duty of candour, negligence and causation. These concern such medical questions as sterilisation, abortion, blood transfusions, anorexia, euthanasia and termination of life, all against the background of the requirements of the law and the GMC guidelines on ethical practice.

One might start by asking what is the purpose of obtaining the patient's consent to a specified treatment. The answer is clear: it is a protection to the doctor against committing the actionable tort of battery. It has often been described as the key which unlocks the door, but Lord Donaldson MR in *Re W (a minor)* in 1992 preferred a different simile, a legal flak jacket, which protects doctors from litigious claims by giving them the right to proceed. That is the legal purpose of consent, but Lord Donaldson pointed out that the clinical purpose is of prime importance in medical practice, because a patient's confidence in the efficacy of treatment is a major factor contributing to the treatment's success.

But before they can don their flak jackets, doctors have to be clear on our three elements. So let us look for a moment at the first, the patient's capacity. It may seem obvious and superfluous to say that an adult of sound mind can and must make his or her own decision, but that statement conceals a number of serious practical problems. The American surgeon Arul Gawande in his book *Complications* tells a heartbreaking story of a patient in his early sixties with extensive and untreatable cancer who insisted on having spinal surgery which might prolong his life a little but which contained severe risks of serious damage and the certainty of a long, difficult and painful recovery. He was very thoroughly and meticulously warned of the risks and informed of the options – the overwhelming preference of the doctors was to do nothing and let him go home and receive hospice care, which gave him the best chance of dying peacefully. He insisted on proceeding and despite the best care – and the account given of the care devoted to him was impressive – the result was very unhappy indeed, described in harrowing detail by Dr Gawande, and he died in severe discomfort after fourteen days. Yet legally and, I think, ethically the doctors were right. He had to make the choice, and the ability to choose must imply the freedom to make the wrong choice. The patient's decision may appear irrational to any doctor or lawyer, but he is entitled to make it, even to the extent of refusing life-saving treatment or instructing the cessation of life-preserving treatment.

In her O'Connell Lecture in St Malachy's College last autumn Dame Elizabeth Butler-Sloss gave an example of the latter from her own experience. Ms B was an able and talented woman of 43, holding a responsible position in the NHS, who through a devastating illness had become tetraplegic and who no longer wished to be kept alive by artificial means. To begin with, her doctors took the view that she must be incompetent. They focused on the decision she had made, rather than on her actual state of mind, and decided that this decision could not be the product of a competent mind. However when the medical experts came to give evidence in court, it was universally agreed that Ms B was quite clearly mentally competent. It was clear that her right to choose to come off the ventilator without which she could not breathe had to be respected. Dame Elizabeth so decided and gave a declaration that the hospital must follow Ms B's instructions to withdraw her artificial ventilation. In so doing the judge hoped, though faintly, that Ms B might reconsider her decision, but she did not, and she died peacefully a short time later.

If the patient does not have proper mental capacity, no one can give consent on his or her behalf and it has to be obtained from the court (I leave out of account the exceptions, treatment under the mental health legislation for conditions affecting mental health and treatment in an emergency). There may be difficulties in practice in assessing mental capacity, but the rule is clear enough.

When we come to look at the position of minors, the difficulties fairly bristle. One might innocently suppose that because the age of majority is 18, a patient under that age cannot give or refuse consent to treatment. I regret to say that one would be severely disappointed, and the rules which have been built up are complex and to some extent baffling. Any experienced practitioner will know at once the areas in which the problems lie, the foremost being on the one side contraception and abortion, where the child will be anxious to have medical treatment and the parents may oppose it;

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and on the other side anorexia, where the opposite may prevail.

The first inroad into the simple rule of consent at the age of 18 was made by section 4 of the Age of Majority Act (NI) 1969, by which a child aged 16 or more may give consent to medical treatment – though not the donation of organs or blood or other procedures which do not constitute treatment or diagnosis. The second was made by the courts in the litigation brought by the renowned Mrs Gillick. Mrs Gillick was one of the type of formidable ladies of strong moral fibre and strong moral views who form the backbone of all worthy bodies such as the Mothers' Union and the WI – though I could hardly imagine her posing as Miss November for the famous calendar. The DHSS issued a circular to area health authorities advising them that doctors consulted at family planning clinics could lawfully prescribe contraceptives to girls under 16, if acting in good faith to protect them against the harmful consequences of sexual intercourse. Mrs Gillick took exception to this in principle (I must add at once that it was a question of principle, as her own daughters were not seeking contraceptives). She sued the DHSS and the health authority and the case went right to the House of Lords, where she narrowly but decisively lost. The result is that a child under 16 who is what we now call *Gillick* competent may give valid consent to treatment on his or her own behalf, provided (and the proviso is important) that the treatment is in the child's best interests. The courts have said that what constitutes *Gillick* competence is a question of fact, which they usually say when they want to let someone else take the responsibility. It will depend on the age and level of understanding of the child and also on the complexity and importance of the treatment – consent to setting a fracture of the arm is not rocket science, whereas all doctors can think of difficult clinical decisions which a young person may not have the maturity or judgment to make unaided.

I cannot give you a set of hard and fast rules to govern the case of minors, but two guiding principles can be distilled from the voluminous case-law:

1. No doctor can be required to treat a child, either by the child, the parents or the court. It is a decision for the doctor's own professional judgment, subject to the threshold requirement of a valid consent.
2. There can be concurrent powers to consent. Either the child or the parents may be able to give valid consent, in which event only the failure or refusal by all will create a veto. The somewhat strange position is that the child can give consent under 18, but cannot refuse it, so the parent may give an overriding consent which will be valid if the child refuses (this may be important in anorexia cases).

The court can, however, give its consent and override a refusal which would block treatment, provided it is in the best interests of the child. There have been many carefully thought out statements of the law about the extent of the court's power and the occasions on which it should be exercised, but I need not trouble you with them tonight. All I need say is that sometimes the decision is not difficult to make, as I found in a recent case of a boy with vCJD (though there was no question of going against the family wishes in that case, they were very keen on the treatment). In other cases it may be fiendishly difficult, and you will remember how the Court of Appeal in England wrestled like Jacob with the angel when presented with the problem of the conjoined twins.

Once you have determined that the patient or some person on his behalf can give consent, the next question which arises is the amount of information which a doctor is required to furnish to him in order to make that consent valid. It is here that the law has some rather strange answers which I am not at all sure are very sound in principle. If you read the GMC or the Royal College of Surgeons guidelines on seeking consent you will find constant references to "informed consent", a concept which requires that the patient be given all the facts in a complete and comprehensible form, that all possibilities, including non-operative methods and non-treatment, are discussed, that a description of the expected outcome for each alternative procedure be given and that the patient should take part and share in decisions and give active, not passive, consent. This is not only excellent practical advice to doctors, but it constitutes the ethical requirement of their professional bodies, which of course they must observe. I think that it may represent the reaction of the profession to the conclusion reached in a 1986 study that doctors at that time regularly underestimated the amount that patients wanted to know.

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Oddly enough perhaps, it does not represent the law. In our law it does not take very much information to ground a valid consent. Consent is consent, even if the patient only knows the outline of what the treatment is; so long as he is aware what he is agreeing to, his consent is valid in law. There is, however, a catch, as you might suppose. It is part of the comprehensive duty owed by the doctor to give the patient proper information about the proposed treatment, and in particular to warn of the risks which it may entail, and failure to do so to the standard of a reasonable practitioner will be actionable negligence. So obtaining the rugged consent required by English law is not enough: you must observe the professional standards of a reasonable medical practitioner practising in that field in order to discharge your legal duty.

Let me give you a couple of examples which have occurred in cases which I myself tried as a judge in the High Court:

1. A young woman was plagued with Raynaud's Disease, which caused blueness and swelling in her feet and ankles and severe pains in her legs. She was referred to a vascular surgeon, who after carrying out tests recommended that she should have a sympathectomy, done by the chemical method, involving the injection of a solution of phenol to burn the tissue of the sympathetic nerve. The object of the treatment was to destroy the lumbar sympathetic chain which supplies nervous control to the small blood vessels in the feet, and that should have removed the cause of the spasm and cured the affliction.

The injection was done by a consultant anaesthetist and it was accepted that it was done with proper professional skill and competence. Unhappily there occurred one of the known side-effects, the irritation of the genitofemoral nerve resulting in hyperaesthesia. Normally this lasts at most a few weeks, but in the case in question it persisted and undoubtedly caused the patient much distress and discomfort. The case turned on what she had been told about the risk and what it was good practice at the time to tell patients about it.

2. A patient was advised to have a hysterectomy carried out. She was particularly concerned about the location of the incision and the conspicuous nature of the resulting scar. She claimed that she was assured that it would be done by means of a Pfannenstiel's incision, leaving what the lady referred to throughout the case as a bikini-line scar. In the event the surgeon did not find it possible to make that type of incision and for good medical reasons made a mid-line vertical incision, which left a much more conspicuous scar. The patient became very distressed when she discovered the location of the operation scar and claimed that she had been given a guarantee that she would be left with a bikini-line scar. The surgeon for his part maintained that he could never have given such a guarantee, as the final decision on the incision could only be made on proper surgical grounds at the commencement of the operation.

Neither of these patients succeeded in her claim for negligence, because the doctors established on the facts that they had given proper information and warning in the circumstances of the case. But this sort of case is not going to go away, and my own view is that it may become more prevalent as people become more demanding and complaints-oriented, in medical matters as in everything else. How should doctors guard against it?

Let me return to the question of informed consent. That is a concept adopted in many other common law jurisdictions, notably in North America. It starts from the premise that medical treatment is a trespass or battery and that will be actionable unless proper consent is given by the patient, which is interpreted as informed consent. In order to obtain an informed consent the doctor must disclose all material risks. What are material risks? They are determined by the "prudent patient" test, formulated as follows in the leading American case of *Canterbury v Spence*, decided in 1972:

> "A risk is material when a reasonable person, in what the physician knows or should know to be the patient's position, would be likely to attach significance to the risk or cluster of risks in deciding whether or not to forego the proposed therapy."

It is subject to the exception of the "therapeutic privilege", which enables a doctor to withhold information as to risk when a reasonable medical assessment would have indicated to the doctor that disclosure would have posed a serious threat of psychological detriment to the patient.

This standard is rather good advice to doctors who wish to know the extent of their ethical

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obligation under the professional guidelines, though my personal advice would be to be extremely cautious about exercising the therapeutic privilege. But it does not represent our law, at least not at the present time. I insert this caveat because our law is moving into an era of rights-based doctrines, particularly since the Human Rights Act incorporated the European Convention on Human Rights into our law. And fairly recently Lord Irvine of Lairg in an article in the Medical Law Review suggested that the rights-based approach may encourage the courts to move away from the traditional doctrine towards that of informed consent. It does seem to me fairly likely that lawyers will cross-examine doctors about their observance of the guidelines, so be warned.

I referred a moment ago to the standard of care of a reasonable medical practitioner, but much as I might hesitate to burden you with complications, I fear that I have to do it, for we are getting into what is known as *Bolam* territory. I think that I had better go back to basics for a moment, and I hope that the lawyers will forgive me for stating what to them is obvious and elementary.

In general the standard of care which members of any profession are expected to reach in the exercise of the skills of their avocation is that of a reasonably competent member of that profession, the professional equivalent of that paragon of prudence, the man on the Clapham omnibus (I am afraid that this mythical character is a classic example of how the law clings to outdated institutions: the Clapham omnibus ceased to run in 1914).

If you are an architect or engineer, a landscape gardener or a marine hydrographer, that is the rule which will apply in unqualified form to the issue of your liability if your client has sustained damage and seeks to hold you liable. One will generally find that an expert in your field will give evidence on each side about the standard of care which a reasonable professional should adopt, and at the end of the day the judge has to decide whether that standard has been reached or whether you the defendant have fallen short of it. In the process he may have to weigh up the evidence of the experts if it conflicts and decide which should be preferred.

Not so for doctors. Their liability is governed by the well known *Bolam* test. Under that test if a doctor has followed a practice adopted by a responsible body of practitioners he or she is not to be regarded as having been negligent. In short, medical judgment rules, or doctor knows best. This is not the law in other spheres of activity. In the realm of industrial accidents it was thought for many years that following the established practice was a sufficient defence. But the employers' confidence in trade practice was rudely shattered when a case from this jurisdiction, *Cavanagh v Ulster Weaving Ltd* went to the House of Lords in 1959 and their Lordships held that trade practice is not conclusive. It may be strong evidence of lack of negligence if the defendant has followed it, but it is still open to the tribunal of fact to hold that that was not good enough.

One might have thought that medical negligence would be approached in the same way. But the issue was dealt with in 1957 by a puisne judge in the Queen's Bench Division charging a jury in *Bolam v Friern Hospital Management Committee* a case where the plaintiff had been undergoing ECT for treatment of a psychiatric disorder. In the course of this treatment he sustained dislocation of both hip joints, with fractures of the acetabulum and pelvis on each side. It was claimed that relaxant drugs should have been administered or manual control exercised, but it was proved that different views were held among competent doctors about the advisability of taking either step. The trial judge directed the jury in these terms:

> "A doctor is not guilty of negligence if he has acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art."

He went on to say that it was not essential for the jury to decide which of two practices was the better practice, as long as they accepted that what the doctor did was in accordance with a practice accepted by responsible persons. You can see at once that this has got away from the general rule that the standard is that of reasonable care in all the circumstances, to be determined by the tribunal of fact.

