Volume 65 No. 2 NOVEMBER 1996
ISSN 0041-6193

[continued on back cover

THE ULSTER MEDICAL JOURNAL

Published by
THE
ULSTER MEDICAL SOCIETY

The Ulster Medical Journal, Volume 65, No. 2
November 1996

Contents continued from front cover

Another Seizure-Fr

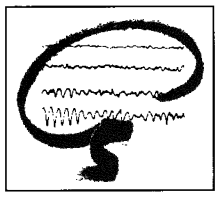
Adjunctive treatment for partial seizures, with or without secondary

TOPAMAX Abbreviated Prescribing Information
Please read the data sheet before prescribing
Presentation: Tablets each imprinted "TOP" on one side and strength on the other containing 25mg (white), 50mg (light yellow), 100mg (yellow), and 200mg (salmon) topiramate. **Uses:** Adjunctive therapy of partial seizures, with or without secondarily generalised seizures, in patients inadequately controlled on conventional first line antiepileptic drugs. **Dosage and Administration:** *Adults and Elderly:* Oral administration. Usual dose: 200mg - 600mg/day in two divided doses. Maximum recommended dose: 800mg/day. Initiate therapy at 50mg bd then titrate to an effective dose. See data sheet for titration. Do not break tablets. It is not necessary to monitor topiramate plasma concentrations. Patients with renal disease/haemodialysis may require a modified titration schedule. (See data sheet). *Children:* Not recommended

Contra-indications: Hypersensitivity to any component of the product. **Precautions and Warnings:** Withdraw all antiepileptic drugs gradually. Maintain adequate hydration to reduce risk of nephrolithiasis (especially increased in those with a predisposition). Drowsiness likely. TOPAMAX may be more sedating than other antiepileptic drugs therefore caution in patients driving or operating machinery, particularly until patients' experience with the drug is established. Do not use in pregnancy unless potential benefit outweighs risk to foetus. Women of child bearing potential should use adequate contraception. Do not use if breastfeeding. **Interactions:** *Other Antiepileptic Drugs:* No clinically significant effect except in some patients on phenytoin where phenytoin plasma concentrations may increase. Phenytoin level monitoring is advised. *Effects of other antiepileptic drugs:* Phenytoin and carbamazepine decrease topiramate plasma concentration. No clinically significant changes in plasma concentrations on sodium valproate addition or withdrawal.

ee Day

generalisation.



TOPAMAX®

topiramate

At the end of the day, it works.

Digoxin: A decrease in serum digoxin occurs. Monitor serum digoxin on addition or withdrawal of TOPAMAX. *Oral Contraceptives:* Should contain not less than 50µg of oestrogen. Ask patients to report any change in bleeding patterns. *Others:* Avoid agents predisposing to nephrolithiasis. **Side Effects:** In 5% or more: ataxia, impaired concentration, confusion, dizziness, fatigue, paraesthesia, somnolence and abnormal thinking. May cause agitation and emotional lability (which may manifest as abnormal behaviour) and depression. Less commonly: amnesia, anorexia, aphasia, diplopia, nausea, nystagmus, speech disorder, taste perversion, abnormal vision and weight decrease. Increased risk of nephrolithiasis. **Overdosage:** If ingestion recent, empty stomach. Activated charcoal not recommended. Supportive treatment as appropriate. Haemodialysis is effective in removing topiramate. **Pharmaceutical Precautions:** Store in dry at or below 25°C. **Legal Category:** POM. **Package Quantities and Prices:** Bottles of 60 tablets. 25mg (PL0242/0301) = £22.02; 50mg (PL0242/0302) = £36.17; 100mg (PL0242/0303) = £64.80; 200mg (PL0242/0304) = £125.83. **Product Licence Holder:** JANSSEN-CILAG LIMITED, SAUNDERTON, HIGH WYCOMBE, BUCKINGHAMSHIRE HP14 4HJ
Further information is available on request from the Marketing Authorisation Holder: Janssen-Cilag Limited, Saunderton, High Wycombe, Buckinghamshire HP14 4HJ.

Date of Preparation July 1996

JANSSEN-CILAG Ltd

0098063 A2 JUL/96

The Ulster Medical Journal, Volume 65, No. 2, November 1996.

The Ulster Medical Journal

The Journal of the Ulster Medical Society. First published in 1932.
Successor to the Transactions of the Ulster Medical Society (1884-1929), and the Transactions of the Belfast Clinical and Pathological Society (1854-1862)

The Ulster Medical Society was founded in 1862
by the amalgamation of the Belfast Medical Society (founded 1806)
and the Belfast Clinical and Pathological Society (founded 1853)

THE ULSTER MEDICAL JOURNAL

NOTICE TO CONTRIBUTORS

1. Authors are reminded that concise and clearly expressed papers are those most welcomed by readers and the Editorial Board. All manuscripts are independently refereed.

   All manuscripts should be accompanied by a covering letter signed by all the authors agreeing to publication and stating that the work has not been published elsewhere, also stating that they have been actively involved in the preparation of the paper.

2. Manuscripts should be typewritten in double spacing, with wide margins. They should be fully corrected and alterations in proof may be disallowed or charged to the author. A sample typescript showing layout is available on request from the editorial office. Three copies of each manuscript should be submitted, including tables and figures.

3. The text should indicate the purpose of the paper, and should include an introduction, sections on materials and methods, results, and a discussion relevant to the findings. A brief factual summary should be provided at the beginning of the paper.

4. Scientific measurements should be in Sl units *(Units, symbols and abbreviations; a guide for biological and medical editors and authors,* 3rd ed. London: Royal Society of Medicine, 1977). Blood pressure may be expressed in mmHg and haemoglobin concentration as g/dl.

5. Tables must be kept simple and vertical lines should be avoided. Tables and illustrations must be kept to a minimum and data should not be given in both text and tables. Line drawings should be used where possible and symbols must be large enough to be legible when reduced to text size. Where possible, size of illustrations and tables should be planned so that one or more can easily fit the page size of 19·5 x 12·5 cm. Photographs and other illustrations should be unmounted, and authors may be charged for these at cost price. Authors' names and the top of the figure should be marked in soft pencil on the back.

6. References should be restricted to those really necessary and useful. This journal uses the 'Vancouver' style (see British Medical Journal 1982; **1**: 1766 -70 and Lancet 1979; **1**: 429 - 30). Text references are numerical. Each reference should include:

   i) a list of all authors when six or less (when seven or more only the first three should be listed followed by *et al).*

   ii) the title of the article.

   iii) the title of the journal (abbreviated to the form published by Index Medicus).

   iv) the year;

   v) volume number:

   vi) first and last pages.

   eg

   McCoy GF, Dilworth GR, Yeates HA. The treatment of trochanteric fractures of the femur by the Ender method. *Ulster MedJ* 1983; **52**: 136-41.

   Book references should give the author, title, edition, town of publication, name of publisher, year of publication, and, where appropriate, volume and page numbers.

7. Ten reprints of each article will be forwarded free of charge to the corresponding author. Further reprints can be obtained from the printers, Messrs Dorman & Sons Ltd, 1-3 Holmes Street, Belfast BT2 7JG, who should be approached directly.

8. Editorial communications should be sent direct to the Editor who will be pleased to advise on the preparation of manuscripts if requested.

   Fellows and Members of the Ulster Medical Society receive the Journal free. Individuals may subscribe directly (see back page). The journal contents are covered by *Current Contents: Clinical Practice, Index Medicus, Excerpta Medica* and *Science Citation Index.* This publication is available in 16mm and 35mm microfilm and 105mm microfiche from University Microfilms, 300 North Zeeb Road, Ann Arbor, Michigan 48106, USA.

9. For reprint information in the United States contact: International Reprint Corporation, 968 Admiral Callaghan Lane, Apt 268, PO Box 12004, Vallejo, California 94590 USA. Telephone (707) 553-9230, Fax (707) 552-9524.

The Ulster Medical Journal

VOLUME 65

PUBLISHED BY

THE ULSTER MEDICAL SOCIETY

1996

CONTENTS

The Ulster Medical Journal, Volume 65, No. 2, pp. 179, November 1996.

NOTICE

The Royal Victoria Bicentenary Scientific Meeting
Waterfront Hall, Belfast
24th-26th September 1997

The Royal Victoria Hospital will celebrate its two hundredth anniversary in 1997. To mark this important occasion a series of events have been arranged. One such is a scientific meeting to be held at the new Waterfront Hall in Belfast in September. It is proposed that this meeting will be a celebration not only of the "Royal" but of two hundred years of medicine in this part of Ireland. The programme has been carefully constructed to cover a broad range of topics which will be of interest not only to hospital and general practice based doctors but to other professional groups. The speakers include international experts, many with links to the Royal Victoria Hospital. The main theme is to "look forward to the year 2000" and sessions include the history of "The Royal", medicine and surgery in the next millennium, resuscitation, wound healing, neurosurgery and rehabilitation, the future of nursing to name but a few. An equally entertaining social programme has also been arranged.

We would urge you to mark the event in your diary now and encourage friends at home and abroad to come. This will be an unique opportunity to renew old friendships. A truly international gathering of doctors proud of their association with the Royal Victoria Hospital will ensure that news of our best scientific work is relayed to all corners of the globe.

For further information please contact Dr Julian Johnston, consultant anaesthetist, or the Bicentenary co-ordinator Mrs Mary Graham, Directorate of Corporate Affairs, Royal Hospitals Trust, Grosvenor Road, Belfast BT12 6BA, Northern Ireland. Tel 01232 263232 or Fax 01232 263296.

R J Barr, MD, FRCS,
on behalf of the Scientific Committee.

The Ulster Medical Journal, Volume 65, No. 2, pp. 180, November 1996.

The Editorial Board gratefully acknowledge the generous financial contributions from the following for the Ulster Medical Journal:

Northern Ireland Council for Postgraduate Medical Education.

Royal Victoria Hospital Medical Staff Committee.

Editorial Board announcement

The board have been informed that a paper published in the last issue of this journal will shortly appear elsewhere. This error was brought to our attention by one of the authors. The authors and the publishers of the second journal (Blackwell's) have accepted full responsibility and offered their apologies to the Ulster Medical Journal. A statement to that effect will be published in the journal concerned. The editorial board of the UMJ has accepted that no deceit was intended, but wish to stress that authors must not send a manuscript to more than one journal.

The Ulster Medical Journal, Volume 65, No. 2, November 1996.

THE ULSTER MEDICAL SOCIETY

Whitla Medical Building
97 Lisburn Road
Belfast BT9 7BL

If you are not a member of the Ulster Medical Society, we would appeal to you to give the question of joining your consideration. The Society was formed in 1862 through the amalgamation of the Belfast Medical Society (founded in 1806 and revived in 1822) and the Belfast Clinical and Pathological Society (founded in 1853). Meetings are held in the Society's room in the Whitla Medical Building at fortnightly intervals from the autumn to the spring. There is an opportunity to meet informally after each lecture and enjoy a cup of tea. *The Ulster Medical Journal, the official organ of the Ulster Medical Society, is issued to all Fellows and Mernbers free of charge.*

By joining the Ulster Medical Society you will enable us to widen its influence and sphere of usefulness still further. The only requirement is that you should be registered under the Medical Acts. A proposal form will be found overleaf. Your proposer and seconder should belong to the Society. Please contact the Honorary Secretary if you do not know any members. The annual subscription is claimable against income tax.

Anyone may enter their name as a subscriber to *The Ulster Medical Journal,* without joining the Society. See overleaf for details.

R L MILLER, *President*

D R McCANCE, *Honorary Secretary*

M J J GORMLEY, *Honorary Treasurer*

MEMBERS **£10.00.**

All medical practitioners registered under the Medical Acts who graduated in medicine less than eight years before the date of their membership application shall be eligible for election as Members. At the end of the eighth year after the date of medical graduation, Members shall become Fellows and shall pay the Fellows' subscription.

FELLOWS **£25.00.**

All medical practitioners registered under the Medical Acts who graduated in medicine eight years before the date of their membership application shall be eligible for election as Fellows.

If a husband and wife are members of the Society they shall, on application, be entitled to pay a joint annual subscription of £30.00.

Ties, cufflinks and brooches bearing the crest of the Society may be obtained from the Honorary Treasurer.

SUBSCRIPTIONS: Any individual wishing to take out a direct subscription may do so. The cost is £30.00 for one volume (two numbers) of the Journal. Please apply for a banker's order to :

THE HONORARY TREASURER,
ULSTER MEDICAL SOCIETY,
WHITLA MEDICAL BUILDING,
97 LISBURN ROAD,
BELFAST BT9 7BL,
NORTHERN IRELAND.

EXCHANGES: Exchange journals and all relevant correspondence should be addressed to:

ULSTER MEDICAL JOURNAL,
QUEEN'S UNIVERSITY MEDICAL LIBRARY,
INSTITUTE OF CLINICAL SCIENCE,
GROSVENOR ROAD,
BELFAST BT12 6BJ,
NORTHERN IRELAND.

MEMBERSHIP: All Registered Medical Practitioners may apply for Fellowship or Membership of the Ulster Medical Society. Applicants should complete the form below and return it to:

THE HONORARY SECRETARY,
ULSTER MEDICAL SOCIETY,
WHITLA MEDICAL BUILDING,
LISBURN ROAD,
BELFAST BT9 7BL,
NORTHERN IRELAND.

APPLICATION FOR FELLOWSHIP OR MEMBERSHIP
OF THE ULSTER MEDICAL SOCIETY

Please enter your full name as recorded by the GMC *This form may be photocopied.*

Forenames _____ Surname _____

Address _____

_____ Postcode _____

Degrees _____ Date of Graduation _____

Proposer (Print) _____ Seconder (Print) _____

Your proposer and seconder should be Fellows or Members of the Ulster Medical Society. Please contact the Honorary Secretary if you have difficulty in finding a proposer or seconder.

The Ulster Medical Journal, Volume 65, No. 2, November 1996.

Editorial

Medical Education for the Millenium

This year students entering the Medical School at Queen's University will begin a new course. The success of this in equipping doctors for practice in the 21st century will depend on our ability to predict the environment in which medicine will be practised. Trends already in evidence are likely to be further developed. The need to apply new discoveries and new technologies will lead to increasing specialisation. Increasing numbers of elderly in the population will mean that the pattern of disease will change with an increasing emphasis on the management of chronic disease and disability. Doctors will be required not only to treat illness in their patients but to actively promote health in the populations which they serve. They will be required increasingly to work in teams with other health professionals and they will have to recognise more and more that clinical decisions also have economic implications which will require them to work with Government and other funding agencies to ensure cost effective care. Doctors will therefore need skills not just in clinical areas but also in the ethical, social, economic and political aspects of medicine. It will be important that Medical Education provide experiences which reflect the reality of contemporary medical practice and not that of another era.

Much has been written about the problems of Medical Education. There is first the pressure to extend the scope of courses to encompass the increasing knowledge and technology attached to every discipline which burdens the student with information. The process of education thus becomes distorted with the student emphasis centring on the passive acquisition of knowledge in order to achieve examination success rather than the development of an attitude to learning based on enquiry and the exploration of knowledge. A major aim of change must be to reduce factual content and yet retain those skills which are fundamental to the practice of medicine. At the very least the undergraduate course should provide students with the knowledge and skills sufficient to enable them to undertake the duties of the pre-registration year. This objective has allowed us to identify elements of a core curriculum and to define more clearly that which we would expect all doctors to share. The course should also enable students to develop cognitive skills so that they can use their knowledge from across all disciplines to define problems and identify solutions. In addition it should create in students a desire to continue learning throughout their professional career.

There have been criticisms not only of the process of Medical Education but also of its product. Doctors describing their experiences as patients have commented that while technical aspects of their care were superb, those which related to their emotional and psychological needs were often seriously deficient. Surveys of our own graduates demonstrate a concern that not sufficient attention is given to skills in communication and to the values which should provide the moral and intellectual basis of medical practice.

Achieving all of these educational goals will require much more than a definition of curricular aims and objectives. A key element will be the enthusiasm, motivation and ability of those involved in teaching. It is through effective teaching in clinical settings that students will develop the cognitive skills and appropriate attitudes which relate to patient care. Teachers need to be able to demonstrate in themselves and to develop in others the capacity to think critically, to have both scientific and humanitarian values and to respect the dignity and autonomy of the patient. In changing the educational process we should not neglect the powerful influence of role models on student behaviour. This will represent a considerable challenge for clinicians. I hope that in spite of the many pressures on their time, many will still want to echo the words of Sir William Osler; 'I desire no other epitaph than that I taught medical students in the wards as I regard this as by far the most useful and important work I have been called upon to do'.

Prof. Randal Hayes

The Ulster Medical Journal, Volume 65, No. 2, pp. 106-112, November 1996.

Cancer in Northern Ireland by 2002

A T Gavin, D O'Reilly

Accepted 1 September 1996

Summary

An estimate of cancer deaths and incidence for the years 1997 and 2002, taking account of current trends and population projections for Northern Ireland is presented below. These numbers will be of value to those planning services and, in particular, for those implementing the report "Cancer Services – Investing for the Future".[1] Cancer deaths are expected to rise by almost 13% to 4056 by the year 2002. Marked rises are expected in the number of deaths from cancer of the lung, oesophagus, kidney, bladder and prostate with smaller rises in deaths from breast and pancreatic cancer.

The fall in stomach cancer is expected to continue as is the trend of lower deaths from cervical cancer. Deaths from cancer of the colon and rectum are expected to remain static. Estimates of cancer incidence currently and for the years 1997 and 2002 are also included. The impact of tobacco use by the population, which poses a current and future serious threat to public health is highlighted.

INTRODUCTION

In April 1995, following wide consultation, the Secretary of State for Health unveiled a strategic framework for the future development of cancer services This was based on a policy framework for commissioning cancer services: "A report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales" (the Calman Report).[2] The Expert Advisory Group considered evidence regarding the current position of cancer services in England and Wales and made recommendations. These were to ensure equal access to high quality cancer care for all people, irrespective of where they live. It was recommended that cancer services should be organised as a network which included primary care and care in the community, secondary care in District General Hospitals, designated as cancer units, with tertiary care provided in large cancer centres. The cancer unit and cancer centres would be closely integrated with good communication between the three levels of care.

The Department of Health and Social Services in Northern Ireland established a Cancer Working Group under the chairmanship of the Chief Medical Officer, Dr Henrietta Campbell. Their remit was to consider how the recommendations of the Expert Advisory Group's report might best be implemented in Northern Ireland. The Cancer Working Group's report "Cancer Services – Investing for the Future"[1] includes recommendations which emphasise multidisciplinary, multiprofessional team management of patients, and effective communication between the newly designated cancer centre, cancer units and primary care. Unfortunately, the absence of accurate information on the numbers of cancers occurring in the population could hamper the planning of these important changes. Incidence data will be available from the re-established Cancer Registry by mid 1997, alas too late for this Cancer Working

N. Ireland Cancer Registry, Department of Epidemiology & Public Health, The Queen's University of Belfast, Mulhouse Building, Grosvenor Road, Belfast BT12 6BJ.

Anna Gavin, MB, MSc, MFPHM, Director.

Previously at the Northern Ireland Cancer Registry now at Health & Health Care Research Unit, The Queen's University of Belfast, Mulhouse Building, Grosvenor Road, Belfast BT12 6BJ.

Dermot O'Reilly, MB, MSc, MRCP, MFPHM, Deputy Director.

Correspondence to Dr O'Reilly.

Email: oreilly@v1.eph.qub.ac.uk

Group. Anyone working on planning services for haematological malignancies, colorectal cancer and malignant melanoma can thank those far-sighted enough to establish disease-specific registries for these tumours. The N. Ireland Cancer Registry has already produced trends for cancer deaths over the past 25 years.[3] This has given a basis from which to estimate the number of cancer deaths and further extrapolate an expected number of cancers in various major groups for Northern Ireland.

METHODS

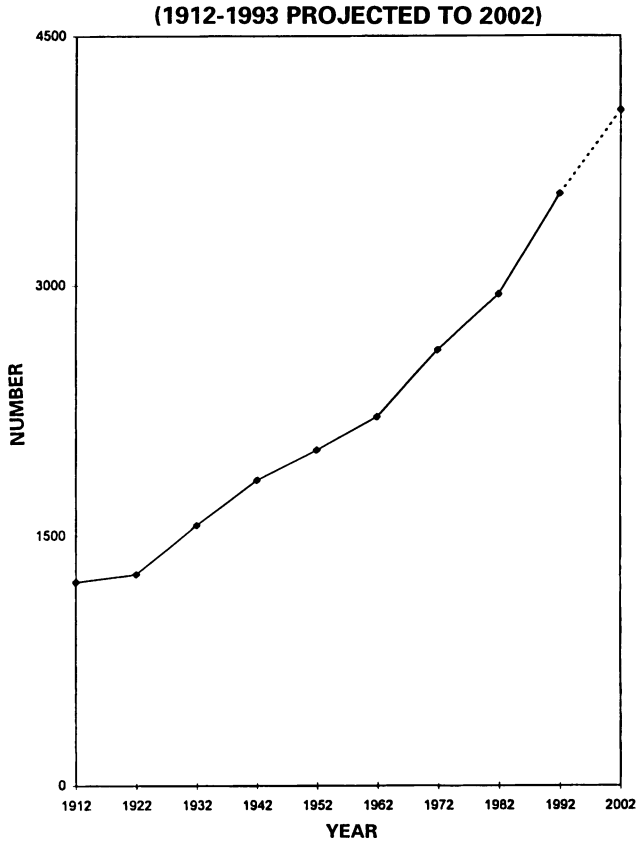
The trends in the World Health Organisation age standardised mortality rates[4] for each sex and age band were calculated for those under 65 years and those over 65 years. The standard errors of these trends were also calculated. The average age-specific rates for the two age groups (under and over 65 years) were calculated using deaths 1985-1993 and the 1991 mid year population estimates.[5] This was to produce the reference points to which the trends would be applied. The historical trends were applied to the 1991 rates and extrapolated forward to 1997 and 2002 to produce the expected number of deaths in those years. 95% confidence intervals were calculated for each year using the standard error of the beta co-efficient of the regression lines to provide an estimate of the variation associated with the projections. These were scaled up, using incidence to mortality ratios,[6,7] to estimate the numbers of new cases per year.

RESULTS

It is estimated that by 2002 the total number of cancer deaths will have risen by 13%, from 3,595 (the average 1989-1993) to 4,056. (See Figure 1). The number of lung cancer deaths will rise by 30% to 1,033. The fall in deaths in men under 65 from 160 to 129 will be offset by an increase in deaths among older men and women (see Table I). The number of lung cancers diagnosed is expected to rise from current estimates of 953 to 1,239 by 2002 (see Table II). The fall in levels among younger men will again be offset by the rise in levels among older men and both older and younger women.

Deaths from cancer of the oesophagus are expected to rise 35% by 2002 to 157. The biggest increases will be in younger men while in women the rise will be mainly in those over 65, giving rise to an expected 58 female oesophageal cancer deaths.

Figure 1



New cases diagnosed are expected to rise to 181 per year by 2002 (see Table I).

Cancer of the stomach should continue to fall so that by 2002 there should be 104 male cancer deaths and 59 stomach cancer deaths in women (see Figure 2 and Table I). The numbers of stomach cancers diagnosed is also expected to fall to 212 by 2002 (see Table II).

The number of deaths from cancers of the colon and rectum are expected to remain unchanged over this period. A fall in deaths among older women and, to a lesser extent amongst younger women is predicted to be offset by the rise in deaths of older men (see Table I).

Deaths from cancer of the pancreas are expected to rise by about 4% to 165 per year with 190 new cases predicted in 2002 (see Tables I & II).

Deaths from breast cancer are expected to rise by 8.6% to 342 by the year 2002 though the confidence intervals in this are fairly wide. New cases diagnosed each year are expected to rise from an estimated 630 in 1991 to 685 by the year 2002. Deaths from cancer ofthe cervix which are showing a downward trend may fall further by 2002 (see Figure 3 and Table III).

TABLE I

Estimated deaths from selected cancers in N. Ireland 1997 and 2002

			Male			*Female*			*Total*			
			Current Annual Average	*Predicted*	*Predicted*	*Current Annual Average*	*Predicted*	*Predicted*	*Current Annual Average*	*Predicted*	*Predicted*	
Site	*ICD*	*Age*	*1989-93*	*1997*	*2002*	*1989-93*	*1997*	*2002*	*1989-93*	*1997*	*2002*	*95% CI±*
Oesophagus	150	<65	25	32	38	6	6	6	31	38	44	0
		>65	43	53	61	41	48	52	85	100	113	12
		Total	68	84	99	48	54	58	116	138	157	12
Stomach	151	<65	36	29	25	17	13	11	53	43	35	4
		>65	93	86	80	75	59	48	168	145	128	9
		Total	129	116	104	92	72	59	221	187	163	13
Colon	153	<65	40	41	42	36	34	33	76	75	74	2
		>65	112	119	123	149	144	138	261	263	261	9
		Total	152	160	165	185	178	171	337	338	336	11
Rectum	154	<65	18	18	18	11	10	9	29	28	28	1
		>65	51	54	56	39	35	31	90	89	88	2
		Total	69	73	75	50	45	40	119	117	115	3
Pancreas	157	<65	22	20	18	19	19	19	40	39	37	1
		>65	53	57	58	65	68	69	118	124	127	0
		Total	75	76	77	84	87	88	158	163	165	1
Lung	162	<65	160	144	129	71	83	91	232	227	220	27
		>65	391	446	490	171	250	323	563	697	813	40
		Total	552	590	619	243	333	413	794	923	1033	65
Bladder	188	<65	12	12	12	40	42	42	52	54	54	0
		>65	51	57	61	47	49	50	98	1906	111	5
		Total	62	69	73	88	91	92	150	160	165	5
Kidney	189	<65	16	17	17	1	2	2	17	18	19	0
		>65	26	32	39	10	13	16	36	45	54	5
		Total	42	49	55	11	15	18	53	64	73	5
All Cancers		<65	536	536	527	527	543	547	1063	1079	1074	11
		>65	1320	1480	1602	1212	1319	1380	2532	2799	2982	64
		Total	1856	2017	2129	1738	1861	1927	3595	3878	4056	75

Deaths from cancer of the kidney and renal parenchyma (ICD 189) are expected to rise by 39% from 53 in 1991 to 73 in 2002. Most of this increase will be accounted for by a continued rise in deaths in older men (see Figure 4 and Table I). It is calculated there will be 132 new cases of kidney cancer diagnosed in the year 2002 (see Table II).

Deaths from cancer of the prostate are expected to rise by 20% to 219 by the year 2002. This increase based on current trends (see Figure 5) will be totally in men over 65. The predicted number of new cases diagnosed is 416 for the year 2002 (see Table III).

Deaths from bladder cancer are predicted to rise by 10% to 165 in the same period. This increase will be largely in men over 65. It is expected there will be 496 new cases of this cancer diagnosed by the year 2002.

TABLE II

Estimated incidence of selected cancers in N. Ireland 1997 and 2002

			Male			*Female*			*Tota*			
			Estimated	*Predicted*	*Predicted*	*Estimated*	*Predicted*	*Predicted*	*Estimated*	*Predicted*	*Predicted*	
Site	*ICD*	*Age*	*1993*	*1997*	*2002*	*1993*	*1997*	*2002*	*1993*	*1997*	*2002*	*95% CI±*
Oesophagus	150	<65	29	36	43	7	7	7	36	44	51	1
		>65	50	61	70	48	55	60	98	116	130	14
		Total	79	97	114	55	62	67	133	159	181	15
Stomach	151	<65	47	38	32	22	17	14	69	55	46	6
		>65	121	112	103	97	76	63	218	188	166	11
		Total	168	150	135	119	93	77	287	244	212	17
Colon	153	<65	54	56	56	48	46	44	102	102	100	3
		>65	151	161	167	201	194	186	352	355	353	12
		Total	205	217	223	249	240	230	454	457	453	15
Rectum	154	<65	21	22	22	13	12	11	35	34	33	2
		>65	61	65	68	47	42	38	108	107	105	3
		Total	83	87	90	60	54	49	143	141	138	5
Pancreas	157	<65	25	23	21	21	22	22	46	45	43	1
		>65	61	65	67	75	78	79	136	143	147	0
		Total	86	88	88	96	100	101	182	188	190	1
Lung	162	<65	192	173	155	86	99	109	278	272	264	30
		>65	469	536	589	206	300	387	675	836	976	48
		Total	662	708	743	291	399	496	953	1108	1239	78
Bladder	188	<65	35	36	37	121	125	126	156	161	162	0
		>65	152	170	183	142	148	151	295	318	334	16
		Total	187	206	219	263	273	277	451	479	496	16
Kidney	189	<65	29	30	30	3	3	4	31	33	34	2
		>65	46	58	69	18	24	28	64	82	98	4
		Total	75	88	100	21	27	32	95	115	132	6

TABLE III

Estimated deaths and incidence from cancers of the breast, cervix and prostate in N. Ireland 1997 and 2002

			Deaths				Incidence			
			Estimated	Predicted	Predicted		Estimated	Predicted	Predicted	
Site	*ICD*	*Age*	*1993*	*1997*	*2002*	*95% CI±*	*1993*	*1997*	*2002*	*95% CI±*
Breast (female)	174	<65	148	159	165	11	296	318	330	21
		>65	167	175	177	0	334	349	354	0
		Total	315	334	342	11	630	667	685	21
Cervix	180	<65	21	18	17	3	56	50	45	7
		>65	16	15	13	2	43	39	36	6
		Total	37	33	30	5	99	89	82	13
Prostate	185	<65	15	15	15	0	28	29	29	0
		>65	168	188	204	13	319	357	387	25
		Total	182	203	219	13	347	386	416	25

Figure 2

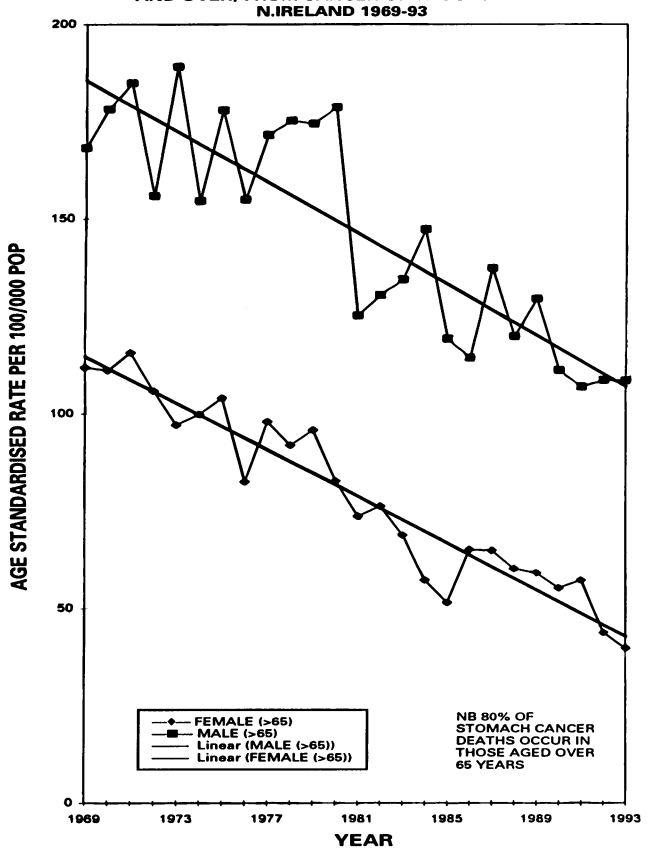


Figure 3

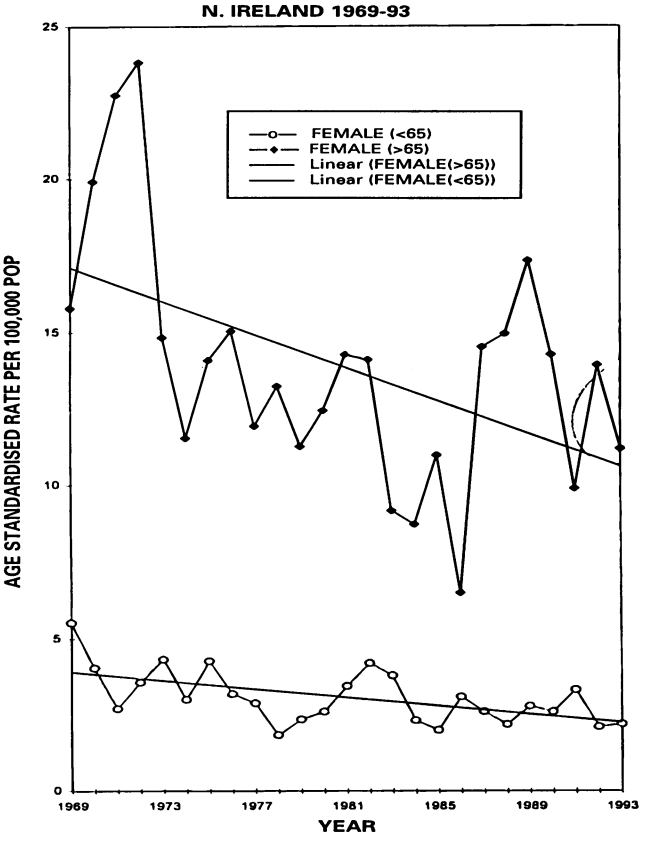


Figure 4

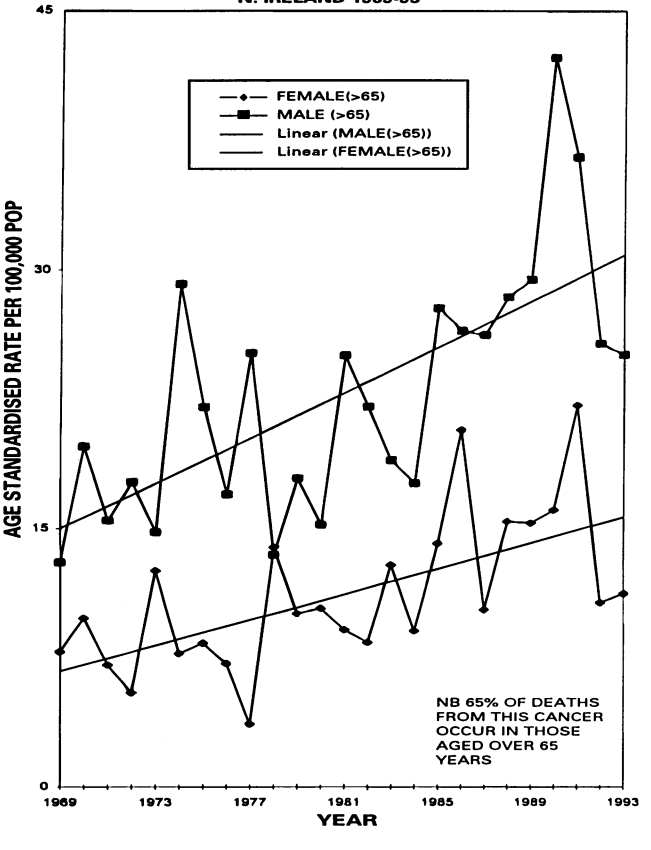
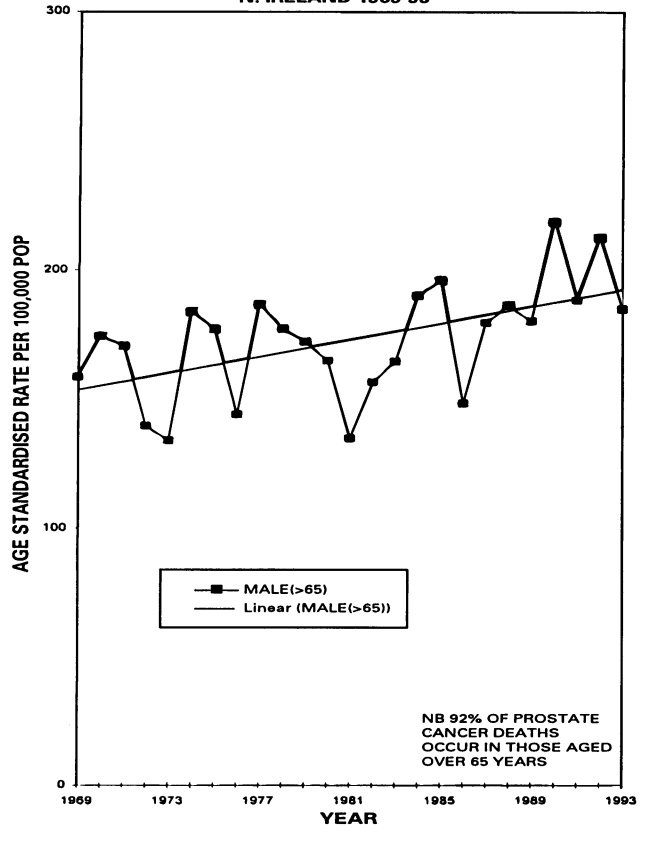


Figure 5



DISCUSSION

Planning for the future is fraught with difficulties though it is better to best-guess than not to plan at all. It is important, however, that the assumptions built into a planning model are explicit so that they can be challenged and if necessary modified. The assumptions used to calculate the deaths and numbers of new cases are as follow:

1. That the population projections are correct.
2. That the trends in cancer mortality rates, over the previous 25 years 1969-1993, for Northern Ireland continue into the near future.
3. That the ratios for incidence to mortality (the number of new cases per year compared to the number of those who died from the cancer) do not alter significantly and the Northern Ireland population has similar characteristics to the Welsh and Scottish populations.