The *Bolam* test has remained part of law for nearly 50 years now, though often criticised, and with some modification: in *Bolitho v City and Hackney Health Authority* in 1997 the House of Lords emphasised that to satisfy the requirement the body of medical opinion relied upon must be

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not only responsible but respectable and reasonable. In order to qualify it must have a logical basis, formed by experts who have directed their minds to the question of comparative risks and benefits and reached a defensible conclusion on the matter. Once such a body of opinion has been proved to exist, however, that is a sufficient defence and the judge is not at liberty to pick and choose between the opinions expressed by medical experts, even though he might do that very thing in the next case involving the liability of a structural engineer.

One might have thought that even if it is justifiable on pragmatic grounds to judge the standard of actual treatment by this *Bolam* test, that should hardly apply to the issue of liability for failing to give a patient sufficient warning of adverse consequences of a proposed treatment, and one might have hoped that the courts would not apply the *Bolam* test in this area.

Unhappily for the law, at least in my own view, that was not to be, and the courts became distracted once again by the siren call of *Bolam.* In the case of *Sidaway v Bethlem Royal Hospital Governors*, decided in 1985, the House of Lords came down once again on the side of the application of the *Bolam* test and held that it should be applied in the sphere of warning of risks just as much as in diagnosis and treatment.

The patient, a woman of 63, had suffered from persistent pain in her neck and shoulders. She was advised by a neuro-surgeon, correctly as the court found, to have an operation on her neck to relieve pressure on a nerve root. The operation consisted of a laminectomy of C4 and a facetectomy or foraminectomy of the disc space between C4 and C5. The trial judge described the procedure as follows:

> "A laminectomy is an excision of the posterior arch of the vertebra. It gives the surgeon access to the foramen or channel through which nerves travel from the spine laterally... [The surgeon] freed the fourth cervical nerve root by removing the facets, or small bony protuberances, from the fourth vertebra and used a dental drill to free the nerve within the foramen."

It was found that the surgeon carried out the operation with proper skill and care, but sadly in its course some damage occurred to the spinal cord which caused a partial paraplegia. It was known that there was a risk of this occurring, the extent of which the medical witnesses placed at less than one per cent. The issue was whether sufficient warning had been given by the surgeon before the operation. The evidence was less than clear, because the surgeon had died before trial, but the judge held that it was probable that he did not refer specifically to the danger of cord damage when discussing the operation with her. There was, however, a responsible body of medical opinion which would not have given such a warning. The judge held that this concluded the matter, and the Court of Appeal and House of Lords upheld his decision. So once again the law has got away from the standard test of reasonable care, to be decided by the tribunal of fact.

The extension of the *Bolam* test to cases of warning has been strenuously criticised, I think with some justification. One can see a case for saying that it is extremely difficult for a layman to make a proper judgment about matter of diagnosis and treatment, and so in that sphere one should accept that if a body of responsible doctors would have taken the same course that should be a good enough defence. As I have said, I don't accept this, but one can at least see the force of the argument. But why should this be so when the issue is one of giving a sufficient warning, on which a layman can far more readily comprehend the issues and form a judgment? The courts have not allowed experts' opinion to be conclusive in other fields, so why should they do so in this one?

I think myself that it was a pity that the House of Lords did not see fit to adopt the regular method of determining the standard of care and take the opportunity to reject *Bolam* in this segment of medical negligence, which might have opened the way for jettisoning it altogether in some future case. But it was not to be, and one can only hope that it may reconsider the subject in time and reverse the rule. What are the prospects of this? Who knows? It might, but don't hold your breath waiting for it.

Let us suppose then that the doctor has failed to give the patient a sufficient warning and is to be regarded as having been negligent in that respect. What would the patient have done if a proper warning had been given? It would hardly accord with most people's sense of justice to hold the doctor liable for damages if that patient was set on having that treatment and would not have been put off in the slightest if the fullest warning of the

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risks had been given. I am glad to be able to say that the law does not perpetrate such an injustice, but I am also sorry to say that it has got itself into some rather tortuous complications in trying to achieve a proper result. This part of the thicket is one for the lawyers to struggle through, rather than the doctors, who have done their best, or rather worst, and have to leave the unravelling to the other profession; but the difficulties involved may serve as a cautionary tale which will remind doctors of the need to stay alert to the need for warnings.

It is a necessary part of a plaintiff's proofs that the defendant's act or omission, in these cases the failure to warn of risks, caused the loss sustained, that is, the actual occurrence of one of the possible eventualities of which warning should have been given. Our law has always had problems with the concept of causation. One sees in the reported cases depressingly frequent references to causation being a matter of common sense, often described as "ordinary" common sense or "good" common sense. But one man's sense may be another man's nonsense, and whole books have been written on causation without producing any clear and workable tests. A celebrated article on the topic by the distinguished academic Sir Arthur Goodhart commenced with a passage to the following effect:

> "My grandson, aged three, fell over a chair. Being an intelligent child, he thereupon proceeded to kick the chair."

I fear that the discussion of the subject, certainly in decided cases, all too frequently fails to get above this level of philosophical subtlety.

Let me pose a couple of scenarios to you, taken from actual decisions, and ask you how you would have decided each case. The first is an Australian case, *Chappel v Hart*. The patient suffered from a pharyngeal pouch, a relentlessly progressive throat condition which required surgery. No matter how carefully or well the surgery was performed, it entailed a very slight risk of injury to the vocal cords which would leave the patient with a weak and gravelly voice. The doctor failed to warn her of the risk of damage to her vocal cords. She consented to the surgery and suffered damage to her cords. Understandably, then, she was very upset that the doctor had performed the operation with precisely the result she had feared.

It was not disputed that the doctor had performed the operation with reasonable care, but it was accepted that he was in breach of his duty to inform the patient. The difficulty in the case arose from a combination of several other of its features. First, she would sooner or later have needed an operation of the type he performed on her (although it was not essential at the time it was done), and she would have had the operation at some time even knowing of the risk of damage to her vocal cords. Secondly, the risk of what happened to her was inherent in that type of operation no matter who performed it, or when or how well it was performed. But, thirdly, if the doctor had performed his duty to inform the patient of the risk, she would have sought a second opinion and would have had the operation performed by the most skilled and experienced surgeon available. What do you think was the result? Did the patient win or lose? Well, after a long legal battle the High Court of Australia held by a majority that she could recover substantial damages.

The second case is an English decision, *Chester v Afshar*, decided in 2002. The patient was a journalist who had a history of miserable back pain. She saw a surgeon, who advised her that she needed three bulging discs removed and that in his hands the operation (microdiscectomy L3/4 and L4/5) would be straightforward; he gave her the impression that it was virtually risk-free. Unfortunately, things did not go as planned. The patient suffered both motor and sensory impairment, which was not cured by a second operation. The only explanation forthcoming was one of cauda equina contusion that may have occurred during the first operation. She sued for damages, alleging that the surgery was negligently performed. This part of the case did not succeed at trial. So she was back to the case based on failure to inform her of the risks. The relevant factors are hard to fit into a logical pattern:

1. The risk of nerve damage was very small, perhaps 1 to 2 per cent (though the surgeon himself estimated it at the remarkably precise figure of 0.9 %).
2. Nevertheless, if he had warned her, she would not have proceeded with surgery at that time.
3. As it was elective surgery and there was no need for speed, she would have postponed the surgery, but would probably have sought another opinion and had the procedure done at

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a later stage.

4. Since the risk was so small, the odds were strongly in favour of her being less unfortunate the next time.

Should she win? Should she recover full substantial damages? The trial judge and the Court of Appeal held that she should.

This is very difficult territory, and I am rather reluctant to be critical of decisions which I should have found extremely difficult if faced with them myself. But I do wonder if a better approach might not have been via the concept of measuring a chance, which is used in other areas of tort law, and is very familiar to practitioners negotiating settlements. It would then not be a question of all duck or no dinner, but of what proportion of the full value of the damage sustained the plaintiff should recover. That has not found favour with our courts in this area of the law, or at least not yet. But some day perhaps it might . . .

Can I draw the threads of these rambling disquisitions together in order to see if there are any nostrums which I can offer to doctors – with, I may say, all the diffidence with which a practitioner in one discipline should feel when offering advice to experts in another:

1. I have no doubt that you have all made yourselves familiar with the ethical guidelines of the GMC and Royal College of Surgeons, for these are prime sources of guidance and instruction for members of your profession.
2. Obtaining consent is a more difficult matter in some cases than might have been thought in the past, and you might consider the wisdom of having it done at a suitably experienced level, not delegated to colleagues who are too junior.
3. Taking time to understand the concerns of the particular patient is important, and then to explain to that patient at a level of detail which he or she can understand what the treatment involves and where any material problems or risks may lie.
4. Above all, keep as good a note as you can. I know how difficult that must be when you are under pressure to deal with many things and time is at a premium – nor is it the most riveting task. But it can save you enormous worry and possible exposure to liability if you can prove months or years later, when ordinary recollection has naturally disappeared with time, what you said and what the patient agreed to.

One of the favourite hoary old stories of lawyers is of F. E. Smith, when he was a brash young man who frequently crossed swords with a particular county court judge. On one occasion that judge, after listening to an elaborate argument from F. E., remarked rather testily that he had listened to counsel's argument and was no wiser for it, to which F. E .replied silkily "No wiser, your Honour, but much better informed." I venture to doubt whether any of you present tonight are much wiser for listening to this paper, but I hope that you may be a little better informed and may be able to take something of benefit away from this evening.

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Case Report

Effort-induced thrombosis of the subclavian vein – a case of Paget-Schroetter syndrome

P G McGlinchey, S A Shamsuddin, J C Kidney

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Paget-Schroetter syndrome is thrombosis of the subclavian or axillary vein due to repetitive use of the upper limbs. We present a case of Paget-Schroetter syndrome in a man who regularly performed weightlifting as part of his routine workout at the gymnasium. The mechanisms of the disease and its treatment are discussed. This diagnosis should be considered in unexplained subclavian or axillary vein thrombosis.

CASE REPORT A 53 year old male taxi driver presented with left arm swelling. There was no history of trauma. The limb was not painful. He had noticed a hard swelling in his left axilla. He was previously healthy, with no relevant past medical history. In particular, there was no personal or family history of deep venous thromboses or any clotting disorder. He was a lifelong non-smoker, and had no respiratory symptoms.

On examination, the left upper limb was mildly erythematous, obviously swollen and oedematous. The axillary vein was felt to be palpable. There was no lymphadenopathy present. Respiratory examination was normal. There was no swelling in any other region, including the other three limbs. Chest X-ray was normal.

The provisional diagnosis was left subclavian or axillary vein thrombosis and the patient was commenced on a therapeutic dose of low molecular weight heparin.

D-dimer was not elevated. A venogram of the left arm showed an occluded left subclavian vein with collateral circulation connecting to the neck veins. Investigation of an underlying cause was initiated. A thrombophilia screen consisting of antithrombin III, protein C, protein S and factor V Leiden assays was normal. A CT of thorax was also normal.

On further questioning, the patient admitted to attending a gymnasium three times a week for many years. Part of his routine at the gymnasium included weightlifting, with obvious repetitive use of the arms. This information led to the diagnosis of effort-induced thrombosis of the subclavian vein, otherwise known as Paget-Schroetter syndrome.

The patient was commenced on warfarin for a period of six months with a target international normalised ratio of between 2.0 and 3.0. When he last attended the outpatient clinic, the swelling in his left arm had completely resolved. He has been advised to discontinue activities at the gymnasium, such as weight lifting, that involve repetitive use of the arms.

DISCUSSION

Primary thrombosis of the axillary/subclavian vein was described in 1875 by Sir James Paget and in 1884 by Leopold von Shroetter.[1] Paget-Schroetter syndrome usually develops in young, healthy persons with a history of repetitive motion of the arms. Spontaneous thromboses in the arms have been reported in athletes such as golfers, American football players, weight lifters, baseball players, wrestlers, tennis players and cheerleaders, as well as in painters and beauticians.[1,2] Most

Department of Medicine, Mater Infirmorium Hospital, Crumlin Road, Belfast BT14 6AB.

P G McGlinchey, MB, BCh, BAO, MRCP, Specialist Registrar.

S A Shamsuddin, MB, BCh, BAO, Senior House Officer.

J C Kidney, MD, MRCPI, Consultant Physician.

Correspondence to Dr McGlinchey.

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patients present with symptoms of venous obstruction such as pain, swelling and bluish discolouration of the limb.[3]

Repetitive shoulder-arm motion, extrinsic compression of the subclavian vein, and in some, a hypercoagulable state, may contribute to the development of primary thrombosis of the subclavian vein.[4] There are a number of mechanisms by which repetitive motion of the shoulder and arm may predispose to thrombosis. The subclavian vein may be compressed during lateral abduction of the arm, causing turbulence or obstruction to flow.[2,5] Microscopic intimal injury may occur, stimulating the coagulation cascade. Repetitive motion may also contribute to anatomical narrowing of the thoracic outlet through hypertrophy of the tendon of the subclavian muscle, the anterior scalene muscles, or both. Finally, lifting of heavy weights may cause further narrowing of the costoclavicular space through depression of the shoulder.[5]

Although most patients with the Paget-Schroetter syndrome have isolated vascular compression, some also have classic symptoms of thoracic outlet compression such as paraesthesia, numbness and muscle weakness.