This analysis takes into account projected changes in the population albeit at the safer aggregate levels of over and under 65 years.

The number of cancers in a population is dependent on the incidence rate and the size and age structure of that population. It is estimated that the population of N. Ireland will increase by 4.8% between 1991 and 2002[5] (5.5% for males and 4.2% for females). This alone will increase the numbers of cancers and cancer deaths. Other things being equal, an older population will generate more cases, as cancer is largely a disease of older ages. The population of N. Ireland is not only increasing but it is also becoming older. Between 1991 and 2002 the number of males over 65 are predicted to increase by 10.8%, females by 6.0%.

Almost half of the anticipated increase in female cancer deaths and 60% cancer deaths in males will be due to demographic change. The remainder is mostly due to risk factor change, although the interaction between demography and risk will account for approximately 2.5% and 4.5% respectively.

An important premise is that the incidence to mortality ratio should remain constant. Only time will tell if this was valid. It is possible that risk factor change may affect both incidence and survivorship and that new therapies and/or better organisation of cancer services may reduce mortality rates independently of incidence rate change. Also, the calculations cannot take account of newer methods of diagnosing cancers which may become common-place by the year 2002. An example of this would be the use of Prostatic Specific Antigen in the detection of prostatic cancer. This would increase the numbers of prostatic cancers diagnosed, although experience from elsewhere indicates that the death rates from the disease would not be affected.[8] The 20% increase in prostatic cancer deaths predicted reflects the changing numbers and age structure of the population. The rise in breast cancer deaths by 8.6% is also largely due to demographic changes with more older women in the population. The calculation has not taken account of the possible impact of the N. Ireland Breast Screening Programme which aims to reduce breast cancer deaths by 25% in the screened population by 2002 (estimated deaths prevented at 20 per year). The standardised mortality ratio 1980-1992 for breast cancer, which takes age into account, fell from 27.7 to 24.5 while the numbers of deaths rose by 41 to 331 deaths by 1993.[3]

The predicted rise in deaths from cancer of the lung, oesophagus, pancreas and bladder reflects not only the changing demography but is also a legacy from the use of tobacco in previous years. It is known there is an approximately 20 year lag between tobacco use and the development of lung cancer in a population.[9] The patterns of tobacco use in the 1980's should, with population changes, determine the rise or fall in numbers of tobacco-related cancers in the early 21st century. There has been a reduction in the prevalence of smoking in N. Ireland, yet in 1994 almost a third, 31% of men and 32% of women, were recorded as current smokers, higher than 28% for England and Wales. Smoking levels were highest in the age group 35-54 where 42% of men and 39% of women smoked. These smokers, especially the women tended to smoke more than the average. Tobacco-related cancers may also occur in the population of ex-smokers. In 1994 half of men and a quarter of women aged 55-74 were ex-smokers as were 26% of men and 19% of women aged 35-54.[10]

The trend of rising deaths from lung cancer among young women more than offsets the health gain achieved by falling tobacco use by younger men. This is likely to continue. Currently 27% of men and 33% of women aged 16-34 are smokers. This identifies an area for urgent attention to protect the health of the population in N. Ireland and achieve the targets of the N. Ireland Regional

Strategy for reduction in lung cancers.[11] The target for 2010 is to reduce the death rate from lung cancer by at least 30% in men under 75 and 15% in women under 75.

The need for accurate incidence information on cancer, a major disease group which accounts for 23% of deaths, over 20,000 hospital admissions and an unmeasured amount of health service resources is again highlighted. We look forward to the time when the N. Ireland Cancer Registry is regularly producing timely accurate information on cancer in N. Ireland for the purposes of research, education and planning of services. In the meanwhile these predictions should assist the N. Ireland Cancer Working Group in making decisions on the future of cancer services and enhance the precision of data available to those planning cancer services.

ACKNOWLEDGEMENTS

We wish to thank Breige Torrans, Lorraine Crichton, Dr Richard Middleton and Nuala Brady in the N. Ireland Cancer Registry for assistance with the production of the manuscript and figures. Thanks are also due to DHSS (NI), the Ulster Cancer Foundation and the NI Breast Screening Service which fund the work of the Cancer Registry.

REFERENCES

1. Cancer Working Group – Chair: Dr Henrietta Campbell. Cancer Services – Investing for the Future. DHSS NI, April 1996.
2. Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales. A Policy Framework for Commissioning Cancer Services, A Report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales, April 1995 (E L (95) 51).
3. O'Reilly D, Gavin A T, "Cancer Deaths in Northern Ireland – An Analysis of Pattern and Trends" published by the N. Ireland Cancer Registry. November 1995.
4. World Health Statistics Annual 1991. World Health Organisation, Geneva. 1992.
5. Registrar General Reports for Northern Ireland.
6. Kirkpatrick R, Cotter M, "Cancer Registration in Wales: 1984-1988". Welsh Office HMSO. 1994.
7. Scottish Cancer Intelligence Unit. "Cancer Registration Statistics Scotland 1981-1990". The NHS in Scotland 1993.
8. Lynch C F, Oppliger R A, McKeen K M. "Cancer in Iowa. State Health". Registry of Iowa. 1994.
9. Hill G B, Yang Mao, Laidlaw J. et al. Canadian Cancer Statistics 1988. Canadian Cancer Society 1988.
10. MacAuley D, McCrum E, Stott G. et al. Northern Ireland Health and Activity Survey Report. HMSO 1994.
11. Department of Health and Social Services. Health and Wellbeing: into the next millennium. Regional Strategy for Health and Social Wellbeing 1997-2002. Published 1996.

The Ulster Medical Journal, Volume 65, No. 2, pp. 113-117, November 1996.

Hereditary Breast Cancer in Northern Ireland

A G McKinley, S E H Russell, R A J Spence, W Odling-Smee, N C Nevin

SUMMARY

The aim of this investigation was to document hereditary breast cancer in Northern Ireland. Family history details from over nine hundred women were obtained by postal survey and one hundred and twenty nine home visits were carried out to collect pedigree information. The families documented varied in the number of affected women from three, which was the minimum criteria for inclusion, to a maximum of nine and many families described other features of hereditary disease such as bilateral breast cancer, ovarian and gastrointestinal malignancies.

INTRODUCTION

A family history of breast cancer is recognised as one of the most important risk factors for the disease.[1,2] In the majority of women breast cancer is due to a multifactorial combination of environmental and genetic factors. However breast cancer in some women is due to a major genetic influence. Several epidemiological[1,2,3] studies have suggested that an autosomal dominant gene may be present in approximately three per thousand individuals, and that this is responsible for a substantial proportion of the familial clustering of breast cancer in the population. It is now established that in some families the high incidence of breast cancer is due to a mutation in a gene, known as BRCA1, which is located on the long arm of chromosome 17.[4,5]

Hereditary breast cancer has a number of distinguishing features[6] which include early age of onset of breast cancer, an autosomal dominant pattern of inheritance, an association with other malignancies, an excess of bilateral disease and a better prognosis. It was decided to undertake a study to document hereditary breast cancer families within the community.

METHODS

Suitable families were identified by selecting pre-menopausal women who had developed breast cancer. In addition, specialist breast clinics, a charity cancer screening organisation and general practitioners were involved in identifying families containing at least three women who had developed breast cancer.

All women in Northern Ireland who developed pre-menopausal breast cancer in the five years between January 1986 and January 1991 were identified through pathology records. Patients with a diagnosis of invasive breast carcinoma, either ductal or lobular, were selected. Most histopathology records are computerised but manual documentation was necessary in two of the hospitals in Northern Ireland.

Details of women with a family history of breast cancer were obtained from three sources.

1. 'At risk' patients attending specialist breast clinics in either the Royal Victoria or Belfast City Hospitals.
2. General Practitioners were contacted by letter and referral of suitable families requested.
3. Women attending 'Action Cancer' for breast cancer screening within the period January 1986 - January 1991 were ascertained, although

Department of Surgery, Belfast City Hospital and Royal Victoria Hospital, The Queen's University, Belfast.

A G McKinley, MD, FRCS, Senior Registrar.

R A J Spence, MD, FRCS, Consultant Surgeon.

W Odling-Smee, MD, FRCS, Senior Lecturer/ Consultant Surgeon.

Department of Medical Genetics, Belfast City Hospital, The Queen's University, Belfast.

S E H Russell, BSc, PhD Lecturer/Scientist.

N C Nevin, BSc, MD, FFCM, FRCPath, FRCP, Professor of Medical Genetics.

Correspondence to Mr A G McKinley, Department of Surgery, Belfast City Hospital, Lisburn Road, Belfast BT9 7AD.

the medical records for a longer period were available.

All women identified were sent a postal questionnaire requesting details regarding family history of breast and other cancers. The returned questionnaires were manually checked and details were stored on computer (Amstrad Locofile) which prevented inclusion of any family already identified, and avoided multiple ascertainment.

Those families which fulfilled the criteria of at least three affected women were contacted and a home visit was arranged to obtain a pedigree and clinical details necessary for pathological verification of diagnosis.

RESULTS

The numbers of women identified from the various sources are shown in Table I. There was a total of 3425 new patients with breast cancer diagnosed in Northern Ireland within the five year period, of which 727 were aged 47 years or less. For 632 of these patients we were able to establish a name and address; the remaining 95 women could not be contacted as hospital records had insufficient information.

TABLE I

Number of pre-menopausal women with breast cancer: source of referral, number identified and number with at least three affected women.

Source of Patients	*Number identified*	*Number with three affected relatives*
Pre-menopausal women	632	47
Clinical referral	87	35
General practitioner referral	13	4
Action Cancer records	170	78
Total	902	164

From other sources two hundred and seventy women were identified and in total nine hundred and two women were sent a questionnaire. Six hundred and forty-seven questionnaires were returned, (58%) and one hundred and sixty-four families fulfilled the criteria of three or more affected women.

One hundred and twenty-nine women were visited at home. Of the remaining thirty-five families, twenty-one were reluctant to take any further part in the study, and nine who did not include a telephone number in their returned questionnaire failed to respond to a posted request to arrange a home visit. In five instances although the family agreed to a home visit, various family circumstances prevented this during the study period. In four families the death of a family member from breast cancer meant that the family were too distressed to discuss details of the pedigree. One family moved to another part of

TABLE II

Number of families identified with number of affected women per family *

Number of affected women in family	*Number of families identified*
3	63
4	37
5	12
6	12
7	2
8	1
9	2
	Total 129

* Previously published data – Br J Surg 1995; 82: 1086-1088.

TABLE III

Additional features of hereditary disease in the families

Additional Feature	*Number of families affected*
Bilateral breast cancer	38
One ovarian malignancy	18
Two or more ovarian malignancies	4
One gastrointestinal malignancy	10
Two or more gastrointestinal malignancies	17
Male breast cancer	3

the United Kingdom before a visit could be arranged. Pedigree details are shown in Table II. Many families revealed additional features in their pedigree suggestive of hereditary disease. These include bilateral breast cancer, other malignancies in the family and male breast cancer (Table III).

Families were also classified into three groups depending on age at onset of disease. There were forty-six families in which all affected women in the family were aged 47 years or less at diagnosis. There was a group in which the majority, but not all, of the breast cancers developed in the pre-menopausal period. This group, which contained fifty-four families, was described as Mixed. Twenty-nine families showed predominantly post-menopausal onset of breast cancer.

DISCUSSION

Five hundred and nine women with hereditary breast cancer have been identified in Northern Ireland using multiple sources of ascertainment. The sources used are similar to those reported in other studies although many of these relied on a single source of ascertainment and a realistic comparison between methods of family identification is not possible.

The majority of breast cancers develop in the post-menopausal period; pre-menopausal disease normally accounts for approximately 20% of the total.[7] This is borne out in our study from histopathology records in which 727 (21%) women developed pre-menopausal disease. Previous studies have shown that 20% of women who develop pre-menopausal breast cancer will have another relative with breast cancer.[7, 8] Analysis of pedigrees in this study allowed identification of 28% hereditary breast cancer families. However from the total 632 pre-menopausal breast cancers it might have been expected to identify more than the 47 (7.5%) families (Table I).

Action Cancer provided an important source of breast cancer-prone women, contributing more than 50% of the total families identified as containing three or more affected women. Women attending Action Cancer are often self-referrals for breast cancer screening. This suggests that the availability of a Breast Cancer Family clinic will attract concerned families. The number of referrals from the general practitioners was low and this possibly reflects the use of a manual system for medical records in some practices which would prevent rapid, easy identification of families containing several members with cancer.

The criteria for inclusion in the study of three or more affected family members has been used in most other studies. However breast cancer is common in Northern Ireland (142 per 100,000)[9] and three affected members within a family could also result from the clustering of sporadic breast cancers. There is evidence from local genetic analysis studies that some families with three affected members do trace susceptibility to the gene BRCA1.[10] These families which contain only three affected members demonstrate the difficulties associated with genetic analysis when the pedigree shows a nuclear family pattern.

It may be that some families containing a smaller number of affected members represent the effect of environmental influence in combination with the incomplete penetrance documented for BRCA1.[5] It is also possible that there are several BRCA1 mutations in the population with variation in expression depending on the degree of penetrance of some mutations.

The majority of families (78%) described either three or four affected women but twenty-four families contained either five or six affected women. Despite such a high incidence of disease less than 30% of unaffected women from these families attended either Action Cancer or a specialist breast clinic. Both the families containing nine affected women were identified through the attendance of an unaffected relative at a specialist breast clinic but even in these families many unaffected women, despite the availability of such a facility, do not attend for surveillance. This may seem surprising but a study of breast cancer families has shown that a common reaction to the serious threat of breast cancer is denial. This type of denial reaction is associated with a reluctance to attend for surveillance, and a delay in seeking medical attention when a breast lump is discovered.[8] A more recent study reports that many women from breast cancer prone families underestimate their risk of breast cancer and despite counselling feel that their risk of breast cancer is only slightly greater than that of the general population.[11]

The development of bilateral breast cancer is very suggestive of hereditary disease[6] and a study has shown that a woman with unilateral hereditary breast cancer has almost a 50% risk of developing a second breast cancer if she survives over a

twenty year period.[8] In addition women who develop breast cancer when aged less than fifty years have more than five times the risk of developing a second breast cancer than those women who exhibit post-menopausal disease.[8] In our study 38 families showed evidence of bilateral breast cancer although this trait was not confined to the families with particularly large numbers of affected women. However there did seem to be more bilateral disease in the families in which the majority of women had developed pre-menopausal disease, in that all of the women with bilateral breast cancer were from families classified as either pre-menopausal or mixed age at onset of disease.

In 22 families at least one woman had developed ovarian cancer. Although there is some evidence that a small number of families with multiple breast and ovarian cancers are not linked to BRCA1 most publications suggest that BRCA1 is responsible for disease in the majority of these families.[4, 5] If appropriate surveillance is undertaken then clearly women in such families must be offered regular monitoring for gynaecological neoplasia. It is recommended that unaffected women from these families have six monthly pelvic ultra-sound surveillance.[6]

Twenty-seven families (25%) contained at least one relative with a gastrointestinal cancer. Large bowel cancer is common in Northern Ireland with approximately 620 new cases per year[12] and the prevalence of gastrointestinal cancers amongst relatives in these families may be due to a common sporadic disease.

Early onset of disease is perhaps the most characteristic feature of hereditary breast cancer[2] and there were forty-six families in which all affected women were aged less than 47 years at diagnosis. In a study including combined results from ten different centres throughout the United States and Europe involving 214 families in which DNA analysis was used to investigate familial susceptibility to BRCA1, there was strong evidence for an association between early onset breast cancer prone families and BRCA1 but little evidence for families showing post-menopausal onset of disease.[5]

In this study twenty-nine families showed predominantly late-onset of breast cancer. A similar study noted 19 late-onset families.[5] However, the majority of reports made no comment on late-onset disease. This may be due to family identification methods, as clinical referral may select early-onset breast cancer families. A Swedish study in which there was a number of late-onset families used a postal survey system to ascertain families.[13] It is possible that in families with late onset of breast cancer another gene may be involved, for example a region on chromosome 6[14] or indeed on another as yet unidentified gene.

Those families which were classified as mixed, in which the majority of women showed pre-menopausal breast cancer but one or more women developed breast cancer post-menopausally may represent variation in penetrance of hereditary breast cancer genes, or the post-menopausal cases may be due to the development of sporadic breast cancer within a hereditary breast cancer family which has been documented.

There are many undiscovered families in the community, as evidenced by a continued accumulation of families through Action Cancer and clinical referral. If the frequency of BRCA1 in the general population is 0.003[1, 2, 5] then it would be expected that in the population of Northern Ireland of roughly one and a half million there will be approximately 2250 female carriers. If 5%[6] of breast cancers are hereditary, then in Northern Ireland about 30 women could be expected to develop breast cancer each year as a result of a major gene.

CONCLUSION

Women with a family history of breast cancer, whether linked to BRCA1 or to some other gene, have a high risk of developing the disease.[1, 2, 5] Frequently these women are young, and they have the added risk of bilateral disease.[5, 15, 16] Little information from controlled clinical trials is available as to the effectiveness of screening for breast cancer in young, high-risk women and it may be very difficult to obtain.[17]

There are increasing requests for information, counselling and surveillance from patients and general practitioners. The rapid development of molecular genetic diagnostic techniques and general public awareness through media publicity demand an organised team approach.

It is suggested that this demand is best served by a breast cancer family clinic where women with a family history of breast cancer can obtain accurate risk counselling from a medical geneticist with back up from a molecular genetic laboratory.

In addition appropriate surveillance requires a specialist breast surgeon, with the availability of both cytopathology and radiology breast imaging services.

Apart from families who were identified either through attendance at specialist breast clinics or 'Action Cancer' breast screening we found little evidence that breast cancer-prone women attend for genetic assessment or screening investigation. When the possibility was discussed, usually when obtaining a pedigree, many women expressed an interest in attending a breast cancer family clinic but at present this type of service is unavailable in Northern Ireland. This study shows that families and women can be identified in the Northern Ireland community who are at risk of developing breast cancer and who may benefit from such a clinic.

REFERENCES

1. Iselius L, Slack J, Littler M, Morton N E. Genetic epidemiology of breast cancer in Britain. *Ann Hum Genet* 1991; **55**: 151-9.
2. Claus E B, Risch N J, Thompson W D. Genetic analysis of breast cancer in the cancer and steroid hormone study. *Am J Hum Genet* 1991; **48**: 232-42.
3. Goldstein A M, Haile R W C, Marazita M L, Paganini-Hill A. A genetic epidemiologic investigation of breast cancer in families with bilateral breast cancer. I. segregation analysis. *J Nat Cancer Inst* 1987; **78**: 911-8.
4. Narod S A, Feunteun J, Lynch H T, Watson P, Conway T, Lynch J, Lenoir G M. Familial breast-ovarian cancer locus on chromosome 17q12-q23. *Lancet* 1991; **338**: 82-3.
5. Easton D F, Bishop D T, Ford D, Crockford G P. Genetic linkage analysis in familial breast and ovarian cancer: results from 214 families. The Breast Linkage Consortium. *Am J Hum Genet* 1993; **52**: 678-701.
6. Lynch H T, Harris R E, Organ C H, Lynch J F. Management of familial breast cancer 1. Biostatistical-genetic aspects and their limitations as derived from a familial breast cancer resource. *Arch Surg* 1978; **113**: 1053-8.
7. Dunn J, Farndon J R. Review – Familial breast cancer. *J R Coll Surg Edin* 1991; Vol. **36**: 147-51.
8. Lynch H T. The family history and cancer control – hereditary breast cancer. *Arch Surg* 1990; **125**: 151-2.
9. Kee F, Gorman D, Odling-Smee W. Confidence intervals and interval cancers... needles and haystacks. *Public Health* 1992; **106**: 29-35.
10. McKinley A G, Russell S E H, Spence R A J, Odling-Smee W and Nevin N C. Hereditary breast cancer and linkage analysis to BRCA1. *Br J Surg* 1995; **82**: 1086-8.
11. Smyth E H, Anderson E D C, Steel C M. Experience with a breast cancer family screening clinic. Presented at the Nottingham EORTC. Joint Breast Cancer meeting September 1993, abstract published in Breast November 1993.
12. Wilson R W, Moorehead J R. Preliminary Report 1990-1991. Northern Ireland Colorectal Cancer Register, N.I. Radiotherapy Centre, Belvoir Park Hospital, Hospital Road, Belfast.
13. Lindblom, Rotstein S, Nordenskjold M, Larsson C. Linkage analysis with markers on 17q in 29 Swedish breast cancer families. *Am J Hum Genet* 1993; **52**: 749-53.
14. Zuppan P, Hall J M, Lee M K, Ponglikitmongkol M, King M C. Possible linkage of the estrogen receptor gene to breast cancer in a family with late-onset disease. *Am J Hum Genet* 1991; **48**: 1065-8.
15. Egan,R L. Bilateral breast carcinomas. *Cancer* 1976; **38**: 931-8.
16. Lynch H T, Harris R E, Organ C H, Lynch J F. Management of familial breast cancer 2. Case reports, pedigrees, genetic counselling and team concept. *Arch Surg* 1978; **113**: 1061-7.
17. Evans D G, Fentiman I S, McPherson K, Asbury D, Ponder B A J, Howell A. Familial breast cancer. *Br Med J* 1994; **308**: 183-7.

The Ulster Medical Journal, Volume 65, No. 2, pp. 118-122, November 1996.

Babies born under 1000 g – Perinatal Outcome

D C Wilson, G McClure

Accepted 29 June 1996

SUMMARY

Improved survival of very pre-term infants is a result of advances in obstetric and neonatal medicine. To provide relevant data for a Northern Ireland population group, we evaluated mortality and morbidity of extremely low birthweight (ELBW; <1000 g) infants from a tertiary referral neonatal unit. Seventy-seven ELBW infants were admitted on the first day of life during the period April 1990 to April 1992. Mean (SD) gestational age (GA) was 26.2 (2.1) weeks and birthweight (BW) was 781 (132) g. The degree of severity of initial illness was high, with a mean (SD) CRIB (clinical risk index for babies) score of 7.4 (4.2). Fifty (65%) babies survived, being discharged home at a mean (SD) age of 95 (34) days. Survivors were more likely to have received maternal steroid therapy or been born in this hospital. Ten (20%) of the survivors had evidence of severe neonatal brain injury on cranial ultrasonography – Papile grade 3 or 4 intraventricular haemorrhage (IVH) or periventricular leucomalacia (PVL). Survival rate of ELBW infants without severe brain injury was 54% overall; this ranged from 0% in ELBW infants born at 23 weeks GA and 33% at 24 weeks GA to 85% at 27 weeks GA.

INTRODUCTION

There have been great improvements in the survival of tiny babies in the last decade. These have been due to advances in obstetrical management such as the use of tocolytic agents to prevent pre-term birth[1] and the use of antenatal corticosteroids to increase maturity of fetal lungs,[2] and in neonatal intensive care, such as surfactant replacement therapy.[3] However, our goal is not survival at all costs, but rather the highest quality of survival.

Studies of neonatal outcome for tiny babies have been reported from geographical regions[4, 5] or from tertiary referral hospitals.[6, 7] Some have only been of ELBW infants,[6] others have been of babies born at less than a defined gestational age.[5, 7] Some have excluded babies born <500 g,[6] others have excluded babies transferred for intensive care after initial resuscitation elsewhere.[7] To provide comparative data, the aim of this descriptive study is to provide information on mortality and morbidity in ELBW infants surviving to neonatal unit admission from a Northern Ireland population in the 1990s. This information will aid the counselling of parents at risk of having a tiny pre-term baby.

METHODS

Detailed prospective records were maintained on all 77 ELBW infants admitted to a regional neonatal intensive care unit (NICU) from April 1990 to April 1992. Babies who died in the labour ward or who were transferred to our NICU later than the first day of postnatal life were excluded from this study.

Gestational age was estimated from the date of the last menstrual period, fetal ultrasonography, and physical examination of the baby.[8] Small for gestational age (SGA) babies are those with a weight <10th centile for age. The presence of congenital infection was determined by one or more of the following criteria[9] – prolonged rupture of membranes, signs of chorioamnionitis and clinical signs suggesting infection of the infant at delivery. The criteria for rescue treatment of neonatal respiratory distress syndrome (RDS) have been previously defined.[10] Initial disease severity was calculated by the clinical risk index for babies (CRIB) score.[11] Chronic lung disease (CLD) was defined as the need for supplemental oxygen at 28 days and bronchopulmonary dysplasia (BPD) as CLD plus classic chest

Royal Maternity Hospital, Belfast, and Department of Child Health, The Queen's University of Belfast.

David Wilson, MD, MRCP.

Garth McClure, MB, FRCP, Professor.

Correspondence to Dr Wilson.

radiographic changes.[8] Intraventricular haemorrhage (IVH) was graded 0-4 on the Papile classification of cranial ultrasonographic appearances.[12] Periventricular leucomalacia (PVL) was defined as cyst formation, but not transient echodensities, on cranial ultrasonography.[8] Severe neonatal brain injury was defined as IVH grade 3 or 4 and/or PVL. Other indicators of neonatal morbidity included cholestasis (conjugated bilirubin >30 umol/l for >1 week), necrotising enterocolitis (NEC – suspicious clinical signs plus gas in the bowel wall on abdominal radiograph),[8] retinopathy of prematurity (ROP) and need for cryopexy,[13] confirmed bacterial or fungal septicaemia, duration of parenteral nutrition, amount of transfused blood product (blood or plasma), need for postnatal steroid therapy for ventilator dependency,[8] and growth parameters at discharge.

For statistical analysis the chi-squared test and student t test were used as appropriate. A p value < 0.05 was considered significant.

RESULTS

Initial clinical data on entry to the NICU are shown in Table I. These babies were born at a mean (SD, range) GA of 26.2 (2.1, 23-33) weeks with a mean (SD, range) BW of 781 (132, 345-991) g. The range of initial disease severity is shown by the mean (SD, range) CRIB score of 7.4 (4.2, 1-19).

TABLE I

Clinical details of 77 ELBW infants on the first day of life. Figures are number (%)

Male sex	41 (53)
Singleton	54 (70)
Antenatal steroids	46 (60)
Birthweight <750 g	28 (36)
Small for gestational age	21 (27)
Inborn	69 (90)
Congenital infection	7 (9)
Respiratory distress syndrome	45 (58)
Requiring supplemental oxygen	68 (88)
Requiring ventilation	54 (70)
Requiring surfactant	33 (43)

Fifty (65%) infants survived. There was a non-significant difference in survival rate of 28 infants born with a BW < 750 g and 49 with a BW of 750-999 g. Fifteen (54%) of the < 750 g group and 35 (71%) of the 750-999 g group respectively survived. Forty-six (67%) of inborn and 4 (50%) of outborn babies survived. Thirty-three (72%) of babies whose mothers had received some or all of a course of antenatal steroids survived compared to 17 (55%) surviving of those born before antenatal steroid therapy could be commenced. There was a significant ($p < 0.0001$) difference in mean (SD) CRIB score of survivors and non-survivors, at 5.8 (2.6) and 10.4 (4.8) respectively.

Table II shows relative survival at differing gestational ages and birthweights for ELBW infants. Not all babies born at less than 34 weeks gestation weigh less than 1000 g. During the study period the number of babies admitted with a birthweight ≥1000 g were 0 at 23-25 weeks, 2 at 26 weeks and 11 at 27 weeks gestation. Of these only 1 baby died, giving a total survival of 48 (64%) of the 75 babies born <28 weeks. Of the 27 ELBW infants who died, 10 died in the first 48 hours of life and 24 by day 21. All these deaths were expected in view of their clinical condition. Three babies died of complications related to BPD, at ages of 139, 202 and 206 days respectively, whilst still in the NICU.

TABLE II

Number of ELBW babies surviving when grouped in gestational age (GA) and birthweight (BW) categories.

Group	*Number*	*Survivors (%)*
GA: 23 weeks	4	0 (0)
GA: 24 weeks	12	5 (42)
GA: 25 weeks	16	9 (56)
GA: 26 Weeks	17	10 (59)
GA: 27 Weeks	13	12 (92)
GA: 28 weeks	5	4 (80)
GA: 29-33 weeks	10	10 (100)
BW: <500 g	2	0 (0)
BW: 500-749 g	26	15 (58)
BW: 750-999 g	49	35 (71)

Morbidity in the neonatal unit is shown in Table III for the 50 babies who survived. Of the 23 babies with IVH, three had grade 3 and three also had grade 4. Of the babies with ROP, only four had grade 3 and two had grade 4. Thirty-seven babies had at least one episode of coagulase-negative staphylococcal septicaemia. The mean (SD, range) of duration of supplemental oxygen was 52 (34, 0-164) days and of mechanical ventilation was 21 (19, 0-77) days. These babies had a mean (SD, range) of 1.4 (1.0, 0-4) episodes of septicaemia and a mean (SD, range) of 16 (8, 1-34) transfusions of blood products.

Details of condition at time of hospital discharge are shown in Table IV. Babies were discharged at a mean (SD, range) of 95 (34, 39-203) days at a weight of 2555 (687, 1715-5574) g. Forty (54%) babies had intact survival, defined as survival without severe brain injury. Incidence of infant survival of ELBW infants at differing gestational ages and birthweights is shown in Table V. The incidence of intact survival of babies of all birthweights born < 28 weeks was 37 of 75 (49%) over this time period.

TABLE III

Incidence of neonatal morbidity in 50 surviving ELBW infants while in the NICU. Figures are number (%).

Required supplemental oxygen	47 (94)
Required mechanical ventilation	41 (82)
Developed chronic lung disease	37 (74)
Developed bronchopulmonary dysplasia	19 (38)
Required steroid therapy for CLD/BPD	27 (54)
Required oxygen at term	6 (12)
Developed intraventricular haemorrhage	23 (46)
Developed periventricular leucomalacia	5 (10)
Developed retinopathy of prematurity	28 (56)
Required cryotherapy for ROP	5 (10)
Developed cholestatic jaundice	2 (4)
Developed necrotising enterocolitis	5 (10)
Developed bacterial septicaemia	42 (84)
Developed fungal septicaemia	2 (4)

TABLE IV

Condition at hospital discharge of 50 surviving ELBW infants. Figures are number (%).

Weight < 10th centile	46 (92)
Weight < 3rd centile	31 (62)
Length < 10th centile	43 (86)
Length < 3rd centile	31 (62)
Head circumference < 10th centile	15 (30)
Head circumference < 3rd centile	4 (8)
Home with supplemental oxygen	2 (4)
Severe brain injury	10 (20)

TABLE V

Numbers (%) of surviving ELBW infants without severe neonatal brain injury when grouped into gestational age (GA) and birthweight (BW) categories.

GA: 23 weeks	0 (0)
GA: 24 weeks	4 (33)
GA: 25 weeks	7 (44)
GA: 26 weeks	5 (29)
GA: 27 weeks	11 (85)
GA: 28 weeks	4 (80)
GA: 29-33 weeks	9 (90)
BW: < 500 g	0 (0)
BW: 500-749 g	13 (50)
BW: 750-999 g	27 (55)

DISCUSSION

There are many reasons for examining closely the results of intensive care for tiny babies. We would contend that the most important is that involved physicians can accurately counsel parents who are at risk of delivering an ELBW infant. This will prevent expectations being too high, and lower the risk of letting absolute numbers of survivors become more important

than their quality of life.[14] Other reasons include audit of obstetric and neonatal practice, the provision of accurate data for follow-up studies and the relation to health care costs. The cost of producing and looking after a new pre-term survivor with modern intensive care has been estimated at £10,000-£15,000.[15] However, the emotional and physical cost to caregivers and lifelong financial cost of a severely neurologically damaged survivor must also be considered. It is also important to examine recent data from ongoing scientific and technological advances; had these babies been born in 1996 they would have been likely to have had steroid therapy for ventilator dependence at an earlier age.[16]

These results can be set in context with other published neonatal outcome data. A study of all pre-term babies born in Scotland in 1984 showed survival of 78 of 204 ELBW infants, a rate of 38%.[4] When all registered births in England and Wales in 1989 were examined, 357 of 923 babies born at BW of 500-799 g survived, a rate of 39%.[17] Both these studies were based on geographical region. In a hospital study from Melbourne, 92 of 194 ELBW infants survived in the period 1985-7, a rate of 47%.[6] Other studies have examined outcomes of babies based upon gestational age. In a tertiary referral centre in the Mersey region, 465 of 823 babies born at less than 29 weeks gestation during 1980-89 survived, a rate of 57%.[18] In the Oxford region, 164 of 342 babies born at less than 29 weeks gestation during the period 1984-86 survived, a rate of 48%.[5]

Analysis of survival figures in this study showed no survivors who were born less than 500 g birthweight or 24 weeks gestational age. Major neurodevelopmental handicap has an incidence of 50-100% in pre-term infants with grade 3-4 IVH or PVL,[7] that is, those babies defined as having severe neonatal brain injury in this study. The survival rate without severe neonatal brain injury of ELBW infants in this regional NICU in the period of 1990-92 was 0% at GA of 23 weeks or BW < 500 g, and 33% at 24 weeks GA. We and others[7] suggest that aggressive resuscitation should only be provided after mature discussion among physicians and parents of babies at the current limit of viability – that is < 500 g BW and < 24 weeks gestation. Survival of ELBW infants of < 25 weeks gestation should be closely monitored, both in terms of early and longterm outcome.[19] Longterm outcome is being monitored for the surviving ELBW infants in this study and we will report results of their neurodevelopment, growth and medical problems in early childhood.

REFERENCES

1. The Canadian Pre-term Labour Investigations Group. Treatment of pre-term labour with the beta-adrenergic agonist ritodrine. *N Engl J Med* 1992; **327**: 308-12.
2. Garite T J, Rumney P J, Briggs G G et al. A randomized, placebo-controlled trial of betamethasone for the prevention of respiratory distress syndrome at 24 to 28 weeks gestation. *Am J Obstet Gynecol* 1992; **166**: 646-51.
3. Collaborative European Multicenter Study Group. Surfactant replacement therapy for severe neonatal respiratory distress syndrome: an international randomized clinical trial. *Pediatrics* 1988; **82**: 683-91.
4. The Scottish Low Birthweight Study Group. The Scottish low birthweight study: I. Survival, growth, neuromotor and sensory impairment. *Arch Dis Child* 1992; **67**: 675-81.
5. Johnson A, Townshend P, Yudkin P, Bull D, Wilkinson A R. Functional abilities at age 4 years of children born before 29 weeks of gestation. *Br Med J* 1993; **306**: 1715-8.
6. Kitchen W H, Doyle L W, Ford G W et al. Changing two-year outcome of infants weighing 500 to 999 grams at birth: A hospital study. *J Pediatr* 1991; **118**: 938-43.
7. Allen M C, Donohue P K, Dusman A E. The limit of viability – neonatal outcome of infants born at 22 to 25 weeks gestation. *N Engl J Med* 1993; **329**: 1597-601.
8. Halliday H L, McClure B G, Reid M McC. Handbook of neonatal intensive care, 3rd ed. Eastbourne: Baillere-Tindall, 1989.
9. Edgar J D M, Wilson D C, McMillan S A et al. Predictive value of soluble immunological mediators in neonatal infection. *Clin Sci* 1994; **87**: 165-71.
10. Halliday H L, Tarnow-Mordi W O, Corcoran J D, Patterson C C. Multicentre randomised trial comparing high and low dose surfactant regimens for the treatment of respiratory distress syndrome (The Curosurf 4 trial). *Arch Dis Child* 1993; **69**: 276-80.
11. The international neonatal network. The CRIB (clinical risk index for babies) score: a tool for assessing initial neonatal risk and comparing performance of neonatal intensive care units. *Lancet* 1993; **342**: 193-8.
12. Papile L A, Munsick-Bruno G, Schaefer A. Relationship of cerebral intraventricular haemorrhage and early childhood neurologic handicaps. *J Pediatr* 1983; **103**: 273-7.
13. Watts J L. Retinopathy of prematurity. In: Sinclair J C, Bracken M R, eds. Effective care of the newborn infant. Oxford: *Oxford University Press*, 1992: 617-40.

14. McClure G. Surfactant replacement therapy – time for thought. *Arch Dis Child* 1992; **67**: 1228-30.

15. Tubman T R J, Halliday H L, Normand C. Cost of surfactant replacement treatment for severe neonatal respiratory distress syndrome. A randomised controlled trial. *Br Med J* 1990; **301**: 842-5.

16. Yeh T F, Torre J A, Rastogi A, Anyebuno M A, Pildes R S. Early postnatal dexamethasone therapy in premature infants with severe respiratory distress syndrome: a double-blind controlled study. *J Pediatr* 1990; **117**: 273-82.

17. Roberton N R C. Should we look after babies less than 800 g? *Arch Dis Child* 1993; **68**: 326-9.

18. Cooke R W. Factors affecting survival and outcome at 3 years in extremely pre-term infants. *Arch Dis Child* 1994; **71**: F28-31.

19. Hack M, Fanaroff A A. Outcomes of extremely immature infants – a perinatal dilemma. *N Engl J Med* 1993; **329**: 1649-50.

The Ulster Medical Journal, Volume 65, No. 2, pp. 123-125, November 1996.

Experience with Schistosomiasis in Northern Ireland

P J Ingram, D C Allen, S T Irwin

Accepted

SUMMARY

Five cases of schistosomiasis have been recorded in the Belfast City Hospital Histopathology Laboratory over the last three years. The sites of infection have included the colon, bladder, uterus and seminal vesicles. All the infected individuals had visited Africa. Three of them were health care workers. The clinician must maintain a high index of suspicion when treating those with a history of travel and risk of exposure to this infection. Diagnosis is made even more critical as the condition is treatable, and serological markers can identify those with occult infection.

CASE 1: 23 year old physiotherapist

A physiotherapist and colleague had visited Zimbabwe. Upon their return the colleague was diagnosed as having schistosomiasis. The physiotherapist was therefore advised to seek medical attention. Urinalysis revealed the presence of blood, though a 24-hour urine collection was negative for parasites. However a follow-up rectal biopsy contained schistosoma ova. Serological testing was positive. The patient is currently well.

CASE 2: 30 year old civil engineer

This patient swam in Lake Malawi which he had been assured was schistosome - free. He contracted malaria falciparum, schistosomiasis and amoebic dysentery in 1992. These were appropriately treated at that time. Two years later he presented with testicular pain and haemospermia. A urine collection was negative, though cytological examination of his seminal ejaculate showed it to be contaminated with schistosoma haematobium. He is currently schistosomiasis-free and is under the review of the urology service.

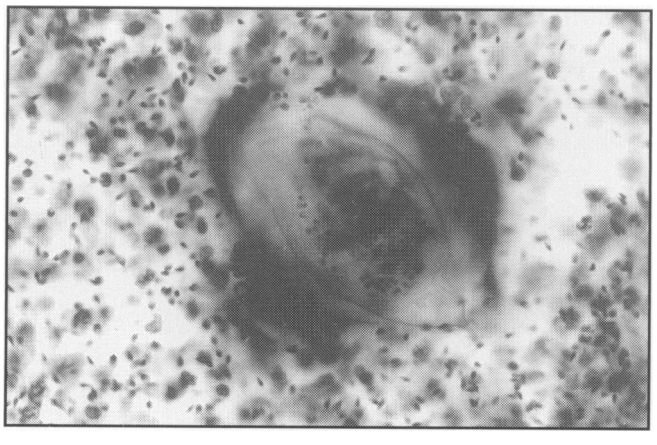


Fig 1. Direct examination of seminal fluid showing schistosoma ova.

CASE 3: 27 year old doctor

As a medical student this doctor had been on an elective in Africa had swum in Lake Malawi. Two years later she experienced several episodes of rectal bleeding. Colonoscopy showed small pale raised lesions which were biopsied and found to contain the ova of schistosoma mansoni. Serological markers were positive for both the

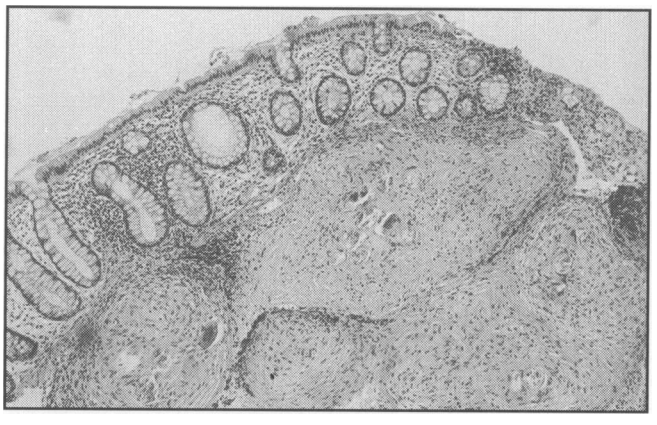


Fig 2. Granulomatous reaction to submucosal schistosoma ova in the large intestine.

Histopathology Department, Belfast City Hospital, Belfast BT9 7AD.

P J Ingram, MB, BCh, BAO, Senior House Officer.

D C Allen, MD, MRCPath, Consultant Pathologist.

S T Irwin, MD, FRCS, Consultant Surgeon.

Correspondence to Dr Ingram.

student and a colleague who had also been on the elective. Both were subsequently treated, though the student has since had a recurrence two and a half years later.

CASE 4: 26 year old barman

Whilst travelling from Kenya to Zimbabwe this man and a friend passed through Malawi and swam in the lake. After returning home he was admitted to hospital with epididymo-orchitis and haematuria which was treated with antibiotics. His symptoms returned however, and he was readmitted for investigation. During this admission it was discovered that his friend with whom he had travelled had been diagnosed as having schistosomiasis. Cystoscopy revealed multiple white spots in the bladder mucosa which on biopsy contained multiple schistosoma ova. He is currently under review; he has had no further bladder biopsies.

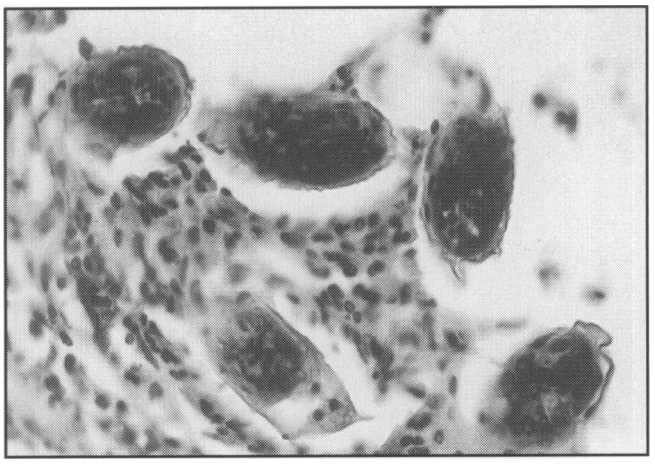


Fig 3. Schistosoma haematobium demonstrating terminal spine.

CASE 5: 40 year old nurse

This nurse had worked in Africa with a friend who was found to have schistosomiasis. This patient only came to medical attention following a diagnosis of Stage IB cervical carcinoma. A radical hysterectomy was performed with subsequent radiotherapy. Examination of the uterus confirmed the presence of a squamous cell carcinoma which had metastasised to regional lymph nodes. Pale seedlings were also noted in the cervical stroma, parametria and serosal aspect of the specimen. Histological sections showed these to be aggregates of schistosoma ova. Serological markers were negative in this case. Unfortunately, despite surgery, chemotherapy and radiotherapy, this patient died.

DISCUSSION

Schistosomiasis is a chronic trematode infection affecting around 200 million people worldwide and is one of the leading causes of morbidity in developing countries.[1] Theodore Bilharz was the first to describe the parasitic blood flukes of the genus schistosoma in Cairo in 1851. Infection occurs while bathing in fresh water contaminated with the larval stage of the worm (or cercaria) which penetrates the skin and enters the venules. It then travels through the systemic circulation to the liver where it matures to form adult worms. These then migrate to the mesenteric veins and lay their eggs (fig 2). Subsequently the eggs are passed into the intestinal lumen and are excreted in the faeces. The life cycle is completed in slow-moving water contaminated by egg-containing faeces. The former hatch releasing larvae which are ingested by the intermediate host, the freshwater snail, where the second larval stage of cercariae develop and emerge in a free swimming form.[2]

Several sub types of schistosoma exist. Infestation of the large intestine is usually due to schistosoma mansoni and schistosoma japonicum. The first is endemic in Africa and central South American countries including the Caribbean islands. The latter is found in Japan, China, the Philippine Islands and the countries of South East Asia. Schistosoma haematobium infects the bladder and only rarely involves the intestine. It is found in Africa, particularly Egypt, and in countries of the near Middle East.

Over the last few years a schistosoma enzyme linked immunosorbent assay (ELISA) against soluble egg antigen has been developed. This can be used to confirm a clinical or histological diagnosis as well or to screen those who may be harbouring occult infection.

Positive results are graded according to their predictive value. The test will not be positive for 6 to 12 weeks after infection. It is in this early period that false negatives will occur.

Out of the five cases reported here, four sites of infection are represented, two in the large bowel and one each in the bladder, uterus and seminal vesicles. In the bowel, schistosomiasis infection can manifest itself both as subserosal and submucosal pseudotumour[3] – a potential pitfall for surgeons, and there is also an association between colonic cancer and chronic schistosomal infection. Pseudopolyps may form in

schistosomiasis with potential for progression to focal mucosal atypia and ultimately carcinoma.[4] Another known association is between urinary tract infection and squamous cell carcinoma of the bladder. It is interesting to note that in case 5 the schistosomiasis infection was in close juxtaposition to a cervical squamous carcinoma. It is therefore postulated that as in the case of bladder and bowel carcinoma, chronic carriage of this trematode may be a co-factor in malignant transformation within the cervix. Studies from Malawi have shown that 60 per cent of gynaecological infections by schistosomiasis have involved the cervix.[5] However, we are unaware of other reports linking schistosome infection to cervical carcinoma.

Several subtypes of schistosoma exist each having its own predilection for a particular infection site. Subtyping is dependent upon the shape of the ova and positioning of its spine (fig 3). Subtyping can be problematic on formalin fixed specimens. A more accurate result is obtained if fresh stool, urine or seminal fluid is examined directly (fig 1). The ova can be clearly seen within the media suspension and there is no crush artefact.

Praziquantel is the drug of choice as it combines successfully effectiveness, broad spectrum activity and low toxicity. The exact regime varies with the subtype of schistosome. However the treatment is not totally effective[6] so careful review is essential.

Health care workers, students and tourists from Ireland work and visit many of the countries with schistosomiasis. Our paper illustrates that this disease should be considered carefully in these groups.

ACKNOWLEDGEMENTS

The authors wish to thank Mr R A Donaldson, Mr B Lee and Mr J H Price for permission to review the records of their patients, and also the Department of Microbiology, Belfast City Hospital, for their guidance.

REFERENCES

1. Whitehead R. Gastrointestinal and Oesphageal Pathology, 1st Edition, London, Churchill Livingstone 1989; 504-5.
2. Morson B, Dawson I, Day D, Jass J, Price A, Williams G. Morson & Dawson's Gastrointestinal Pathology, 3rd Edition, London, Blackwell Scientific Publications 1990, 491.
3. Prosser J, Kasznica J, Gottlieb L, Wade G. Bilharzial pseudotumours – dramatic manifestation of schistosomiasis: report of a case. *Hum Path* 1994; **25**: 98-101.
4. Ming-Chai C, Chi-Yuan C, Pei-Yu C, Jen-Chun H. Evolution of colorectal cancer in schistosomiasis. Transitional mucosal changes adjacent to large intestinal carcinoma in coleatomy specimens. *Cancer* 1980; **46**: 1661-75.
5. Wright E D, Chiphangwi J, Hutt M S. Schistosomiasis of the female genital tract. a histopathological study of 176 cases from Malawi. *Trans R Soc Trop Med Hyg* 1982; **76**: 822-9.
6. Goldsmith P C, Leslie T A, Sams V, Bryceson A D B, Allason-Jones E, Dowd P M. Lesions of schistosomiasis mimicking warts on the vulva. *BMJ* 1993; **307**: 556-7.

The Ulster Medical Journal, Volume 65, No. 2, pp. 126-130, November 1996.

Casualties of the Sun

C E Willis, B Smyth

Accepted September 1996

Summary

A retrospective review was carried out of all sunburn related attendances, during the periods 1/6/94 – 31/8/94 and 1/6/95 – 31/8/95, at the four A&E departments and at one of the general practices within the Northern Health and Social Services Board area. Four hundred and thirty patients had attended. The modal age group was 16-30 years. More males presented than females. Within the sexes more males presented in the under 16 years and over 30 years age group, while females were more common in the 16-30 years age group. There was documentation of blisters in 30% of patients. Those with blisters were more likely to be under 16 years and male. In females the most and least commonly affected areas correlated with the most and least commonly affected areas for cutaneous malignant melanoma. In these days of limited resources it is important to use epidemiological data such as this in order to contribute to the development of health promotion programmes and campaigns.

INTRODUCTION

The evidence relating cutaneous malignant melanoma to previous sun exposure is now very strong.[1] However, despite this widely established relationship and extensive health promotion within the public domain, sunburn and sun-related illness continue to be a major problem within Northern Ireland.

Epidemiological studies suggest that sun exposure up to age 20 initiates a process of carcinogenesis that manifests 40 – 60 years later.[2] About 90% of skin cancers are non-melanoma cancers, approximately 80% of these being basal cell carcinomas and most of the rest being squamous cell carcinomas.[3] In the UK the incidence of basal cell carcinoma has risen by 238% in 14 years.[2]

Non-melanoma skin cancers rarely metastasize and are seldom fatal. Malignant melanoma is the third form of skin cancer which is comparatively rare but much more serious. Between the periods 1974-78 and 1984-88 the incidence of cutaneous malignant melanoma (CMM) within the province doubled.[4] This reflects the worldwide increase in this disease which is greater than most reported studies.[4]

Many factors contribute to this growing problem, including Celtic skin type, the greater availability of sunbeds, package holidays, the suntan status symbol, the continuing failure of many to recognise the dangers of solar damage and diagnostic delay.[4]

It was as a response to the growing incidence of CMM that the four Health and Social Services Boards developed a "Care in the Sun" Health Promotion programme. This began in 1990, and included among its objectives are programmes:

1. To raise public awareness of the dangers of overexposure to the sun, both at home and abroad.
2. To raise awareness among primary school children of the long term dangers of sunburn.
3. To promote the primary prevention message among those professionals involved in care of pre-school children.
4. To raise awareness and increase recognition of CMM by general practitioners.

However, despite this ongoing work, during the unusually hot summer of 1995 the authors became

Department of Public Health Medicine, Northern Health & Social Services Board, 182 Galgorm Road, Ballymena, BT42 1QB.

C E Willis, MB, BCh, DPH, Registrar.

B Smyth, MSc, FRCP, MFPHM, Consultant in Public Health Medicine.

Correspondence to Dr C E Willis.

aware of a marked increase in A&E attendances due to sun-related problems. It was decided, therefore, to review data from A&E attenders to see if this could help target future public awareness initiatives.

MATERIALS AND METHOD

Of the people who develop adverse symptoms as a result of exposure to the sun, only a small, but unknown, fraction will ever seek medical attention. This may be in the form of a GP visit, attendance at an A&E department or advice from a pharmacist. Hospital records are one of the few ways of retrieving epidemiological data in a relatively short and inexpensive manner. An attempt was made to relate the numbers attending A&E to those going to their GP by reviewing data from a 9,500-patient practice within the Northern Board.

All four Northern Board A&E departments were visited by one of the authors in September 1995. A retrospective search was carried out for sun-related attendances during the periods 1/6/94 – 31/8/94 and 1/6/95 – 31/8/95.

This was done either manually by going through registers, looking for a diagnosis of sunburn/ sunstroke or other term implying sun-related injury, or by computer using the Read codes relating to sunburn and looking for free text relating to sunburn. Data from the health centre was downloaded from the practice computer. Details of age, sex, presenting symptoms, area of skin affected, treatment given and follow-up required were extracted from the notes, along with any other relevant information.

The data was entered into a Statistical Package for Social Sciences (SPSS). Descriptive and inferential analyses were carried out as appropriate.

RESULTS

There were 394 patients who attended the A&E departments and 36 patients who presented to their GP during the studied periods in 1994 and 1995. The results were analysed in two groups, according to the place of presentation.

Hospital A&E Departments

Of the 394 attenders, 74 patients presented in the period from 1st June – 31st August 1994 and 320 from 1st June – 31st August 1995.

In June 1994 sun-related injury accounted for 0.3% of the total new patient attendances, whereas in June 1995 it accounted for 2.9%; this represents almost a ten-fold increase.

Of the total attenders, 215 (55%) were male and 179 (45%) were female. The ratio was similar for both years and in each A&E department.

The patients were divided into age bands for statistical purposes as shown in Table I.

In two cases there was no date of birth available.

Further analysis of the <16 years group revealed that there were 52 (13% of total attenders) in the <11 and 25 patients (6%) in the <5 years age group. When each A&E department was studied individually the ages showed a similar pattern of spread.

The mean and median ages of presentation were 24 years and 22 years respectively with a range of six months to 82 years. This pattern was the same for both years.

Using combined figures for 1994 and 1995, there was a significant difference in ages presenting between the sexes, with significantly more males presenting in the <16 years and >30 years groups and significantly more females in the 16-30 year age group ($p = 0.04$).

On review of the case notes for both years, three had a diagnosis of sunstroke and eleven others had symptoms of sunstroke, i.e. nausea, headache and dizziness, documented. None required admission. Fourteen patients were sun-burnt on holiday outside the United Kingdom. Two were burnt under a sunlamp, one on the face and the other on the back. Three patients were pregnant and two had an underlying skin condition – psoriasis and systemic lupus erythematosus respectively.

TABLE I

Age of Presenting Patients

Age Group (years)	*1994*	*1995*	*Total (%)*
<16	16	73	89 (23)
16-30	35	166	201 (51)
31-45	18	58	76 (19)
46-60	2	17	19 (5)
>61	3	4	7 (2)

TABLE II

Areas Affected by Sun

Area Affected	*Males*	*Females*
Trunk	123	65
Legs	61	84
Arms	39	32
Head and neck	28	26
Feet	12	21

The areas of the body affected are presented in Table II. The frequencies for the sexes are presented in Figure 1 for comparison. The numbers add up to >394, and >100%, as some patients had more than one area affected. The pattern of areas affected was similar for the patients in 1994 and 1995. No information was available regarding area affected in 26 patients.

In 118 cases (30%) there was documentation of blisters being present; in 55 cases it was documented that no blisters were present, in 221 cases blisters were not mentioned in the notes. Of those with blisters 75 were male (63.6%), and 43 were female (36.4%). The correlation between blisters and sex was statistically significant ($p = 0.006$). The blistered group were also significantly younger, i.e. in the <16 years age group ($p = 0.001$), with 32 of the 118 being in the <11 primary school age group. The commonest areas affected in the blistered group were legs, shoulders and back.

Treatment administered to the patients included topical cream (66%), analgesia (42%), antihistamines (5%), incision of blisters (4%); antibiotics (2%) were prescribed where it was felt that secondary infection was present. This number adds up to >394 as in some cases more than one treatment was given.

Follow-up was arranged for 123 (31%) patients: 24 were to be reviewed at the A&E department and 99 by their GP. Forty-six (12%) patients were told to come back if their symptoms did not resolve and one did so, while four other patients also reattended when it hadn't been previously arranged. The remaining 221(56%) were not reviewed.

Nine (2%) patients had already seen their GP before attending the A&E department, ranging from four hours to one day previously.

Health Centre Data

Data available from the health centre consisted of age, sex, date of presentation, treatment required and review.

Thirty-six patients presented within the period studied, four patients between 1/6/94 – 31/8/94 and 32 patients between 1/6/95 – 31/8/95.

The data was analysed and comparisons made between it and the group presenting to hospital. Due to the small number in 1994, data from the two time periods were combined.

The mean age of presentation to the GP was 26 years, (median 24 years, range 2 – 53 years). There was no significant difference in age between this group and the group presenting to hospital. The age grouping is shown in Table III.

Thirty-one percent of those who presented to their GP were male and 69% were female. This was significantly different from those presenting at hospital ($p=0.006$).

More patients were treated with creams ($p= 0.002$), analgesia ($p=0.00004$), and antihistamines ($p=0.001$) within the hospital setting than in general practice. No data was recorded on the severity of the signs and symptoms of the GP attenders.

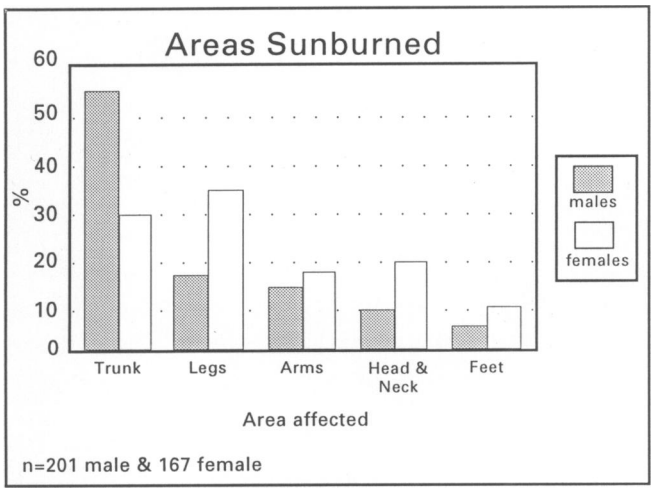
None of the patients seen in general practice were reviewed, in contrast to the 123 patients who returned to hospital for review.

TABLE III

Age of Presenting Patients

Age Group (years)	*Total*
<16	10
16-30	14
31-45	7
46-60	5
>61	0

Fig 1.



DISCUSSION

Exposure to UV radiation is a major contributor to skin cancer. It is repeated sunburn, especially in childhood, which increases the risk of malignant melanoma in later life.

In the UK CMM is the 13th most common cancer in women and the 15th most common in men. In the age group 15-34 years, it is the cause of one in twelve cancers.[3] Females still outnumber males but the gap between the sexes is narrowing. In Northern Ireland it had fallen from 3:1 to 2:1 from the mid 70s to mid 80s.[4]

The present study is a descriptive one of sun-related attendances at A&E departments and may not be representative of sun-related problems within the wider population.

In terms of areas affected by CMM in Northern Ireland, leg is most common in the female, followed by head and neck, then arm and hand, foot and trunk. In the male CMM is commonest on the head and neck, then trunk, leg, arm and hand and foot.[4] The most and least common areas affected by CMM in females are reflected by the areas burnt in this study. In males the pattern of burns correlates more closely with the areas for CMM in the UK, where the trunk is the most common area for CMM.[3]

The fact that younger people were more frequent attenders could be due to reduced tolerance of symptoms, easier access to A&E departments, less inhibition about coming forward for treatment, greater awareness of the danger due to health promotion campaigns or to greater incidence of sunburn in this age group. The same biasing factors could explain why more males attended than females, but more males had blisters, indicating a greater severity of burn, which could explain the higher attendance rate.

A possible explanation for the differences between the GP practice and A&E could be that patients with less severe symptoms attended the practice, therefore requiring less in the way of treatment and review.

The main target population for the "Care in the Sun" campaign has been the pre-school and primary school age groups, and it is encouraging that the numbers presenting in these groups are small, although disappointing that 62% of those in this age group had blisters. The results have identified males under 16 and over 30 years, and females between 16 and 30 years as being the most frequent attenders at A&E departments after a period of hot weather. Perhaps future public awareness programmes should also be directed at these groups.

Key points to be included in health promotion programmes include:

- Identifying suitable areas for targeting, such as the workplace, leisure centres, shops, (in particular where sun screens are sold), and the media, such as fashion magazines.
- The need to explore the development of programmes tailored to particular settings, for example, health visitor consultations with the parents of young children, pharmacists with the general public, as well as continuing the work of nursery and primary school teachers with their pupils and parents.
- The fact that most people in Northern Ireland who attended a medical establishment with a sun-related injury did so as a result of normal local summer activity, not as part of a foreign holiday.

Market research to identify how best to access these groups and impart health promotion messages is therefore essential.

Health promotion is always an uphill struggle, and in these days of limited resources it is important to direct time and energy in a way to achieve maximum benefit for the maximum number. Therefore it is important to review lifestyle factors and use information, such as that provided in this study, to refine and target health promotion interventions.

ACKNOWLEDGEMENTS

The authors thank Dr R S Matthews, Consultant Dermatologist, for his advice and comments; and Miss P McDonald for her help with the data analysis. Thanks also go to the consultant and medical records staff in the A&E departments visited and to Coleraine Health Centre for facilitating the data collection.

REFERENCES

1. Elwood J M. Melanoma and sun exposure: contrasts between intermittent and chronic exposure. *Wld Surg* 1992; **16**: 157-65.
2. Goldberg L H. Basal cell carcinoma. *Lancet* 1996; **347**: 663-7.
3. Cancer Research Campaign. Malignant Melanoma in the UK, Fact Sheet 4.1, 1995.
4. The Melanoma Study Group (1995) The Wolfson Foundation Report on Cutaneous Malignant Melanoma in Northern Ireland.

The Ulster Medical Journal, Volume 65, No. 2, pp. 131-136, November 1996.

Randomised controlled trial of ranitidine versus omeprazole in combination with antibiotics for eradication of *Helicobacter pylori*

T C K Tham, J S A Collins, C Molloy, J M Sloan, K B Bamford, R G P Watson

Accepted September 1996

SUMMARY

This study compared high dose ranitidine versus low dose omeprazole with antibiotics for the eradication of *H pylori*. 80 patients (mean age 48 years, range 18-75) who had H pylori infection were randomised in an investigator-blind manner to either a two-week regime of omeprazole 20 mg daily, amoxycillin 500 mg tid and metronidazole 400 mg tid (OAM), or ranitidine 600 mg bd, amoxycillin 500 mg tid and metronidazole 400 mg tid (RAM), or omeprazole 20 mg daily and clarithromycin 500 mg tid (OC), or omeprazole 20 mg daily and placebo (OP). H pylori was eradicated in 6 of 19 patients in the OAM group (32%); 8 of 18 in the RAM group (44%), 4 of 15 in the OC group (27%); none of 18 in the OP group (0%). [<P0.005 for OAM, RAM, OC vs OP; P=N. S. between OAM, RAM, OC]. Overall metronidazole resistance was unexpectedly high at 58%. Eradication rates in metronidazole sensitive patients were 71% (5/7) and 100% (3/3) for OAM and RAM respectively. In conclusion, H pylori eradication rates using high dose ranitidine plus amoxycillin and metronidazole may be similar to that of low dose omeprazole in combination with the same antibiotics or omeprazole with clarithromycin. Overall eradication rates were low due to a high incidence of metronidazole resistance but were higher in metronidazole-sensitive patients. Even high dose ranitidine with two antibiotics achieves a relatively low eradication rate. These metronidazole-based regimens cannot be recommended in areas with a high incidence of metronidazole resistance.

INTRODUCTION

Helicobacter pylori infection is found in most patients suffering from chronic active gastritis or peptic ulceration.[1] Eradication of *H pylori* prevents relapses of duodenal ulcer[1,2] and probably lessens the risk of ulcer complications.[3-6]

The optimal therapeutic regimen for eradicating *H pylori* is not yet determined. Numerous studies have evaluated the combination of a proton pump inhibitor, omeprazole, with a single or double antibiotic regimen such as amoxycillin or clarithromycin, reporting eradication rates of around 80%.[7-9] In contrast, fewer studies have evaluated the role of histamine-2 receptor antagonists when combined with antibiotics. Hentschel et al[10] found that ranitidine in combination with amoxycillin plus metronidazole produced an eradication rate of 89%. Ranitidine

Royal Victoria Hospital, Grosvenor Road, Belfast, Northern Ireland, UK

Division of Medicine

Tony C K Tham, MD, MRCP, Senior Registrar in Gastroenterology.

John S A Collins, MD, FRCP, FRCPI, Consultant Physician and Gastroenterologist.

Caroline Molloy, RGN, Research Nurse.

R G Peter Watson, BSc, MD, MRCP, Consultant Physician and Senior Lecturer.

Department of Pathology

James M Sloan, MD, FRCPath, Consultant Histopathologist and Senior Lecturer.

Department of Microbiology

Kate B Bamford, MD, FRCPath, Consultant Microbiologist and Senior Lecturer.

Correspondence to Dr Tham.

combined with triple therapy (bismuth, metronidazole and tetracycline) produced an eradication rate of 84%.[11] Thus ranitidine in combination with antibiotics may be as effective as omeprazole plus antibiotics in the eradication of *H pylori*. However few randomised studies have compared ranitidine and antibiotics with omeprazole and antibiotics in the eradication of *H pylori*.

The aims of our study were to evaluate the efficacy of *H pylori* eradication using ranitidine compared to omeprazole when they are combined with antibiotics. The antibiotics used were amoxycillin and metronidazole to produce a triple therapy regimen without bismuth, as there is some evidence that the addition of bismuth is not necessary in achieving high eradication rates with this type of triple therapy.[10] These two regimens were compared to a control regimen of omeprazole alone and the regimen of omeprazole plus clarithromycin which has been associated with high eradication rates.

METHODS

The study was approved by the Research Ethical Committee of the Queen's University of Belfast and written informed consent was obtained from all patients.

80 dyspeptic patients who underwent upper gastrointestinal endoscopy and were found to have *H pylori* infection were studied. Patients were excluded if they were allergic to any of the study medication, pregnant or liable to become pregnant, lactating, had recent gastrointestinal haemorrhage, severe disease of any other kind or had taken antibiotics in the month before entry.

The presence of *H pylori* infection was assessed by endoscopy and antral biopsies were taken for histology and culture; rapid urease (CLO) test and the 13C-urea breath test (UBT) were also performed. *H pylori* infection was confirmed if at least two of the tests were positive. Two antral biopsies were taken for histology, and the presence of *H pylori* identified using a Giemsa stain. Two antral biopsies were taken for culture using non-selective medium of Columbia-based agar and selective medium (Dent's medium), incubated in micro-aerophilic conditions at 37°C for up to 10 days; then checked for metronidazole resistance in Columbia blood-agar with 5 mcg metronidazole disc incubated for 72 hours. One antral biopsy was taken for the CLO test (Delta West, Australia).

The 13C-urea breath test was performed according to the European 13C-urea breath test protocol and assessed by the Bureau of Stable Isotope Analysis Ltd., England. A positive result was taken as excess deltal3 C02 excretion > 5 per ml, standard delta notation.[12]

The patients were randomised in an investigator blind manner to a two-week regime of (1) omeprazole 20 mg daily, amoxycillin 500 mg tid and metronidazole 400 mg tid (OAM); (2) ranitidine 600 mg bd, amoxycillin 500 mg tid and metronidazole 400 mg tid (RAM); (3) omeprazole 20 mg daily and placebo (OP); or (4) omeprazole 20 mg daily and clarithromycin 500 mg tid (OC).

Repeat endoscopy for histology and culture and 13 C-UBT were undertaken 4 weeks after completion of therapy. Eradication of *H pylori* was considered successful if all three tests were negative.

Compliance was assessed by return tablet counts. Side-effect profile was determined by visits at two and six weeks after commencement of treatment, and patients were asked to contact the investigators if they had side-effects. Symptoms were assessed before treatment and four weeks after completing the treatment and graded by a scoring system. Patients were questioned in a standardised manner about five predefined symptoms: epigastric pain, nausea or vomiting, heartburn, postprandial discomfort or regurgitation. The presence of each symptom was scored as: 0-absent; 1 – recalled on direct questioning; 2-present but not impairing activities; 3-interfering with daily work and life. Frequency of symptoms was scored as: 1-one day or less per week; 2-several times each week; 3-daily. The scores were added for each patient giving a possible score ranging from 0 to 30.

The Chi-square test was used to compare the eradication rates between treatments; a P value of less than 0.05 was considered significant.

RESULTS

80 patients with *H pylori* infection entered the study. Their demographic and clinical details are summarised in Table 1. All four groups had similar demographic and clinical characteristics. Some of the patients had become asymptomatic at the time of the initial endoscopy.

Side effects occurred in two (10%) of the patients in the OAM group. On complained of nausea and rash and withdrew from the study, and another

TABLE I

Patient demographic and clinical characteristics

	Omeprazole Amoxycillin Metronidazole (n=20)	*Ranitidine Amoxycillin Metronidazole (n=20)*	*Omeprazole Placebo (n=20)*	*Omeprazole Clarithromycin (n=20)*
Mean age (range) (y)	40 (18-75)	50 (18-65)	52 (26-82)	49 (28-75)
Men/women (n)	8/12	13/7	7/3	15/5
Diagnosis (n):				
Duodenal ulcer disease	14	14	17	12
Oesophagitis	3	1	3	5
Gastric ulcer	1	0	0	0
Normal	3	4	3	7
Median symptom score (range)	12 (0-23)	14 (0-22)	10 (0-22)	15 (0-30)
Smoker (n) (%)	4/7 (57%)	5/10 (50%)	3/12 (25%)	3/9 (33%)
Alcolol use (n) (%)	3/7 (43%)	7/9 (78%)	9/12 (75%)	7/9 (78%)

had diarrhoea but continued with the study. Two (10%) of the patients in the RAM group complained of nausea and vomiting and they both withdrew from the study. Two (10%) of the patients in the OP group complained of diarrhoea, one of whom withdrew from the study. Three (15%) of the patients in the OC group complained of diarrhoea (one) and vomiting (two); they all withdrew from the study. In total, 11% of patients suffered from side-effects and of these 9% withdrew from the study as a result.

Compliance was good in all the groups (>90% consumption of the delivered study medication) with no significant differences between them except for two patients who withdrew from the study because of poor compliance in the OC group. Compliance was 97% (range 86 - 100; n=12) in the OAM group; 94% (74 - 100; n=12) in the RAM group; 95% (72 - 100; n=13) in the OP group; 92% (72 - 100; n=8) in the OC group.

H pylori resistance to metronidazole was assessed. The metronidazole resistance was 50% (n = 7/14) in the OAM group; 73% (11/15) in the RAM group; 60% (9/15) in the OP group; 47% (7/15) in the OC group. There was no significant difference in the metronidazole resistance between the groups. The overall metronidazole resistance was 58%.