The optimal treatment of Paget-Schroetter syndrome has not been determined by a prospective, randomised study. Traditionally, treatment has consisted of limb elevation and anticoagulation. More recently, catheter-directed thrombolytic therapy followed by surgical decompression of the thoracic outlet has been advocated.[6]

In conclusion, this case has been presented to raise awareness of Paget-Schroetter syndrome. A history of repetitive use of the upper limbs should be sought in cases of unexplained subclavian or axillary vein thrombosis.

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Case Report

Elevated serum ß-hCG due to a tumour of unknown origin

L Kenny, J J McAleer

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We report a patient with an elevated level of serum beta human chorio-gonadotrophin (ß-hCG) due to cholangiocarcinoma. This case demonstrates the need for consideration of diagnoses other than germ-cell tumours when a patient presents with a raised ß-hCG level.

CASE REPORT A 45-year-old man presented initially to a surgical unit with a history of epigastric pain radiating to the right hypochondrium for four months, nausea, vomiting, obstructive jaundice and weight loss of 15kg over two months. After initial investigations, he was transferred to the regional oncology centre.

He was deeply icteric on examination, with marked ascites and a four-fingerbreadth hepar palpable in the abdomen. He had sinus tachycardia (rate 100bpm) and was tachypnoeic (respiratory rate 20 breaths per minute). Decreased air entry was noted bibasally, more marked on the right; oxygen saturation was normal. Bilateral pitting oedema to the knees and presacral oedema were also evident. Testes were normal on examination.

Ultrasound and CT scan showed a moderate right-sided pleural effusion, a small left pleural effusion, small soft tissue masses involving the right anterior pleura and right lung parenchyma and bilateral basal pulmonary collapse/consolidation. Extensive lesions replaced the entire left lobe of liver; smaller deposits in the right lobe, ascites and a peritoneal nodule were noted.

Liver function tests were deranged (bilirubin 102 umol/l (normal = 3-18 umol/l), alkaline phosphatase (ALP) 769 U/l (normal = 30-120 U/l). gammaglutaryl transferase (GGT) 235 U/l (normal = 12-58U/l), aspartate transaminase (AST) 139U/l (normal = 10-40 U/l, alanine transaminase (ALT) 54 U/l (normal = 10-56U/l), albumin 21g/l (normal = 35-50 U/l), prothrombin 17.3 seconds (normal = 12-17 seconds), coagulation otherwise normal. Haemoglobin was 10.9 g/dl – normochromic, normocytic, white cell count elevated at 16.7x 10^9 (neutrophil leucocytosis). Serum tumour markers showed serum beta human chorio-gonadotrophin (ß-hCG) 1274 IU/l, alpha- fetoprotein (AFP) 2.4 kU/l, prostate specific antigen (PSA) 0.1 ng/ml, carcinoembryonic antigen (CEA) <0.5 ng/rnl, and CA 19-9 34992 IU/ml. A liver biopsy (performed under ultrasound guidance) revealed poorly differentiated adenocarcinoma. Immunohistochemistry of the tumour cells was negative for CEA, AFP, ß-hCG, and cytokeratin 20, positive for cytokeratin 7 and positive for mucin. A repeat CT scan of chest, abdomen and pelvis suggested a lesion in the pancreatic head with a dilated main pancreatic duct. Given the possibility that the patient had a germ cell tumour, and considering his poor performance status he received a single cycle of carboplatin AUC 6 using a dose based on creatinine clearance (calculated by the Cockroft formula using ideal body weight[1]). Serum CA19-9 and ß-hCG levels were repeated on several occasions – the peak values for these were 96,000 IU/ml and 6739 IU/l respectively two days before his death which occurred 25 days after chemotherapy.

Postmortem examination revealed that the bulk of the tumour was in the left lobe of the liver, obliterating the biliary tract and directly infiltrating the pancreas. There were metastases to the porta hepatis, adrenal glands, kidneys,

PET Oncology Group, Room 241, MRC Cyclotron Building, Hammersmith Hospital, Du Cane Road, London, W12 0NN.

L Kenny, MRCP, Clinical Research Fellow.

Belvoir Park Hospital, Hospital Road, Belfast BT8 8JP.

J J McAleer, Consultant Oncologist/Senior Lecturer.

Correspondence to Dr Kenny.

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abdominal wall, multiple ribs and vertebrae and multiple pulmonary infarcts. Histology was in keeping with an intrahepatic bile duct carcinoma, though pancreatic carcinoma could not be excluded.

Human chorionic gonadotrophin is produced by syncitiotrophoblasts, and is a glycoprotein which consists of an α and a ß subunit. A serum level of ß-hCG> 1000 pg/ml (equivalent to 9.3 IU/l) is believed to be highly diagnostic of gonadal (especially nonseminomatous germ cell) tumours.[2,3] Lower levels of elevation of the free ß-hCG subunit (>100 pg/ml) have previously been demonstrated in patients with gonadal and non-gonadal tumours; in some patients (1-2%) with nonseminomatous germ cell tumours the free ß-hCG subunit may he the only identifiable form in the serum.[4] The nongonadal tumours in the series by Marcillac *et al* included bladder, biliary, pancreatic, and cervical neoplasms. Microparticle enzyme immunoassay was used to measure ß-hCG (i.e. free ß-hCG and intact hCG) in our case (Axsym system®, Abbott laboratories, Illinois, USA). The degree of elevation of CA19-9 is consistent with the post mortem findings.

The high total ß-hCG level is extremely unusual, but may relate to the poorly differentiated nature of this tumour. Serum levels of ß-hCG greater than or equal to 4 IU/l have been demonstrated to correlate with poor prognosis in patients with gastric carcinoma, and may represent an independent factor reflecting not just the tumour burden but aggressive biology.[5]

Raised levels of free ß-hCG have also been found to be a poor prognostic factor in advanced colorectal cancer.[6] In a small series from Japan, patients with cancer of unknown primary origin and female patients with peritoneal adenocarcinomatosis with elevated ß-hCG (more than 10 IU/l) who received platinum based chemotherapy showed higher response rates than patients with lower values (83.3% and 80% respectively versus 15.3%).[7] Elevated preoperative levels of free ß-hCG may also correlate with prognosis and survival in patients with epithelial ovarian cancers.[8] The method of analysis of ß-hCG is important for comparisons between different reports as assays report either free ß-hCG or total ß-hCG.

Tissue expression of ß-hCG does not always correlate with serum expression of ß-hCG.[6] Reasons for this may include a lower detection threshold of the serum assay, and the degree of shedding of antigen which is related to lymphovascular invasion, basal membrane degradation and the extracellular matrix. Elevation of ß-hCG measured in the serum can also occur due to heterophilic antibodies,[9] and an alternative serum assay would have been useful to exclude this phenomenon.

In summary, ß-hCG remains a valuable marker in patients with germ cell tumours and trophoblastic disease. We must however, consider other diagnoses in the setting of an elevated serum ß-hCG (even very high levels as seen in our patient) and a tumour of unknown origin. The atypical clinical presentation as a germ cell tumour should prompt further investigations for alternative primary tumours, although this is unlikely to have affected the management of this patient due to his poor general condition.

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Case Report

Crutch induced axillary artery injury

B McFall, N Arya, C Soong, B Lee, R Hannon

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Chronic use of axillary crutches is sometimes associated with axillo – brachial thrombo-embolic disease. Inappropriate placement of the patient's body weight on the axillary pad of the crutch causes repetitive trauma to the axillary artery leading to stenosis or aneurysm formation. We report a case of acute occlusion of the axillary artery caused by the use of the axillary crutch.

CASE REPORT A 53-year-old female presented with sudden onset of pallor and decreased sensation of the right hand and forearm, without loss of power. She had rheumatoid arthritis for the last 30 years, and had been using axillary crutches for the last 10 years. She had undergone bilateral knee and left hip replacements. There were no other significant cardiovascular risk factors, nor any previous history of deep venous thrombosis or miscarriages suggesting a hypercoagulable state. She was a non-smoker.

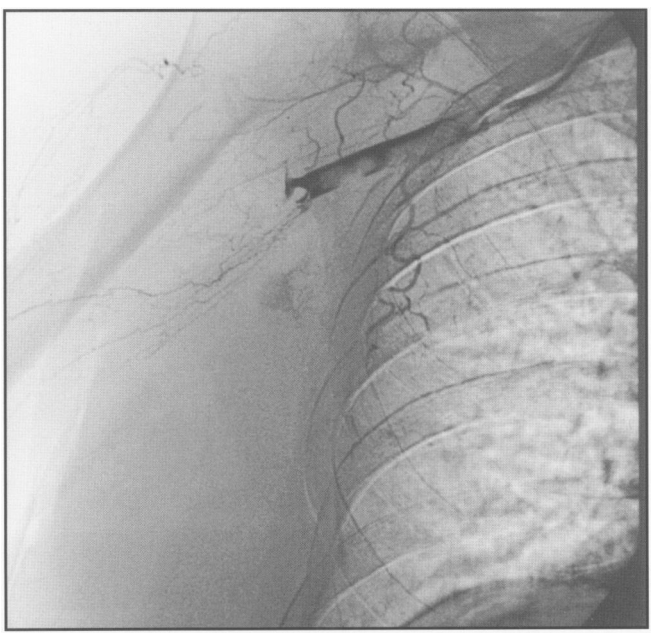

Fig 1. Arteriogram demonstrating complete occlusion of the right axillary artery.

On examination, she was in normal sinus rhythm. Both hands showed classical deformities of burnt out rheumatoid arthritis. The right hand was cold and pale, with delayed capillary return. Sensation was impaired over the fingers. Right brachial, ulnar and radial pulses were absent.

X ray of the thoracic inlet showed no evidence of bony cervical rib. ECG and echocardiogram were normal. An urgent angiogram showed an acute occlusion of the right axillary artery, with poor filling of the distal vessels (*figure*).

Because of severity and persistence of symptoms, surgical exploration of the brachial artery above the antecubital fossa was performed.

Fresh clot was retrieved from distal radial and ulnar artery with balloon thrombo -embolectomy. Further clots were obtained from the proximal axillary artery. Subsequently a good forward pulsatile flow was achieved. After closure of arteriotomy and restoration of blood flow, the hand became warm and pink, with a palpable radial and ulnar artery at the wrist. Follow up duplex scan showed no evidence of residual stenosis or thrombus in the axillary artery. No obvious aneurysm formation was demonstrated.

She was subsequently assessed and trained in the use of a rollator with wrist braces, as a walking aid.

Department of Vascular Surgery, Belfast City Hospital, 91 Lisburn Road, Belfast BT9 7AB.

B McFall, BSc, MB, BCh, Senior House Officer.

N Arya, MS, FRCS, Specialist Registrar.

C Soong, MD, FRCS, Consultant Surgeon.

B Lee, FRCS, Consultant Surgeon.

R Hannon, MD, FRCS, Consultant Surgeon.

Correspondence to Mr Soong.

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DISCUSSION

Radial nerve and axillary artery are the commonest structures injured with the long term use of axillary crutch. It usually presents in the form of traumatic radial nerve palsy or a thromboembolic episode in the upper limb.[1]

Radial nerve palsy affects motor supply to the extensor muscles of the arm and forearm. Damage to it causes the forearm to adopt a characteristic position with a flexed, limp wrist. In this state, grip strength is lost since for maximum power in the digital long flexors, the wrist has to be held in extension. If the lesion occurs above the upper third of the arm, the triceps muscle is also affected and elbow extension will be absent. Sensation is tested over the area of the anatomical snuffbox. Sensation here is lost with a radial nerve lesion at any level.

Repetitive trauma due to the use of axillary crutch causes disruption and degeneration of the tunica intima and tunica media leading to the formation of an aneurysm or stenosis. Pathological examination of the axillary artery reveals fragmentation of the intima and elastica associated with a perivascular fibrous reaction.

Crutch induced aneurysms of the axillary artery was first reported as early as 1930.[2] The commonest presentation is in form of sudden ischaemia of the upper limb, with no reported case of rupture.[3,4,5] The patients are usually elderly, suffering form chronic arthritis or weakness of the lower extremities, and have used axillary crutches to mobilize for many years. Muscle wasting around the pectoralis, latissimus dorsi and shoulder joint are often seen in rheumatoid patients, and one could postulate that this muscle wasting and/or loss of body fat may make such an injury more likely.

Intimal disruption leads to thrombogenesis and repetitive trauma dislodges showers of small emboli, which gradually occlude distal vessels and may compromise the results of revascularisation during a later ischaemic episode.[1] For this reason surgical treatment is suggested on discovery of an aneurysm even if asymptomatic. Surgical alternatives include thrombectomy, axillo-brachial bypass or primary repair of the axillary artery. For non-aneurysmal disease, percutaneous thrombolysis and angioplasty may be safer, less invasive and equally efficacious.

Thrombolytic agents have been successfully used to dissolve the occluding thrombus, reconstitute blood flow, and improve the status of the tissue bed supplied by the involved vascular segment. Thrombolytic agents in clinical use are actually plasminogen activators and plasmin is the active molecule that cleaves fibrin polymer to cause dissolution of thrombus. Peripheral thrombolytic therapy is administered through a catheter-directed approach to achieve regional thrombolysis with minimal systemic fibrinolysis. However a moderate systemic proteolytic state often results, culminating in haemorrhagic complications and hence limiting their use to patients with no contraindications (*Table*). There is no overall difference in limb salvage or death between surgery and thrombolysis in the initial management of acute limb ischaemia.[6] Thrombolysis may be associated with a higher risk of continued limb ischaemia, and of haemorrhagic complications including stroke and this must be balanced against the risks of surgery in each patient.