The eradication of *H pylori* with the different regimens are summarised in Table II. The evaluable patient group includes the patients who completed the study and the intention-to-treat group includes all patients who participated in the study. The statistical results were the same for both evaluable and the intention to treat groups. The eradication rates with the regimens which included antibiotics were significantly higher than that for omeprazole alone ($P<0.005$). There were no significant differences in the eradication rates between the regimens which included antibiotics. In patients who had metronidazole sensitive *H pylori*, the eradication rates were 71% (5 out of 7) in the OAM group and 100% (3 out of 3) in the RAM group.

TABLE II

H pylori eradication rates with the different regimens

Treatment	*Evaluable (n; %)*	*Intention to treat (n; %)*
Omeprazole Amoxycillin Metronidazole	6/19 (32%)	6/20 (30%)
Ranitidine Amoxycillin Metronidazole	8/18 (44%)	8/20 (40%)
Omeprazole Placebo	0/19 (0%)	0/20 (0%)
Omeprazole Clarithromycin	4/15 (27%)	4/20 (20%)

P,0.005 for all regimens with antibiotics versus omeprazole/ placebo.

No significant differences between regimens which included antibiotics.

DISCUSSION

This study utilised the optimal design for an *H pylori* eradication study which is a randomised, investigator-blind, controlled design. We were stringent in our definition of eradication as we used three test methods – histology, culture, 13C-urea breath test. *H pylori* was considered eradicated if all three tests were unable to detect it. In contrast, the recommendations regarding the definition of eradication relies on only two test methods[13] and some published studies only use one method.[8, 14] In addition to an efficacy analysis, we have also analysed our data on an intention-to-treat basis to avoid over-estimating the expected success of treatment used in routine clinical practice. This aspect has been neglected in many previous studies.[7] Our conclusions were the same regardless of the method of analysis.

At present it is uncertain which factor is more important for antimicrobial therapies using omeprazole-pH or antimicrobial activity. Omeprazole has intrinsic *in vitro* antimicrobial activity[15, 16] and may also improve the antimicrobial action of the co-administered acid-sensitive antibiotics when the intragastric pH approaches 7.[17, 18] We found that monotherapy with omeprazole did not eradicate *H pylori*, confirming previous reports that omeprazole alone merely suppresses *H pylori* but does not eradicate it.[19]

The eradication rates achieved in this study were low compared to some previous similar studies. The eradication rates of ranitidine 1200 mg with amoxycillin plus metronidazole, and omeprazole 20 mg with the same antibiotics were 44% and 32% respectively. One group has found that the combination of omeprazole 40 mg daily with amoxycillin and metronidazole for 14 days gave an overall eradication rate of 91% but only 47% with metronidazole-resistant strains.[20] As the majority of our patients had metronidazole resistance, our results are similar to this group's eradication rates in those with metronidazole resistance. The only previous controlled randomised trial using ranitidine 300 mg daily in combination with amoxycillin and metronidazole for 10 days achieved an eradication rate of 89% which is comparable to that of bismuth triple therapy.[10] However their incidence of metronidazole resistance was low (11%) which could explain why they achieved higher eradication rates than us. Our eradication rate with omeprazole 20 mg daily and clarithromycin was low at 27% compared to previous studies which have found eradication rates of 63 to 80%.[8, 9, 21, 22] This could be explained by the low dose of omeprazole used in our study in contrast to omeprazole 40 mg daily which has been used in the other studies.

Although there may be a trend towards higher eradication rates in the ranitidine, amoxycillin and metronidazole group compared to omeprazole, amoxycillin and metronidazole (44% versus 32%), this lacked statistical significance because of the rather small sample size. However a study with the power to show clearly that a 12% difference was truly present or absent would have required a prohibitively high number of 400 subjects (power 80%).

Several other factors affect *H pylori* eradication. Compliance is important as eradication is low with poor compliance.[23, 24] The compliance of our patients was good, ranging from 92 to 97% and it would therefore seem unlikely that this factor would account for the low eradication rates in this study. Metronidazole resistance is associated with a marked reduction in eradication rates. We found an unexpectedly high prevalence of metronidazole resistance (58%) in this group of

patients. In comparison, the overall prevalence of metronidazole resistance in Europe is 28% with figures ranging from 7 to 49%.[25] This is the most likely explanation for the low eradication rates achieved with our regimens of metronidazole with amoxycillin and ranitidine or omeprazole. The reasons for the high prevalence of metronidazole resistance are uncertain. It could be speculated that there is a high usage of metronidazole in this community. Eradication rates increase with the total daily dose of omeprazole in combination with amoxycillin[7] and it may be that the low dose of omeprazole used in our study could have influenced the low eradication rates. The reason we used a low dose of omeprazole was to try to achieve comparable acid suppression with high dose ranitidine.

The frequency of side-effects found in this study (11%) is lower than that of triple therapy which includes bismuth, where the overall frequency of side-effects is 32%.[7] Our results are more comparable to the reported frequency of side-effects with omeprazole plus amoxycillin which is 11%. However the side-effects associated with our regimens appear to be more severe than bismuth triple therapy or omeprazole plus amoxycillin, as 9% withdrew from our study in consequence of side-effects compared to about 4% and 2% for the latter two regimens.[7]

Using the doses outlined in our study, a two-week regimen of omeprazole 20 mg daily plus amoxycillin and metronidazole would have cost £23.79 and ranitidine 1200 mg daily plus amoxycillin and metronidazole £56.25 (prices from British National Formulary, number 28, 1994). Thus using high dose ranitidine plus amoxycillin and metronidazole to eradicate *H pylori* does not give any definite cost/benefit advantage compared to low dose omeprazole with the same antibiotics. The most expensive regimen in this study was omeprazole with clarithromycin which cost £73.26.

In conclusion, *H pylori* eradication rates using high dose ranitidine plus amoxycillin and metronidazole may be similar to that of omeprazole in combination with the same antibiotics or clarithromycin. Eradication rates were probably low due to a high incidence of metronidazole resistance. The eradication rate was higher in metronidazole sensitive patients. Prior to using metronidazole-based regimens, the local metronidazole resistance rates should be determined to ensure that efficacy is not compromised. Even if ranitidine plus amoxycillin and metronidazole had higher eradication rates than omeprazole with the same antibiotics (12% difference) undetected by the small sample size, the former regimen would still not have been as cost effective as the latter, and would have involved taking a larger number of tablets.

ACKNOWLEDGEMENTS

We are grateful to Dr Chris Patterson from the Department of Epidemiology and Public Health Medicine for advice on statistical analysis, Dr Michael Callender, Consultant Physician, for help with subject recruitment and Mr Barney O'Loughlin from the Department of Microbiology for performing the cultures for *H pylori*.

REFERENCES

1. NIH Consensus Development Panel on *Helicobacter pylori* in Peptic Ulcer Disease. *Helicobacter pylori* in Peptic Ulcer Disease. *JAMA* 1994; **272**: 65-9.
2. Tytgat G N J. Review article: Treatments that impact favourably upon the eradication of *H pylori* and ulcer recurrence. *Aliment Pharmacol Ther* 1994; **8**: 359-68.
3. Chung S C, Sung J Y, Hosking S W, et al. One week therapy for *H pylori* eradication: follow-up study of a randomized trial at one year after treatment. *Gastroenterology* 1993; **104**: Suppl. A56 (Abstract).
4. Graham D Y, Hepps K S., Ramirez F C, Lew G M, Saeed Z A. Treatment of *Helicobacter pylori* reduces the rate of rebleeding in peptic ulcer disease. *Scand J Gastroenterol* 1993; **28**: 939-42.
5. Labenz J & Borsch G. Role of *H pylori* eradication in the prevention of peptic ulcer bleeding relapse. Proceedings of the II United European Gastroenterology Week, Barcelona, 1993: A96 (abstract)
6. Rokkas T, Mavrogeorgis A, Rallis E, Giannikos N. *Helicobacter pylori* eradication reduces the possibility of rebleeding in peptic ulcer disease. Proceedings of the II United European Gastroenterology Week, Barcelona, 1993: A3 (Abstract).
7. Penston J G. *H pylori* eradication – understandable caution but no excuse for inertia. *Aliment Pharmacol Ther* 1994; **8**: 369 - 89.
8. Logan R P H, Gummett P A, Hegarty B T, Walker M W, Baron J H, Misiewicz J J. Clarithromycin and omeprazole for *Helicobacter pylori* (Letter). *Lancet* 1992; **340**: 239.
9. Logan R P H, Bardhan K D, Celestin L R, Theodossi A, Palmer K, Reed P I for the BHURG study. Clarithromycin (CL) and omeprazole (OM) in the prevention of duodenal ulcer (DU) recurrence and eradication of *H pylori* (Hp). *Am J Gastroenterol* 1994; **89**: 1378 (Abstract).

10. Hentschel E, Brandstatter G, Dragosics B, Hirschl A M, Nemec H, Schutze K, Taufer M, Wurzer H. Effect of ranitidine and amoxicillin plus metronidazole on the eradication of *Helicobacte Pylori* and the recurrence of duodenal ulcer. *N Engl J Med* 1993; **328**: 308-12.

11. Labenz J, Gyenes E, Ruhl G H, Börsch G. Amoxicillin plus omeprazole versus triple therapy for eradication of *Helicobacter pylori* in duodenal ulcer disease: a prospective, randomized, and controlled study. *Gut* 1993: **34**: 1167-70.

12. Logan R P H. Detection of *Helicobacter pylori* by the 13C-urea breath test. In: Rathbone B J, Heatley R V, eds. *Helicobacter pylori* and gastroduodenal disease. Blackwell Scientific Publications, London, 1992; 88-106.

13. Korman M G, Marks I N, Hunt R H, Axon A, Blaser M J, McCarthy D M, Tytgat G N J. *Helicobacter pylori*: a workshop review. *Eur J Gastroenterol Hepatol* 1993; **5**: 963-7.

14. Peterson W L, Graham D Y, Marshall B, Blaser M J, Genta R M, Kleiln P D, Stratton C W, Drnec J, Prokocimer P, Siepman N. Clarithromycin as monotherapy for eradication of *Helicobacter pylori*: a randomized, double blind trial. *Am J Gastroenterol* 1993; **88**: 1860-4.

15. Suerbaum S, Leying H, Klemm K, Opferkuch W. Antibacterial activity of pantoprazole and omeprazole against *Helicobacter pylori*. *Eur J Clin Microbiol Infect Dis* 1991; **10**: 92-3 (Letter).

16. Bugnoli M, Bayeli P F, Rappuoli R, Pennatini C, Figura N, Crabtree J E. Inhibition of *Helicobacter pylori* urease by omeprazole. *Eur J Gastroenterol Hepatol* 1993; **5**: 683-5.

17. Paulsen O, Höglund P, Walder M. No effect of omeprazole-induced hypoacidity on the bioavailability of amoxycillin or bacampicillin. *Scand J Infect Dis* 1989; **21**: 219-23.

18. Goodwin C S, McNulty C A M. Bacteriological and pharmacological basis for the treatment of *Helicobacter pylori* infection. In: Rathbone B J, Heatley R V (eds). *Helicobacter pylori* and Gastroduodenal Disease, Blackwell Scientific Publications, London, 1992; 224-31.

19. Bayerdorffer E, Mannes G A, Sommer A, et al. High dose omeprazole treatment combined with amoxicillin eradicates *Helicobacter pylori*. *Eur J Gastroenterol Hepatol* 1992; **4**: 697-702.

20. Bell G D, Powell K U, Burridge S M, Bowden A N, Rameh B, Bolton G, Purser K, Harrison G, Brown C, Gant P W, Jones P H, Trowell J E. *Helicobacter pylori* eradication: efficacy and side effect profile of a combination of omeprazole, amoxycillin and metronidazole compared with four alternative regimens. *Q J Med* 1993; **86**: 743-50.

21. Schaufelberger H D, Logan R P H, Gummett P A. The effect of patients compliance on Helicobacter. Proceedings Digestive Disease Week, Barcelona 1993, A-104.

22. Greaves R G, Cayla R, Mendelson M G. Omeprazole versus clarithromycin and omeprazole for eradication of Hp. Proceedings Digestive Disease Week, Barcelona 1993, A-101.

23. Graham D Y, Lew G M, Klein P D, et al. Effect of treatment of *Helicobacter pylori* infection on the long-term recurrence of gastric or duodenal ulcer. a randomized, controlled study. *Ann Int Med* 1992; **116**: 705-8.

24. Cutler A F, Schubert T T. Patient factors affecting *Helicobacter pylori* eradication with triple therapy. *Am J Gastroenterol* 1993; **88**: 505-9.

25. European Study Group on Antibiotic Susceptibility of *Helicobacter pylori*. Results of a multicentre European survey in 1991 of metronidazole resistance in *Helicobacter pylori*. *Eur J Clin microbiol Infect Dis* 1992; **11**: 777-81.

The Ulster Medical Journal, Volume 65, No. 2, pp. 137-141, November 1996.

A comparison of intra-arterial digital subtraction angiography with doppler sonography in the assessment of carotid arterial stenosis

P K Ellis, B E Kelly, D Bennett, E M McIlrath

Accepted September 1996

SUMMARY

A comparison is made of the use of selective intra-arterial digital subtraction angiography and doppler sonography in the assessment of disease in 206 carotid arteries. Maximal stenoses in each of the internal, external and common carotid arteries were recorded and compared using both modalities. In 93% of cases, arteries reported as normal ultrasonically were also found to be normal on angiography. However, agreement between the modalities in the assessment of severe stenoses was rather less at 79%. Overall agreement between the two modalities was good using statistical analysis (weighted Kappa). It is our view that ultrasound is reliable in normal vessels, but where significant disease is present the rate of error between the two modalities is too high to warrant omission of angiography.

INTRODUCTION

With the advance in ultrasound technology there has been recent speculation that angiography is not always necessary prior to endarterectomy.[1] In this study we compare the maximal stenosis measurements (by area) recorded by intra-arterial digital subtraction angiography (DSA) and doppler sonography in each of the common, internal and external carotid arteries. We also aim to draw conclusions as to the role of each modality in the diagnosis of carotid artery disease.

METHODS

This retrospective study consisted of 103 patients who underwent both selective carotid arteriography and doppler sonography during 1993.

The carotid arteriography was performed in a dedicated angiographic suite using digital subtraction facilities (Polytron-Siemens, Erlangen, Germany). In all cases a 5 French intra-arterial catheter was introduced via a femoral artery and a single 35 degree, left anterior oblique (LAO) view of the aortic arch was obtained to visualise the origins of the great vessels. Using a 5 French headhunter (Cook) or 5 French sidewinder (Cordis) catheter both common carotid origins were selected and images obtained of the common carotid artery, its bifurcation, the internal carotid and the external carotid arteries. Our standard protocol comprised a single lateral projection of each carotid artery with a 35 degree LAO arch projection. However, where necessary, additional 45 degree oblique and posteroanterior (PA) views were obtained. The region of maximum stenosis was identified in each of the common, internal and external carotid arteries and calculations obtained from aboard computer software (Siemens, Erlangen, Germany). In three patients it proved impossible to selectively

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

P K Ellis, MB, MRCP, FRCR, Registrar in Radiology.

B E Kelly, MB, FRCS, FRCR, FFRRCSI, Consultant Radiologist.

E M McIlrath, MB, FRCR, FFRRCSI, Consultant Radiologist.

Department of Epidemiology and Public Health, Mulhouse Building, Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA.

D Bennett, BSc(Hons) Msc, Lecturer in Medical Statistics.

Correspondence to Dr Ellis.

cannulate the left common carotid artery and in these cases stenosis measurements were obtained using the non-selective arch projection to visualise the left bifurcation. All examinations were either performed or supervised by a consultant radiologist.

The doppler sonography examinations were performed using an Ultramark 9 scanner (Advanced Technical Laboratories, California, USA). Each vessel was visualised in the transverse and longitudinal plane, and doppler spectra were obtained. The doppler frequency used was 3 MHz and the pulse repetition frequency (PRF) was 3.8 KHz. The scanning angle used was <68 degrees in all cases. Real time B-scan images were obtained of the common, internal and external carotid arteries and maximal stenosis measurements were inferred from the doppler spectra by Fast Fourier Transformation of data by computer software. No reference to plaque morphology was considered. The examinations were performed by experienced vascular sonographers in a dedicated vascular laboratory setting.

The Kappa statistic was used to assess agreement between the categorisation schemes using sonography and DSA. It has a maximum of one when agreement is perfect, a value of zero indicates no agreement better than chance. Where the categories are ordered it is preferable to give a weight to disagreements according to the magnitude of the discrepancy. Thus in this paper a weighted Kappa statistic has been reported. Values of Kappa in the range 0.4 – 0.6 indicate moderate agreement, 0.61 – 0.80 indicate good agreement and values in the range 0.81 – 1.00 indicate very good agreement.[2]

RESULTS

The results are presented in Tables I - III with the maximum stenosis detected in each vessel placed in groups according to severity.

TABLE I

Common Carotid Artery

		DSA					
	% stenosis	*normal*	*0-15*	*16-40*	*41-70*	*71-99*	*occluded*
ultrasound	normal	104	0	0	0	0	0
	0-15	38	14	1	0	0	0
	16-40	14	3	7	0	0	0
	41-70	5	1	2	8	1	0
	71-99	0	0	0	2	4	1
	OCC	0	0	0	0	0	1

Total = 206 Arteries

Weighted Kappa = 0.579 (95% CI = 0.48, 0.673)

TABLE II

Internal Carotid Artery

		DSA					
	% stenosis	*normal*	*0-15*	*16-40*	*41-70*	*71-99*	*occluded*
ultrasound	normal	62	5	4	2	0	0
	0-15	3	11	1	2	0	0
	16-40	4	3	13	3	<u>2</u>	0
	41-70	0	0	4	14	3	0
	71-99	0	0	3	2	42	<u>6</u>
	OCC	0	<u>1</u>	0	<u>1</u>	0	9

Total = 206 Arteries. 6 not seen on ultrasound

Weighted Kappa = 0.819 (95% CI = 0.770, 0.869)

(underlined = a particularly surprising result)

The figures in Table I show that in the common carotid artery there was reasonable agreement between the two modalities with a weighted Kappa of 0.579 (95% CI = 0.486, 0.673). It is interesting that all 104 cases by ultrasound described as normal were also found to be normal angiographically. However in 47 cases (23%), mild to moderate disease revealed by ultrasound was described as normal on angiography.

Table II demonstrates the results obtained from the internal carotid artery. Again, good agreement between DSA and doppler sonography was obtained with a weighted Kappa of 0.819 (95% CI = 0.770, 0.869). Of 73 cases described as normal by ultrasound 62 were also passed as normal by DSA. None of the remaining 11 cases had severe disease (greater than 70% stenosis angiographically). Perhaps the most important indicators are those that place the patients in a group with severe disease (greater than 70% stenosis) that would suggest endarterectomy as a beneficial procedure for management (in symptomatic cases). Of 47 cases of severe disease detected angiographically, 42 were similarly described on ultrasound. The remaining 5 (or 12%) were placed in a group of lower severity. On the other hand, of 53 cases of severe disease detected on ultrasound, 42 were similarly described on DSA. Six of these patients demonstrated an occlusion on DSA and five were placed in groups of lower severity. Fifteen complete occlusions were reported on DSA of which nine were seen on ultrasound, the remaining six were reported as severe stenoses (70 - 99%). A total of six internal carotid arteries were not seen on ultrasound.

Table III demonstrates the results obtained from the external carotid artery. DSA and ultrasound placed patients in the same group of disease severity in 80% of cases. There was good reciprocity in those patients described as normal: 128 cases reported as normal on angiography compared with 116 cases (or 91%) on ultrasound. There was less close agreement in the detection of occlusion with only two out of 6 occlusions reported on DSA being detected on ultrasound. Overall agreement between the two modalities was good with a weighted Kappa of 0.724 (95% CI = 0.631, 0.818).

DISCUSSION

When taken as a whole intra-arterial digital subtraction angiography (DSA) and ultrasound agree on the severity of stenosis in just over seventy percent of cases and are within one grade of each other in ninety percent of cases. It is more interesting, however, to look at areas where discrepancies occur. One such area is in the detection of mild disease. Colquhoun et al[3] concluded that ultrasound was more sensitive in the detection of mild disease than intravenous digital subtraction angiography; we have found this also to be true of intra-arterial DSA, with 44% of lesions estimated at less than 40% stenosis on ultrasound reported as normal on angiography Ultrasound also reliably detects a normal vessel with 93% of cases reported as normal on ultrasound giving a similar result on DSA. Zierler et al[4] found that a normal doppler sonographic examination predicted a benign clinical outcome without operation, confirming the validity of using ultrasound as a screening procedure to

TABLE III

External Carotid Artery

		DSA			
	% stenosis	*normal*	*0-50*	*51-99*	*occluded*
	normal	116	4	<u>5</u>	<u>1</u>
	0-50	9	21	5	<u>1</u>
ultrasound	51-99	<u>3</u>	3	25	2
	OCC	0	0	0	2

Total = 206 Arteries. 9 not seen on ultrasound
Weighted Kappa = 0.724 (95% CI = 0.631, 0.818)
(underlined = a particularly surprising result)

detect those patients without significant carotid disease.

Of most critical interest are significant stenoses (greater than 70%) particularly of the internal carotid artery. Of 47 severe stenoses reported on DSA, 42 (or 89%) were similarly outlined on ultrasound. Of 53 severe stenoses reported on ultrasound, 42 (or 79%) were also similarly grouped on DSA. Poindexter et al[5] in a study of 238 cases felt that the error rate in this clinically significant group was too high to manage these patients by ultrasound alone. On the other hand Hill et al[1] in a study of 101 patients concluded that a preoperative arteriogram is generally not necessary if a duplex scan is performed.

Farmilo et al have expressed the view that routine angiography is unnecessary in selected patients but that a suspected occlusion should be confirmed by angiography.[6] Our results would support this opinion with a rate of agreement of just over 50% on the finding of occlusion on ultrasound and DSA. However, we conclude that the rate of error in those patients with significant stenoses is also too high to warrant management decisions on the basis of an ultrasound examination alone.

In this study we did not analyse plaque surface morphology. Previous studies have demonstrated that ulceration is more likely to be found in symptomatic patients and that plaque morphology as well as stenosis severity should be considered when deciding management.[7] Steinke et al found a 70 % agreement in detection of plaque ulceration between angiography and ultrasound; however, no haemodynamic patterns successfully predicted those patients who were more likely to be symptomatic.[7] It is clear that ultrasound has a leading role to play in the definition of plaque morphology and its clinical consequences and in this respect it has clear advantage over angiography.

Inadequate visualisation of the internal carotid artery occurred in six cases of this study. Recently work by Meents et al has attempted to address this problem.[8] Twenty-nine cases with insufficient signal intensity, mainly due to dorso-medial origin of the internal carotid artery, were contrast-enhanced with galactose microspheres (SHU 508A, Schering, Berlin). In all cases signal intensity increased and no complications were reported. Galactose microspheres increase the echogenicity of blood by trapping small volumes of air, thus increasing the visibility of vessels.

Recently attention has focused on the comparison of magnetic resonance angiography (MRA) with conventional angiography and duplex scanning. Toh et al described 70% agreement between measurements reported on MRA and those on conventional angiography.[9] Riles et al found reasonable correlation except in the detection of occlusion, where MRA tended to overread angiographically patent vessels as complete occlusions.[10] With the increasing availability of magnetic resonance imaging the technique of MRA of the extracranial carotid vessels will no doubt assume a greater role. However, limitations of cost, availability and safety with regard to metallic surgical clips ensure that doppler sonography and angiography will have a dominant role for some time to come.

In conclusion our results suggest that doppler sonography is extremely reliable in the detection of normal and moderately diseased vessels and is therefore a good first line investigation for patients with suspected carotid disease. Its role in post-operative endarterectomy follow-up is also well described.[11] Ultrasound also has a leading role in the detection of plaque morphology. However, with lesions above 70% stenosis, error rates between the modalities are sufficiently high to require angiography as part of the imaging protocol.

ACKNOWLEDGEMENT

The authors would like to thank Mr A A B Barros D'Sa, Mr J H Hood and the Vascular Laboratory, Royal Victoria Hospital for their help in this study.

REFERENCES

1. Hill J C, Carbonneau K, Baliga P K et al. Safe extracranial vascular evaluation and surgery without preoperative arteriography. *Ann Vasc Surg* 1990; **4**: 34-8.
2. Landis J R, Koch G G. The measurement of observer agreement for cateorical data. *Biometrics* 1977, **33**: 159-74.
3. Colquhoun I, Oates C P, Martin K et al. The assessment of carotid and vertebrae arteries: a comparison of CFM duplex ultrasound with intravenous digital subtraction angiography. *Br J Radiol* 1992; **65**: 1069-74.
4. Zierler R E, Kohler T R, Strandness D E Jr. Duplex scanning of normal or minimally diseased carotid arteries: correlation with arteriography and clinical outcome. *J Vasc Surg* 1990; **12**: 447-55.

5. Poindexter J M Jr, Shah P M, Clauss R H, Babu S C. The clinical utility of carotid duplex scanning. *J Cardiovasc Surg* 1991; **32**: 64-8.
6. Farmilo R W, Scott D J, Cole S E et al. Role of duplex scanning in the selection of patients for carotid endarterectomy. *Br J Surg* 1990; **77**: 388-90.
7. Steinke W, Hennerici M, Rautenberg W et al. Symptomatic and asymptomatic high-grade carotid stenoses in Doppler colour-flow imaging. *Neurology* 1992; **42**: 131-8.
8. Meents H, Burkand A. Contrast-enhanced colour duplex sonography of carotid arteries. *Europ Radiol* 1994; **4**: 533-7.
9. Toh K H, Tan K P. Comparison of accuracy of magnetic resonance angiogrraphy with conventional angiography: a report of 45 cases. *Ann Acad Med, Singapore* 1993; **22**: 742-8.
10. Riles T S, Eidelman E M, Litt A W et al. Comparison of magnetic resonance angiography conventional angiography and duplex scanning. *Stroke* 1992; **23**: 341-6.
11. Maiuri F, Gallicchio B, Iaconnetta G et al. The role of real time B-mode ultrasonography in the follow-up of patients submitted to carotid endarterectomy. *J Neurosurg Sci* 1992; **36**: 73-7.

The Ulster Medical Journal, Volume 65, No. 2, pp. 142-144, November 1996.

Re-admission of elderly patients after in-patient rehabilitation

Janet Haines-Wood, D H Gilmore, T R O Beringer

SUMMARY

The re-admission rates of a cohort of 97 elderly patients discharged from hospital were ascertained. The overall re-admission rate at 30 days was 15%, at 90 days 24% and at 180 days, 30%. On 4 occasions (9%) re-admission was deemed avoidable by the general practitioner. Deterioration of existing disease accounted for 16 (36%) and a new medical event for 22 (49%) re-admissions.

INTRODUCTION

Re-admission rates may be used as a measure of the effectiveness of hospital treatment, and are increasingly scrutinised by purchasing authorities. Rates of re-admission to hospital of elderly patients vary widely and are likely in part to reflect differences in case-mix and dependency, in addition to efficacy of clinical care. Reported re-admission rates include 15.1% at 28 days from North East Thames,[1] 28% at 3 months in Edinburgh,[2] 38% at 6 months in London[3] and 19.3% at one year from Belfast.[4] As the lengths of inpatient stay reduce, scrutiny and monitoring of re-admission are increasingly relevant, particularly with the growing numbers of elderly patients requiring acute hospital care. As patients in Belfast are often re-admitted to different units or hospitals, current record systems are unlinked and do not provide a complete record of re-admissions. This may result in a falsely low perception amongst hospital staff of true re-admission rates.

It was considered important therefore to establish current re-admission rates from a rehabilitation ward for elderly patients for three reasons. Firstly to provide hospital staff with a complete record of the true re-admission rate, secondly to allow future changes in the rate of re-admission to be compared with current rates, and thirdly to enable the proportion of admissions deemed avoidable to be measured using a classification scheme previously proposed.[5]

METHODS

All elderly patients discharged from a 24-bedded rehabilitation ward in Musgrave Park Hospital in Belfast over a 6-month period were included in the study. To ascertain the number of patients re-admitted, the hospitals they were admitted to and the circumstances of re-admission, information was sought from the patients' general practitioner. A questionnaire was devised and sent to general practitioners after an interval of six months requesting details of hospital re-admissions, and asking the general practitioners to adjudge, using the classification scheme proposed by Clarke,[5] whether re-admission was avoidable or unavoidable. Avoidable reasons included (a) recurrence or continuation of disorder leading to first admission, (b) recognised avoidable complication or (c) re-admission for social or psychological reason within control of hospital services. Unavoidable reasons included (a) chronic or relapsing disorder, (b) re-admission for social or psychological reason probably beyond control of hospital services or (c) completely different diagnosis from previous admission. The opinion of the general practitioners regarding need for re-admission was sought to provide a primary care perspective rather than assessment by hospital staff. Additional information regarding outpatient therapy, pre-discharge home visits and receipt of social services support was obtained from hospital records.

Meadowlands, Care of the Elderly Unit, Musgrave Park Hospital, Belfast BT9 7JB.

Janet Haines-Wood, Clinical Audit Co-ordinator.

David H Gilmore, MB, FRCP, Consultant Physician.

Timothy R O Beringer, MD, FRCP, FRCPI, Consultant Physician.

Correspondence to Dr Beringer.

TABLE

Demographic details of subjects re-admitted vs not re-admitted

	Not re-admitted	*Re-admitted*
Number of subjects	51	33
Male : Female %	33:65%	40:60%
Mean Age	82 years	81 years
Number of deaths (%) at 180 days	11(22%)	4(12%)
Living alone	19(37%)	12(37%)
Receipt of social services support	30(59%)	20(61%)
Occupational therapy pre-discharge home visit	11(22%)	8(24%)
Mean (median) length of hospital stay in days	31(17)	30(18)

RESULTS

A total of 97 patients were entered in the study and responses obtained from general practitioners for 84 (87%) patients (Table). A total of 33 (39%) were re-admitted to hospital and 15 (19%) died during the 6-month follow up period. A second re-admission occurred in nine subjects during the study period and three patients had a third re-admission, making a total of 45 re-admissions. The overall re-admission rate at 30 days was 15%, at 90 days 24% and at 180 days 30%. Of the 33 patients re-admitted, four (12%) died during the re-admission episode, with the earliest death occurring 53 days after initial hospital discharge. On four occasions (9%) re-admission was deemed avoidable by the general practitioner on account of drug-induced bradycardia, complications of lung carcinoma and recurrence of anaemia and diarrhoea. Of the remainder, re-admission was attributed to deterioration of existing disease in 16 (36%) and to a new medical event in 22 (49%), with unavoidable factors including chest infection, chest pain, cholecystitis, fracture, hyperthyroidism, melaena, oesophageal stricture and stroke.

DISCUSSION

This study demonstrates a high rate of re-admission to hospital of elderly patients, with 15% at 30 days and 30% at 180 days. The higher proportion of males re-admitted has been described in previous studies[5,6,7] and may reflect the increased likelihood of highly dependent males returning home to be supported by spouses, a situation often denied to females due to the previous death of their husbands.

The rates of re-admission of 15% at 30 days and 24% at 90 days recorded in this study are equivalent to that of 15.1% at 28 days reported from North East Thames[1] and 23% at three months in Middlesex,[8] but significantly higher than those previously reported in Belfast.[4] The mean age of patients was similar in the two studies, but it is probable that the average length of hospital stay of 31 (median 18) days in this study is considerably shorter than that current in 1985. The likely relationship of length of hospital stay to re-admission rate indicates that caution is necessary in the interpretation of re-admission rates in isolation from other variables. One such additional variable that was not obtained in this study was severity of illness.

The observed rate of 9% for avoidable re-admissions indicates some opportunity to reduce re-admission rates, but in the remaining 91% no avoidable factors could be identified. While strengthening community services may reduce hospital re-admissions,[8] there is a need to ensure adequate provision of hospital rehabilitative care for elderly patients in view of the projected demographic rise in numbers of elderly people in the population.

Careful monitoring of length of hospital stay allied to re-admission rates will assist in the provision of hospital services as well as providing a marker for the quality and effectiveness of medical care for elderly people, but only if avoidable unplanned re-admissions are accurately recorded. Establishing our current re-admission rate will enable future comparisons to be made as hospital length of stay reduces further. The

implementation of medical record linkage would greatly assist the gathering of such information in Belfast.

REFERENCES

1. Chambers M, Clarke A. Measuring re-admission rates. *Br Med J* 1990; **301**: 1134-6.
2. Tierney A J, Worth A. Readmission of elderly patients to hospital. *Age Ageing* 1995; **24**: 163-6.
3. Victor C, Jefferies S. Are readmission rates a useful indication of outcome? *Geriatric Med* 1990; March: 19-20.
4. Kelly J F, McDowell H, Crawford V, Stout R W. Re-admission to a geriatric medical unit: is prevention possible? *Ageing Clin Exp Res* 1992; **4**: 61-7.
5. Clarke A. Are re-admissions avoidable? *Br Med J* 1990; **301**: 1136-8.
6. Graham H, Livesley B. Can re-admissions to a geriatric medical unit be prevented? *Lancet* 1983; **1**: 404-6.
7. Fethke C C, Smith I M, Johnson N. "Risk" factors affecting re-admission of the elderly into the health care system. *Med Care* 1986; **24**: 429-37.
8. Townsend J, Piper M, Frank A O, Dyer S, North W R S, Meade T W. Reduction in hospital re-admission stay of elderly patients by a community based hospital discharge scheme: a randomised controlled trial. *Br Med J* 1988; **297**: 544-7.

The Ulster Medical Journal, Volume 65, No. 2, pp. 145-148, November 1996.

Clinical trial comparing artificial rupture of membranes plus oral PGE_2 tablets versus artificial rupture of membranes plus intravenous oxytocin for induction of labour in primigravid patients at term

S A Nassief, P McFaul, A Rane

Accepted: 1 May 1996

SUMMARY

We report the results of a pilot study conducted to compare the efficacy of oral prostaglandin E_2 versus intravenous oxytocin in inducing labour after lower amniotomy in 20 primigravid patients at term.

The results suggest no significant differences in the performance of each group for the induction to delivery interval, the mode of delivery, the Apgar score at five minutes or for third stage abnormalities. However, the use of oral PGE_2 allows the patient unrestricted mobility and avoids the discomfort of IV infusions.

INTRODUCTION

The secret of successful induction of labour lies in replicating as accurately as possible the physiological processes of spontaneous labour. In the presence of a favourable cervix, a small dose of prostaglandin E_2 (PGE_2) is often enough to induce a labour very similar to spontaneous labour. This method of induction is also associated with a decrease in postpartum haemorrhage and neonatal jaundice.[1]

The timing of amniotomy is crucial. If performed too early, before the cervix is ripe, it may lead to complications for both mother and fetus. If left too late, we may lose the advantage of its uterine sensitising influence and its augmentatory effect.

Women are requesting less interference with labour and, in particular, as little restriction of mobility as possible during its early stages. A combination of oral PGE_2 and a judiciously timed amniotomy for induction may allow such mobility and may offer a non-invasive alternative to intravenous oxytocin.

PATIENTS AND METHODS

Ethical committee approval of the protocol was obtained and informed written consent obtained from all patients. Twenty patients were recruited. They were all nulliparous at term, with an indication for induction of labour and in the age group 18 to 35 years. Patients with major systemic illness, such as severe bronchial asthma and cardiac disease, and those with existing contraindications to the use of PGE_2 and oxytocin were excluded from the study.

Patients were eligible for the study if, on vaginal examination, the Bishop score was greater than 4.[2]

Each of the twenty patients had low amniotomy (fore water rupture) performed under aseptic conditions using a disposable amnihook. None of the twenty patients were experiencing uterine contractions at the time of artificial rupture of membranes (ARM). They were then randomly

West Dorset Hospital, Damers Road, Dorchester DT1 2JY.

S A Nassief, MRCOG, Registrar.

Belfast City Hospital, Belfast BT9 7AB.

P McFaul, MD, MRCOG, Consultant.

A Rane, MRCOG, FRCS, Senior Registrar.

Correspondence to: Dr McFaul

assigned to two treatment groups. Treatment was commenced within 30 minutes of ARM.

Group 1

Intravenous oxytocin (Syntocinon) was administered according to the standard labour ward regime:

Five units of Syntocinon are added to 500 ml Hartmann's solution and an IVAC pump is used to control the rate of infusion which is commenced at 5 drops per minutes. The dose is increased by 5 drops per minute every 15 minutes until regular uterine contractions are established and are occurring once every three minutes and lasting for at least 40 seconds.

Group 2

PGE_2 (Prostin oral tablets, Upjohn) was administered as an initial dose of 0.5 mg tablet, followed one hour later by 1 mg tablet, and one hour later of 1.5 mg tablet, if the patient is not in established labour. If after three doses the response was poor the options were either to give another 1.5 mg oral dose or to commence intravenous Syntocinon infusion according to the regime prescribed above.

ASSESSMENT

The Bishop score was assessed on entry to the study at the time of low amniotomy (Table I). Cervical dilatation was measured at least every two hours. The frequency, strength and duration of uterine contractions were recorded by the attending midwife, and the time required from commencement of treatment till labour was established (as defined by regular uterine contractions occurring once every three minutes and lasting for at least 40 seconds).

TABLE I

Pre-treatment characteristics (standard deviations in brackets)

	GROUP 1 Amniotomy and IV oxytocin	*GROUP 2 Amniotomy and oral PGE2*
Gestation (weeks)	40.1	40.0
Mean	(2.18)	(2.16)
Bishop score	7.0	6.1
Mean	(1.7)	(1.9)

The duration of the first, second and third stages of labour were recorded, together with the total amniotomy-delivery interval and method of delivery. Analgesic requirements, adverse effects such as vomiting, abnormal cardiotocogram, uterine hypertonus, and presence or development of meconium-stained liquor, were all reported. Apgar scores at one and five minutes and the condition of the baby on transfer from the labour ward were assessed. All maternal and fetal adverse events were carefully documented. The attending doctor and midwife were asked for their subjective assessment and the mother was questioned as to the acceptability of the treatment she had received.

The interval between amniotomy and delivery (Table II) was greater in the oral PGE_2 group, 9.8 hrs, compared with 7.5 hrs for women receiving oxytocin, although these differences were not statistically significant.

TABLE II

Outcome of induction of labour (Standard deviations in brackets)

	GROUP 1 *IV oxytoicin*	GROUP 2 *Oral PGE_2*
– Duration of first stage (hours) (Amniotomy to full cervical dilatation)		
Mean	5.73 (3.40)	7.98 (3.87)
– Duration of second stage (hours)		
Mean	1.63 (1.34)	2.62 (12.8)
– Amniotomy-delivery interval (hours)		
Mean	7.46 (3.95)	9.84 (2.75)
– Mode of delivery		
Normal delivery	7	6
Vacuum extraction	1	0
Forceps	2	2
Caesarean section		1

* 1 patient from the PGE_2 group was changed to IV oxytocin and had a normal delivery.

It was noted that patients went into established labour within one hour of starting IV oxytocin infusion, but not until the third dose of oral PGE_2 was given, ie three hours after ARM. The incidence of spontaneous and instrumental deliveries was similar in the two groups. The two Barnes-Neville forceps deliveries in the oral PGE_2 group were performed because of persistent late decelerations (with 60-90 seconds lag time) on the cardiotocogram. In the IV oxytocin group, two Barnes-Neville forceps deliveries were also performed, the first because of fetal bradycardia and the second because of persistent late decelerations. One vacuum extraction delivery was also performed in this group because of persistent left occipito-transverse position of the head. The patient who required caesarean section (in the oral PGE_2 group) progressed to full cervical dilatation but the fetal head was grossly deflexed in the occipito-posterior position at spines minus one. There were no caesarean sections in the IV oxytocin group.

Of those taking oral PGE_2, one patient developed severe nausea and vomiting after the second dose and had to be changed to IV oxytocin. (In this particular patient, prior to starting IV oxytocin infusion, vaginal examination showed that the cervix was 5-6 cm dilated and fully effaced, and the patient had spontaneous vaginal delivery 3 hours 27 minutes after starting oxytocin infusion.)

The analgesic requirements of those receiving oral PGE_2 were similar to those who had IV oxytocin. Two patients in the IV oxytocin group required epidural analgesia immediately after the oxytocin infusion was commenced. The remaining 18 patients all started with intramuscular pethidine but then requested epidural analgesia. It can be seen from Table III that the mean neonatal birthweight and Apgar scores at one and five minutes were almost the same for each treatment group.

TABLE III

Neonatal outcome

	GROUP 1 IV oxytocin	*GROUP 2 Oral PGE_2*
Number of neonates	10	10
Birthweight (grams) (mean)	3256	3299
Apgar score at 1 minute (mean)	7.9	7.7
Apgar score at 5 minutes (mean)	9.3	9.2

The midwives evaluated both treatments as equally effective in inducing labour.

Of the patients receiving oral PGE_2 tablets, 90% expressed satisfaction with this method of induction, compared with 60% of the women in the oxytocin group. The main reasons for dissatisfaction were the discomfort of the IV line and the restricted mobility in the first stage of labour.

DISCUSSION

The use of oral PGE_2 for the induction of labour has previously been reported and other workers have drawn attention to the ease of administration and increased patient acceptability of this route compared with the use of intravenous infusion. However, previous use was mostly in parous patients with spontaneous rupture of membranes.[3]

Calder et al[1] also reported that oral PGE_2 has been shown to be as effective and safe as oxytocin. Side effects mainly in the form of nausea and vomiting are rarely encountered unless the dose exceeds 1 mg/hour, and they also claimed that the method is more successful in multiparous women, with few side effects seen in this group as the majority respond to low doses.

The problem of nausea, vomiting and diarrhoea appears to be dose-related[4] and can be overcome by applying a low dose regime such as the one used in this study. Hauth et al[5] reported that only one woman vomited in a group of 50 receiving between 0.5 and 1 mg hourly. In this study, only one woman developed severe nausea and vomiting in the oral PGE_2 group and this occurred only with the higher dose of 1 mg tablet.

The mean amniotomy-delivery interval was shorter in the oxytocin group but this did not reach statistical significance (probably because women in the oxytocin group went into established labour quicker than those in the oral PGE_2 group). However, the majority of women in the oral PGE_2 group were in established labour within three hours of initiating treatment and progressed satisfactorily thereafter.

A common criticism of oral administration of oxytocic agents is the prolonged duration of action which can produce problems in patients who develop uterine hypertonus following the

ingestion of the oxytocic agent. However, there were no reported cases of uterine hypertonus in this trial and, in addition, uterine hypertonus can be reversed by urgent administration of a tocolytic, either by infusion or inhalation, to reverse the hypertonia; after an hour, normal labour can usually be allowed to continue.[6]

The women considered oral PGE_2 tablets to be highly acceptable. The most frequently expressed benefits were the ability to be mobile and not being attached to an intravenous infusion.

The midwives did not make any distinctions in the helpfulness of either treatment; this was probably due to initial lack of familiarity with the oral PGE_2 regimen. However, they soon adapted to the new procedure and commented on the simplicity of tablet administration and the fact that PGE_2 patients enjoyed greater mobility during labour.

REFERENCES

1. Calder A A, Johnston A T A. Greer I. A Prostaglandins and the induction of labour. *Curr Obstet Gynaecol* 1991; **1**: 221-8.
2. Bishop E H. Pelvic scoring for elective induction. *Obstet Gynaecol* 1964; **2**: 266-8.
3. Lange A P, Secher N J, Neilsen F H, Pedersen G T. Stimulation of labour in cases of premature rupture of membranes at or near term. *Acta Obstet Gynaecol Scand* 1981; **60**: 207-10.
4. Craft I. Amniotomy and oral prostaglanding titration for induction of labour. *Br Med J* 1972; **2**: 191-4.
5. Hauth J C, Cunningham F G, Whalley P J. Early labour initiation with oral PGE_2 after premature rupture of membranes at term. *Obstet Gynaecol* 1977; **49**: 523-6.
6. Khor P P T, Kalshekar M, Joyce M, Elder M G. Induction of labour with PGE_2 vaginal tablets. *Eur J Obstet Gynecol Reprod Biol* 1981; **11**: 313-8.

The Ulster Medical Journal, Volume 65, No. 2, pp. 149-151, November 1996.

Laparoscopic-assisted vaginal hysterectomy:
Initial experience

J H Price, S A Nassief

Accepted 27 August 1996

SUMMARY

We reviewed the charts of 36 women who had had laparoscopic-assisted vaginal hysterectomies (LAVH) at Belfast City Hospital over a 3 year period. The average operating time was 105 minutes. However, patients had a shorter duration of hospitalisation (<4 days for 96% of patients) with rapid recuperation (3.4 weeks). Complications occurred in 7 patients. One patient developed a vesico-vaginal fistula which was diagnosed post operatively and successfully repaired 5 months later. Technical difficulty was reported in one patient because of significant adhesions and poor access due to obesity. She went on to develop a pelvic abscess which was drained. Patient satisfaction with the operation was high. LAVH is an effective operation in selected cases and in experienced hands the complication rate is low. In the future it may become a valid alternative to open abdominal hysterectomy.

INTRODUCTION

Hysterectomy is one of the most frequently performed of all surgical operations. Traditionally the uterus has been removed by either the abdominal or the vaginal route. In a recent study from a single centre in Scotland, of women under the age of 35 requiring hysterectomy, 87.5% had the operation performed per abdomen.[1]

The aim of using the laparoscopic mode of access for any procedure is to avoid a large laparotomy skin incision and all the sequelae associated with such a painful and disfiguring approach. Laparoscopic hysterectomy is an alternative to abdominal, but not vaginal, hysterectomy. If a uterus can safely and easily be removed by a traditional vaginal approach, the operation should be performed in this way.

The first laparoscopic hysterectomy (LH) was reported by Reich et al in 1989[2] and an ever-growing number of variations of this technique and even radical hysterectomies have been described.[3] According to the definition by Reich et al (1989), an LH must include laparoscopic division of the uterine arteries. If the arteries are divided vaginally, the operation is designated a laparoscopically-assisted vaginal hysterectomy (LAVH). We describe the results of this operation in a series of patients treated at the Belfast City Hospital.

PATIENTS AND METHODS

Medical records of 36 women who underwent LAVH in Belfast City Hospital between 1.7.91 and 31.7.94 were reviewed. A questionnaire was sent to each patient seeking information about satisfaction with post operative analgesia, convalescent time until they felt able to return to domestic activities, the time before they returned to work and the degree of satisfaction with the operation. The average age of the women at the time of surgery was 42 years, with a range of 32-52 years. Average parity was 2.6. Indications for surgery are shown in Table 1.

Of the 36 patients, 11 had been previously sterilised laparoscopically, two patients had cholecystectomy and appendicectomy, and one patient had left salpingectomy for an ectopic pregnancy. All were performed as open technique.

Examination under anaesthesia was performed before proceeding to LAVH. There was no report of uterine descent in any of the 36 patients. It was

Belfast City Hospital, Belfast BT9 7AB.

J H Price, MD, FRCOG, Consultant.

West Dorset Hospital, Damers Road, Dorchester, DT1 1JY.

S A Nassief, MRCOG, Registrar.

Correspondence to Dr Price

TABLE I

Indication for surgery

Indication for surgery	*No. of patients*
Menorrhagia	11
Menorrhagia and dysmenorrhoea	15
Menorrhagia and pelvic pain	5
Menorrhagia, dysenorrhoea and pelvic pain	2
CIN III (Cervical Intraepithelia Neoplasia)	1
Postmenopausal bleeding	2

the opinion of the surgeon that if there was any uterine descent the patient could have been offered vaginal hysterectomy.

24 patients (66.6%) were reported to have a bulky uterus (size ranged between 8 and 14 weeks gestation). Three patients (8.3%) were reported to have an adnexal swelling.

The technique of LAVH employed was similar to that described by Raju & Auld.[4]

RESULTS

1. INTRA-OPERATIVE

The average operating time was 105 minutes, with a range of 60-150 minutes. Surgery was performed primarily by one operator; about a quarter of the procedures were done by other surgeons being supervised or during teaching workshops. It was noted that the operating time fell as experience was gained. Technical difficulty was reported in one patient mainly due to gross obesity and pelvic adhesions; she had previously had cholecystectomy and appendicectomy. In 25 cases bilateral salpingo-oöphorectomy was performed at the same time as LAVH. There were no reports of operative repair of bowel, bladder or ureter.

2. POST OPERATIVE

Three women (8.3%) had urinary tract infections which were satisfactorily treated by antibiotics. Two patients (5.5%) developed vault haematoma which manifested itself as painless vaginal bleeding five to seven days post operatively. In both cases the haematoma discharged spontaneously and no further action was required apart from prophylactic antibiotic cover. In one case the procedure was complicated by a pelvic abscess which was drained on the eighth post operative day.

One patient continued to have vaginal bleeding and dysuria three weeks post operatively. Cystoscopy was performed and showed a small vesico-vaginal fistula at the base of the bladder. An indwelling catheter was inserted for three months and successful repair of the fistula was carried out five months after LAVH.

Twenty three patients had their post operative opioid analgesia discontinued 24 hours after the operation. Four patients requested analgesia for 36 hours, while nine patients required analgesia for 48 hours after the operation.

TABLE II

Recovery Time

		Average	*No. of weeks Range*
Return to normal domestic activities	36 patients	1.5	0-4
* Return to work	14 patients	3.4	0-6

* 22 patients were housewives
* 14 patients had other work

Except for one patient who developed a pelvic abscess twenty-four patients were discharged on the third post operative day and eleven patients were discharged on the fourth post operative day.

Overall, recovery as judged by return to normal domestic activity (Table II) was fast. Thirty two patients were satisfied (Table III).

TABLE III

Satisfaction with the operation

Very satisfied	27	(75.0%)
Satisfied	5 patients	(13.8%)
Not sure	2 patients	(13.8%)
* Dissatisfied	2 patients	(5.5%)

* Bladder fistula and pelvic abscess.

In eighteen patients the histopathology report showed leiomyoma. Fourteen patients had endometriosis while five patient had dysfunctional uterine bleeding.

DISCUSSION

The main advantages of minimally invasive surgery in general, and LAVH in particular, are found in the convalescent phase. Replacing long and painful incisions with multiple small punctures results in less disfigurement, less post operative pain, shorter inpatient hospital stay and shorter convalescence.

Comparisons between the morbidity and cost of vaginal, abdominal and laparoscopic hysterectomy are needed to justify this approach. Complication rates may be similar more or less frequent, compared with open and vaginal hysterectomy.[5, 6, 10]

The laparoscopic procedure requires the acquisition of much new expensive equipment and many new technical skills, and it usually takes longer to perform than the equivalent open procedure. However, the present study has shown that this time is shortened with more experienced operators, both surgeon and ancillary operating staff. In the series of LAVH performed by the first author (31 out of the 36 cases) the operating time (from induction of anaesthetic) for the first 14 procedures ranged from 130-150 minutes, thereafter dropping to between 95-120 minutes. This finding has also been observed by others.[7, 8]

In this study, a vesico-vaginal fistula occurred in a patient (the fifth performed) at a stage before the operator had developed sufficient confidence to dissect fully the pelvic peritoneum. It occurred during dissection of the anterior pouch vaginally in a nulliparous patient with no prolapse, and a small hole was made in the midline of the base of the bladder. Unfortunately, this was not recognised during the procedure.

This highlights the importance of acquiring experience and, as also reported by other observers,[6] complications will be encountered in the learning phase. This barrier to laparoscopic surgery will diminish as trainee gynaecologists routinely learn operative laparoscopic techniques.

Detractors of the concept of laparoscopic hysterectomy argue that vaginal hysterectomy is faster, less expensive and results in a similar short hospital stay and convalescence. However, more than 80% of hysterectomies are currently performed abdominally.[9] If laparoscopic hysterectomy is added to the gynaecological armamentarium almost all hysterectomies may be done without an abdominal incision.

REFERENCES

1. El Torkey M M. Hysterectomy in patients aged 35 years and under: indications and complications. *Obstet Gynecol Today* 1991; **1**: 44-9.
2. Reich H, De Caprio J, McGilpin F. Laparoscopic hysterectomy. *J Gynaecol Surg* 1989; **5**: 213-6.
3. Querleu D, Leblanc E, Casterlain B. Laparoscopic pelvic lymphadenectomy in the staging of early carcinoma of the cervix. *Am J Obstet Gynecol* 1991; **164**: 579-81.
4. Raju K S, Auld B J. A randomised prospective study of laparoscopic vaginal hysterectomy versus abdominal hysterectomy each with bilateral salpingo-oöphorectomy. *Br J Obstet Gynaecol* 1994; **101**: 1068-71.
5. Carter J E, Bailey T S. Laparoscopic assisted vaginal hysterectomy utilising contact-tip Nd: YAG laser. *J Clin Laser Med Surg* 1993; **11**: 75-7.
6. Wood C, Maher P, Hill D, Lolatgis N. Laparovaginal hysterectomy. *Aust NZ J Obstet Gynecol* 1994; **34**: 81-4.
7. Liu CY. Laparoscopic hysterectomy: a review of 72 cases. *J Reprod Med* 1992; **37**: 351-4.
8. Phipps J H, John M, Nayak S. Comparison of laparoscopically assisted vaginal hysterectomy and bilateral salpingo-oöphorectomy with conventional abdominal hysterectomy and bilateral salpingo-oöphorectomy. *Br J Obstet Gynaecol* 1993; **100**: 698-700.
9. Vessey M P, Villard-Mackintosh L, McPherson K, Coulter A, Yeates D. The epidemiology of hysterectomy: findings in a large cohort study. *Br J Obstet Gynaecol* 1992; **99**: 402-7.
10. Reich H, McGlynn F M, Sekel L. Total laparoscopic hysterectomy. *Gynaecol Endoscopy* 1993; **2**: 59-63.

The Ulster Medical Journal, Volume 65, No. 2, pp. 152-161, November 1996.

Thomas Ferrar, MB, LRCSI (1797-1837):

The absentee professor of surgery at the Royal Belfast Academical Institution

Peter Froggatt, MD, PhD, FRCP, FRCPI, FFCM, FFOM, DPH, MRIA

SUMMARY

Thomas Ferrar was the second professor of surgery in the short-lived (1835-1849) medical school of the Royal Belfast Academical Institution. Appointed on 5 July 1836 he failed to turn up for the winter session and was accordingly discharged on 29 November. He died in Sligo in the following June aged 39.

Nothing has been written about Ferrar who survives as a mere foot-note in Belfast medical history. The events leading to his dismissal are, however, unusual, equivocal, and worth recounting. The facts suggest that the Institution was clearly justified in its action but that Ferrar emerges with some credit for a certain if misplaced high-mindedness though overshadowed by his patent derelictions.

INTRODUCTION

The board of faculty of the 'medical department' of the Royal Belfast Academical Institution (hereafter 'Inst') met for the first time on 8 October 1835.[1,2] There were five members – the 'president', James Lawson Drummond (professor of anatomy and physiology, and of botany)[3], the honorary secretary, James Drummond Marshall (professor of materia medica and pharmacy),[3] the honorary treasurer, Robert Little (professor of midwifery and diseases of women and children),[4,5] Thomas Andrews (professor of chemistry),[6,7] and John MacDonnell (professor of surgery).[8] MacDonnell soon resigned[9] on being appointed to the House of Industry and Richmond Hospital in Dublin and was replaced on 5 July 1836 by Thomas Ferrar.

Ferrar was 'deposed' on 29 November: as the history of Inst says he 'failed to put in an appearance . . . and was dismissed for neglect of duty'[10] though the Centenary Volume more diplomatically observes 'he removed to Sligo'.[11] So far as posterity is concerned[1,10,11] Ferrar simply returned to his former impeccable obscurity.

Ferrar is a shadowy and, as it has turned out, elusive figure, but he was not a wayward one. This paper examines the circumstances of his dismissal and it also completes the set of biographical sketches of the six 'professors' appointed to the Inst medical department during its first year, 1835-1836.

BIOGRAPHICAL DETAILS [12]

Antecedents

The Irish Ferrars were descendents of Nicholas Ferrar, a prosperous London merchant, who in 1626 with his widowed mother founded a religious community in the derelict hamlet of Little Gidding in Huntingdon which as an ancillary avocation carried on the 'useful' trade of binding mainly religious books.[13] William (b.1665), first of the Irish cadet line, was a captain in Schomberg's cavalry during the Williamite wars and settled in Limerick after the peace of Ryswick (1697). His son, also William (1700-1753), followed the family trade of book-binding, married a local girl (Rose Payne) and prospered.[14] His son John (1742-1804) continued the trade, likewise prospered,[15] married the mayor's daughter,[16] became the first historian of Limerick,[17] and published poems,

Peter Froggatt, MD, PhD, FRCP, FRCPI, FFCM, FFOM, DPH, MRIA, 3 Strangford Avenue, Belfast BT9 6PG. Formerly Vice-Chancellor, Queen's University Belfast.

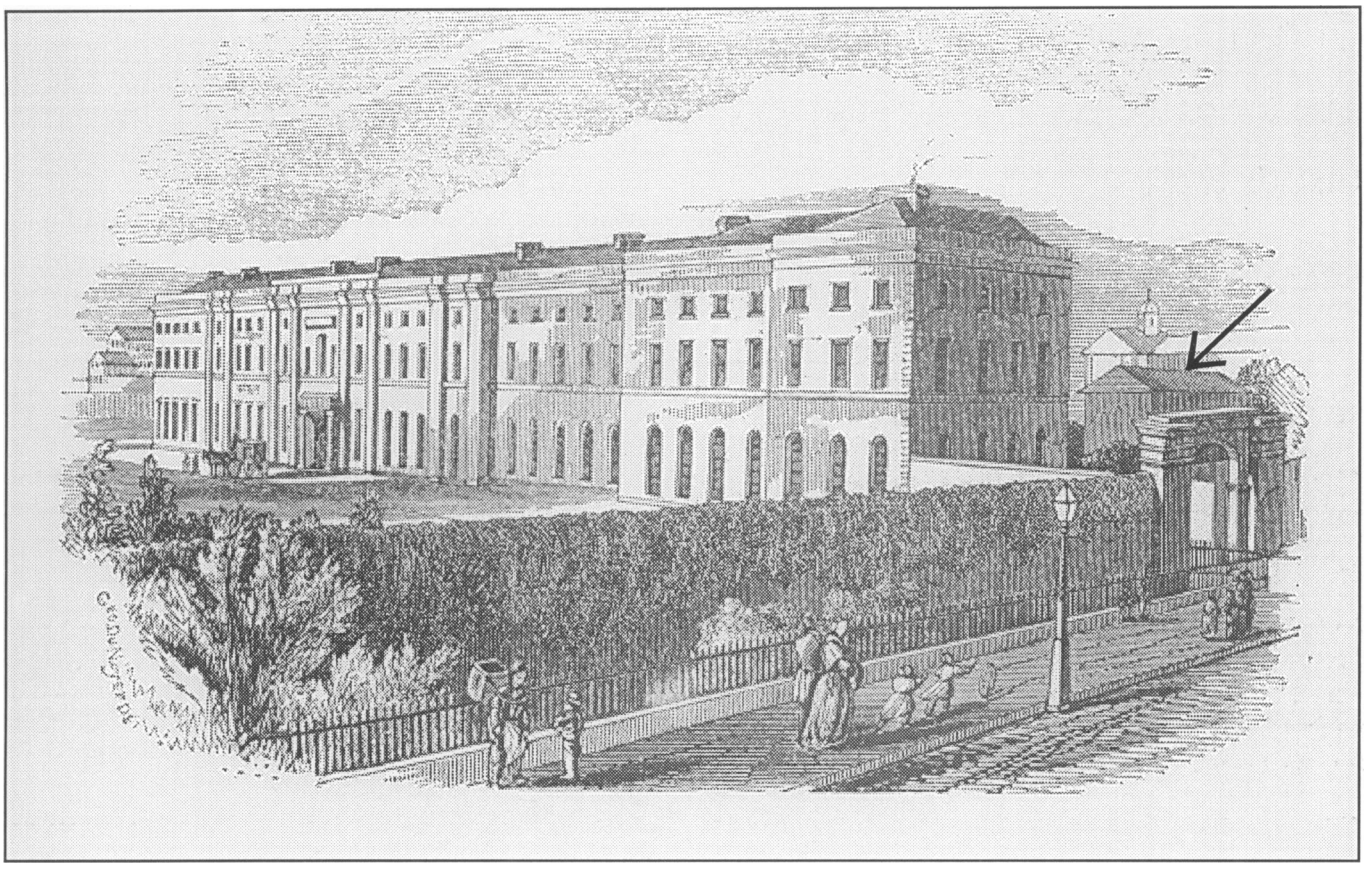


Figure The Royal Belfast Academical Institution with the three-roomed medical school (arrowed) of lecture theatre, dissecting room and museum. This building and the adjoining "botanic garden" were enclosed and separated from the main building by a brick wall. From a print of about 1840 and reproduced in: Smith, J H. Belfast and its environs with a tour of the giant's causeway. Dublin: Wm Curry, 1842, facing p.14).

social histories and topographical books.[18] His eldest son, William Hugh, the father of our subject, Thomas, was born in Limerick in 1771, married Maria Lloyd a member of a prominent local family,[19] joined the Bank of Ireland in Dublin in 1795 and in 1800 was posted to Larne as pro-collector of the customs. Concerned to further the schooling of his growing family[20] he moved to Belfast in 1809[21] and in 1816 was appointed the town's first 'magistrate of police'. He died of typhus at his residence, 83 Donegall Street, at Christmas 1826 aged 55 – 'active, upright, intelligent, and a very vigilant Magistrate . . . loyal to the King, true to his country'.[22] His wife followed him on 2 April 1850.[23]

Thomas Ferrar

Thomas, William Hugh's third son, was born in Dublin on 24 August 1797.[24] He attended the Belfast (Royal) Academy – 'Dr Bruce's Academy' – then in Donegall Street close to the family residence, and he matriculated at Trinity College Dublin on 6 November 1815 as a 'pensioner', ie. with neither the privileges of a 'fellow commoner' nor the menial obligations of a non-fee-paying 'sizar', but he did not proceed BA until the spring of 1826,[25] over ten years later! He took the MB in the summer of 1829[25] and the 'letters testimonial' of the Royal College of Surgeons in Ireland (LRCSI) on 23 July 1830.[26] This leisurely progress would have included time spent in obtaining professional class credits but he must have been more than somewhat dilatory or perhaps absent for long periods – possibly travelling adventurously like his brother Michael,[27] possibly dawdling on some *grand* or not-so-*grand tour*, possibly studying or employed elsewhere, possibly unwell. There is no way of knowing.[28]

After qualifying LRCSI Ferrar remained in Dublin for up to two years.[29] He then (in 1833) disappears from (Wilson's) *Directory*[30] but reappears for 1834 now without address, and for 1835 and 1836 is entered as 'at Sligo', the latter entry showing him as being also authorised to practise midwifery.[31] While in Sligo he visited Belfast in

connection with the chair of surgery (vacant after 19 January 1836[9]) in which he showed a close interest,[32] and was elected professor on 5 July his home address being Castle Street, Sligo.

After his dismissal (on 29 November) he disappears until a brief entry in the (Belfast) *Newsletter* for 9 June 1837 that Thomas Ferrar MD (sic.) 'second surviving son of W H Ferrar of this town' had died at Sligo on 2 June. His sole obituarist wrote briefly and somewhat tritely that, 'he was a just ornament to his profession being endowed with talents of a superior order. His death is regretted by all to whom he was known'.[33] He had no recorded attachment to any medical institution in Sligo or elsewhere.[34] He was unmarried.[12]

THE PROFESSORSHIP OF SURGERY

Ferrar's appointment

On John MacDonnell's resignation (on 19 January 1836)[9] Inst moved quickly to appoint a successor even though there were still no endowments from government for the medical chairs, the emoluments being solely the class fees of the students.[1] Ferrar at once enquired about the post[32] and his application with those of Robert Coffey and Henry Purdon was considered at a thinly attended meeting on 29 February. The election, however, was deferred; the Inst honorary secretary (Joseph Stevenson) had received a letter 'from a person who was considered by him a warm friend of the Institution . . . strongly recommending postponement'.[35] At a better attended meeting the next day the retabled motion for postponement was easily carried when a member disclosed that the unmasked correspondent had written similarly to him. The writer's reasons were not revealed but were probably the continued lack of medical professors' endowments.[36] The medical school nevertheless needed an incumbent in surgery for the 1836-7 session, and so on 23 June they agreed to re-advertise.[37]

Ferrar, Coffey and Purdon at once re-applied.[38] Twenty electors assembled on 5 July.[39] One late application (from Edward John Burton) was deleted. The first ballot gave nine votes for Coffey, seven for Ferrar, and four for Purdon. Since none had an overall majority Purdon was eliminated and the second ballot showed Ferrar ten and Coffey nine (one of the 20 electors was suddenly absent!)[39] On the face of it this was a strange albeit a narrow preference. Coffey was a respected local surgeon, had been through the accepted Belfast career ranks as medical attendant to the General Dispensary 1823-27, attending surgeon at the Fever Hospital 1826-1836, had just recently (April 1836) been elected consulting surgeon [40,41] and was a long-serving member of the hospital's management committee and of the Belfast Medical Society.[40] Ferrar on the other hand was virtually unknown and had no hospital attachment which meant that he could not have access to the General Dispensary or to the Fever Hospital wards for teaching or pupilages. Coffey had been *proxime accessit* to John MacDonnell for the chair in 1835 (Ferrar had not even applied) and within six months was to be unanimously appointed to succeed Ferrar[42] and two years later was elected 'president' of the medical faculty. Moreover, he was an MD (of Glasgow), Ferrar was only an MB (of Dublin), and Inst had a stated preference for holders of an MD because 'it is preferred . . . by the Royal Colleges' though those without it 'would not be excluded'.[43] There were undoubted factional and sectarian interests in appointments at Inst and the 'new light' Coffey was implacably opposed by the General Synod[44] (whose opinion could be made known to the electors before the vote) whereas its attitude to Ferrar (a Church of Ireland member[45]) may have been more tolerant. There is no way of confirming this supposition – only the numbers and not the identity of those voting for each candidate are recorded – but it seems likely.

Ferrar attended the faculty of medicine meetings on 1st and 19 August[46] and received the usual professor's grant (£50) for procuring 'preparations and specimens to illustrate his lectures'.[47] There seemed no reason to doubt his resolve to move to Belfast and assume his duties in time for the 1836-7 session. However, it was not to be.

Ferrar's predicament

On 16 August Ferrar wrote to Inst expressing concern that the proposed courses in the medical school had still not been recognised by the Colleges of Surgeons. These 'had to be in connection with an hospital and have the use of a museum containing surgical and anatomical preparations', and he reasonably, indeed prudently, sought some comfort on these points.[48] His letter (written from 'Belfast') was referred on 6 September to the medical faculty.[49] By this time an embryo museum was being put in place, course recognition was being energetically sought, and the former cavalry barracks in Barrack Street was in the process of being purchased by Inst to fit out

as a wholly owned 100-bed 'teaching' hospital.[1,2,50] Ferrar may not have known of these developments since he was, somewhat surprisingly, absent from all the no less than seven faculty meetings in September and October[51] and probably from Belfast as well.

On 10 October Inst publicly advertised their medical classes for the winter session 1836-7, concluding 'The lectures will be delivered in conformity with the Regulations of the Royal Colleges of Surgeons, London and Dublin'.[52] On the 17th the Inst honorary secretary, Stevenson, sought to reassure Ferrar now that the purchase of the former barracks was complete.[53] Ferrar's continued absence from faculty meetings and doubt as to his whereabouts[54] prompted the cautious Stevenson to add 'of course your presence will soon be required. This I am communicating without any order from the Boards'.[53] But Ferrar though absent from campus had not been completely *incommunicado*. He had seen the course advertisement of 10 October and considered it to be misleading, or at best ambiguous, and 'well calculated to lead astray and to cause students to suppose they could receive at [Inst] advantages of education equal to those offered by the "recognised" schools in Ireland. This however is far from the fact . . .'.[55] Much concerned he now acted high-handedly and on 29 October, only four days before the scheduled start of classes, placed a notice in the press that his lectures were adjourned 'until the completion of sound measures necessary to ensure the recognition of the Certificate of Attendance . . . as qualification available to students when candidates for the Degree or Licence granted by the different Collegiate Bodies in the United Kingdom'.[56] This notice was clearly damaging both to Inst and its fledgling medical school. Moreover, placing it was outwith Ferrar's authority.[57] Inst, gravely provoked, reacted vigorously. A board of visitors meeting was convened that same day which *inter alia* wrote to Ferrar 'who it appears is now in Sligo' requiring him to start his classes on 2 November as advertised.[58] The board also placed a notice in the press to reassure aspiring students that 'the lectures in Materia Medica, Chemistry and Midwifery have been recognised by the Royal College of Surgeons London and Dublin; the lectures in Anatomy will be recognised by the . . . College in London as soon as the course will have been delivered; and all the lectures at present delivered in [Inst] are recognised by Apothecaries Hall Dublin'.[59] Ferrar however did not start his classes on 2 November and this led inexorably to his dismissal four weeks later.

Ferrar's dismissal

The board of visitors letter of 29 October[58] reached Ferrar in Sligo in the evening of 1st November. He did not comply with its requirement to attend forthwith at Inst claiming, rather opaquely 'as at the present moment urgent and inevitable business occurring within the last ten hours renders my absence from my present post altogether out of my own power'.[60] He promised to explain his actions 'in a post (or two at furtherest)' which he did on 6 November.[61] This letter was considered on 15 November and the board unanimously resolved that his explanations were unsatisfactory and recommended to the joint boards (of managers and visitors) that they hold a special meeting on the 22nd (under the medical department *Plan*, rule 9) to consider 'deposing' him (under the *Plan*, rule 13),[62] and wrote appropriately to Ferrar that same day.[63] Ferrar (in Sligo) acknowledged the letter's receipt[64] and on the 19th replied in an exculpatory yet temporising letter in time to reach Inst for the crucial special meeting on the 22nd.[65] He argued again that he was not aware of this 'defective element' (non-recognition of classes) at the time of his appointment, and that furthermore he was ignorant of the rules under which he was contracted (including that of regular attendance) since 'I was . . . only just aware of the existence of the Regulations for the Medical School . . . I have not most certainly ever read them and saw them but once at the house of one of the professors'.[65] He closed with a hope to be in Belfast 'before or on Tuesday next [the day of the joint board meeting]' and added in the circumstances a remarkable PS, 'Has anything yet been done relative to the Barrack Hospital? If circumstances permit I shall gladly become resident Surgeon of it gratuitously'! Did he not understand the precariousness of his situation? Was it an exercise in 'leverage'? Or was it meant as a genuinely generous offer?

The joint boards duly met on the 22nd. Eight members were present including two of Ferrar's faculty colleagues (Drs James MacDonnell and J D Marshall). They were unimpressed with Ferrar's letters of the 6th and 19th and concluded that he 'has neglected the duty of his office' and in consequence, by the necessary two-thirds

majority, deposed him under the *Plan*, rule 9 subject only to the mandatory confirmation at a second meeting.[66] Ferrar was at once informed (by letter to Sligo)[67] and understandably he at once replied.[68] His letter is not an *apologia* or one of specious or special pleading but has a certain dignity, clarity of argument, integrity of purpose, and a strength of resolve. It is also well-written and highly literate!