TABLE

Contraindications to use of thrombolytic agents

Absolute Contraindications
1. Active bleeding disorder
2. Gastrointestinal bleeding within 10 days
3. Cerebrovascular event within 6 months
4. Intracranial or spinal surgery within 3 months
5. Head injury within 3 months
Relative Contraindications
1. Major surgery or trauma within 10 days
2. Hypertension (systolic >180 mm Hg or diastolic >110 mm Hg)
3. Cardiopulmonary resuscitation within 10 days
4. Puncture of noncompressible vessel
5. Intracranial tumour
6. Pregnancy
7. Diabetic haemorrhagic retinopathy
8. Recent eye surgery
9. Hepatic failure
10. Bacterial endocarditis

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However, in this case no aneurysm formation was found. The lack of a local stenotic lesion raised the possibility of embolus arising from a more central source. However the absence of any previous symptoms or signs of cardiac disease, and a normal echocardiogram suggest that this was unlikely.

Therefore the presentation of acute upper limb ischaemia in this case was most probably due to axillo-brachial thrombosis secondary to chronic axillary crutch use, even though no focal stenotic lesion could be identified.

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Case Report

Spontaneous rupture of kidney with peri-renal haematoma: a conservative approach

V Koo, B Duggan, G Lennon

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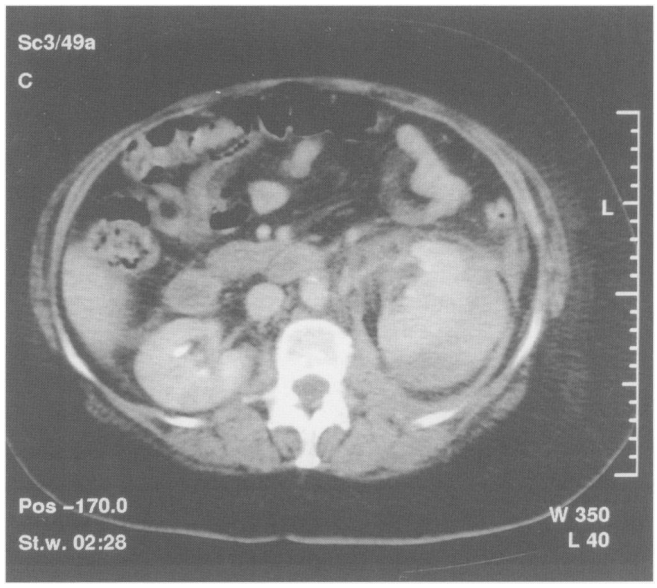
Spontaneous peri-renal haemorrhage (SPH) is an uncommon entity. Its diagnosis requires the absence of recent instrumentation, surgery or trauma.[1] It may present with 'Lenk's triad' consisting of acute flank pain, tenderness and symptoms of internal bleeding.[2] In many cases, the severe haemorrhage necessitates surgical exploration. We discuss conservative management of such a case.

CASE REPORT A healthy 65 year old lady was admitted to our department with 10 days history of left flank pain. She had no previous history of renal disease or recent trauma, and was not on anticoagulants. On examination, she was pyrexic 37.8°c, tachycardic with left flank tenderness. Blood investigations (i.e. full blood picture, electrolyte profile, liver function, coagulation screen) revealed haemoglobin (Hb) of 7.8g/L, haematocrit (HCT) of 0.232 and white cell count (WCC) of 23.0 g/L. She received blood transfusion and antibiotic therapy. Her MSSU and blood culture returned as negative. Computed tomography (CT) scan showed a left 6cm by 3cm peri-renal haematoma. (*figure*) Because an infected haematoma could not be ruled out completely, the collection was drained (50mls of altered blood) under CT-guidance with a pigtail catheter. The drainage stopped on day 3 and was removed, Hb remained stable, WCC normalised and she was discharged 1 week later.

Six weeks later, she was reviewed with a follow-up CT scan which showed a recurrent 5 by 4cm collection in the left kidney with retroperitoneal extension along psoas muscle. She also developed a new onset hypertension (200/120mmHg) and was treated with ACE inhibitor. This was thought to be secondary to the renal damage done by the haematoma (vasculitis profile, autoantibody



Figure

profile, ESR, thyroid function test, urinary catecholamines, cortisol level creatinine clearance were normal). She was re-admitted for a repeat pigtail drainage procedure. About 15mls of bloody material with clots was drained and was negative for culture and malignancy. An intravenous urography (IVU) did not show any obstruction in the left kidney. On day 3 the drainage stopped and was removed, and she was discharged. Two months later, a repeat CT scan showed that the

Department of Urology, Altnagelvin Hospital, Glenshane Road, Londonderry, BT47 1SB.

V Koo, MB, BCh, BAO, SHO.

B Duggan, MD, FRCS, Sp. Registrar.

G Lennon, MCh, FRCSI, Consultant.

Correspondence to Dr Koo, 102 Locksley Park, Belfast BT10 0AT.

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haematoma had resolved completely. DTPA renogram did not demonstrate reno-vascular disease. She remains well and is presently being followed up by the Urology and Medical Team.

DISCUSSION

Originally reported by Bonet,[3] and later described by Wunderlich[4] in 1856, various terms have been used including spontaneous ptri-renal haematoma, spontaneous subcapsular renal haemorrhage, non traumatic peri-renal haematoma and spontaneous ptri-nephric haematoma. Causes of SPH includes benign (eg. angiomyolipomas, renal cyst, adenoma, lipoma, hamartoma) and malignant (eg. oncocytomas, clear cell carcinoma, Wilms, renal secondary), vasculitis, nephritis and blood dyscrasias (coumarin anticoagulation, polycythaemia). McDougal *et al*[5] reviewed the English literature in 1975 and found 78 cases; Cinman *et al*[6] reviewed from 1974 to 1985 and found 27 cases; Zhang *et al*[7] reviewed from 1985 to 1999 and found 165 cases of SPH as shown in Table 1. In Zhang' s meta-analysis, the male-to-female ratio was 6:5 and the average age was 46.8 years (range from 4 months to 89 years) with most cases (85%) occurring between ages 20 to 70 years. Table II illustrates the aetiology of these cases.

Flank pains with disproportionate low Hb, low haematocrit level and elevated serum lactate dehydrogenase (LDH) level[8] raises the suspicion of SPH. Intravenous urography[10] with nephrotomography may demonstrate the presence of non-opacified haematoma compressing the opacified renal parenchyma and provide information on renal function of the opposite kidney. Ultrasonography (US) is effective in the identification of renal/peri-renal fluid collection, although it may be difficult to differentiate between tumour and abscess[9] Here, CT scan may provide the aetiologic diagnosis and well as providing details of the contralateral kidney. There is little data on the use of magnetic resonance imaging (MRI), but it would be useful in situations where contrast enhance CT is contraindicated (eg. contrast allergy, pregnancy). Selective angiography may demonstrate pathological

TABLE I

Spontaneous repture of renal parenchyma: underlying causes and its incidence

References	*No. of cases*	*Tumour* %	*Vascular* %	*Infection* %	*Idiopathic* %
McDougal *et al* [5]	78	58	18	10	2.6
Cinman *et al* [6]	27	63	26	7	–
Zhang *et al* [7]	165	61	17	4	6.7

TABLE II

Etiology of spontaneous renal haemorrhage and its incidence in 165 cases (adapted from Zhang et al [7])

Etiology	*Percentage of patients %*
Tumour:	61.5
(Benign – 31.5% and Malignant – 29.7%)	
Vascular	17
Infection	2.4
Miscellaneous	12.7
Idiopathic	6.7

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vascularisation and active bleeding from a renal tumour, but is generally thought to be unhelpful.[2] Diagnostic accuracy of retroperitoneal haemorrhage was 100% sensitive in CT and MRI and 56% in US; and diagnosis of an underlying renal mass in CT yielded a sensitivity of 57% and specificity of 82% compared to 11% and 33% respectively in US.[7]

In some cases,[10, 11] US, CT and angiography may not be able to discern the underlying cause and this constitutes a therapeutic dilemma. The rationale for management of these cases must take account that the commonest cause of SPH is tumour, of which benign and malignant nature have almost equal incidence and can occur in young and elderly population. Bagley,[12] Kendall *et al* [13] and Novicki *et al* [14] advocate radical nephrectomy due to the possibility of a small clinically unapparent renal cell carcinoma. In Kendall's series, six cases of SPH were due to rupture of small renal cell carcinoma that CT had failed to reveal at the time of acute haemorrhage. While Morgentaler *et al* [8] proposed nephrectomy for patients with non-fatty lesions (other than haematoma) on CT, which are suspicious for carcinoma. They recommended that all other cases should be followed up with serial CT.

In contrast, Howalt & Squirs[15] have advised a conservative approach when diagnostic studies fail to demonstrate a significant pathology. Uson *et al* [16] and Bosniak[17] advocated serial CT at 2-3 months interval until the haematoma resolves and a definite diagnosis may be possible. Bosniak claims that surgical exploration is not necessary in most unexplained cases because of the diagnostic accuracy of CT using 5mm sections. In the context of conservative management, Gupta *et al* [18] recommended that drainage of haematoma should be individualised: a large infected haematoma needs drainage, while smaller uninfected haematoma should be left alone.

In Zhang' s review,[7] malignancy was present in 49 of 113 (43%) patients undergoing total nephrectomy; and in 64 of 113 (57%) patients one with normal kidney or benign disease underwent total nephrectomy. They have recommended that repeat imaging following resolution or evacuation of haematoma seems prudent to avoid unnecessary nephrectomy. In our case, three separate CT scans did not demonstrate any renal parenchymal disease. Although the cause for this patient's haematoma remains unknown, we have shown that conservative management can be appropriate where clinical signs stabilise.

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Cervical osteophyte causing perforation of the nasopharynx

A Khan, T Farnan, SJ Hall, MJ McClure

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Cervical osteophytosis causing perforation of the nasopharynx has not been reported. We record a case of a 70-year-old man who fell from a horse and developed surgical emphysema in his neck. The possible aetiology is discussed.

CASE REPORT

A 70-year-old man fell from a horse and landed on his head. He did not lose consciousness, but immediately noticed a slight change in the tone of his voice and was able to continue his normal activity. Later that day he noticed increasing swelling of his neck with associated dysphagia. He went to his local hospital Casualty Department and was referred to the Otorhinolaryngology Service after having his cervical spine x-rayed.

On admission ten hours after the injury, he complained of dysphonia and odynophagia. He also complained of decreased hearing and a blocked sensation in the right ear. Past medical history included benign prostatic hyperplasia and hypercholesterolaemia. He had long standing cervical spine osteoarthritis treated with simple analgesia. On examination, there was gross surgical emphysema of the neck. The cervical spine was diffusely tender on palpation, and no neurological deficit was evident. He was apyrexial and vital signs were stable.

Indirect laryngoscopy was not possible. Flexible laryngoscopy confirmed that his airway was patent and rigid nasendoscopy revealed a bony elevation in the nasopharynx with a small overlying tear.

There was obvious swelling of the posterior pharyngeal wall. Otoscopy of the right ear was normal.

Haematological investigations were normal. A lateral cervical spine radiograph (Fig. 1) demonstrated gross surgical emphysema, with abnormal gas seen in the retropharyngeal space and soft tissues of the neck. Prominent anterior osteophytes were noted at C2 and C3 vertebral endplates, with preservation of disc height. Multi-level anterior osteophyte formation and disc space narrowing were also seen at C5-7, consistent with osteoarthritis, rather than diffuse idiopathic sclerosing hyperostosis (DISH). An emergency CT neck examination confirmed gross surgical emphysema of the neck and clearly delineated the prominent osteophytes (Fig. 2). There was no evidence of other bony injury.

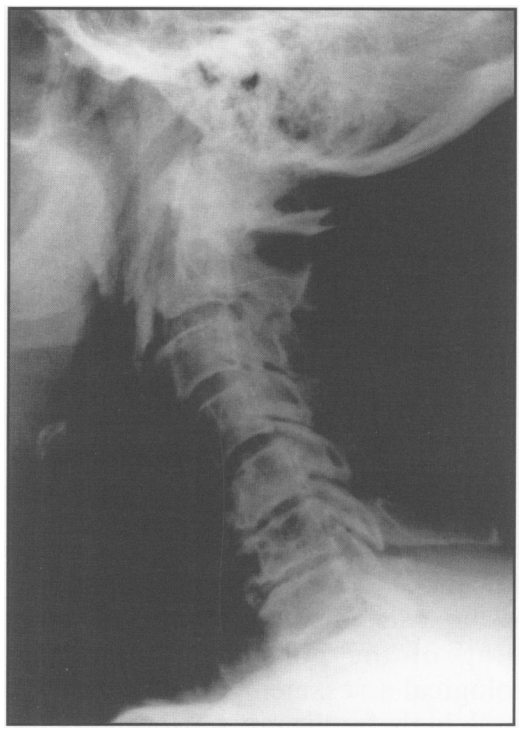

Fig 1. Lateral cervical spine radiograph demonstrating gross surgical emphysema.