Briefly, Ferrar refused to retract his view that the Inst advertisement for prospective students[52] was misleading – 'Is such a being [penurious student] a fit one to deceive or lead astray in any matter connected with his studies, or their probable, nay certain, tendering?' It was, he averred, in their interests that he had put his notice in the press.[56] He pleaded ignorance of the regulations: no copy had been given to him, if it had 'my conduct might have been modified in some degree as to appearance in Belfast'. He would not, however, compromise on the 'misleading' of the students. He concluded by saying that he would commence lectures if and when the regulations of the (London) College of Surgeons were met, *or* when the 'anatomical certificates will be recognised in Dublin' (this was a crucial point with Ferrar and he seems to have written to Drummond about it though without reply), *or* 'I will lecture provided that the students be publicly informed of the nature and value of the certificates as far as their diplomas are concerned'. This eloquent defence fell on the deafest of deaf ears; the joint boards confirmed their decision to depose him, now unanimously![69] Ferrar accepted the decision with grace[70] and without prompting at once returned the £50 earlier voted to him for surgical specimens.[47] The very next day the board of visitors advised the joint boards to advertise the chair 'immediately'[71] and Robert Coffey, *proxime accesit* in July and now the sole candidate, was appointed on 19 January 1837.[72] The faculty of medicine at its meeting on 11 March 1837 pronounced Ferrar's epitaph: 'having refused to deliver the course of lectures on surgery during the present winter . . . he was deposed'.[73] The next (and final) reference to Ferrar are the brief notes in the press of his death some three months later.

COMMENT

Ferrar appears to have been convinced of the propriety, good sense, and ultimate correctness, of his actions, and his impugning of Inst's good faith to be justified. Inst for their part accepted that Ferrar was in breach of regulations in failing to report for the start of the session despite their repeated requests for him to do so, and in deferring his course on his own authority. Crucially, their much-vaunted probity had been publicly called in question. Were there grounds for Ferrar's actions? This is now examined.

Course recognition

Inst's public advertisement of 10 October stated that 'The lectures will be delivered in conformity with the Regulations of the Royal Colleges of Surgeons, London and Dublin'.[52] It did not say that they *were already* or would *necessarily be recognised* though the phraseology could be held to be somewhat ambiguous. Recognition by appropriate licensing bodies was essential if Inst were to attract career students; without these the medical school would be a mere conduit for lectures for non-medical students and 'improving' *dilettantes*. The faculty had early considered this at its second meeting (on 14 October 1835) but deferred the matter because 'it was stated by one of the members that no lectures would be recognised by any of the Colleges [of Surgeons] until after the delivery of at least one course'.[74] Moreover, only anatomy and midwifery lectures were being given during the 1835-6 session because of inadequate facilities.[75] During August 1836, Drs Drummond and Marshall (as faculty 'president' and honorary secretary) had written to various licensing bodies with results which I have given elsewhere.[1, 2] Pertinently, the Apothecaries Society of Ireland and the Faculty of Physicians and Surgeons of Glasgow agreed to recognise the courses for 1836-7, the latter including surgery if the course was extended to 'six months of daily lectures 5 days in the week'.[76] Recognition by the Royal Colleges of Surgeons in London, Dublin and Edinburgh was critical. Here the Inst archives are incomplete: particularly, no letters from the London and Dublin Colleges during 1836 survive. It would appear however that responses from them had been received by end-October (1836) because in its public rebuttal on 2 November[59] of Ferrar's notice (of 29 October),[56] Inst said:

> 'As that advertisement might possibly lead students to suppose that none of the lectures . . . have been recognised . . . the [Joint] Boards state that the lectures in Materia Medica, Chemistry, and Midwifery have been recognised by the Royal Colleges of

> Surgeons in London and Dublin, that the lectures in Anatomy will be recognised by the London College of Surgeons as soon as a course shall have been delivered in conformity with their regulations which will be during this [1836-7] and all other subsequent sessions . . .'.

These facts were further endorsed at the faculty meeting on 3 April 1837 when the minutes record that 'the courses in chemistry, midwifery, practical midwifery, surgery, and materia medica *have already been recognised* by the Royal College of Surgeons London and Dublin . . .'[77] (my italics); on 13 June Inst informed various synod moderators that 'the courses *already delivered* [1836-7] have been recognised by the principal Medical Corporations of the United Kingdom'[78] (my italics), while the Inst board of proprietors in July were specifically assured that 'the Ticket of the Medical Courses which have been given in the Institution *are already recognised* by . . . the College of Surgeons London . . . and in most instances by the College of Surgeons Dublin'.[79] (my italics). The qualified approval to all the courses was given by the Royal College of Surgeons of Edinburgh though not until August 1837 and is fully documented.[80]

CONCLUSIONS

Since Inst was presumably not intent on deliberately misinforming the public, its own proprietors and the moderators of the presbyterian synods, Ferrar was incorrect in fact in his notice of 29 October;[56] had he attended any faculty meetings in September and October, or even been on campus, he might have known this. But in one detail he was right: Drummond's course in anatomy was seemingly not recognised or necessarily immediately due to be recognised by the 'Dublin' College of Surgeons (it was specifically omitted from the Inst rebuttal of 2 November (1836)[59]) and it was this very course which caused Ferrar much concern. In his view Drummond's 'professorship is that on which the weal and prosperity of the Medical School [at Inst] depend; all the others are but secondary to the Anatomical Chair . . . that until the certificate of the Anatomical professor shall be recognised, the school cannot . . . flourish'.[68] Though strongly held this was a viewpoint and not a fact; and indeed Drummond's classes would soon be recognised by the Colleges.[81] Ironically, had Ferrar given his course in surgery from November 1836 as scheduled it would have been recognised just as it was to be under his successor Coffey.[82] There are in short no grounds to suppose that Inst had any deliberate intention to mislead. Their prospectus may have been upbeat but if so this is one of the many examples of that sublime faith in their future which was their ethos and their style. We can give an appreciative nod to Ferrar's concerns on behalf of prospective students but we must be critical of his reading far too much into an advertisement and for taking unauthorised action, and deprecate his prolonged sojourn in Sligo during a crucial period for the future of his subject and of Inst, and especially his failure, for obscure reasons, to answer the several due summonses to Belfast. Inst was unquestionably sorely provoked by his behaviour and had no other reasonable course of action than to discharge him. The adverse votes cast at the joint boards by his medical faculty colleagues, the highly principled James MacDonnell and James Drummond Marshall, endorses this view.

EPILOGUE[83]

William Hugh, Thomas's father and the founder of the Belfast Ferrar line, had eight children (two girls; six boys) who reached adulthood. The girls married into local families – Wallace[84] and Patterson.[85] Of the six boys, the two eldest, Richard Lloyd and William Augustus, served in the armed forces and died abroad;[24] Thomas (our subject) was unmarried; Edward removed to Dundalk;[86] John entered Holy Orders in England.[87] Only Michael, the fourth son, settled in Belfast.[88] He became a distiller (in 1829) but also later held more menial employments.[89] Thomas stayed with him in Belfast periodically during 1836 and he sponsored at Inst the two sons of his then deceased brother Richard Lloyd. Only one of Michael's own six sons remained in Belfast – Augustus Minchin, a deputy lieutenant of Antrim, and a prosperous director of the linen merchants Jaffé Brothers.[90] Four emigrated including Michael Lloyd, compiler of the family history.[91] The eldest, William Hugh, was professor of Latin at TCD,[92] and *his* son and grand-son were well known in Dublin.[93] The non-*émigré* son, Augustus Minchin, had in turn four sons: three were army men[94] (including Michael Lloyd (Junior) the historian of the Green Howards and compiler of the register of the Royal School Armagh), while the fourth, William Augustus, was a JP and a prosperous flax merchant in Belfast.[95] The family disappears from the Belfast *Directory* in 1944 with Michael

Lloyd (Junior's) death (at his late father's house, 33 Windsor Avenue), and there are now no Ferrars in the Northern Ireland telephone or street directories. Like our subject, Thomas, the family itself has become a mere foot-note in Belfast history. I hope this article rescues both from near obscurity.

POSTSCRIPT

The poet, T S Eliot, visited Little Gidding in May 1936, and saw in the cycle of the foundation of a religious community (by Nicholas Ferrar in 1626) and its later dispersal by Cromwell's forces in 1646 a theme for his religious-patriotic expressions of man's progression from nature's bonfire to the fire of God: 'To be redeemed from fire by fire', as he put it in his poem, *Little Gidding*, one of his three great wartime Quartets.[96] Perhaps it is not altogether fanciful to see an analogous cycle in the Belfast Ferrars – from the founder, William Hugh, through his descendents including our subject (his son) Thomas, to the family's ultimate disappearance from Belfast with Michael Lloyd Ferrar's death in 1944.

Acknowledgements

I am grateful to the Deputy Keeper of the Records, the Public Record Office of Northern Ireland, for permission to cite from documents in the Office. Professor Richard Clarke, honorary archivist, the Royal Victoria Hospital, made many helpful suggestions. Mrs Julie Frost as usual supplied an exemplary typescript. Professor J B Lyons (RCSI) and Dr P J Henry (Sligo) helped with sources as I am pleased to acknowledge in the notes nos. 26, 33 and 34.

NOTES AND REFERENCES

The Royal Belfast Academical Institution archive is in the Public Record Office of Northern Ireland (PRONI – Series SCH 524). The following abbreviations are used:

Minute Book of the Faculty of Medicine, 1835-1849 (SCH 524/3C/5): FM, followed by the date of the meeting, e.g. 8 October 1835 is 8.10.35.

Minute Books of the Joint Board of Managers and Visitors (SCH 524/3A/1-6): JB followed by the volume number, *viz.* **IV** (1828-1836), **V** (1836-1842), and the date of the meeting.

Letter Book (SCH 524/7A/2-4): Lett Bk, followed by the volume number, *viz.* **III** (1833-1846), and the date of the correspondence, and the pagination (the entries are not always chronological).

Minute Book of the Board of Visitors (SCH 524/3A/3/1): BV, followed by the date of the meeting.

Belfast Commercial Chronicle: *BCC*

(Belfast) News Letter: *NL*

1. Froggatt P. The foundation of the 'Inst' medical department and its association with the Belfast Fever Hospital. *Ulster Med J* 1976; **45**: 107-45.
2. Froggatt P. The first medical school in Belfast, 1835-1849. *Med Hist* 1978; **22**: 237-66.
3. Froggatt P. Two neglected Belfast medical professors: James Lawson Drummond (1783-1853) and James Drummond Marshall (1808-1868). In: McCann W W J, Gray J (Edits.) An uncommon bookman. Belfast: Linenhall Library, 1996, pp. 74-99.
4. Froggatt P. The resignation of Robert Little from the chair of midwifery at 'Inst'. *Ulster Med J* 1979; **48**: 19-31.
5. Froggatt P, Wheeler W G. Robert Little MA, MD, LAH, LM, professor of midwifery and diseases of women and children, Royal Belfast Academical Institution, 1835-1840: a biographical note. *Ulster Med J* 1983; **52**: 58-66.
6. Tait P G, Crum Brown A. The scientific papers of the late Thomas Andrews MD, FRS, with a memoir. London: Macmillan, 1889.
7. Riddell H. Thomas Andrews, the great chemist and physicist. *Proceedings of the Belfast Natural History and Philosophical Society, 1920-21*, pp. 107-38.
8. Froggatt P. MacDonnell father and son. James (1763-1845), physician of Belfast; John (1769-1892), surgeon of Dublin. *J Ir Coll Phys Surg* 1984; **13**: 198-206.
9. On 18 January 1836 (SCH 524/7B/30/5; JB, **IV**, 19.1.36).
10. Jamieson J. The history of the Royal Belfast Academical Institution 1810-1960. Belfast: Mullan, 1959, p.70.
11. Fisher J R, Robb J H. Royal Belfast Academical Institution: centenary volume 1810-1910. Belfast: McCaw, Stevenson and Orr, 1913, p.82.
12. Unless otherwise stated the authorities are: Ferrar M L. The Limerick-Huntington Ferrars. Plymouth, 1903. Fifty copies only were printed for private circulation but the original MS is in PRONI (MIC 338/5); Dodds J. The Ferrar family. *Journal of the Limerick Field Club* 1905-8; **III**: 181-2; Dix, E R McD. An early Limerick book-binder. *Ibid*, 183; *Dictionary of National Biography*. London: Smith Elder, 1889, vol. XVIII, pp. 377-80. Ferrar M L (*op. cit.*) is not always reliable on dates where verifiable.
13. A 'concordance' (or 'harmony') prepared for Charles I and dated 1635 is in the British Museum (BM, Bibl. Reg. C23, e3).
14. He was admitted a burgess of Limerick on 28 January 1731; occupation, 'bibliopagus' i.e. book-binder.
15. Also admitted a burgess. In 1766 he founded *The Limerick Chronicle*.

16. Mary *née* Johns. John died in Dublin on 2 May 1804 and Mary on 15 September 1826 (*NL*, 26.9.26).
17. Ferrar J. An history of the city of Limerick, etc. 2nd edition. Limerick, 1767 (first edition 1761); also – An history of Limerick . . . from the earliest records to the year 1787. Limerick: Watson, 1787.
18. Crone J S. A concise dictionary of Irish biography. Dublin: Talbot Press, 1928.
19. The Lloyds of Drumsallagh and Kildromin, Co. Limerick, and of Castle Lake, Co. Tipperary. Maria was born in 1769.
20. Six boys and two girls between two and 15 years.
21. Belfast Street Directory (of about 1813) (PRONI, ref. 212), *Bradshaw's Belfast Directory*, 1819, and *Pigot's City of Dublin and Hibernian Provincial Directory*, 1824, show Ferrar as at 83 Donegall Street.
22. *NL*, 29.12.26; *BCC*, 27.12.26.
23. At her son Michael's house (*NL*, 5.4.50).
24. The eldest was Richard Lloyd (*b.* 15 Sept. 1793). Commissioned into the 41st regiment he died in Burma on 5 Dec. 1825. The second was William Augustus (*b.* 6 Feb. 1796). Commissioned into the royal navy he died at Portsmouth on 20 Jan. 1867. (Ferrar ML, *op. cit.*, note 12 above).
25. Burtchaell G D, Sadleir T U. Alumni Dublinenses. A register of the students, graduates, professors and provosts of Trinity College in the University of Dublin (1593-1860). Dublin: Alex Thom, 1935, pp. 274, 278. Thomas's age is given as 17 at matriculation but it would have been 18 on the dates in Ferrar M L (*op. cit.*, note 12 above).
26. I am grateful to Professor J B Lyons, Royal College of Surgeons in Ireland, for this information.
27. Michael (*b.* 14 Dec. 1799) served for a while before the mast before settling in business in Belfast in 1824 (Ferrar, M L, *op. cit.*, note 12 above).
28. Thomas rates only two lines in the family history (*Ibid.*) with an erroneous date of death (2 May 1837 instead of 2 June 1837) and possibly also of birth! (Burtchaell and Sadleir, *op. cit.*, note 25 above).
29. At 'Stephens Green West' (*Wilson's Directory*, 1831, 1832). This was also the address of RCSI but was unlikely to have been a *poste restante* for Ferrar since none of the other 234 licentiates of RCSI listed for 1831 gave it.
30. He could have been abroad (or in arrears of the College fees!) since these names were withheld.
31. This was the midwifery diploma awarded under the RCSI Royal Charter of 1828.
32. Ferrar to Inst of 19.11.36 (SCH 524/7B/30/135). Various letters suggest that Ferrar when in Belfast stayed with his brother Michael at 39 Barrack Street.
33. *Sligo Journal*, 9.6.36.
34. Henry P J. Sligo: medical care in the past, 1800-1965. Dublin: Colour Books, for North Western Health Board, 1995, pp. 115-6. I am indebted to Dr Henry for making exhaustive local inquiries about Ferrar including details of his interment. Nothing was discovered.
35. JB, 29.2.36. Unfortunately Ferrar's 'testimonial' has not been discovered.
36. JB, 1.3.36.
37. JB, 23.6.36.
38. JB, 28.6.36.
39. JB, 5.7.36.
40. Malcolm A G. The history of the general hospital, Belfast, and the other medical institutions of the town. Belfast: Agnew, 1851, appendices, pp. ii, iii-v, vi-vii, xxvii.
41. Annual medical report of the dispensary and fever hospital of Belfast. Belfast: Mackay, under dates.
42. JB, 19.1.37.
43. JB, 4.8.35.
44. JB, 10.9.35, 29.9.35, 19.1.37. The moderator gave no recorded opinion at the July 1836 election (JB, 5.7.36). Coffey was a 'new-light' (ie, non-subscribing) presbyterian who was married by Rev. Henry Montgomery the bitter theological opponent of the General Synod (*NL*, 23.5.20).
45. The Ferrar family was Church of Ireland though I can find no reference to Thomas in any church records in Belfast or Sligo.
46. FM, under dates.
47. JB, 9.8.36.
48. Ferrar to Inst of 16.8.36 (SCH 524/7B/30/90).
49. Lett. Bk., **III**, 6.9.36, p.131; JB, 6.9.36.
50. Froggatt P. The early medical school: foundation and first crisis - the 'college hospital' affair. Ulster Med J 1986; **56 (Suppl.)**: S5-S14.
51. FM, 1, 17, 30.9.36; 8, 15, 17, 22.10.36.
52. *BCC*, 10.10.36.
53. Lett. Bk., **III**, 17.10.36, p. 148.
54. The letter was 'sent to his [Dr Ferrar's] brother [Michael] to be forwarded'.
55. Ferrar to Inst, 27.11.36 (SCH 524/7B/30/143).
56. *BCC*, 29.10.36.
57. Ferrar must have known that adjourning classes was a matter requiring faculty approval since he was present at the faculty meeting when this rule was agreed (FM, 1.8.36, Regs. 2 and 3).
58. The board also passed nine resolutions on the matter including: '5. We have reason to believe that Dr Ferrar has already received an intimation from the Royal College of Surgeons Ireland that his lectures will be recognised as soon as his course shall have actually

been delivered – it being the rule and practice uniformly to recognise no lectures until after the delivery of one course in conformity with their regulations' (BV, 29.10.36; JB, **V**, 1.11.36).

59. *BCC*, 2.11.36. The board also requested the editors of the (Belfast) *Newsletter*, *Northern Whig*, *Ulster Times*, and the *Belfast Commercial Chronicle* not to publish any notices unless authorised by the honorary secretary of Inst (Lett. Bk. **III**, 7.11.36, p.148).
60. Ferrar to Inst of 2.11.36. This is dated '2 am Wednesday 2nd November 1836, Castle Street, Sligo' (SCH 524/7B/30/121). His 'present post' and the 'urgent and inevitable business' are unknown. The board of visitors considered this letter on 4th November (a Saturday) but adjourned to await the promised second letter (BV, 4.11.36).
61. This letter has not been traced but much of its argument is repeated in Ferrar's letter of 18th November (SCH 524/7B/30/134).
62. BV, 15.11.36; JB, **V**, 15.11.36. Rule 9 states that a professor can only be deposed 'by a vote of two-thirds of the members present at two meetings of the Joint Boards summoned for that especial purpose, for impropriety of conduct, or neglect of duty'. Rule 13 requires each professor *inter alia* 'to deliver a lecture of an hour's duration on each day of his session'. (Plan for the establishment of a medical department in the Royal Belfast Academical Institution, adopted by the joint boards, 4th August 1835. Belfast: J Smyth, 1835).
63. The joint boards agreed the letter (JB, **V**, 15 and 22.11.36).
64. Ferrar to Inst, 18.11.36 (SCH 524/7B/30/134).
65. Ferrar to Inst, 19.11.36 (SCH 524/7B/30/135).
66. JB, **V**, 22.11.36.
67. Lett. Bk., **III**, 23.11.36, p.149.
68. Ferrar to Inst, 27.11.36 (SCH 524/7B/30/143).
69. JB, **V**, 29.11.36. The board of visitors had given the benefit of any doubt as to Ferrar's intentions in challenging their advertisement when they said that his public notice was 'calculated, though probably not intended, to injure the success of the Medical School' (BV, 29.10.36).
70. Ferrar to Inst, 1.12.36 (SCH 524/7B/30/146).
71. BV, 3.12.36.
72. JB, **V**, 19.1.37.
73. FM, 11.3.37. The faculty had not met since 12.11.36.
74. FM, 14.10.35.
75. FM, 8.10.35.
76. FM, 15 and 29.10.36; 12.11.36.
77. FM, 3.4.37.
78. Inst to moderators of the General and the Secession Synods, 13.6.37 (Lett. Bk., **III**, 13.6.37, pp. 180-2).
79. JB, **V**, 4.7.37 (pp.97 *et seq*).
80. FM, 4.9.37.
81. Drummond's anatomy classes were fully recognised by the Colleges at least as early as 1837-8 (JB, **V**, 3.7.38).
82. *BCC*, 29.4.37.
83. Unless otherwise stated the authority is – Ferrar M L (*op. cit.*, note 12 above).
84. Frances, *b.* 1805, *d.* Melbourne, Australia, 1879, *m.* Andrew Wallace, 18 Oct. 1831 (*NL*, 21.10.31; Parish register, St. Anne's Belfast (Shankhill), marriages May 1830 – September 1841 (PRONI – T679/255)). Nine children. Andrew is described progressively as 'accountant', 'merchant', and 'gentleman'. Originally the family were of St. Anne's parish but the three youngest children were baptised in St. George's (Index to St. George's church records, 1817-1870 (PRONI – printed lists)).
85. Mary Elizabeth, *b.* 1806, *d.* 1889, *m.* Robert Patterson 11 June 1833 (Register of marriages 1790-1930 and of births 1757-1977, First Belfast Congregation (Rosemary Street) (PRONI – MIC 1B/2/1)). Eleven children. Robert became FRS for his geological researchers.
86. *b.* 4 April 1802, *d.* 28 July 1846, *m.* Margaret Carroll of Drumgoolen, Co. Louth, 1 Aug. 1827 (*NL*, 3.8.27; 4.8.46; PRONI – Dundalk parish Church Records (MIC 1/204A/3)). Four children. Margaret *d.* 18 Dec. 1889 leaving effects worth £941 (*Calendar of grants of probate . . . , 1889*. Dublin: HMSO, 1891).
87. *b.* 20 Dec. 1807, *d.* 18 Feb. 1884 at Bury St. Edmunds. Matriculated TCD, 4 June 1825, BA, 1830 (*op. cit.*, note 25 above). *m.* Elizabeth Angus. Entered Holy Orders. Three children.
88. *b.* 14 Dec. 1799, *d.* 27 Feb. 1884 at No. 1, Camden Street, Belfast. *m.* Mary Minchin of Dundrum, Co. Dublin (his cousin) in Taney church, 19 Sept. 1834 (*NL*, 23.9.34). Assistant accountant in Dublin, common seaman, variously employed in England, settled in Belfast 1824. Partner (with John Mackenzie and James King) in distillery in Barrack Street in 1829 (PRONI - T877 (417)). Nine children. His orphaned nephews were William and Frederick (School album, 1814-1876 (SCH 524/1A/1, p.141)). Frederick was briefly proprietor of the *Mercury* newspaper, Winecellar Entry (*Directory*, 1858-9).
89. He was also employed in wine and spirit merchants and in 'Henderson's steam-packet office' (*Directory*, 1852, 1854). His effects were valued at £455-0-7 (*Calendar of grants of probate . . . for 1884*. Dublin: HMSO, 1886).
90. Second son. *b.* 17 April 1837, *d.* 1 Aug. 1913, *m.* Rebecca Hughes at Killymard church, Co. Donegal, 27 April 1858 (Killymard parish records, PRONI – MIC/1/145/1). Left property valued at £17,291-4-2 (*Calendar of grants of probate . . . for 1913*. Dublin: HMSO, 1915).
91. *b.* 24 Nov. 1839. Scholar TCD. Career in Bengal civil service. The three other *émigrés* brothers were: Howard

Minchin, *b.* 3 Feb. 1841, *d.* 11 June 1872 in India; Henry Stafford, *b.* 10 July 1850 (*NL*, 23.7.50), went to USA; John Edgar, *b.* 8 Nov. 1852 (*NL*, 12.11.52), went to South Africa. The last two were pupils at Inst (School album, 1814-1876 (SCH 524/1A.1 p.216); Register of baptisms at St. Anne's parish Belfast, Sept. 23, 1842-Nov. 19, 1852. (PRONI – T679/259, p.220).

92. *b.* 14 Nov. 1835, *d.* Sydney, Australia, 15 May 1871 on voyage to recover lost health. Matriculated TCD, 1853, scholar, 1855, BA, 1857, fellow and MA, 1859, junior dean, 1864-6. Foundation professor of latin, 1870-1. (Webb D A, Bartlett J R. (edits.). Trinity College Dublin record volume 1991. Dublin: College Press, 1992, pp. 62, 127-8; A catalogue of graduates who have proceeded to degrees in the University of Dublin . . . with a supplement to December 16, 1868. Compiled by Todd J H. Dublin: Hodges, Smith and Foster, 1869).

93. Dr Benjamin Banks Ferrar became curator of the Dublin Zoological Gardens in 1912; and Michael Lloyd Ferrar was warden of Divinity Hostel Dublin, 1939-60. (Simms G O (edit.). Addresses and papers of Michael Lloyd Ferrar, 1909-1960. London: SPCK, 1962).

94. Major Michael Lloyd F (*b.* 8 Jan 1861, *d.* 5 Nov. 1944); Major Henry Minchin F (*b.* 25 March 1863); Captain Walter Hughes F (*b.* 29 June 1876; killed in action Gheluveldt, 31 Oct. 1914) (Ferrar M L, Register of the Royal School Armagh. Belfast: W and G Baird, 1933, pp. 107-8). The histories were: Ferrar M L. With the Green Howards in South Africa 1899-1902. London: Eden Fisher, 1904; Officers of the Green Howards, 1688-1931. Belfast: W and G. Baird, 1931; and others.

95. *b.* 8 Jan. 1861, *d.* 24 Feb. 1929 at Cloona, Dunmurry. His effects amounted to £5,707-14-6 (*Calendar of grants of probate . . . for 1929*. Belfast).

96. Moody A D. Thomas Stearns Eliot: poet. Cambridge: Cambridge University Press, 1979, pp. 242-259.

The Ulster Medical Journal, Volume 65, No. 2, pp. 162-164, November 1996.

Case Report

A left sided neck mass

A Paterson, S K Kaluskar, C S McKinstry

Accepted 1 September 1996

Carotid body tumours are slow-growing hypervascular lesions arising from nonchromaffin cells within the neural crest in the region of the carotid bifurcation.[1] They are also referred to as paragangliomas and it is well documented that they may be multiple.[2] These lesions have characteristic magnetic resonance imaging (MRI) features that permit accurate diagnosis and precise definition of tumour extent. This report serves to illustrate the radiological appearances in such a case.

Case Report A 72 year old man presented with a 6 month history of a painless lump in the left side of his neck. There was no associated dysphagia, hoarseness, otalgia or weight loss. He was a non-smoker. Examination revealed a 3 x 4 cm mobile mass in the anterior triangle of the neck on the left side, just below the angle of the mandible. Otological and neurological examination was normal.

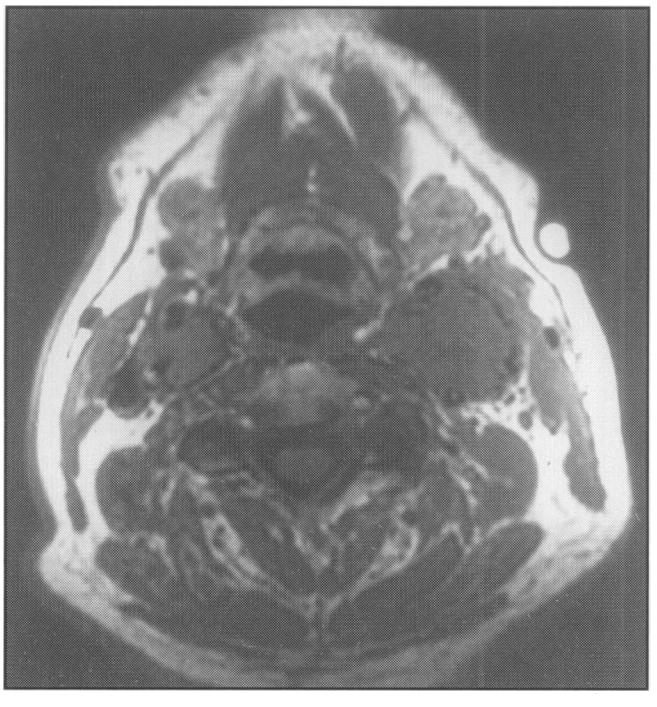


Fig 1. Axial T1-weighted (TR600/TE11) image through the neck (at the level of the carotid bifurcation).

The clinical impression was of an occult primary tumour with metastases in the neck. The patient was booked for excision biopsy of the mass. At operation the tumour was found to be adherent to the carotid artery. On the basis of this finding the lesion was left intact, the wound closed, and the patient referred for MRI of his neck. Axial T1-weighted images, both before and after

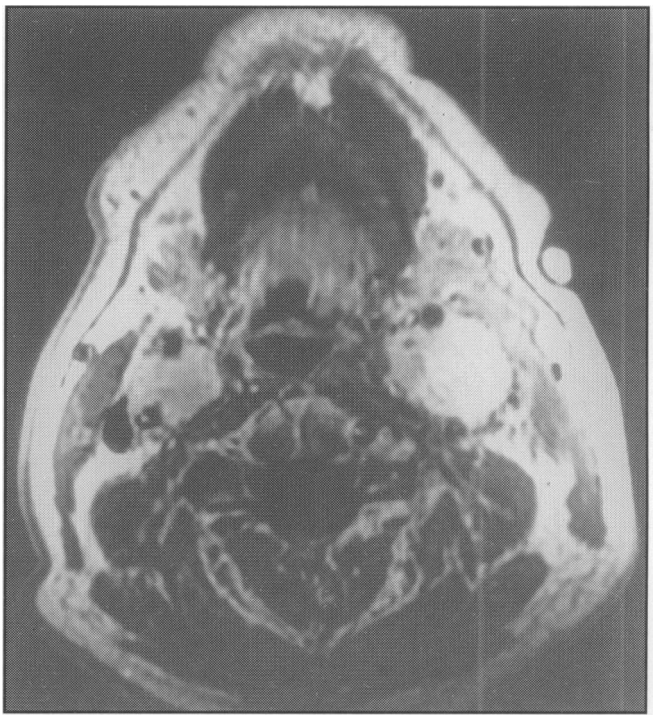


Fig 2. Axial T1-weighted image at the same level following intravenous gadolinium-DTPA.

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

Anne Paterson, MB, BS, MRCP, Specialist Registrar in Radiology.

C S McKinstry, FRCR, Consultant Neuroradiologist.

ENT Department, Tyrone County Hospital, Hospital Road, Omagh BT79 0AP.

S K Kaluskar, MS, FRCS, DLO, Consultant ENT Surgeon.

Correspondence to Dr McKinstry.

intravenous gadolinium-DTPA enhancement are shown above.

Figure1 shows well-defined lobular soft-tissue masses arising in the carotid spaces bilaterally. Both lesions are isointense with muscle. The left sided lesion is larger measured 3 cm across in its widest extent, and is seen to arise at the carotid bifurcation, causing splaying and displacement of internal and external carotid arteries. Further sections showed the mass to extend superiorly to the level of the tip of the epiglottis, but it did not reach the skull base. On the right side, the lesion is smaller, but otherwise its features are the same as the left-sided mass.

Following intravenous contrast, the left-sided lesion enhanced markedly, particularly in its lateral portion. The right-sided lesion enhanced moderately (see Figure 2). The site of these soft tissue abnormalities in conjunction with their enhancement characteristics is consistent with bilateral carotid body tumours.

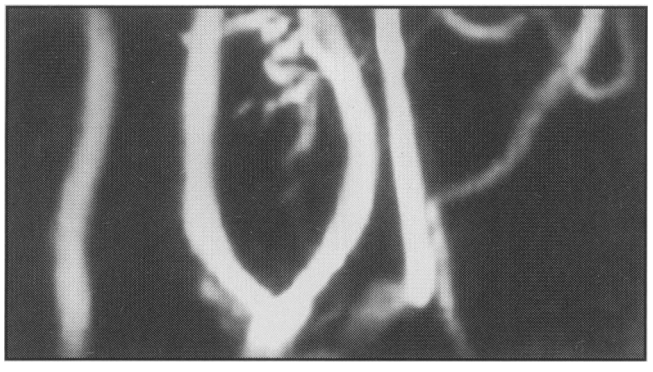


Fig 3. Three dimensional phase contrast MR angiographic study (TR24/TE8.6/20° flip angle). Targeted reconstruction showing a lateral projection of the left carotid bifurcation.

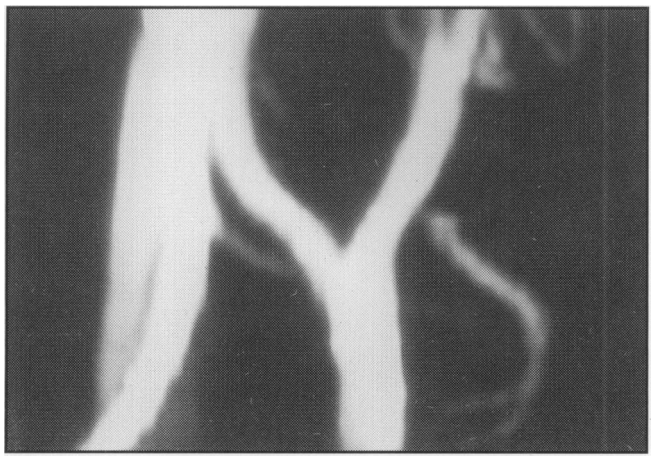


Fig 4. Three dimensional phase contrast MR angiographic study. Targeted reconstruction showing a lateral projection of the right carotid bifurcation.

Figures 3 and 4 show images from a three dimensional phase contrast MR angiogram that was also performed. This confirmed the vessel splaying shown on the axial images, and also showed the left-sided lesion completely obstructing the internal jugular vein. At the upper limit of the left-sided lesion some pathological vessels are seen to arise from the external carotid artery. On the right side, the splaying of the internal and external carotid arteries is also apparent, but to a lesser degree. The right internal jugular vein is displaced but not obstructed.

DISCUSSION

Carotid body tumours usually present as a slowly enlarging neck-mass below the angle of the mandible, and they may or may not be associated with a variety of symptoms such as pain, hoarseness, dysphagia and stridor. On examination they are classically pulsatile but not expansile, and they are mobile from side to side but not up and down.[3] Approximately 25% will be associated with a bruit.[4] The patient can present with an Horner's syndrome or palsies of the lower cranial nerves,[5] reflecting the anatomical location of the lesion.

Reports suggest 3% of all patients with this tumour and 26% of patients with a family history of this disease have bilateral lesions.[6] Several authors have described an autosomal dominant mechanism of inheritance in these instances.[7, 8] There is an increased incidence of carotid body tumours in those populations living at altitude, which is thought to be related to hyperplasia of the carotid body secondary to chronic hypoxaemia. A similar mechanism presumably accounts for the reported increase in these tumours in patients with chronic obstructive airways disease or intra-cardiac shunts with flow reversal.[9]

These lesions have the ability to produce catecholamine-like substances, but the majority of them do not.[10] Malignancy as defined by those lesions with associated metastases occurs in approximately 5-10% of cases.[3] Secondary spread is generally to the regional lymph nodes, but may be to distant organs such as the lungs, liver, kidney, pancreas, thyroid, heart or bone.[3]

Histologically these tumours are shown to be composed of clusters of neoplastic cells, which are located within a vascular connective-tissue stroma. The degree of associated fibrosis is variable.[9, 10]

A variety of imaging techniques can be used to demonstrate these lesions, including ultrasound, computer assisted tomography, scintigraphy[11] and conventional angiography. With MRI, well circumscribed masses which are hypointense or isointense with muscle on T1-weighted images and hyperintense on T2-weighted images are seen. Signal void within the tumours on T2-weighted scans gives the so called "salt and pepper" pattern which is attributed to blood flow within the vascular structures of the tumour.[2] However lack of signal void does not discount the diagnosis because the vessels may be very small or thrombosed. Intense enhancement after intravenous gadolinium-DTPA helps to improve the diagnostic accuracy of the scan.[12] MR angiography shows the displacement of the carotid arteries secondary to the tumour and may also demonstrate pathological feeding vessels. This of course is of value to the surgeon if resection of the lesion is being considered, although conventional angiography is still considered superior in this respect by some authors.[2, 13]

In this case the surgeon's impression of a left-sided carotid body tumour at the time of biopsy was confirmed by MRI scanning. The demonstration of a second lesion was entirely unexpected. Further questioning at a later date failed to reveal any definite family history of similar tumours.