Craigavon Area Hospital, 68 Lurgan Road, Portadown, Craigavon, BT63 5QQ.
Department of otorhinolaryngology,
A Khan MBBS,
T Farnan MRCS,
SJ Hall FRCS, Consultant ENT Surgeon
Department of Radiology
MJ McClure FRCR, Consultant Radiologist
Correspondence to Mr Hall

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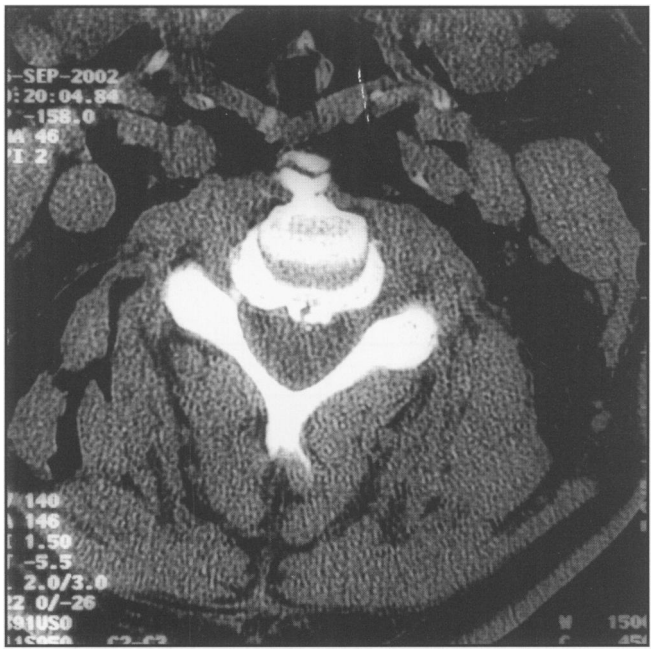

Fig 2. CT neck examination confirming gross surgical emphysema of the neck.

He was given an immediate dose of intravenous Dexamethasone and started on intravenous Co-amoxiclav thrice daily. He was allowed a soft diet. His voice and swallowing improved over a period of three days. There was also a reduction of the neck swelling. Repeat flexible and rigid endoscopy carried out on day three showed mild swelling of the posterior pharyngeal wall. Audiological assessment showed a symmetrical bilateral high frequency sensorineural hearing loss in keeping with presbycusis. He was discharged on day four on oral Co-amoxiclav.

At review in the outpatient clinic three days later, his symptoms had almost completely settled. There was no palpable surgical emphysema. Rigid nasendoscopy and indirect laryngoscopy were normal. He was discharged from follow-up.

DISCUSSION

To our knowledge, there are no previous case reports of cervical osteophytes causing perforation of the nasopharynx following a neck injury. A case of surgical empysema following a flexion-extension sports injury has been reported[1]. In that particular case, it is postulated that anatomical weakness at the pharyngo-oesophageal junction predisposed to perforation with minimal force of impact leading to surgical emphysema in the neck. Nasopharyngeal perforation as a complication of nasogastric intubation has been described in a patient who developed surgical emphysema in the neck after three failed attempts of nasogastric intubation[2]. Flexible endoscopy carried out the following day revealed a vertical 1 cm laceration in the midline of the nasopharynx.

Patients with diffuse idiopathic sclerosing hyperostosis (DISH), or Forestier's diesease, have extensive osteophyte formation of the anterior cervical vertebrae. However, in this condition the intervertebral disc spaces are preserved, which helps differentiate from the much more common condition of cervical osteoarthritis, in which disc space narrowing is the hallmark[3]. In this case, the narrowed disc height in the lower cervical region was consistent with osteoarthritis. The degree of osteophytosis seen on radiological investigation is however somewhat unusual. Chronic dysphagia may be associated with DISH[4].

We feel that our patient's dysphonia and dysphagia were due to the marked surgical emphysema of the pharynx and neck. The blocked sensation in his ear was probably due to eustachian tube dysfunction secondary to surgical emphysema of the nasopharynx. His presbycusis was incidental to this injury.

CONCLUSION

We postulate that prominent cervical osteophytes in this patient caused perforation of the nasopharynx due to the trauma sustained by falling from a horse. Air tracked through the perforation resulting in gross surgical emphysema in the neck as evident on clinical examination and supported by the findings on endoscopy, cervical spine radiograph and CT imaging. Symptoms resolved rapidly with conservative treatment.

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Carcinoid tumour of the extrahepatic bile duct - report of a case and literature review

A A C Menezes, A J Diver, D McCance, T Diamond

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Carcinoid tumors of the extrahepatic bile duct are rare and account for only 0.2-2% of all gastrointestinal carcinoids [1,2].

CASE REPORT

A 30 yr old man presented with obstructive jaundice while on holiday in Australia. Physical examination was otherwise normal. Abdominal ultrasound, CT scan and MRI scan confirmed marked dilatation of the intrahepatic biliary system. ERCP revealed a stricture in the common hepatic duct (Figure 1). A stent was inserted. Brush cytology was inconclusive. CA19-9 and CEA levels were normal. Following return to the UK, laparotomy was performed and revealed a 3cm tumour at the junction of cystic duct and CHD. Excision of the bile duct with portal lymphadenectomy and Roux-en-Y hepaticojejunostomy was performed. He had an uneventful postoperative course.

Histopathology revealed a white firm tumour obliterating the lumen of the CHD. Microscopically, the tumour contained round and polygonal cells arranged in nests and separated by fibrous stroma. Tumour cells were tested for neuroendocrine markers incuding chromogranin S and serotonin, but were positive only for protein gene peptide and neurone specific enolase (Figure 2). Ultrastructural appearances on electron microscopy showed dense-cored neuroendocrine granules consistent with a mid-gut carcinoid tumour. Margins were free of tumour but one out of eleven lymph nodes showed a metastatic deposit.

Postoperatively, gastrointestinal hormone levels including NeurokininA, Gastrin Release Peptide, and Pancreatic Polypeptide were normal. Daily urinary excretion of 5 hydroxyindoleacetic acid (5-HIAA) was also within the normal range. SPECT octreotide scan did not reveal any metastases and he remains well at follow up 18 months later.

DISCUSSION

Carcinoid tumours of the bile duct are rare. As with other tumors of the bile duct, these lesions are difficult to diagnose preoperatively and nearly impossible to distinguish from cholangiocarcinoma. They are derived from embryonal neural crest cells (Kulchitsky cells) and have the potential to produce serotonin[3]. These cells are also known as argentaffin cells, because of their affinity for silver staining compounds and are located in the crypts of Leiberkühn.

Most of the information about this malignancy is from case reports. A comprehensive search of Medline and Embase revealed forty two cases of carcinoid of the extrahepatic duct, including our case. In 1959, Davies first published a case of biliary carcinoid although this may have been a periampullary carcinoid[4]. Pilz has been credited with the first reported case of carcinoid of the biliary tract[5]. Clinical characteristics, pathology and follow up data of previously described cases are summarized in Table 1[3-22].

The age of patients ranged from 12 to 79 years with a median of 47 years[12,13]. The female to male ratio was 2:1. The commonest symptom was jaundice (69% of cases), often associated with abdominal pain (30%) and pruritis (21%).

Mater Hospital Trust, Crumlin Road, Belfast BT14 6AB.

AAC Menezes, FRCS, Surgical research Registrar

AJ Diver, MB, BCh, BAO, Senior House Officer

T Diamond, BSc, MD, FRCS, FRCSI, Consultant Hepatobiliary Surgeon

Royal Victoria Hospital, Grosvenor Road, Belfast, BT12 6BJ.

D McCance, MRCP, Consultant Endocrinologist

Correspondence to Mr Diamond.

E-mail: tdiamond-stc@mater.n-i.nhs.uk

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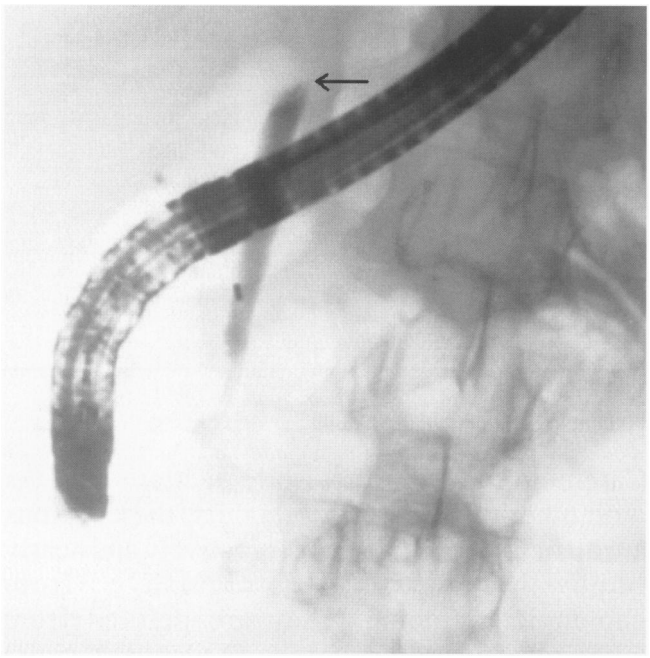

Fig 1. ERCP showing a stricture in the common hepatic duct (arrow)

Investigations ranged from abdominal ultrasonography to endoscopic retrograde pancreaticography and more recently CT scan and Magnetic Resonance Cholangiography. However, a preoperative diagnosis of carcinoid tumour was made in just one case [5] and in only 11 cases was a diagnosis of primary CBD tumour suspected. In three cases the diagnosis was made at autopsy[13].

The commonest site of malignant stricture was the common bile duct (55%) followed by the hilar confluence of the bile ducts and the common hepatic duct (33%). Notably, pain in the right upper quadrant was a predominant symptom of tumours in the cystic duct.

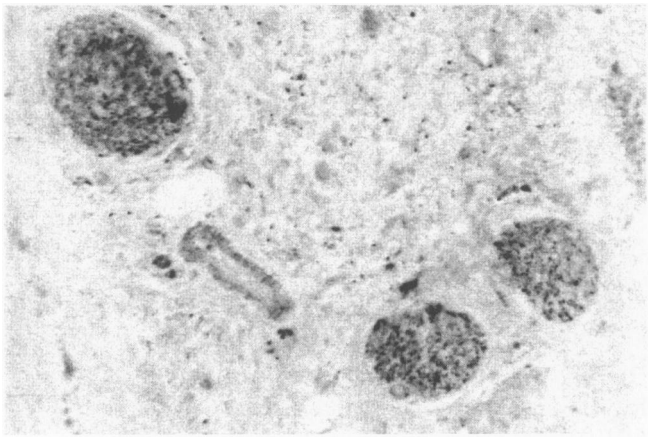

Fig 1. (200x magnification) Shows large malignant cells with neuroendocrine granules positive for Neurone Specific Enolase by immunohistochemistry. (Image inverted for clarity)

Metastatic spread was present in 14 cases (33%) in which lymph node involvement was most common site. Immunomarkers were not performed in any case preoperatively and even after diagnosis not all cases were tested. Positive immunomarkers neurokinin, cromogranin, gastrin, serotonin or argyroffin were detected in 10 cases and normal levels found in three, including the present case.

Follow up varied from 6 to 72 months but was not recorded in all cases. Survival in seven patients was more than 24 months and four patients, including two patients with lymph node metastases, survived for more than 4 yrs.

In conclusion, carcinoid tumours of the extra hepatic biliary tree are rare and occur in a young age group with a preponderance in females. Preoperative diagnosis is difficult but may be improved with assessment of neuroendocrine markers in suspected cases. Disease free survival is prolonged following surgical excision despite the presence of metastases and these patients should be treated aggressively.

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TABLE I

Data on 42 Reported Cases of Bile Duct Carcinoids

Case	Author/Series	Year	Age	Gender	Symptoms	Site	Metastases	Immunomarkers	Status
1	Pilz	1961	55	f	jaundice,RUQ pain	CBD	PV		
2	Little	1968	41	f	jaundice,RUQ pain	Hilar			died PE 3 weeks
3	Bergdahl	1976	79	f	incidental finding	CBD	no		autopsy finding
4	Judge	1976	19	m	jaundice,RUQ pain	CBD	LN		autopsy finding
5	Gerlock	1979	32	m	jaundice	CBD	LN		N/A
6	Vitaux	1981	30	m	jaundice	CBD	LN		NED 4 yrs
7	Abe	1983	64	m	RUQ pain	CBD	liver		died 10 months
8	Goodman	1984	28	f	RUQ pain	Cystic Duct	LN	argyrophin	NED 9 months
9	Jutte	1986	62	m	back pain	CHD	no	argyrophyn others negative	Ned 24
10	Nicolescu	1986	50	f	RUQ pain	CBD	no		N/A
11	Alexander	1986	64	f	haematemesis	CBD	no		NED 8 months
12	Chittal	1989	46	f	RUQ pain	Cystic Duct	no	CEA,cytokine,	NED 3yrs
13	Fujita	1989	55	f	RUQ pain	CBD	no	all negative	NED6m
14	Bickerstaff	1989	57	f	jaundice	CBD	no		NED 6 mos
15	Brown	1990	35	f	jaundice	Hilar	no		alive 7 days
16	Bumin	1990	38	f	jaundice	CBD	no		N/A
17	Angeles-Angeles	1991	39	f	jaundice, pruritis, pain	CBD	LN	serotonin,somatostatin	NED 42 months
18	Barron-Rodriguez	1991	36	m	jaundice	CBD	liver		died 4 days,Autopsy
19	Rugge	1992	64	f	jaundice	Cystic Duct	no		NED 12 m
20	Gembala	1993	28	m	jaundice	Hilar	liver		N/A
21	Mandujano-Vera	1995	53	f	jaundice	CBD	no		N/A
22	Sankary	1995	47	f	jaundice	Hilar	no		NED 4 yrs
23	Hao	1996	47	m	incidental finding	CBD		chromogranin,gastrin, serotonin	N/A
24	Kopelman	1996	44	m	jaundice	CBD	liver		N/A
25	Belli	1996	78	m	jaundice, pruritis	CBD	N/a		N/A
26	Bembenek	1998	12	f	jaundice	Hilar		chromogranin, gastrin	
27	Nahas	1998	61	f	jaundice	Hilar	n/a		NED 6m
28	Hermina	1999	69	m	RUQ pain	Cystic Duct	LN		
29	Perakath	1999	36	f	jaundice,pain	CHD	LN		N/A
30	Ross	1999	65	f	jaundice	CBD	no		NED 17
31	Chamberlain	1999	37	f	pruritis	Hilar	no		NED 18 m
32	Chamberlain	1999	67	f	pruritis	Hilar	no		NED 15 Months
33	Chan	2000	14	m	jaundice	Hilar		chromogranin,synaptophysin,	
34	Maitra	2000	53	f	jaundice	CBD	no		NED 6 yrs
35	Maitra	2000	61	f	jaundice, pruritis	Hilar	no		NED 4 yrs
36	Juturi	2000	43	m	jaundice, pruritis	CBD	no	HIAA -ve	NED 3.5yrs
37	Turrion	2002	51	f	jaundice, pruritis	Hilar	no		NED 18 m
38	Pawlik	2003	59	m	jaundice	Hilar	LN		
39	Podnos	2003	65	f	cholecystitis	CBD	no	chromogranin, serotonin,	NED 37 m
40	Podnos	2003	27	m	jaundice, pruritis	CBD	no		NED 7.5 years
41	Volpe	2003	19	m	jaundice, abdominal pain	CBD	no	chromogranin	NED12 m
42	Present case	2003	30	m	jaundice, pruritis	CBD	LN	Normal Neurokinin A, HIAA -ve	NED 18 m

RUQ: right upper quadrant, CBD: common bile duct, CHD:common hepatic duct, PV: portal vein, LN: Lymph node, CEA: carcinoembryonic antigen, HIAA: hydroxyindole acetic acid, NED: no evidence of disease, N/A: not available,

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Case Report

Diclofenac suppositories and acute ischaemic proctitis

N Arya, M J G Hawe, C Ozo

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Nonsteroidal anti - inflammatory drugs are widely prescribed because of their high efficacy as both anti-inflammatory and analgesic agents. The adverse effects of NSAIDs such as damage to the gastroduodenal mucosa, renal toxicity and bronchospasm are well known. In recent years, many cases have been reported of NSAID induced damage to the small and large intestine.[1,2] We report a case of acute ischaemic proctitis following diclofenac suppository.

CASE REPORT A fifty three year old healthy male patient was admitted for elective repair of his left inguinal hernia. He had a history of peptic ulcer symptoms following ibuprofen tablets, but no lower gastro-intestinal symptoms.

Under spinal anesthesia, Lichtenstein mesh repair of the inguinal hernia was performed. He had a 100 mg diclofenac suppository in the immediate post-operative period for pain relief, with no other medications given per rectum. There was no intra -operative or post-operative hypotension.

Five hours after the operation he complained of crampy abdominal pain, associated with six to seven episodes of haematochezia over the next twelve-hour period. He remained hemo-dynamically stable. Flexible sigmoidoscopy showed congested erythematous rectal mucosa with confluent erosions extending to 15 cm from the anal verge. The proximal rectal mucosa above 15 cm was macroscopically normal.

Coagulation screen, platelet count, CRP and ESR were within the normal range. The serum levels of Protein C and Functional Protein S were normal and a test for activated Protein C resistance was negative. The stool culture revealed no evidence of *Salmonella, Shigella, Campylobacter, Escherichia coli* 0157 or *Cryptosporidium oocyst* and it was negative for *Clostridium difficle* toxin A.

He was discharged home on prednisolone suppositories. Histology of the inflamed rectal mucosa showed widespread areas of acute ischaemic necrosis and ulceration which were limited predominantly to the superficial half of the mucosa. There were fibrin thrombi in the mucosal and submucosal capillaries (Figure). The biopsy of macroscopically normal proximal rectal mucosa showed no evidence of inflammation.

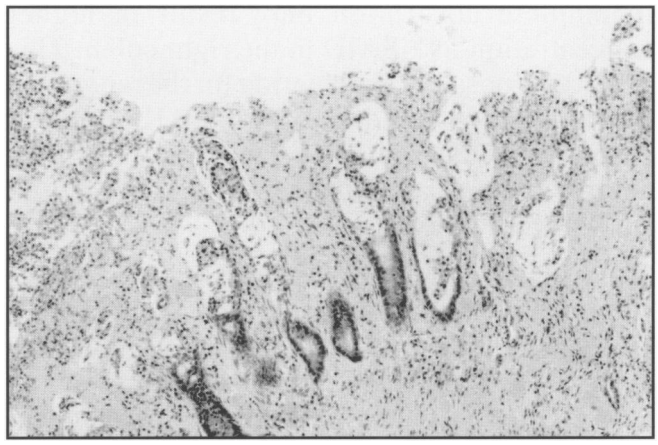

Fig Rectal biopsy showing necrosis of superficial half of the mucosa.

Prednisolone suppositories were subsequently discontinued and he remained asymptomatic. Eight weeks later, flexible sigmoidoscopy and biopsy showed complete clinical and histological resolution of the lesions.

Department of Surgery, Mid Ulster Hospital, Magherafelt, Co. Londonderry, BT45 5EX.

N Arya

M J G Hawe

Department of Pathology, Antrim Area Hospital, 45 Bush Road, Antrim, Co. Antrim, BT41 2RL.

C Ozo

Correspondence to Mr Arya, Department of Vascular Surgery, Level 5, Belfast City Hospital, Lisburn Road, Belfast BT9 7AB.

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DISCUSSION

The exact mechanism of NSAID-induced damage to the colonic/rectal mucosa is not fully understood. The inhibition of prostaglandin synthetase in the colonic mucosa causes decrease in the level of endogenous protective prostaglandins and increased production of Leukotriene B4.[1,3] Another significant factor may be due to local toxicity owing to the high local concentration of NSAID. Increased use of slow-release NSAID preparations associated with incomplete absorption may result in higher concentration of NSAID in the right colon. This provides a possible explanation for the report that the maximum incidence of NSAID-induced stricture and ulceration is on the right side of the colon .[1] It also explains the rectal lesions caused by NSAID suppositories[4,5]

There have been previous reports of NSAID suppositories induced rectal lesions presenting as tenesmus and bleeding.[4,5] The endoscopic appearance of erosions and ulcers progressing to stenosis may be related to the duration of treatment with NSAID suppositories. At endoscopy, the appearance of NSAID proctitis may be difficult to differentiate from infectious colitis or idiopathic inflammatory bowel disease.

A review of histology of 11 cases of NSAID-induced colitis suggests a remarkable similarity to ischemic colitis.[1] In other cases, it showed features of non specific colitis, with mixed inflammatory cell infiltrate and focal erosions.[2,4] Absence of crypt architectural distortion differentiates NSAID colitis from ulcerative colitis.[1]

In our case the pathological picture was classical of acute ischaemic proctitis. Infectious causes were excluded and there was no thrombogenic tendency or pen-operative hypotension. The absence of any other etiology, the rapid anatomic and histological resolution along with classical pathology suggest that the lesions were caused by diclofenac suppositories.

In spite of widespread use of NSAID suppositories, the number of cases of rectal lesions reported is small. It is quite possible that a large number of rectal lesions remains undetected or misinterpreted. NSAID should be considered as a cause of acute ischaemic proctitis and haematochezia in the appropriate clinical setting.

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Can transdermal nicotine patch cause acute intoxication in a child? A case report and review of literature.

A A Wain, J Martin

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Nicotine poisoning has been observed in children from ingestion of cigarettes, chewing gums & tobacco.[1,2] Application of several patches to skin can cause serious over dosage resulting in serious toxicity due to first pass metabolism. A case is reported of nicotine overdose from patch application. A brief review of presentation and management of this condition is presented.[3]

INTRODUCTION

Transdermal nicotine patches (TNPs) are in use as an efficient method of drug delivery, helping adults to avoid cigarette smoking. We report an interesting case, where a child out of curiosity used these resulting in intoxication.

CASE REPORT

An 11 year old boy brought to our accident & emergency department by emergency ambulance. He described feeling nauseated, weak and unwell during play. He walked home, vomited twice complained of palpitation and fell to the floor from a settee feeling weak. He remained fully responsive. On arrival at A & E he was alert but anxious and complained of head and stomach ache and weakness. On examination he was unable to stand and his skin was cold and clammy. Breathing, circulation and level of consciousness were all norma, in particular he had a regular full volume pulse 90beats/min, BP 115/80. No neurological deficiency was noted. Random blood sugar and ECG were normal. The nicotine patch was found applied on left upper outer arm during the application of ECG electrode. A patch mark was evident below the in situ patch. They actually belonged to mother under treatment for smoking cessation. The first was applied the previous night and the second midday at the day of presentation. A diagnosis of nicotine poisoning was made. Patches were immediately removed and the skin washed with water. Patient monitored in A & E Department for four hours. During stay BP dropped to 90/60, pulse 70beats/min. A fluid bolus was initially administered and repeated. No improvement was noticed. Injection Atropine Sulphate (.02mg/kg body weight) was administered intramuscularly. His condition improved gradually and he was asymptomatic after 4 hours. He was discharged home later.

DISCUSSION

Symptoms arising from inadvertent exposure to nicotine can be wide ranging in severity. These depend on dose, duration of exposure and route of administration.[4]

As transdermal route may cause serious toxicity due to first pass metabolism. TNPs are available for the treatment of smoking cessation without prescription. Therapeutic use has been associated with a variety of adverse effects including skin rashes, allergic skin reactions, nausea and vomiting, sleep disturbances, headache, chest pain. Symptoms following oral ingestion in children include gastrointestinal symptoms, increased salivation, pallor, weakness, and dizziness.[5]

In one series, as little as 0.2mg / kg of ingested nicotine caused mild toxic symptoms.[2] Complications such as lethargy, seizure, coma, respiratory depression, apnoea, hypertension, hypotension & dysrythmia are seen in significant intoxication.[6] In a study conducted by Woolf et al[4] at 34 United States poison centres Patients were triaged to home observation or to the

Downe Hospital, 9a Pound Lane, Downpatrick, Co Down, BT30 6JA.

Accident and Emergency Department

AA Wain FRCS, Associate Specialist

J Martin FRCS, Consultant

Correspondence to Mr Wain, 21 Glenbrae, Limetree Avenue, Knockmore Road, Lisburn, Co Antrim BT28 2YJ.

E-mail: wain59@aol.com

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emergency department. For patient at home a telephone follow up for 24 hours was carried out. No child seen in emergency department had blood or urine sent for nicotine levels. Nicotine dose was calculated from the estimated time of exposure to TNP as reported by care worker. Higher dose TNPs releases 0.9 mg of nicotine per hour. Dose-response relationship was observed in TNPs releasing higher amount of nicotine. Children with an estimated dose of absorbed nicotine < 0.1mg/kg were unlikely to develop symptoms.

Recommended treatments include removal of patch, wash with water. If patch is ingested repeated doses of activated charcoal orally.Incase of parasympathetic or sympathetic overstimulation use of atropine or phentolamine I/M or IV to be repeated as necessary.

CONCLUSION

As TNPs[7] are available without prescription as aids for the treatment of smoking cessation, they are accessible to children. As data regarding toxic effect on paediatric TNPs exposure is lacking, these cases should be reported. Users need to be educated for safekeeping.

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Northern Ireland Surgical Trainees: Prize Day November 2003

Abstacts from the Northern Ireland Surgical Trainees Prize Day, which was held on Friday 14 November 2003 and hosted by Altnagelvin Area Hospital at the City Hotel, Londonderry. Thirty-nine abstracts were submitted of which eleven were accepted for presentation on the day. There were six in the SHO section and five in the Specialist Registrar section. Winner of the SHO section was Dr Peter Mallon and runner-up was Conor Marron. Winner of the SpR section was Mr Damian Mole and runner-up was Ms Janne Bingham.

THE IMPACT OF A COMPLIANT ROTA ON SHO TRAINING EXPERIENCE AND SERVICE COMMITMENT

C D Marron, C K Byrnes, S J Kirk

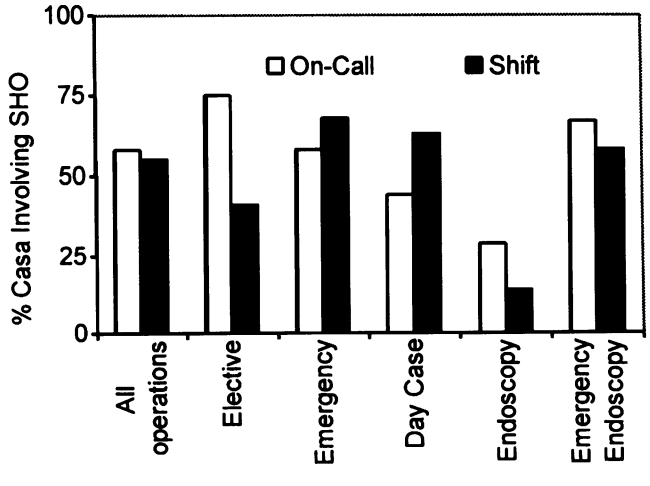
Department of Surgery, Ulster Hospital Dundonald

Introduction

Reduction of junior doctors hours has been driven by health care modernisation, and legislation. Effective reduction has been achieved by the introduction of shift working. This change is not universally accepted, many feel it is detrimental to training and clinical exposure. The aim of this study was to determine the impact of these changes on clinical exposure/experience.