In view of his age, the patient declined further operative treatment of his tumours. He is currently being followed up as an out-patient at his local hospital and to date remains well.

REFERENCES

1. Vogl T J, Jeurgens M, Balzer J O *et al.* Glomus tumours of the skull base: combined use of MR angiography and spin-echo imaging. *Radiology* 1994; **192**: 103-10.
2. DeMarino D P, Mueller D P, Yuh W T C *et al.* Imaging case study of the month; Multiple paragangliomas. *Ann Otol Rhinol Laryngol* 1990; **99**: 85-6.
3. Cottrell E D, Smith L L. Management of uncommon lesions affecting the extracranial vessels. In: Moore W S *et al*, eds. Vascular Surgery 4th edition, Philadelphia; *W B Saunders Company*, 1995; 1623-6.
4. Javid H, Chawla S K, Dye W S *et al.* Carotid body tumor. resection or reflection. *Arch Surg* 1976; **111**: 344-7.
5. Arriaga M A, Lo W W M, Brackmann D E. Imaging study of the month: Magnetic resonance angiography of synchronous bilateral carotid body paragangliomas and bilateral vagal paragangliomas. *Ann Otol Rhinol Laryngol* 1992; **101**: 955-7.
6. Cook R L. Bilateral chemodectoma in the neck. *J Laryngol Otol* 1977; **91**: 611-8.
7. Hamilton J R, Barros D'Sa A A. Radionuclide angiography and surgery for familial bilateral chemodectomas. *Eur J Vasc Surg* 1987; **1**: 97-105.
8. Grufferman S, Gillman M W, Pasternak L R *et al.* Familial carotid body tumors. case report and epidemiologic review. *Cancer* 1980; **46**: 2116-22.
9. Heath D, Kay J M, Flenley D C. Respiratory system. In: MacSween R N M, Whaley K, eds. Muir's Textbook of Pathology 13th edition, London; *Edward Arnold*, 1992; 575-6.
10. Davidge-Pitts K J, Pantanowitz D. Carotid body tumours. *Surg Annu* 1984; **16**: 203-27.
11. Laird J D, Ferguson W R, McIlrath E M, Hamilton J R L. Radionuclide angiography as the primary investigation in chemodectoma: concise communication. *J Nucl Med* 1983; **24**: 475-8.
12. Rippe D J, Grist T M, Uginette J P *et al.* Carotid body tumour: flow sensitive pulse sequences and MR angiography. *J Comput Assist Tomogr* 1989; **13**: 874-7.
13. Rodgers G K, Applegate L, De la Cruz A, Lo W. Magnetic resonance angiography: analysis of vascular lesions of the temporal bone and skull base. Am J Otol 1993; **14**: 56-62.

The Ulster Medical Journal, Volume 65, No. 2, pp. 165-166, November 1996.

Case Report

Phentolamine Mesylate can alleviate the nausea and vomiting associated with liver metastasis

G J McCleane

Nausea and vomiting are common symptoms in a patient with cancer. They may be due directly to the tumour itself or may be side effects of treatment given, this being aimed at achieving either disease remission or symptom relief. With the advent of new anti-emetic agents, such as the anti 5HT3 class of drugs, treatment for nausea and vomiting can be more specifically targeted to the causal factor.

Among factors that can induce nausea and vomiting are liver metastatic deposits. The nausea and vomiting produced by hepatic secondaries can respond to "conventional" anti-emetics but on occasions can be resistant to such treatment and necessitate the use of dexamethasone which can be highly effective but takes 24-48 hours to have the desired effect. Obviously this time delay is unpleasant for the patient and reduces the quality of life when quantity of life is restricted. The following two case reports highlight the potential beneficial effects of intravenous phentolamine in achieving symptom control rapidly and buying time for the more prolonged effects of dexamethasone to become apparent.

CASE 1 A 40 year old female was referred with intractable nausea and vomiting unresponsive to metoclopramide, cyclizine and ondansetron. She had an inoperable gastric carcinoma with liver secondaries, and no radiological or endoscopic evidence of obstruction. Her liver was enlarged. An initial intravenous bolus of 10 mg of phentolamine was given which removed nausea within minutes. This was followed by a bolus of 16 mg of dexamethasone intravenously and a reducing course of oral dexamethasone starting at 8 mg/day.

This patient had good relief for five days but was unfortunately unable to tolerate the dexamethasone which was stopped after 3 days. At this stage a further 10 mg bolus of phentolamine was given with good immediate effect and she was commenced on an intravenous infusion of phentolamine (15 mg/24 hrs) via a syringe driver (Graseby Ltd). After 24 hours the cannula had to be removed due to phlebitis and was replaced by a 15 cm cannula (Vygon Leaderflex) and the infusion recommenced with good effect.

CASE 2 A 77 year old lady was referred with nausea and vomiting associated with a neoplasm involving the head of the pancreas with secondaries in the porta hepatis and liver which were diagnosed at laparotomy. No bowel obstruction was noted. A choledocojejunostomy was performed because of a distended gall bladder. Treatment with metoclopramide and cyclizine was unsuccessful.

On examination she had a tender enlarged liver and was jaundiced. An intravenous injection of 10 mg phentolamine gave relief of nausea in minutes. This treatment was followed by 16 mg intravenously of dexamethasone and an oral reducing course of dexamethasone commencing at 8 mg daily in divided doses over a 9 day period. There was no return of nausea or vomiting in the subsequent 4 weeks until her demise.

DISCUSSION

Phentolamine is a short-acting parenteral alpha blocker which in the past was mainly used in anaesthetic practice as a vasodilator/anti-hypertensive. More recently it has been used in the diagnosis of sympathetically maintained pain. It has a short half-life but when used to diagnose sympathetically maintained pain its beneficial

Department of Anaesthetics, Craigavon Area Hospital Group Trust, 68 Lurgan Road, Portadown BT63 5QQ.
G J McCleane, MD, FFARCSI, Consultant Anaesthetist.
Correspondence to Dr McCleane

effect can last for up to 48 hours. The etiology of the nausea and vomiting associated with liver secondaries is not entirely clear but may be related to stretching of the sympathetically innervated liver capsule (via the hepatic plexus, a derivative of the coeliac plexus,[2]) giving rise not only to nausea and vomiting but also to abdominal pain. Dexamethasone would be expected to have a beneficial effect by reducing peri-tumour oedema and hence stretch on the capsule. On this basis it may be that the blockade of sympathetic nerves around the liver capsule produced by phentolamine is a cause of the reduction in nausea and vomiting associated with this agent. The transient hypotension which accompanies its use (caused by a similar blockade of vascular sympathetic fibres) is rarely troublesome[3, 4] and does not often require intervention. Palpitations may occur but again are short lived.

Perhaps the most marked drawback to phentolamine is the need to administer it parentally but despite this it has proved to be a major asset in acute management of the nausea and vomiting associated with liver secondaries and as such merits further investigation.

REFERENCES

1. Arnér S. Intravenous phentolamine test: diagnostic and prognostic use in reflex sympathetic dystrophy. *Pain* 1991; **46**: 17-22.
2. Warwick R and Williams P L. Gray's Anatomy Longmann Group, London 1973.
3. Raja S N, Treede R D, Davis K D, Campbell J N. Systemic Alpha – adrenergic blockade with phentolamine: a diagnostic test for sympathetically maintained pain. *Anethesiology* 1991; **74**: 691-8.
4. Shir Y, Cameron L B, Raja S N, Bourke D L. The safety of intravenous phentolamine administration in patients with neuropathic pain. *Aneth Analg* 1993; **76**: 1008-11.

The Ulster Medical Journal, Volume 65, No. 2, pp. 167-168, November 1996.

Case Report

Cyst of Pregnancy

G Dorman, W A H Ritchie

Accepted 18 June 1996

Case Report A 29 year old insulin dependent diabetic of 15 years standing presented for antenatal care. In her previous pregnancy a lower uterine segment Caesarean section had been performed for severe pre-eclampsia at 36 weeks gestation. On examination blood pressure was 130/80 mmHg. Urinalysis was clear. There was no retinopathy. On ultrasound scan a viable 6 week intrauterine pregnancy was confirmed. Hospital based antenatal care was arranged and the patient reviewed fortnightly.

At 12 weeks the patient complained of lethargy and general malaise. Diabetic control was satisfactory. However, her serum thyroxin level was low at 3.7 umolL^{-1} (normal range 8.8-23.1), so replacement therapy was given.

At 20 weeks, during a routine 'anomaly' scan, a simple 5 cm left ovarian cyst was seen. However, in view of the nature and relatively small size of the cyst and the normality of the contralateral ovary it was decided to manage the cyst conservatively.

At 24 weeks the blood pressure was mildly elevated for the first time at 130/90 mmHg. There was no proteinuria. The dose of thyroxine was increased to 200ug daily as the patient remained symptomatic. The cyst remained unchanged. Fetal growth was satisfactory.

At 28 weeks the fetus was clinically felt to be small. Blood pressure remained mildly elevated but there was significant proteinuria. Diabetic control remained satisfactory. Ultrasound growth confirmed a symmetrically small for dates fetus with an estimated weight of 630g (<10th centile for gestation). Amniotic fluid volume was markedly decreased. The fetus was active. In view of the fetal compromise, proteinuria and hypertension, the patient was admitted to hospital.

Over the following two days the blood pressure rose significantly and a repeat lower segment Caesarean section was performed. The liquor was heavily meconium-stained. A female infant of 740g was delivered in good condition. An 8 cm ovarian cyst was found on the left. It was smooth-walled, uniloculated and without solid elements. The right ovary was normal and there were no palpable lymph nodes. The left ovary was removed as it was impossible to differentiate ovary from cyst. The mother's recovery was uneventful. The baby was ventilated for 4 weeks and is now well.

Pathological examination showed a solitary luteinised cyst of pregnancy and the puerperium. There were no solid elements or evidence of malignancy.

DISCUSSION

There are only nine other cases of luteinised cyst of pregnancy and the puerperium reported in the literature. In a series of eight cases two were discovered antenatally by ultrasound, two were incidental findings at Caesarean section and four were discovered by abdominal palpation in the puerperium.[1] All eight cysts were surgically removed. The ninth case was diagnosed incidentally at Caesarean section.[2] In all nine cases the cysts were benign, thin-walled, solitary tumours containing clear or blood stained serous fluid or mucoid material. They were lined by multiple layers of heavily luteinised granulosa cells, the cytoplasm of which was densely eosinophilic and or vacuolated.

Although this and one other case occurred in diabetic patients, and in addition our patient was hypothyroid, there is no recognised association

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

G Dorman, MRCOG, Registrar.

W A H Ritchie, FRCOG, Consultant Obstetrician and Gynaecologist.

Correspondence to Dr Dorman

with endocrine abnormalities. It is unclear what the stimulus for the abnormal follicle growth may be. It has been postulated that there is an abnormality in the pituitary release of gonadotrophins or in the stimulus to the ovary from human chorionic gonadotrophin.[3,4,5]

Whilst these cysts are unilateral, the condition *hyperreactio luteinalis* is associated with bilateral ovarian cysts and ovarian enlargement.[6,7] These cysts have similar histological features to the luteinised cyst of pregnancy and the puerperium. This condition is associated with virilisation.[8]

In view of the benign nature of this condition the outlook for this patient is excellent. It is not known, however, if it is likely to recur in the remaining ovary in a subsequent pregnancy.

REFERENCES

1. Clement P B, Scully R E. Large solitary luteinised follicle cyst of pregnancy and puerperium. *Am J Surg Path* 1980; **4**: 431-8.
2. Albukerk J N, Berlin M. Unilateral lutein cyst in pregnancy. *NY State Med J* 1976; **76**: 259-61.
3. Case records of the Massachusetts General Hospital. Case 43461. Follicle cyst with sexual precocity. *New Eng J Med* 1957; **257**: 987-92.
4. Danon M, Robboy S J, Kim S, Scully R, Crawford J D. Cushing syndrome, sexual precocity, and polyostotic fibrous dysplasia (Albright syndrome) in infancy. *J Pediatr* 1975; **87**: 917-21.
5. Caspi E, Schreyer P, Bukovsky J. Ovarian lutein cysts in pregnancy. *Obstet gynaecol* 1973; **42**: 388-98.
6. Barclay D L, Leverich E B, Kemmerly J R. Hyperreactio luteinalis: postpartum persistence. *Am J Obstet Gynaecol* 1969; **105**: 642-4.
7. Girouard D P, Barclay D L, Collins C G. Hyperreactio luteinalis: review of the literature and report of two cases. *Obstet Gynaecol* 1964; **23**: 513-25.
8. Hensleigh P A, Woodruff J D. Differential maternal-fetal response to androgenizing luteoma or hyperreactio luteinalis. *Obstet Gynaecol Surv* 1978; **33**: 262-71.

The Ulster Medical Journal, Volume 65, No. 2, pp. 169-172, November 1996.

Case Report

Malignant lymphoma of the scrotum and Wegener's granulomatosis of the penis – genital presentation of systemic disease

D C Allen, M Y Walsh

The astute clinician occasionally detects herald or concurrent signs of systemic disease in the mouth, perianal area or genitalia. Surgical pathologists are familiar with testicular lymphoma,[1] while scrotal[2] and vulval[3,4] lymphoma are rare. Genital vasculitis may either be isolated or a part of systemic disease and occurs more usually in the testis or spermatic cord.[5] Penile polyarteritis nodosa[6] and Wegener's granulomatosis[7-9] are very infrequent. This report details cases of angiodestructive malignant T-cell lymphoma and Wegener's granulomatosis presenting in the male external genitalia.

CASE 1 A 77-year old male presented with an ulcerative, necrotic lesion in the skin and subcutis of the scrotum measuring up to 3 cm in maximum dimension. Biopsy showed, in the viable dermis adjacent to the necrotic ulcer, a diffuse cellular infiltrate composed of somewhat pleomorphic lymphoid cells with, in areas, a distinct angiocentric/angiodestructive distribution (Figure 1 [a]). A diagnosis of non-Hodgkin's malignant lymphoma was made. Bone marrow trephine biopsy, CT scan of abdomen and pelvis and ultrasound scan of the testes were normal. One month later an irregular 3 cm mass in the right upper lobe of the lung was aspirated, and microscopy showed malignant cells from a non-small cell carcinoma. The lesion was assessed as unsuitable for surgery and treated with radiotherapy. Seven months after this the patient noticed a right sided scrotal swelling, and orchidectomy showed a 120 gram, 9 x 5 x 4 cm pale testicular tumour. Histology showed a partially necrotic non-Hodgkin's malignant lymphoma of the testis with focal infiltration of the tunica vaginalis, rete and inner-most aspect of the epididymis (Figure 1 [b]). It had a polymorphous population of small, medium and large lymphoid cells. Common leucocyte antigen (CLA) staining was strong in both the original scrotal and the testicular tumour cells but B– and T–cell subtyping was somewhat equivocal. A skin nodule on the shoulder was also biopsied and histology showed epidermotrophic cutaneous involvement by T–cell non-Hodgkin's lymphoma, positive for CD_{45} (CLA), CD_3 and $CD45R_0$ ($UCHL_1$) markers (Figure 1 [c]). Bone marrow trephine biopsy and CT scan of abdomen and pelvis were normal. Chemotherapy was given for the lymphoma and further radiotherapy for the chest lesion. The patient died from bronchogenic carcinoma six months later. He had not shown any evidence of immunodeficiency and there was no history of any relevant occupational exposure.

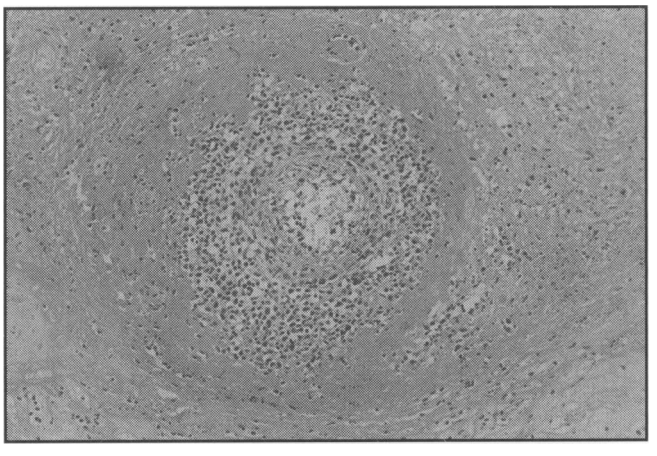


Fig 1[a]. Necrotic scrotal skin with an angiocentric and destructive lymphomatous infiltrate (magnification x 400).

Histopathology Laboratory, Belfast City Hospital, BT9 7AD.

D C Allen, MD, MRCPath, Consultant Pathologist.

M Y Walsh, MB, MRCPath, Consultant Pathologist.

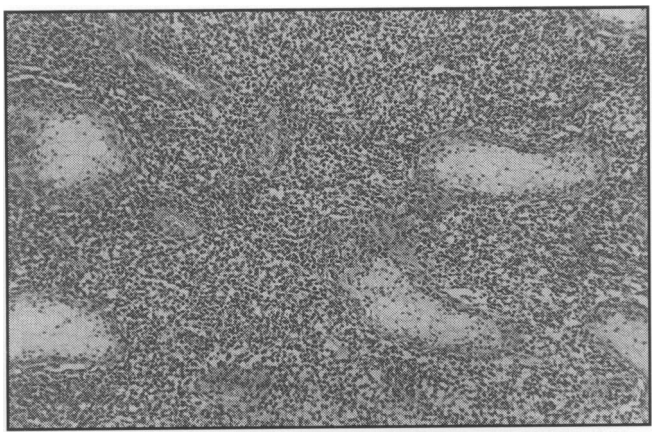


Fig 1[b]. Non-Hodgkin's lymphoma infiltrating the testicular interstitium between residual atrophic tubules (magnification x 250).

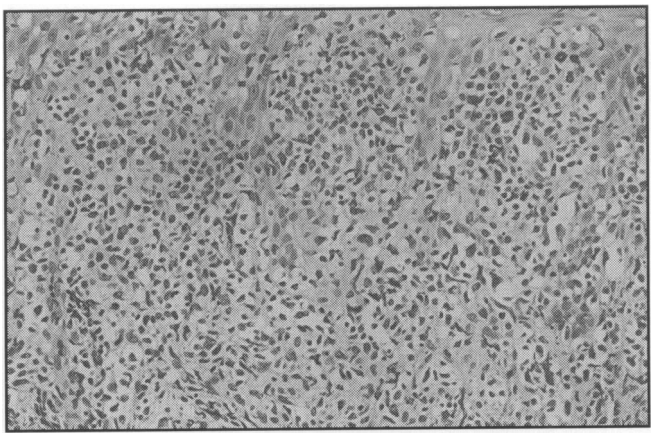


Fig 1[c]. Cutaneous lymphoma with epidermal involvement (magnification x 400).

CASE 2 A 66-year old man presented with an ulcerated mass, suspected clinically to be a neoplasm, on the dorsal aspect of the coronal sulcus of the glans penis. Partial amputation of the penis was performed and on inspection there was a 2.5 x 2 x 1 cm pale ovoid nodule in the sulcus undermining the base of the foreskin. Histology showed the urethral mucosa and corpus spongiosum to be normal. Superiorly Buck's fascia and part of the corpora cavernosa were replaced by an extensive necrotising granulomatous reaction. Irregular, stellate areas of basophilic collagen necrosis containing acute inflammatory debris were oriented to a palisading histiocytic reaction which included multi-nucleated giant cells (Figures 2 [a] and [b]). There was a surrounding lymphoplasmacytic and fibrotic reaction with occasional small necrotic vessels. There was no caseation or malignancy, and stains were negative for tubercle, fungus and bacteria. Various diagnoses such as lympho-granuloma venereum, cat-scratch disease and syphilis were also considered but serological investigations were negative; the pathology report indicated that Wegener's granulomatosis may rarely present as an isolated or peripheral lesion. Over the next six months he lost one stone in weight and had several episodes of haematuria and epistaxis with nasal crusting. Investigations showed normal blood indices, liver and renal function tests (urea 6.1 mmol/l, serum creatinine 104 umol/l), VDRL/TPHA and sputum were negative for tubercle. C-reactive protein was 76 mg/l (normal < 6). Autoimmune screen including pANCA was negative but cANCA was positive to a titre of 1 in 160. Histology showed the nasal mucosa to be ulcerated and heavily inflamed with a diffuse mononuclear inflammatory infiltrate and poorly defined granulomatous foci with some giant cells. Stains for organisms were negative and a diagnosis of Wegener's granulomatosis made. The patient was treated with prednisolone and cyclophosphamide but presented two years later with cough and episodic haemoptysis, biopsy evidence of renal disease (crescentic glomerulonephritis), a cANCA titre of 1 in 1280 and elevated antibody to proteinase 3 of 5.2 u/ml (normal < 2 u/ml). It was felt that the patient had been non-compliant with his drug therapy. Subsequently he has shown a response with a fall in serum creatinine from 300 umol/l to 148 umol/l, a creatinine clearance of 32 ml/minute and cANCA titre of 1 in 20.

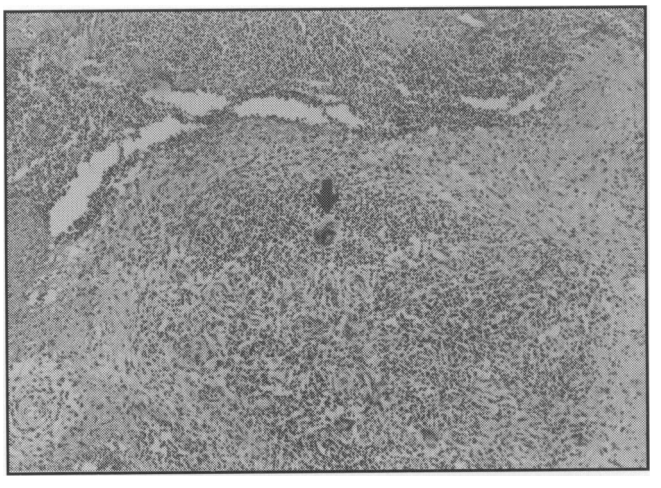


Fig 2[a]. Irregular collagen necrosis with active inflammation (top) and a lymphohistiocytic infiltrate containing giant cells (arrow) (magnification x 250).

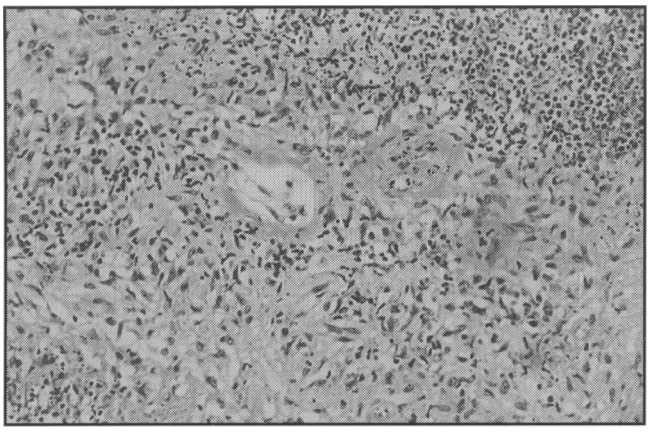


Fig 2[b]. Collagen necrosis with inflammatory debris and an adjacent reaction of histiocytes containing two small necrotic vessels (centre) (magnification x 250).

DISCUSSION

Non-Hodgkin's malignant lymphoma forms approximately one to seven percent of testicular neoplasms and is the commonest tumour at this site in the 60-80 year age group. It is bilateral in 10-25% of cases, mostly immunoblastic B-cell in type and disseminates rapidly to intra-abdominal lymph nodes with a 20% five year survival.[1] It can be present either as localised (Stage I – 55% of cases) or widespread (Stage IV – 34% of cases) disease, often shows complete remission (73% of cases) on initial treatment but ultimately causes death in more than half of patients with a better prognosis for Stage I disease and sclerotic tumours.[10] Sites of spread include central nervous system, bone, bone marrow, liver, kidney, orbit, small intestine and the opposite testis.[1, 10] Spread into the epididymis either by direct extension or as a separate nodule is not unusual and involvement may be isolated to the tunica, epididymis[11] or spermatic cord alone[10] and even the ventral aspect of the base of the penis.[12] Testicular relapse is not uncommon in T-cell leukaemia but only a minority of testicular lymphomas in adulthood are T-cell in type,[1] where there may also be simultaneous cutaneous involvement.[10] Scrotal disease is only fleetingly mentioned in standard texts[2] and our first case is also unusual in that the scrotal cutaneous lesions pre-dated the testicular disease – presumably because of its T-cell nature. T-cell lymphoma may be associated with an angiocentric and angiodestructive distribution and extra-nodal presentation at various sites including upper aero-digestive tract, skin, central nervous system and lung.

Vasculitis of the polyarteritis type can be limited to the penis[6] and testis[5] although testicular lesions may be seen initially or concurrently in 38-86% of cases with widespread disease.[5] Involvement of the genitourinary tract has been noted both in limited and systemic forms of Wegener's granulomatosis. Systemic disease has been associated with vulval[13] and prostatic[14] lesions, renal papillary necrosis,[15] ureteric stenosis,[16] and necrotising granulomatous vasculitis of the mucocutaneous junction of the penis.[8] The latter case required partial amputation of the penis, was associated with an elevated ESR (85 mm/hour) and decreased renal function due to a focal necrotising glomerulonephritis. Dore[7] described Wegener's granulomatosis of the full length of the penile urethra causing a necrotising urethral tumour in a 44 year old male. Genitourinary involvement was noted to be rare and to be a poor prognostic factor when part of systemic disease. Cataldini[9] noted a 40 year old man with an elevated ESR (120 mm/hour) and lesions isolated to the penile prepuce who was alive and well with no further disease one year later. Reed has suggested that up to 5% of cases of Wegener's granulomatosis may present with an initial skin ulcer.[17] There is also some evidence that the limited and protracted superficial (pathergic) forms of Wegener's granulomatosis focus on the lung, skin and upper respiratory tract with either no renal involvement or a long latent period prior to its development.[18] Recent evidence suggests that patients with cutaneous Wegener's granulomatosis showing a leucocytoclastic vasculitis have more rapidly progressive and extensive disease than those with a granulomatous reaction who only infrequently develop subsequent renal and pulmonary lesions.[19] Goulart[20] also noted that Wegener's granulomatosis may present as a localised tumorous lesion in various tissues including retro-peritoneum (where it may cause ureteric obstruction), mediastinum, breast, orbit and gingiva.

Our second case is unusual in that it highlights a cutaneous/penile tumorous lesion predating more widespread systemic involvement and associated with subsequent positive cANCA levels. It also suggested poor compliance with drug therapy.

ACKNOWLEDGEMENTS

The authors thank Drs W Henry, G Varghese, Z Desai, C Doherty and Mr R Donaldson for their permission to report these cases. Dr C Hill kindly provided information about the renal biopsy.

REFERENCES

1. Lee F D. Unusual sites and types of lymphoma. In: Anthony P P, MacSween R N M (Eds). Recent Advances in Histopathology, Vol 16. Churchill Livingstone. Edinburgh 1994, 75-6.
2. McChesney T M, Murphy W M. Diseases of the penis and scrotum. In: Murphy W M. Urological Pathology. W B Saunders. Philadelphia 1989, 404.
3. Tuder R M. Vulvar destruction by malignant lymphoma. *Gynaecol Oncol* 1992, **45**: 52-7.
4. Kaplan M A , Jacobson J O, Ferry J A, Harris N L. T-cell lymphoma of the vulva in a renal allograft recipient with associated hemophagocytosis. *Am J Surg Pathol* 1993, **17**: 842-9.
5. Warfield A T, Lee S J, Phillips S M A, Pall A A, Isolated testicular vasculitis mimicking a testicular neoplasm. *J Clin Pathol* 1994, **47**: 1121-3.
6. Kinn A C, Hedenborg L. Polyarteritis nodosa of the penis. *Scand J Urol Nephrol* 1977, **11**: 289-91.
7. Dore B, Duriez P, Grange Ph, Aubert J. Granulomatose de Wegener à localisation úretro-pénienne a propos d'un cas. *Ann Urol* 1990, **24**: 256-8.
8. Vella E J, Waller D G. Granulomatous vasculitis of the penis with glomerulonephritis. *Postgrad Med J* 1981, **57**: 262-4.
9. Cataldini S, De Simone M, Poti R. Granulomatosi di Wegener ad esordio insolito. Descrizone di un caso. *Recenti Prog Med* 1988, **79**: 249-52.
10. Ferry J A, Harris N L, Young R H, Coen J, Zietman A, Scully R E. Malignant lymphoma of the testis, epididymis, and spermatic cord. A clinicopathologic study of 69 cases, with immunophenotypic analysis. *Am J Surg Pathol* 1994, **18**: 376-90.
11. Schned A R, Variakojis D, Straus F H, Sweet D L. Primary histiocytic lymphoma of the epididymis. *Cancer* 1979, **43**: 1156-63.
12. Carter R D, Smith R, Alpern H D, Healey B M. Primary lymphoma of the penis with rationale of treatment. *Int Urol Nephrol* 1992, **24**: 521-5.
13. Bachmayer K, Ludwig H, Radaszkiewicz T. Eine 60 jahrige patientin mit sialadenitis, lungenrundherden und ulcus vulvae. *Wien Klin Wochensch* 1984, **96**: 289-94.
14. Stillwell T J, de Remee R A, Mcdonald T J, Weiland L H, Engen D E. Prostatic involvement in Wegener's granulomatosis. *J Urol* 1987, **138**: 1251-3.
15. Watanabe T, Nagafuchi Y, Yoshikawa Y, Toyoshima H. Renal papillary necrosis associated with Wegener's granulomatosis. *Hum Pathol* 1983, **14**: 551-7.
16. Ronco P, Mignon F, Lanoe Y, Roland J, Morel-Maroger L, Gattegno B. Ureteral stenosis in Wegener's granulomatosis, a report of a case. *Nephron* 1982, **30**: 201-4.
17. Reed W B, Jensen A K, Konwaler B E, Hunter D. The cutaneous manifestations in Wegener's granulomatosis. *Acta Derm Venereol* 1963, **43**: 250-64.
18. Lever W F, Schaumburg-Lever G. Wegener's granulomatosis. In: Histopathology of the Skin. Lippincott, Philidelphia 1990, 7th Edition, 199-200.
19. Barksdale S K, Hallahan C W, Kerr G S, Fauci A S, Stern J B, Travis W D. Cutaneous pathology in Wegener's Granulomatosis. *Am J Surg Pathol* 1995, **19**: 161-72.
20. Goulart R A, Mark E J, Rosen S. Tumefactions as an extravascular manifestation of Wegener's Granulomatosis. *Am J Surg Pathol* 1995, **19**: 145-53.

The Ulster Medical Journal, Volume 65, No. 2, pp. 173-176, November 1996.

Association of Clinical Pathology, Irish branch Abstracts from Spring Meeting 19-20th April 1996

FATAL PARAQUAT POISONING: THE WEST OF IRELAND EXPERIENCE

K Feeley, C E C Connolly, J Callaghan

Department of Pathology, University College Hospital, Galway.

A review of fatal paraquat poisoning in the West of Ireland over an 18-year period from 1977 to 1995 is presented. There were 44 cases in total, 41 of which were apparently suicidal, 40 of these involving oral ingestion of paraquat (Gramoxone), with 1 case of intramuscular injection. Two accidental cases involved droplet ingestion while spraying, with a third case of Gramoxone being mistaken for an alcoholic beverage. 86% were male, with 52% married; 57% were farmers by occupation. The average volume of Gramoxone ingested was 40 ml, ranging from <1 ml to >1000 ml. The average survival time was 56-72 hours, ranging from <6 hours to 22 days. The survival time was inversely proportional to the volume taken, and to spot urine measurements of paraquat taken shortly after ingestion. At autopsy, the organs involved were lungs (100%, showing intra-alveolar haemorrhage, with 9 cases of fibrosing alveolitis), liver (66%, showing centrilobular necrosis, fatty change and cholestasis), kidneys (62%, ranging from mild nephritis to massive acute tubular necrosis), adrenals (34%, showing massive cortical necrosis, with particular involvement of the zona fasiculata), and heart (9%, showing toxic myocarditis).

PENICILLIN RESISTANT PNEUMOCOCCI

C E Goldsmith, J E Moore, P G Murphy

Molecular Epidemiology Unit, N.Ireland Public Health Laboratory, Bacteriology Department, Belfast City Hospital

Pneumococcal disease is the only infectious disease to rank in the top ten list of fatal conditions in the Western world. *Streptococcus pneumoniae* is the commonest cause of pneumonia in general and of fatal pneumonia in particular. It is also the commonest cause of adult meningitis and childhood bacteraemia. Pneumococcal otitis media affects at least 25% of all children. The emergence of penicillin and multi-resistant pneumococci (PRP) threatens to inflate these already significant mortality and morbidity figures to those of the pre-antibiotic era.

Recently there has been a dramatic increase in the number of PRP isolated at the Northern Ireland Public Health Laboratory. In a study of 488 consecutive isolates of pneumococci here in 1988, only 4 (0.82%) isolates were resistant to penicillin. The figures for 1993 and 1995 were 2% and 18% respectively and 79% PRP were of the identical serotype '9V'. 36% of isolates demonstrated high-level penicillin resistance which cannot usually be treated by increased dosage. Of further concern, 94% were cross-resistant to cefotaxime compared to an expected UK rate of 69%.

The possibility of a clonal outbreak in Northern Ireland following importation of PRP from tourists returning from Spain is currently being investigated using the molecular typing technique of Arbitrary Primed Polymerase Chain Reaction (AP-PCR).

MESENTERIC LYMPH NODE CAVITATION SYNDROME AND COELIAC DISEASE - CASE REPORT

P Lim, M Madden, F A O'Connor

Departments of Gastroenterology and Pathology, Altnagelvin Hospital, Londonderry, Northern Ireland.

Patients with coeliac disease are at higher risk of developing gastro-intestinal malignancy e.g. small bowel lymphoma. In addition, other less common complications of coeliac disease have been described. We report a case of a rare complication of coeliac disease – mesenteric lymph node cavitation syndrome, to draw attention to the unusual lymph node abnormalities. This syndrome is characterised by three features:

cavitation of mesenteric lymph nodes, flat small intestinal mucosa and splenic atrophy.

The patient reported had malabsorption. A jejunal biopsy showed subtotal villous atrophy. She was initially unresponsive to gluten withdrawal but eventually responded when maintained on oral steroids and gluten free diet. She had developed strictures in her jejunum and at laparotomy was found to have large cavitating lymph nodes in the small intestinal mesentery. Subsequent investigations showed that she also had an atrophic spleen.

Review of literature showed 16 previously reported cases of mesenteric lymph node cavitation syndrome. The pathogenesis is unknown and the mortality is about 50%.

A HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL ASSESSMENT OF DIRECTIONAL ATHERECTOMY SPECIMENS

D M O'Rourke, M M Khan,
J M Sloan

Department of Pathology and Regional Cardiology, Royal Group of Hospitals Trust, Grosvenor Road Belfast, Northern Ireland.

Re-stenosis is a relatively common complication of both coronary angioplasty and directional coronary atherectomy (DCA) with an approximate rate of 25-30%. Prediction of those patients more likely to develop re-stenosis would possibly allow therapeutic or surgical intervention and thorough post-procedure monitoring of those at risk. This study was undertaken in an attempt to predict re-stenosis using histological and immunohistochemical markers. The retrieved tissue in 101 DCAs from 98 patients (83 male and 15 female with a mean age of 56.3 years) was formalin fixed for 24 hours embedded in paraffin and 5um sections were cut and stained with H&E, Von Kossa and Masson trichrome. Immunohistochemistry was carried out using monoclonal antibodies to Ki-67(MIB-1) p53, CMV, and smooth muscle actin. The presence of thrombus, intima, media and adventitia was assessed. Semiquantitative grading of calcification (0-3+) was performed. Computerised image analysts was used to accurately count immunopositive staining cells.