Methods

The activities of a cohort of six senior house officers (SHO's) in a general surgical unit were assessed. Information was collected over two consecutive six week periods before and after switching from an "on-call" to a full shift rota. Working pattern information was obtained from, hours monitoring forms, outpatient correspondence, theatre/endoscopy registers, and logbooks.



Results

A total of 792 operations, 710 endoscopies, and 2649 outpatient episodes were analysed. Total hours worked was reduced by the shift system, however, a larger proportion of the hours worked was during the out-of-hours period. Total outpatient and operative throughput did not change.

With the shift system the total number or proportion of operative cases attended did not significantly change. There was a 37% reduction in SHO attendance at inpatient elective cases. Attendance at emergency operations and day case surgery increased by 17% and 42% respectively. There was a marked reduction in exposure to endoscopy and outpatient management (Table).

Conclusion

Change to a shift system leads to reduction in clinical exposure in some key areas. However, increased exposure is noted in emergency and day case experience. If the shift system is not adequately structured valuable learning opportunities may be wasted. Optimising timetable and shift planning may allow adequate and appropriate training opportunities in the available time.

PROMOTING EFFECT OF GASTRO-DUODENAL REFLUX ON OESOPHAGEAL TUMORIGENESIS

A A C Menezes[a], P Bonde[b], Z Bell[a], S Mirvish[c], C Swarbrick[d], J Sloan[d], S McKeown[e], T Robson[e], D Hirst[e], M Hoper[a], K Khosraviani[a], F C Campbell[a], J A McGuigan[b]

[a] Department of Surgery, [b] Department of Cardio-thoracic Surgery, [d] Department of Pathology, Queen's University of Belfast, [c] Eppley Institute for Research in Cancer, University of Nebraska Medical Center, Omaha, NE, USA, [e] School of Biomedical Sciences, University of Ulster.

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Background

There appears to be a link between gastro-oesophageal reflux disease and rising incidence of oesophageal cancer in the West. We hypothesised that increasing severity of reflux enhances proliferation and tumour formation with or without exposure to dietary carcinogen (methyl-n-amyl nitrosamine, MNAN). To achieve this we created a first model of mild to moderate reflux by surgically destroying the cardiac and pyloric sphincter (Model I). The severe reflux model consisted of side to side anastomosis of duodenum with lower oesophagus without gastric bypass (Model II).

Methods

Sprague Dawley (8 week old, male) rats were randomly assigned to 6 groups (as per Table). MNAN (25mg/kg/wk) was injected intraperitoneally at the age of 10 weeks or two weeks following surgery to Group E for one week, and remaining groups for four weeks. The experiment was terminated when the animals reached 38 weeks of age. The study was approved by animal ethics committee.

Results

Hyperproliferative ulcerative lesions (including tumours) increased with severity of the reflux, from 15% in Model I to 81% in Model II with mutagen treatment, ($p<0.01$). Highest tumour yield was in Group F ($p<0.05$). None of the animals in the study suffered weight loss. Twelve animals failed to complete the study.

TABLE

	Group A Control (n=7)	*Group B MNAN (n=15)*	*Group C Model I (n=15)*	*Group D Model II (n=15)*	*Group E ModelI+ MNAN (n=15)*	*Group F Model II +MNAN (n=15)*
Animals completed study	7	15	13	11	13	11
Tumours	0	3(20%)	0	1(9%)	0	5(45%)
Polypoid lesions	0	8(54%)	0	0	0	2(18%)
Hyperproliferative ulcerative lesions	0	0	2(15%)	8(72%)	3(23%)	9(81%)
Normal oesophagus	7	7(47%)	11(85%)	3(27%)	10(77%)	2(18%)
Weight gain in 30 weeks(gms)	299±57	260.7±58.5	245.8±19	291.5±54.7	201.8±25	223±52.8

Conclusions

Gastro-duodenal reflux promotes epithelial proliferation, tumour formation and enhances cancer risk of a dietary mutagen. This stresses the role of anti-reflux treatment.

DOES IRRITABLE BOWEL SYNDROME INFLUENCE THE INCIDENCE OF POST CHOLECYSTECTOMY SYMPTOMS IN THE LAPAROSCOPIC ERA?

P Mallon, J White, N Das, M McMenamin, D Hughes, P Neilly, R Gilliland

Altnagelvin Hospital, Londonderry, Northern Ireland

Aim

An increase in the number of cholecystectomies performed has been noted during the laparoscopic era. Some authors have suggested that this may be due to diagnostic confusion caused by symptoms related to irritable bowel syndrome (IBS). This study aimed to determine whether IBS was causing diagnostic confusion resulting in unnecessary operations being carried out in the laparoscopic era.

Methods

Questionnaires were sent to two patient cohorts who had undergone cholecystectomy between 1988-1990 (open) and 1998-2000 (laparoscopic). Patients were asked about pain, jaundice and indigestion pre- and postoperatively. Questionnaires also incorporated Rome II criteria for the diagnosis of IBS and SF-36 quality of life data. The histological severity of gallbladder disease in both groups was assessed by a single pathologist.

Results

124 of 196 patients in the open group and 264 of 400 patients in the laparoscopic group replied. There was no difference between the groups in gender, age at surgery, incidence of pre-operative symptoms, or the presence of positive Rome II criteria. A higher percentage of patients who had open cholecystectomy had relief of pain compared to the laparoscopic group (81% vs. 70.6%: $p<0.05$)*. There was no difference in the incidence of IBS in patients who had persistent pain (open 50.0%; laparoscopic 50.0%; $p=1.0$) or any symptoms post-cholecystectomy (open 40.0%; laparoscopic 43.5%; $p=0.85$). There was no difference between the groups with regards any of the 8 domains specified within the SF-36 data. The mean histological scores of gallbladder disease were similar in both groups.

Conclusions

While there is a significant increase in the incidence of post cholecystectomy pain in the laparoscopic group this cannot be attributed to IBS and does not appear to influence quality of life.

* Fishers exact test

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DOUBLE CONTRAST BARIUM ENEMAS – HOW FREQUENT ARE REPORTS INCONCLUSIVE AND WHAT ACTION IS TAKEN?

A Wray, G C Beattie, *R E R Wright, W J Campbell

Department of *Radiology and Surgery, Ulster Hospital Dundonald, Belfast, Northern Ireland.

Introduction

Double contrast barium enema (DCBE) in combination with flexible sigmoidoscopy (FS) is considered an adequate means of visualizing the colorectum. In addition to the financial implications of an inconclusive investigation, clinicians are faced with the problem of ongoing management. With a perceived increase in the number of inconclusive DCBE reports and requests for follow-up endoscopic visualization, the aim of this study was to evaluate actual numbers of each.

Methods

Reports of all DCBEs performed in the Ulster Hospital in the calendar year 2001 were obtained from radiology computerized records. Reports were divided into 3 main groups: i. Diagnostic (normal enema or definite mucosal lesion); ii. Complete technical failure; iii. Inconclusive report. The latter reports were further subdivided into 4 groups according to the reason for inadequate views: a. Poor bowel preparation; b. Moderate/severe diverticular disease (DD); c. Possible polyp advising endoscopic visualization; d. Miscellaneous group – 'other' reasons. Charts of all patients in 'inconclusive' group were retrieved and reviewed.

Results

Of 2036 DCBEs performed in 2001, radiologists were confident with the enema (definite pathology or normal) in 1749 (86%). There were 77 (4%) technical failures and 210 (10%) 'inconclusive' DCBE's. Of the 210 inconclusive enemas, the reason stated was poor bowel preparation in 58 (23%), DD in 70 (33%), possible mucosal polyp recommending 'direct visualisation' in 54 (26%) and 28 (13%) for 'other' reasons. Charts were unavailable in 3 (1.4%) patients and 11 (5.2%) patients did not attend for follow-up. In 30 (14%) patients FS had already been carried out pre-DCBE, with 1 abnormality detected. In 96 (46%) patients the referring clinician considered further investigations inappropriate. In 70 (33.3%) patients further investigations (rigid/FS or colonoscopy) were arranged, 35 of whom were from the 'direct visualisation recommended' sub-group. Of 70 endoscopies, 19 (27%) had an abnormality which correlated to that queried on DCBE, and 10 of these 19 were from the 'direct visualisation' sub-group.

Conclusion

A significant number of DCBE reports are inconclusive. The yield of significant mucosal pathology with further endoscopic investigations is low. Outpatient review and clinical risk reassessment is recommended before arranging further investigations in patients with inconclusive DCBE reports.

THE PREVALENCE OF SEXUAL DYSFUNCTION IN MALE PATIENTS FOLLOWING ABDOMINAL AORTIC ANEURYSM REPAIR IN NORTHERN IRELAND

V Koo, A McKinley, P H Blair, J M Hood, L L Lau.

Regional Vascular Unit, Royal Victoria Hospital, Belfast.

Objective

To investigate the frequency of sexual dysfunction in male patients following abdominal aortic aneurysm (AAA) repair in Northern Ireland.

Methods

After an initial screening by telephone contact, a questionnaire-based survey using the validated Sexual Health Inventory for Men (SHIM) was carried out on 142 male patients who underwent open or endovascular AAA (elective and ruptured) repair between April 1999 to July 2002. A SHIM score <21 predicts erectile dysfunction. Demographics, medical history including pre-existing sexual dysfunction, prostate surgery, smoking status and sexual history, operative details and postoperative quality of life (QoL) data were obtained.

Results

56 (40%) patients replied [26 elective open (EO), 21 endovascular (EVR) and 9 ruptured open (RO) repair]. The mean age was 69 (EO), 73 (EVR) and 70 (RO) years old. The prevalence of sexual dysfunction preoperatively was 27% (EO), 63% (EVR) and 45% (RO). About 35% (EO), 33% (EVR) and 33% (RO) admitted to be sexually inactive. Postoperative sexual dysfunction was 58% (EO), 76% (EVR) and 67% (RO). The proportion of patients with postoperative erectile dysfunction (SHIM score <21) was 70% (EO), 95% (EVR) and 78% (RO). The QoL was worsened in 55% (EO), 75% (EVR) and 50%

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(RO) postoperatively. None of patients had any discussion about sexual dysfunction preoperatively. Only 8% (EO), 14% (EVR) and 22% (RO) of patients had sexual dysfunction discussed with their clinician post-surgery.

Conclusion

The prevalence of pre- and post-operative sexual dysfunction is high in male patients who underwent AAA repair. While it is a sensitive issue which is seldom discussed, it poses a significant impact on patient's QoL postoperatively. Elective open repair results in a significantly higher increase of sexual dysfunction compared to endovascular procedure.

SURVIVAL FROM BREAST CANCER IN NORTHER IRELAND - WHAT REALLY MATTERS?

Iain Dobie[1], Karen Bailie[2], Michael Donnelly[3], Stephen Kirk[1]

[1] Ulster Hospital, Dundonald, Belfast, [2]Clinical Research Support Centre, Belfast. [3] Dept Epidemiology & Public Health, QUB, Belfast.

Background

Cancer survival outcomes for patients in the UK are poorer than in Europe and US. Cancer Services reorganisation aims to address this through concentrating care in high volume settings because a positive relationship between high volume and better survival has been reported. However, these studies have inadequate adjustment for casemix, a major determinant of outcome. We examined this issue among patients with breast cancer in Northern Ireland.

Methods

Records of all patients with invasive primary breast cancer in Northern Ireland diagnosed during 1996 (N=809) were reviewed in 1997 and again in 2002. Patient, disease and service variables and treatment decisions and date of death as of 31/12/2001 were extracted. Deaths were corroborated using death registrations. Cox Proportional Hazards models were used to examine the relationship of patient, disease and service variables to the risk of death.

Results

Among 807 (99%) patients traced for follow up, there were 262 deaths. The overall 5 year survival was 68%. Advancing age, late stage disease, poor Nottingham prognostic index, and higher social deprivation (Townsend score), were independently associated with lower survival ($p<0.05$). A survival advantage for radiotherapy treated patients was evident (OR 0.65, 95%CI 0.47-0.90)., and hormonal therapy (OR 0.49, 95%CI 0.30- 0.83). Using ≥30 cases pa to distinguish high/low volume, survival was lower for patients treated in low volume settings (OR 1.40, 95%CI 1.08-1.82) after adjustment for casemix.

Conclusions

Patient and disease variables, radiotherapy and hormonal therapy are the major determinants of outcome for patients with breast cancer. There is limited evidence to support a small advantage to treatment in a high volume setting. Residual confounding by casemix is a strong possibility.

THE ADMINISTRATION OF ENTERAL FATTY ACID REDUCES THE GUT DYSFUNCTION CAUSED BY METHOTREXATE ADMINISTRATION

J Bingham, *M Scott, S J Kirk, K R Gardiner

Departments of Surgery and Pathology*, Institute of Clinical Science, Grosvenor Road, Belfast, BT12 6BJ, Northern Ireland.

Background

A side effect of methotrexate (MTX) administration is gastrointestinal inflammation. This study investigated the effect of enterally administered fish oils on gut mucosal structure and barrier function in an experimental animal model of MTX induced mucositis.

Methods

Sprague-Dawley rats were randomized into 4 groups (n=20 per group). One group received 2.5mls/kg of MaxEPA fish oil, one group received 5.0mls/kg of MaxEPA fish oil, one group received isocaloric safflower oil and one group received 20mls/kg water. Each treatment was administered twice daily by orogastric gavage for ten days. On day seven each animal received 5.0mg/kg MTX by subcutaneous injection for three consecutive days. Food intake and body weight were recorded daily. On day eleven intestinal permeability was assessed by measuring urinary excretion of intragastric ^{14}C-labelled polyethylene glycol 4000. At laparotomy on day twelve, blood was sampled for measurement of plasma EndoCAb and IL-6 concentrations and small bowel excised for assessment of inflammation. Statistical analysis was performed using the Mann-Whitney U test with significance taken as $p<0.05$.

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Results

When compared to the group receiving water, MaxEPA administration increased food intake ($p=0.000$) and reduced plasma EndoCAb ($p=0.000$) and IL-6 ($p=0.017$) concentrations. Doubling the dose of MaxEPA caused weight gain ($p=0.000$) and improved intestinal permeability ($p=0.041$) in addition to increased food intake ($p=0.000$), EndoCAb ($p=0.000$) and IL-6 ($p=0.030$) concentrations. It also reduced small bowel inflammation ($p<0.05$). When compared to the group receiving isocaloric safflower oil, neither dose of MaxEPA improved food intake, weight gain, small bowel inflammation, intestinal permeability or plasma EndoCAb or IL-6 concentration ($p>0.05$).

Conclusions

MTX induces small bowel mucositis. Administration of 5.0mls/kg enteral omega-3 fatty acid reduces the gut mucosal barrier dysfunction caused by MTX when compared with water but not with an isocaloric control. The observed improvement in gut mucosal barrier function may simply reflect a supplemental calorific effect.

INTESTINAL INTRAMUCOSAL pH AS AN INDICATOR OF LONG TERM PROGNOSIS IN PATIENTS UNDERGOING AORTIC SURGERY

J A Reid, G Annamalai, L L Lau, C V Soong

Regional Vascular and Endovascular Unit, Belfast City Hospital, UK

Introduction

The development of intestinal intramucosal acidosis has been shown to be predictive of bowel ischaemia. It is thought that the release of myocardial depressant factor from the ischaemic bowel may be responsible for cardiac complications following abdominal aortic aneurysm repair. However, it is possible that cardiac insufficiency during aortic surgery may result in intestinal ischaemia. The aim of this study is therefore to assess if sigmoid ischaemia is a prognostic indicator of cardiac morbidity and mortality.

Materials and methods

Thirty-eight patients undergoing elective AAA repair were recruited. Demographic details and risk factors for heart disease were recorded. Sigmoid pHi, as an indicator of ischaemia, was measured using a silicone tonometer in all patients during and for 24h after operation. Seven years following surgery the patients and their general practitioners were contacted to determine the patient's health.

Results

Within the follow-up period, 22 patients had died, 3 post-operatively. Eight patients died of cardiac failure or myocardial infarction. There was no significant difference in the demographic and risk factor details between the cardiac and non-cardiac deaths. However there was a strong positive correlation between those with preoperative angina and those who developed cardiac complications postoperatively ($r=0.76$). There was no difference in aortic clamp time and operation time between the two groups. No correlation was observed between clamp time and pHi. The pHi in patients with cardiac related deaths (6.9 ± 0.007) was significantly lower than those with non-cardiac related deaths (7.1 ± 0.006, $p<0.05$). Similarly, patients who suffered cardiac events following AAA repair had lower pHi (6.9 ± 0.05) compared to those who did not (7.1 ± 0.05, $p<0.05$).

Conclusion

The results suggest that global hypoperfusion as a result of an under performing heart may be partly responsible for the sigmoid ischaemia in patients following AAA repair. Therefore, low sigmoid pHi may be a useful prognostic indicator of cardiac complications in this group of patients.

TNF ALPHA, IL-1BETA AND IL-6 PRODUCTION BY THE ISOLATED PERFUSED LIVER IN RESPONSE TO A "SECOND HIT" OF PORTAL ENDOTOXIN IS NOT ENHANCED BY EXPERIMENTAL SEVERE ACUTE PANCREATITIS

D J Mole[1], M A Taylor[1], J Black[1], M Hoper[1], A Stockman[2], N V McFerran[3] and T Diamond[1].

Surgery[1] and Pathology[2], School of Medicine, Queen's University Belfast, and School of Biology and Biochemistry[3], Queen's University Belfast.

Background

Severe acute pancreatitis (AP) may enhance hepatic cytokine production in response to a "second hit", such as portal endotoxaemia resulting from gut-barrier dysfunction.

Aim

To evaluate liver cytokine production in response to a "second hit" of portal endotoxin during severe AP.

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Methods

Twenty-four rats were randomized into 3 groups: AP (n=10), sham-operated (n=8), and non-operated controls (n=6). Severe AP was induced at laparotomy by intraductal glycodeoxycholate injection and intravenous caerulein infusion. 18hr after induction of AP a "second hit" of endotoxin (10μg/kg over 10min) was delivered into the portal vein in an isolated liver perfusion system. TNF-alpha, IL-1beta and IL-6 were measured in effluent perfusate collected at 30-40min and 90-100min into perfusion. Liver viability was assessed by oxygen consumption, biochemistry, histology and electron microscopy. Kupffer cell populations were quantified by immuno-histochemistry.

Results

A systemic inflammatory response to AP was demonstrated by elevated haematocrit, metabolic acidosis and 20% mortality.

At 18hr a pronounced transhepatic serum IL-6 gradient was observed in AP: 96pg/ml (portal) vs 621pg/ml (IVC) ($P<0.001$, Wilcoxon). Sham/control IL-6 was undetectable. IL-1beta was elevated in AP and sham serum. In AP, a small transhepatic serum IL-1beta gradient was detected: 64pg/ml (portal) vs 74pg/ml (IVC) ($P<0.025$, Wilcoxon). Serum TNF-alpha was <6pg/ml in all groups.

"Second hit": Portal endotoxaemia stimulated hepatic TNF-alpha production by 90-100mins: AP: 61pg/ml; sham: 112pg/ml; control: 61pg/ml; $P=0.864$ between groups; 90-100mins vs. 30-40mins, $P<0.001$ for each group (Kruskal-Wallis). No IL-6 or IL-1beta was detected at 90-100mins in any group.

Observation of normal smooth endoplasmic reticulum, mitochondria, oxygen consumption and minor vacuolation indicated minimal liver disruption.

Normal ED1-positive Kupffer cell distributions were seen in perfused livers.

Conclusion

Transhepatic pro-inflammatory cytokine gradients occur during experimental severe AP in rats. The isolated perfused liver TNF-alpha, IL-1beta and IL-6 production response to portal endotoxin is not differentially enhanced in severe AP.

ATTENUATION OF THE "SECOND HIT"-INDUCED HEPATIC CYTOKINE RESPONSE IN OBSTRUCTIVE JAUNDICE USING NOVEL ANTI-ENDOTOXIN PEPTIDES

M A Taylor [1], J M Black [1], A Wallace [2], M Hoper [1], W D B Clements [1], N V McFerran [2], M C Regan [3], T Diamond [1]

[1]Department of Surgery and [2]Centre for Peptide and Protein Engineering, The Queen's University of Belfast, Northern Ireland, [3] University College Hospital, Galway.

Background

Therapeutic intervention in patients with obstructive jaundice (OJ) may be regarded as a second hit, capable of increasing endotoxaemia with subsequent exaggerated hepatic proinflammatory cytokine production. The aim of this study was to assess the efficacy of novel anti-endotoxin peptides (P6 and C1) in attenuating the hepatic TNF± and IL-6 response to a second hit of portal endotoxaemia in OJ.

Methods

Core endotoxin-binding peptides were generated using biopanning of a pVIII random linear phage library with Lipopolysaccharide from *Salmonella minnesota Re995*. A nine-amino acid peptide, P6, was developed which was shown to inhibit LPS-induced TNF± secretion by human monocytic cells and a second peptide, C1, was generated by substituting amino acids of complimentary charge to the original. Bile duct ligation was performed on 15 Male Wistar rats which were randomised to receive either (A) endotoxin (LPS) alone (n=5), (B) LPS + P6 (n=5) or (C) LPS + C1 (n=5) during in-situ hepatic perfusion performed over 2 hours, 1 week post surgery. Effluent perfusate was collected for cytokine analysis (TNF± and IL-6) at 20 min intervals.

Results

Repeated measures analysis over time of the effluent TNF± and IL-6 concentrations between the three groups (A, B and C) was carried out. TNF±: There was a significant difference in effluent levels between the three groups ($p=0.04$) with post hoc analysis (Duncan's test) demonstrating significantly lower concentrations of TNF± in groups B and C compared to A. IL-6: There was no significant difference in effluent levels between the three groups ($p=0.16$) using repeated measures analysis but at 2 hours there appeared to be higher levels of IL-6 in group A.

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Conclusion

These novel anti-endotoxin peptides, capable of attenuating the LPS-induced exaggerated hepatic cytokine response, may offer an exciting new therapeutic strategy for reducing intervention - related complications in OJ.

OPTIMISING BOWEL PREPARATION FOR OUT-PATIENT FLEXIBLE SIGMOIDOSCOPY: A PROSPECTIVE RANDOMISED SINGLE BLIND COMPARISON OF THREE METHODS

A Gidwani, R Makar, D Garrett, R Gilliland

Altnagelvin Area Hospital, Londonderry, United Kingdom

Introduction

Flexible Sigmoidoscopy is a routine investigation for colorectal symptoms. One phosphate enema has been the standard bowel preparation for out-patient sigmoidoscopy but provides adequate preparation in only 80% of patients. This study aimed to compare two methods of bowel preparation with the current standard in an attempt to improve efficacy and acceptability.

Methods

Patients attending for out-patient flexible sigmoidoscopy from January to September 2003 were randomised to 3 groups:- Group 1: One Fleet enema two hours pre-procedure; Group 2: Two Fleet enemas, one during evening prior to sigmoidoscopy and one two hours pre-procedure; Group 3: Lactulose 30mls orally 48 and 24 hours prior to sigmoidoscopy plus a single Fleet enema two hours pre-procedure. A questionnaire was used to assess efficacy, side effects, and patient tolerance. Endoscopists completed questionnaires regarding preparation quality.

Results

261 patients (Group 1:n=105; Group 2:n=81; Group 3:n=75) were included; endoscopist data was available for 251 (Group 1:n=97; Group 2:n=79; Group 3:n=75). No difference was noted between the groups with regards age, gender, procedure indication, or grade of endoscopist.

	Easy to use	*Assistance required*	*No cramps/ pain*	*Alternate method preferred*	*Quality of preparation Excellent/ good*
Group 1	94%	19%	48%	18%	83%
Group 2	85%	11%	46%	28%	88%
Group 3	87%	24%	36%	23%	73%
P value	0.09[1]	0.15[1]	0.35[1]	0.25[1]	0.04[1]

There was no difference in the quality of preparation of patients in Group 1 vs. Group 2 ($p=0.39^2$) or Group 1 vs. Group 3 ($p=0.13^2$). However, two Fleet enemas gave superior preparation compared with the lactulose + Fleet group ($p=0.02^2$).

Conclusions

The addition of a Fleet enema or oral lactulose over and above a single fleet enema gives no significant improvement in acceptability or efficacy.

[1] Chi-squared; [2] Fishers exact test

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A Dictionary of Bookplates of Irish Medical Doctors

A Dictionary of Bookplates of Irish Medical Doctors with short biographies: by Edward A. Martin MD. Dublin De Burca, 2003. ISBN 0-946130-39-8

Bookplates as a means of identifying a book's owner are almost as old as books themselves. They originated in Germany and the first English bookplate is probably that of Cardinal Wolsey of the early 16th century. Irish examples are later and that of Sir Thomas Molyneux MD (1661-1733) may well be the earliest.

This elegant volume by Edward A Martin, a well-known Dublin neurologist, lists some 170 bookplates of Irish doctors. Although the majority are of Dublin physicians, some 50 are from Northern Ireland, such as Dr Thomas Andrews and Dr Alexander Jaffray Nicholson (father of the Brigadier), of the nineteenth century, and Dr Hugh Calwell and Sir Ian Fraser of more recent times. Most bookplates are armorial and the Fraser plate is a good example of this, with its shield of arms, crest of serpent and rod over a stag's head, and the cross of the Order of St John behind. However, the contemplative study of books is seen in the Caiwell plate and one of Dr John Stokes, while the more humorous side is in Dr John Denham's and the alegorical and gloomy side in the Bewley plate.

The biographical notes are a mine of information and must represent many years of work, covering the doctor and often his whole family, as well as the artist where this is known. They have an interest in their own right for their picture of medical education, history, and practise, particularly among the prosperous gentry of Dublin.

Finally, the production of the book by Eamon de Burca is exceptional, with high quality illustrations of nearly all the plates, and a good index and list of references. It is an ideal Christmas present for anyone with an interest in bibliography and/or medical history.

R S J Clarke

Honorary Archivist

Royal Victoria Hospital

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