Repeat angiography in those patients with recurrence of symptoms showed re-stenosis in 28 (27%). Five patients underwent coronary artery bypass grafting due to procedure failure and one patient died following surgery. Of the 93 patients who had successful DCA, histology revealed thrombus in 48% arterial media in 27% and adventitia in 0.9%. There was no correlation between these and re-stenosis or other complications. Re-stenosis was more common in female patients. DCAs with extensive calcification were more likely to require surgery post-procedure and most of the re-stenosis cases had calcific deposits. Thirty two cases stained positively with Ki-67 and the labelling indices varied between 0.3 and 4%. There was, however, no significant correlation with re-stenosis. P53 immunostaining was only positive in 7 cases, 2 of which were also positive for CMV although the results do not reach statistical significance.

In conclusion, the presence of heavy calcification within the atherectomy plaques correlates with an increased risk of surgical intervention, and re-stenosis is also more common in these cases. At present no immunohistochemical marker seems to predict patients more likely to develop re-stenosis.

APOLIPOPROTEIN AI CONTAINING LIPOPROTEINS IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS

P L M Lynch, M J O'Kane, M E Callender,
G S Nesbitt, E R Trimble

Department of Clinical Biochemistry, Liver Clinic, Royal Victoria Hospital, Grosvenor Road, Belfast.

Primary Biliary Cirrhosis (PBC) is a chronic progressive cholestatic disorder associated with an increased serum total cholesterol concentration. Despite this PBC patients do not appear to be at increased risk of cardiovascular disease. There has been recent interest in the role of apoAI containing lipoprotein particles (LpAI and LpAI: AII) in protecting against cardiovascular disease. There is no information on such particles in PBC patients.

Aim:

To define the lipoprotein profile and the apoAI containing lipoprotein particles in patients with PBC.

Subjects:

31 patients with biopsy proven PBC [30F, 1M; age 59.5 yrs (SD11.6)] were compared with 27 control subjects [26F, 1M; age 53.7 yrs (SD11.6)].

Methods:

LpAI and LpAI: AII were measured by differential electroimmunoassay. Other analytes were measured by standard laboratory techniques. ApoAI containing particles were sized by gel permeation chromatography of serum.

Results:

Data from patients with advanced PBC (stage 4) was analysed separately from those with stage 1/2/3 disease. Total cholesterol and HDL cholesterol were increased in the PBC stages 1/2/3 group compared with controls [total cholesterol: 6.27mmol/L(1.74) vs 5.17(1.01) mean(SD) $p<0.02$; HDL: 1.90mmol/L(0.61) vs 1.33(0.36) $p<0.0005$] while triglycerides remained unchanged [1.28mmol/L(0.45) vs 1.48(0.64) $p=0.48$]. Although total apoAI was unchanged [174.4mg/L(38.5) vs 174.1(18.1) $p=0.97$], LpAI was increased in the PBC group [100.1mg/L(23.5) vs 62.6(9.4) $p<0.0001$]. LpAI: AII was decreased in the PBC stages 1/2/3 group [36.7mg/L(10.1) vs 44.4(6.0) $p<0.005$]. ApoB levels were unchanged [121.3mg/L(32.7) vs 137.7(35.0) $p=0.97$]. Lipoprotein abnormalities were dependent on PBC stage, with advanced PBC (stage 4) associated with reduced total and HDL cholesterol, apoAI, LpAI and LpAI: AII with respect to controls and stage 1/2/3 patients. There were no differences in the size profile of apoAI containing particles between PBC patients (n=7) and controls (n=8).

Conclusion:

The lipoprotein abnormalities in PBC are dependent on the stage of disease. Stages 1/2/3 PBC are associated with an increase in the supposedly anti-atherogenic LpAI particles.

BREAST CARCINOMA IN YOUNG WOMEN: A CLINICOPATHOLOGICAL REVIEW

S Curran, K Barry, O Clinton, J Callaghan

Department of Histopathology, Department of Surgery, University College Hospital, Galway.

A retrospective study is reported of all cases of breast carcinoma in women aged 40 years or younger 1982-1994 at U.C.H.G. Comparison was made with a random group of women aged over 40 years with breast carcinoma. There was a trend towards a higher incidence of ductal carcinoma and of high grade tumours in the young women. Thirty-five per cent of the tumours occurring in young women were oestrogen-receptor negative whilst only 8% were oestrogen-receptor rich. Amongst the older women 46% of the tumours were oestrogen-receptor rich ($p<0.01$). There was a positive family history of breast carcinoma in 42% of the young women compared with 8.5% of the older women ($p<0.01$). The most significant differences between the two groups were in terms of family history and oestrogen-receptor status.

CLINICAL ALGORITHMS - HEPATITIS

C McCaughey, H J O'Neill, D E Wyatt, P V Coyle

Regional Virus Laboratory, Royal Hospitals Trust, Grosvenor Road, Belfast BT12 6NB.

The Regional Virus Laboratory computer system is based on a relational database. Clinical details on request forms are entered and are accessible for searching. All requests in which the clinical details indicated that the patient was suspected to have hepatitis were analysed for the calendar year 1995 (9009 tests) and revealed:

1. There were no cases of hepatitis C without risk factors.
2. There were no acute cases of hepatitis C.
3. Hepatitis B coreAg IgG reactivity was often present in patients with acute hepatitis of non HBV origin.
4. No acute or chronic HBV infections were HBcoreAg IgG negative.
5. EBV & CMV were frequent causes of acute hepatitis.
6. Atypical pneumonia screening indicated causes of cases of acute and chronic hepatitis.

These findings were used to construct a proposed algorithm for testing specimens:

Acute Hepatitis:[1]	Chronic Hepatitis:
Hepatitis B surface	Hepatitis B surface
Hepatitis B coreAgG[2]	Antigen

Hepatitis A IgM Hepatitis C antibody
EBV IgM
CMV IgM
Atypical pneumonia screen[3]

[1] A report is issued to indicate this is an acute screen and that if additional tests are required (e.g. hepatitis C) then this would require direct contact with the laboratory.

[2] A further 1-2 year audit with HBsAg/HBcAg IgG as front line assays for acute hepatitis with the intention of dropping either HBsAg or HBcAg IgG.

[3] If respiratory symptoms stated on request form.

THE ROLE OF POULTRY IN THE MOLECULAR EPIDEMIOLOGY OF HUMAN CAMPYLOBACTER INFECTION IN NORTHERN IRELAND BY CYTOTOXICITY ASSAY, ISOENZYME ELECTROPHORESIS PROFILE TYPING AND DNA FINGERPRINT POLYMORPHISM

J E Moore, L O'Riordan, M McCarron, T Stanley, B C Millar, D R A Wareing, T S Wilson, P G Murphy

Molecular Epidemiology Research Unit, Northern Ireland Public Health Laboratory, Belfast City Hospital, Department of Microbiology and Immunobiology, The Queen's University of Belfast, Preston Public Health Laboratory, Royal Preston Hospital.

Campylobacter infections are the most commonly reported cause of acute bacterial enteritis in man both in Northern Ireland and Gt. Britain. Although food and various environmental sources have been implicated in human infection, sub-species typing methods have lacked the ability to discriminate at this level, in order to help elucidate sources of infection and routes of transmission. There is strong epidemiological data that chicken is a major source of human Campylobacter infection. As the majority of poultry consumed in Northern Ireland is produced locally, this allows for a controlled epidemiological study to be carried out in order to ascertain whether chicken is a major source of human infection locally. Campylobacter spp. (n=275) representing C.jejuni (78%), C.coli (20%) and C.lari (2%), were isolated from neck skin of freshly slaughtered chickens at local processors by a selective enrichment technique. Isolations from poultry were carried out from 9 May to 1 July 1994. Clinical Campylobacter isolates (n=62) were obtained from subjects (35 male and 27 female) presenting with acute enteritis over the period, 16 May to 8 July 1994 and were sporadic in nature. All strains were speciated and a representative population (n=30 chickens isolates and n=30 human isolates) were selected for comparison, by phenotyping [Preston biotyping, MAST disc-typing and phage-typing techniques] and by genotyping [multilocus enzyme electrophoresis (MEE) technique and 165 = 235 rRNA typing]. Phenotypically the 30 chicken isolates gave 20 Preston biotypes and 51% of isolates were non-typeable by the Preston phage-typing technique. The 30 human isolates gave 17 different biotypes and 17.7% of isolates were non-typeable by phage-typing. On examination of the preliminary MEE and ribotyping data, there were two distinct clusters, each containing a mixture of human and chicken isolates, indicating a common association between chicken and human Campylobacter spp. Results demonstrated that there were common shared phenotypes and genotypes in chickens and man, indicating chickens' role in the aetiology of this infection. However a lactate dehydrogenase (LDH) release assay with porcine aortic endothelial cells showed that there was a significant difference in the cytotoxic response between strains uniquely seen in chicken and those commonly observed in humans, indicating that not all Campylobacter spp. may be pathogenic for humans and thus parallel the situation with many other Gram-negative enteric pathogens such as E.coli and Salmonella spp.

The Ulster Medical Journal, Volume 65, No. 2, pp. 177-178, November 1996.

Book Reviews

Communication Skills for Medicine – M Lloyd and R Bor. Churchill and Livingstone. ISBN 0-443-05168-2.

Increasingly the focus of medical training is edging away from pure book learning and traditional methods of eliciting clinical signs, and towards the development of problem solving and communication skills. In parallel with this trend is the reality that most surveys of the attitudes of patients towards their doctors have yielded the perception that doctors do not provide sufficient information to patients. Patients all too frequently feel that their contact with doctors does not facilitate the most effective bilateral communication.

This book which is written by a general practitioner and a clinical psychologist is primarily directed towards medical students, but any practising doctor is likely to find it thought provoking and useful.

The ground rules of good communication are well covered and a number of very practical interviewing techniques are described. The book emphasises that despite all the advantages of modern technology most diagnoses are made by taking the history.

With appropriate training students and doctors frequently improve their ability to elicit information. However they would appear to find it more difficult to impart information to the patient. In this context the chapter on breaking bad news is particularly helpful. Lloyd and Bor emphasise the danger on the one hand of being insensitive or too blunt with bad news and on the other hand of the doctor reducing his own anxiety by giving inappropriate reassurance. There is a helpful chapter on how to take a sexual history while two others deal with communication with children and with patients from different cultural backgrounds. Throughout the book the importance of the social context is emphasised. There is a section dealing with the role of patients' relatives, an area of particular importance in psychiatry which is also of great relevance to all doctors.

The book is well laid out and easy to read. A number of exercises, many of which involve role play, are outlined and will be of use to students and their teachers. At various points in the text a 'STOP' sign invites the reader to put aside his medical persona and to look at the issue instead from the perspective of the lay person.

I have no hesitation in recommending this book to all students and teachers of communication skills.

P McGARRY

Handbook of Current Diagnosis and Management. Roy Pounder and Mark Hamilton (Eds). Churchill Livingstone, pp 494. ISBN 0-443-05600-5.

"This book is full of information", as stated in its preface, but to whom is this information directed and is it accessible to the reader? The *Handbook of Current Diagnosis and Treatment*, contains 494 pages of crisp detail and despite having over two hundred contributors is easy to use. This is because the format of the book is uniform, each topic being summarized and limited to two facing pages, one given to diagnosis, symptoms and signs, investigations and complications together with separate columns for differential diagnosis, aetiology and epidemiology; whilst the other is devoted to treatment, management, prognosis and the latest references.

However, this very rigid format means that at times very common and important conditions are lightly brushed over; relative rarities receiving the same coverage in terms of 'quanta' of information given. This results in obvious deficiencies, such as the medical emergencies hardly being mentioned. For a book that claims to provide quick and easy reference on how to diagnose and manage all the major medical diseases, this oversight should be corrected in future editions.

Who should use this book? The direct delivery of facts requires the reader to be familiar with the basics of clinical medicine. A useful aide-memoire for students, if used too early in training it could encourage learning from lists rather than building a logical framework from basics. The section "pharmacological treatment" is of such detail that the book would appear to be aimed at practising physicians, but at what level? Certainly junior doctors will be able to use the book to get 'clued up' on medical topics with which they were previously unfamiliar in addition to increase their ability to order ever more sophisticated investigations, necessary or not. More advice on when to refer patients for specialist consultation and follow up should be available in the section "management and follow-up".

Unfortunately patients present with problems much more frequently than with diagnoses, and this book like all disease based texts assumes that the condition is already known to the patient or doctor. Although a symptom index is present, for the more common complaints this can be time consuming to use and after referencing the symptom it can still be difficult to decide on its aetiology.

However, when a condition is known, information is easily retrieved, is full and as up to date as is possible, so used as an aide memoire, the book achieves a fair level of success.

J CRAIG

Bailie and Love's Short Practice of Surgery. 22nd Edition. Charles V Mann, R C G Russell, N S Williams (Eds.) pp 1041, Price £59.95, London, Chapman and Hall 1995. ISBN 0412-72410-3.

The fact that this textbook has been in circulation for over 60 years and reached its 22nd Edition bears testimony to the pivotal role it has played in communication of surgical knowledge. Whereas the initial text was written by two of the leading surgeons of their day, the current edition is a multi-author textbook with 41 internationally recognised contributors, including its three authoritative editors. The latter have ensured that the final product is a unified volume worthy of the central place it continues to hold in world terms as one of the foremost surgical textbooks.

The editors expressed aim has been to provide an up-to-date volume to meet the requirements of students, surgeons in training and practising general surgeons outside specialist

The Ulster Medical Journal, Volume 65, No. 2, pp. 177-178, November 1996.

Book Reviews

Communication Skills for Medicine – M Lloyd and R Bor. Churchill and Livingstone. ISBN 0-443-05168-2.

Increasingly the focus of medical training is edging away from pure book learning and traditional methods of eliciting clinical signs, and towards the development of problem solving and communication skills. In parallel with this trend is the reality that most surveys of the attitudes of patients towards their doctors have yielded the perception that doctors do not provide sufficient information to patients. Patients all too frequently feel that their contact with doctors does not facilitate the most effective bilateral communication.

This book which is written by a general practitioner and a clinical psychologist is primarily directed towards medical students, but any practising doctor is likely to find it thought provoking and useful.

The ground rules of good communication are well covered and a number of very practical interviewing techniques are described. The book emphasises that despite all the advantages of modern technology most diagnoses are made by taking the history.

With appropriate training students and doctors frequently improve their ability to elicit information. However they would appear to find it more difficult to impart information to the patient. In this context the chapter on breaking bad news is particularly helpful. Lloyd and Bor emphasise the danger on the one hand of being insensitive or too blunt with bad news and on the other hand of the doctor reducing his own anxiety by giving inappropriate reassurance. There is a helpful chapter on how to take a sexual history while two others deal with communication with children and with patients from different cultural backgrounds. Throughout the book the importance of the social context is emphasised. There is a section dealing with the role of patients' relatives, an area of particular importance in psychiatry which is also of great relevance to all doctors.

The book is well laid out and easy to read. A number of exercises, many of which involve role play, are outlined and will be of use to students and their teachers. At various points in the text a 'STOP' sign invites the reader to put aside his medical persona and to look at the issue instead from the perspective of the lay person.

I have no hesitation in recommending this book to all students and teachers of communication skills.

P McGARRY

Handbook of Current Diagnosis and Management. Roy Pounder and Mark Hamilton (Eds). Churchill Livingstone, pp 494. ISBN 0-443-05600-5.

"This book is full of information", as stated in its preface, but to whom is this information directed and is it accessible to the reader? The *Handbook of Current Diagnosis and Treatment*, contains 494 pages of crisp detail and despite having over two hundred contributors is easy to use. This is because the format of the book is uniform, each topic being summarized and limited to two facing pages, one given to diagnosis, symptoms and signs, investigations and complications together with separate columns for differential diagnosis, aetiology and epidemiology; whilst the other is devoted to treatment, management, prognosis and the latest references.

However, this very rigid format means that at times very common and important conditions are lightly brushed over; relative rarities receiving the same coverage in terms of 'quanta' of information given. This results in obvious deficiencies, such as the medical emergencies hardly being mentioned. For a book that claims to provide quick and easy reference on how to diagnose and manage all the major medical diseases, this oversight should be corrected in future editions.

Who should use this book? The direct delivery of facts requires the reader to be familiar with the basics of clinical medicine. A useful aide-memoire for students, if used too early in training it could encourage learning from lists rather than building a logical framework from basics. The section "pharmacological treatment" is of such detail that the book would appear to be aimed at practising physicians, but at what level? Certainly junior doctors will be able to use the book to get 'clued up' on medical topics with which they were previously unfamiliar in addition to increase their ability to order ever more sophisticated investigations, necessary or not. More advice on when to refer patients for specialist consultation and follow up should be available in the section "management and follow-up".

Unfortunately patients present with problems much more frequently than with diagnoses, and this book like all disease based texts assumes that the condition is already known to the patient or doctor. Although a symptom index is present, for the more common complaints this can be time consuming to use and after referencing the symptom it can still be difficult to decide on its aetiology.

However, when a condition is known, information is easily retrieved, is full and as up to date as is possible, so used as an aide memoire, the book achieves a fair level of success.

J CRAIG

Bailie and Love's Short Practice of Surgery. 22nd Edition. Charles V Mann, R C G Russell, N S Williams (Eds.) pp 1041, Price £59.95, London, Chapman and Hall 1995. ISBN 0412-72410-3.

The fact that this textbook has been in circulation for over 60 years and reached its 22nd Edition bears testimony to the pivotal role it has played in communication of surgical knowledge. Whereas the initial text was written by two of the leading surgeons of their day, the current edition is a multi-author textbook with 41 internationally recognised contributors, including its three authoritative editors. The latter have ensured that the final product is a unified volume worthy of the central place it continues to hold in world terms as one of the foremost surgical textbooks.

The editors expressed aim has been to provide an up-to-date volume to meet the requirements of students, surgeons in training and practising general surgeons outside specialist

The Ulster Medical Journal, Volume 65, No. 2, pp. 177-178, November 1996.

Book Reviews

Communication Skills for Medicine – M Lloyd and R Bor. Churchill and Livingstone. ISBN 0-443-05168-2.

Increasingly the focus of medical training is edging away from pure book learning and traditional methods of eliciting clinical signs, and towards the development of problem solving and communication skills. In parallel with this trend is the reality that most surveys of the attitudes of patients towards their doctors have yielded the perception that doctors do not provide sufficient information to patients. Patients all too frequently feel that their contact with doctors does not facilitate the most effective bilateral communication.

This book which is written by a general practitioner and a clinical psychologist is primarily directed towards medical students, but any practising doctor is likely to find it thought provoking and useful.

The ground rules of good communication are well covered and a number of very practical interviewing techniques are described. The book emphasises that despite all the advantages of modern technology most diagnoses are made by taking the history.

With appropriate training students and doctors frequently improve their ability to elicit information. However they would appear to find it more difficult to impart information to the patient. In this context the chapter on breaking bad news is particularly helpful. Lloyd and Bor emphasise the danger on the one hand of being insensitive or too blunt with bad news and on the other hand of the doctor reducing his own anxiety by giving inappropriate reassurance. There is a helpful chapter on how to take a sexual history while two others deal with communication with children and with patients from different cultural backgrounds. Throughout the book the importance of the social context is emphasised. There is a section dealing with the role of patients' relatives, an area of particular importance in psychiatry which is also of great relevance to all doctors.

The book is well laid out and easy to read. A number of exercises, many of which involve role play, are outlined and will be of use to students and their teachers. At various points in the text a 'STOP' sign invites the reader to put aside his medical persona and to look at the issue instead from the perspective of the lay person.

I have no hesitation in recommending this book to all students and teachers of communication skills.

P McGARRY

Handbook of Current Diagnosis and Management. Roy Pounder and Mark Hamilton (Eds). Churchill Livingstone, pp 494. ISBN 0-443-05600-5.

"This book is full of information", as stated in its preface, but to whom is this information directed and is it accessible to the reader? The *Handbook of Current Diagnosis and Treatment*, contains 494 pages of crisp detail and despite having over two hundred contributors is easy to use. This is because the format of the book is uniform, each topic being summarized and limited to two facing pages, one given to diagnosis, symptoms and signs, investigations and complications together with separate columns for differential diagnosis, aetiology and epidemiology; whilst the other is devoted to treatment, management, prognosis and the latest references.

However, this very rigid format means that at times very common and important conditions are lightly brushed over; relative rarities receiving the same coverage in terms of 'quanta' of information given. This results in obvious deficiencies, such as the medical emergencies hardly being mentioned. For a book that claims to provide quick and easy reference on how to diagnose and manage all the major medical diseases, this oversight should be corrected in future editions.

Who should use this book? The direct delivery of facts requires the reader to be familiar with the basics of clinical medicine. A useful aide-memoire for students, if used too early in training it could encourage learning from lists rather than building a logical framework from basics. The section "pharmacological treatment" is of such detail that the book would appear to be aimed at practising physicians, but at what level? Certainly junior doctors will be able to use the book to get 'clued up' on medical topics with which they were previously unfamiliar in addition to increase their ability to order ever more sophisticated investigations, necessary or not. More advice on when to refer patients for specialist consultation and follow up should be available in the section "management and follow-up".

Unfortunately patients present with problems much more frequently than with diagnoses, and this book like all disease based texts assumes that the condition is already known to the patient or doctor. Although a symptom index is present, for the more common complaints this can be time consuming to use and after referencing the symptom it can still be difficult to decide on its aetiology.

However, when a condition is known, information is easily retrieved, is full and as up to date as is possible, so used as an aide memoire, the book achieves a fair level of success.

J CRAIG

Bailie and Love's Short Practice of Surgery. 22nd Edition. Charles V Mann, R C G Russell, N S Williams (Eds.) pp 1041, Price £59.95, London, Chapman and Hall 1995. ISBN 0412-72410-3.

The fact that this textbook has been in circulation for over 60 years and reached its 22nd Edition bears testimony to the pivotal role it has played in communication of surgical knowledge. Whereas the initial text was written by two of the leading surgeons of their day, the current edition is a multi-author textbook with 41 internationally recognised contributors, including its three authoritative editors. The latter have ensured that the final product is a unified volume worthy of the central place it continues to hold in world terms as one of the foremost surgical textbooks.

The editors expressed aim has been to provide an up-to-date volume to meet the requirements of students, surgeons in training and practising general surgeons outside specialist

departments. It is a very difficult task to produce a text at an appropriate level that is ideal for this wide spectrum of readership. Inevitably, there are places where comprehensive coverage of a topic exceeds that required by the undergraduate student while in other areas the text may lack details of management important to the practising surgeon. However, a very reasonable balance has been struck in providing a textbook which contains a great deal of basic as well as advanced information, emphasises the clinical manifestation of disease processes and provides an up-to-date account of evolving investigative and therapeutic technology.

The book is clearly laid out and professionally produced. The text is well written in a clear and concise easily readable style. It is extremely well illustrated with diagrams and high quality monochrome and colour photographs of clinical lesions.

In the 22nd Edition a larger page size, printed in two column format, offers considerable advantages over previous editions. Summary headings of the contents are given at the beginning of each chapter. A concise list of references of recommended further reading is given at the end of most chapters. Again the well selected brief historical footnotes have been maintained.

The book is reasonably priced and represents a good investment for personal use or departmental library.

T G PARKS

Brain Ischaemia: Basic Concepts and Clinical Relevance. Louis R Caplan (Ed). ISBN 3-540-19850-4 Springer-Verlag Berlin Heidelberg New York. ISBN 0-387-19850-4 Springer-Verlag New York Berlin Heidelberg.

This book aims to bring clinicians who treat stroke patients up to date with the basic science aspects of brain, blood, vascular and cardiac functions, and to marry such information with important clinical issues. The pace of change has been such that doctors not directly involved have been unable to keep up. It has become very important to understand the basic science since it now has the potential to be applied to the daily treatment and care of stroke patients. Also it is vitally important for those involved or interested in the current raft of therapeutic trials.

The editor is an eminent and highly respected neurologist from Boston who has written or edited several books on stroke over recent years. He writes in a pleasant style and his thought processes are clear and logical. His claim to know well what clinicians will want to know and how to translate the material into a digestible form appears reasonable. He acts rather like a tour guide, showing clinicians round some rather foreign basic science.

The majority of contributors are clinically experienced. Of the 30 contributors 23 are from the USA and six of these are from around Boston; there are two from the UK, both from London. The book is divided into seven sections, each with prefatory and concluding comments by Caplan, with between one and five chapters in each section. The section headings are the brain, the eye, the blood, the blood vessels, blood flow, blood pressure and intracranial pressure, the heart, clinical research, epidemiology, statistics, databases and trials. The section on the brain has introductory comments that are useful and cautious, but the conclusions strike the optimistic note of the enthusiast – significant bleeding and oedema can be detected. To what end?

The quality and relevance of the chapters vary. PET in acute ischaemic stroke is central to current thinking; excitotoxicity and stroke is useful but dated; growth factors are of only distant relevance and ischaemic cerebral oedema is basic.

At first glance, a chapter on the eye does not appear to rest easily in a book on brain ischaemia. The prefatory comments attempt to justify its inclusion on the grounds that an understanding of the anatomy and physiology is essential to understand ocular ischaemia. Why not similar chapters on the brain? I suppose it could be argued that those dealing with stroke should be well informed in those areas. Surely then ocular ischaemia should be dealt with by those familiar with the eye. Set against this, patients with TIAs are often seen by physicians whose knowledge of the eye may not be as good as with that of the brain. If this book is meant to be read cover to cover it may be useful; if used as a reference who would think to look here for the basic anatomy and physiology of the eye?

The section on coagulation is excellent whereas that on cerebral vasoconstriction is plagued by intrusive references that are irritating and make it difficult to read. The final section on epidemiology also appears out of place.

In summary, this book achieves what it sets out to do with aplomb, and the quibbles I mentioned do not spoil it.

M WATT

The Working Men's Committee. By L A Clarkson & Marianne Litvack. Cost £3.95. Obtainable from The Office of Archives, King Edward Building, Royal Victoria Hospital, or Royal Victoria Hospital Corridor shop.

This slim history records the work of a group who literally kept the Royal Victoria Hospital from collapsing at times over the past century. Professor Leslie Clarkson of the Queen's University Department of Economic and Social History was asked to write this history and, with the help of Mrs Jean Ludlow who carried out the initial research and Ms Marianne Litvack, he has produced a highly readable and informative account of the committee's work. Sadly, their minute books have long since disappeared and for details of the day to day work we have to rely largely on newspaper accounts and Annual Reports of the Hospital. However, the authors have set the committee's work in the wider context of the funding of the hospital as a whole and of other voluntary hospitals. It has therefore a much wider appeal and an educational value to all who have an interest in hospital income and expenditure. We should all be grateful to the working men of Belfast for helping to carry the Royal Victoria Hospital particularly in the difficult days before the National Health Service.

R CLARKE

departments. It is a very difficult task to produce a text at an appropriate level that is ideal for this wide spectrum of readership. Inevitably, there are places where comprehensive coverage of a topic exceeds that required by the undergraduate student while in other areas the text may lack details of management important to the practising surgeon. However, a very reasonable balance has been struck in providing a textbook which contains a great deal of basic as well as advanced information, emphasises the clinical manifestation of disease processes and provides an up-to-date account of evolving investigative and therapeutic technology.

The book is clearly laid out and professionally produced. The text is well written in a clear and concise easily readable style. It is extremely well illustrated with diagrams and high quality monochrome and colour photographs of clinical lesions.

In the 22nd Edition a larger page size, printed in two column format, offers considerable advantages over previous editions. Summary headings of the contents are given at the beginning of each chapter. A concise list of references of recommended further reading is given at the end of most chapters. Again the well selected brief historical footnotes have been maintained.

The book is reasonably priced and represents a good investment for personal use or departmental library.

T G PARKS

Brain Ischaemia: Basic Concepts and Clinical Relevance. Louis R Caplan (Ed). ISBN 3-540-19850-4 Springer-Verlag Berlin Heidelberg New York. ISBN 0-387-19850-4 Springer-Verlag New York Berlin Heidelberg.

This book aims to bring clinicians who treat stroke patients up to date with the basic science aspects of brain, blood, vascular and cardiac functions, and to marry such information with important clinical issues. The pace of change has been such that doctors not directly involved have been unable to keep up. It has become very important to understand the basic science since it now has the potential to be applied to the daily treatment and care of stroke patients. Also it is vitally important for those involved or interested in the current raft of therapeutic trials.

The editor is an eminent and highly respected neurologist from Boston who has written or edited several books on stroke over recent years. He writes in a pleasant style and his thought processes are clear and logical. His claim to know well what clinicians will want to know and how to translate the material into a digestible form appears reasonable. He acts rather like a tour guide, showing clinicians round some rather foreign basic science.

The majority of contributors are clinically experienced. Of the 30 contributors 23 are from the USA and six of these are from around Boston; there are two from the UK, both from London. The book is divided into seven sections, each with prefatory and concluding comments by Caplan, with between one and five chapters in each section. The section headings are the brain, the eye, the blood, the blood vessels, blood flow, blood pressure and intracranial pressure, the heart, clinical research, epidemiology, statistics, databases and trials. The section on the brain has introductory comments that are useful and cautious, but the conclusions strike the optimistic note of the enthusiast – significant bleeding and oedema can be detected. To what end?

The quality and relevance of the chapters vary. PET in acute ischaemic stroke is central to current thinking; excitotoxicity and stroke is useful but dated; growth factors are of only distant relevance and ischaemic cerebral oedema is basic.

At first glance, a chapter on the eye does not appear to rest easily in a book on brain ischaemia. The prefatory comments attempt to justify its inclusion on the grounds that an understanding of the anatomy and physiology is essential to understand ocular ischaemia. Why not similar chapters on the brain? I suppose it could be argued that those dealing with stroke should be well informed in those areas. Surely then ocular ischaemia should be dealt with by those familiar with the eye. Set against this, patients with TIAs are often seen by physicians whose knowledge of the eye may not be as good as with that of the brain. If this book is meant to be read cover to cover it may be useful; if used as a reference who would think to look here for the basic anatomy and physiology of the eye?

The section on coagulation is excellent whereas that on cerebral vasoconstriction is plagued by intrusive references that are irritating and make it difficult to read. The final section on epidemiology also appears out of place.

In summary, this book achieves what it sets out to do with aplomb, and the quibbles I mentioned do not spoil it.

M WATT

The Working Men's Committee. By L A Clarkson & Marianne Litvack. Cost £3.95. Obtainable from The Office of Archives, King Edward Building, Royal Victoria Hospital, or Royal Victoria Hospital Corridor shop.

This slim history records the work of a group who literally kept the Royal Victoria Hospital from collapsing at times over the past century. Professor Leslie Clarkson of the Queen's University Department of Economic and Social History was asked to write this history and, with the help of Mrs Jean Ludlow who carried out the initial research and Ms Marianne Litvack, he has produced a highly readable and informative account of the committee's work. Sadly, their minute books have long since disappeared and for details of the day to day work we have to rely largely on newspaper accounts and Annual Reports of the Hospital. However, the authors have set the committee's work in the wider context of the funding of the hospital as a whole and of other voluntary hospitals. It has therefore a much wider appeal and an educational value to all who have an interest in hospital income and expenditure. We should all be grateful to the working men of Belfast for helping to carry the Royal Victoria Hospital particularly in the difficult days before the National Health Service.

R CLARKE

departments. It is a very difficult task to produce a text at an appropriate level that is ideal for this wide spectrum of readership. Inevitably, there are places where comprehensive coverage of a topic exceeds that required by the undergraduate student while in other areas the text may lack details of management important to the practising surgeon. However, a very reasonable balance has been struck in providing a textbook which contains a great deal of basic as well as advanced information, emphasises the clinical manifestation of disease processes and provides an up-to-date account of evolving investigative and therapeutic technology.

The book is clearly laid out and professionally produced. The text is well written in a clear and concise easily readable style. It is extremely well illustrated with diagrams and high quality monochrome and colour photographs of clinical lesions.

In the 22nd Edition a larger page size, printed in two column format, offers considerable advantages over previous editions. Summary headings of the contents are given at the beginning of each chapter. A concise list of references of recommended further reading is given at the end of most chapters. Again the well selected brief historical footnotes have been maintained.

The book is reasonably priced and represents a good investment for personal use or departmental library.

T G PARKS

Brain Ischaemia: Basic Concepts and Clinical Relevance. Louis R Caplan (Ed). ISBN 3-540-19850-4 Springer-Verlag Berlin Heidelberg New York. ISBN 0-387-19850-4 Springer-Verlag New York Berlin Heidelberg.

This book aims to bring clinicians who treat stroke patients up to date with the basic science aspects of brain, blood, vascular and cardiac functions, and to marry such information with important clinical issues. The pace of change has been such that doctors not directly involved have been unable to keep up. It has become very important to understand the basic science since it now has the potential to be applied to the daily treatment and care of stroke patients. Also it is vitally important for those involved or interested in the current raft of therapeutic trials.

The editor is an eminent and highly respected neurologist from Boston who has written or edited several books on stroke over recent years. He writes in a pleasant style and his thought processes are clear and logical. His claim to know well what clinicians will want to know and how to translate the material into a digestible form appears reasonable. He acts rather like a tour guide, showing clinicians round some rather foreign basic science.

The majority of contributors are clinically experienced. Of the 30 contributors 23 are from the USA and six of these are from around Boston; there are two from the UK, both from London. The book is divided into seven sections, each with prefatory and concluding comments by Caplan, with between one and five chapters in each section. The section headings are the brain, the eye, the blood, the blood vessels, blood flow, blood pressure and intracranial pressure, the heart, clinical research, epidemiology, statistics, databases and trials. The section on the brain has introductory comments that are useful and cautious, but the conclusions strike the optimistic note of the enthusiast – significant bleeding and oedema can be detected. To what end?

The quality and relevance of the chapters vary. PET in acute ischaemic stroke is central to current thinking; excitotoxicity and stroke is useful but dated; growth factors are of only distant relevance and ischaemic cerebral oedema is basic.

At first glance, a chapter on the eye does not appear to rest easily in a book on brain ischaemia. The prefatory comments attempt to justify its inclusion on the grounds that an understanding of the anatomy and physiology is essential to understand ocular ischaemia. Why not similar chapters on the brain? I suppose it could be argued that those dealing with stroke should be well informed in those areas. Surely then ocular ischaemia should be dealt with by those familiar with the eye. Set against this, patients with TIAs are often seen by physicians whose knowledge of the eye may not be as good as with that of the brain. If this book is meant to be read cover to cover it may be useful; if used as a reference who would think to look here for the basic anatomy and physiology of the eye?

The section on coagulation is excellent whereas that on cerebral vasoconstriction is plagued by intrusive references that are irritating and make it difficult to read. The final section on epidemiology also appears out of place.

In summary, this book achieves what it sets out to do with aplomb, and the quibbles I mentioned do not spoil it.

M WATT

The Working Men's Committee. By L A Clarkson & Marianne Litvack. Cost £3.95. Obtainable from The Office of Archives, King Edward Building, Royal Victoria Hospital, or Royal Victoria Hospital Corridor shop.

This slim history records the work of a group who literally kept the Royal Victoria Hospital from collapsing at times over the past century. Professor Leslie Clarkson of the Queen's University Department of Economic and Social History was asked to write this history and, with the help of Mrs Jean Ludlow who carried out the initial research and Ms Marianne Litvack, he has produced a highly readable and informative account of the committee's work. Sadly, their minute books have long since disappeared and for details of the day to day work we have to rely largely on newspaper accounts and Annual Reports of the Hospital. However, the authors have set the committee's work in the wider context of the funding of the hospital as a whole and of other voluntary hospitals. It has therefore a much wider appeal and an educational value to all who have an interest in hospital income and expenditure. We should all be grateful to the working men of Belfast for helping to carry the Royal Victoria Hospital particularly in the difficult days before the National Health Service.

R CLARKE