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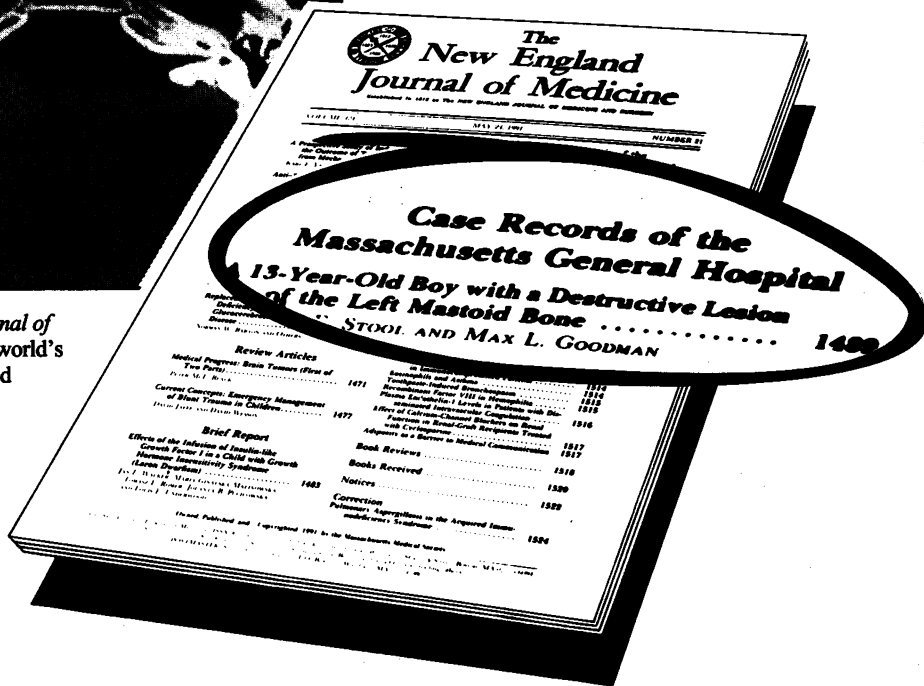
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The Ulster Medical Journal

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Volume 63 No. 1

April 1994

Editorial

“All change . . .”

1948: 1972: 1994. Will these dates be remembered by future social historians as important points of change in the progress of health care organization in the United Kingdom? Perhaps some future student of the economics of health promotion, or death prevention, or whatever it may be called, will consult the *Ulster Medical Journal* to see what contemporary Ulster doctors were thinking on these topics at those seminal times. They will find very little. Doctors write about diseases and how they think they should be cured, or treated. They particularly like to write about unusual diseases, which presumably throw a favourable light on their diagnostic acumen. Some become epidemiologists, which is a form of prospective study of medical history, but that takes a long time, collection of other peoples data is less exciting – and nothing spoils a good long term follow-up study more than a change in the rules of health care. This issue of the *Journal* contains two historical discourses on aspects of late Victorian medicine, seen through the eyes of Sir William Whitla, arguably the most famous Belfast physician, and of the group of citizens who were responsible for the rebuilding of the main hospital in Belfast nearly a hundred years ago.

Whitla could write large books on current treatments, none of which could have been truly curative: but what did he think about junior doctors hours, of the throughput of patients in the hospital beds under his supervision, or even of the budget of the hospital committee? How much did the new Royal Victoria Hospital cost to build, and is it true that Lady Pirrie had accumulated the total cost of £150,000 on deposit from donations before building began? There was no government opinion or finance, but there was certainly support from all the leaders of the time, whether financiers, politicians or working men.

In 1948 the National Health Service was born: in the *Ulster Medical Journal* for that year the then Professor John Henry Biggart contributed a long and detailed pathological dissertation on the hypothalamus which may have presaged the continuing development of endocrinology in Belfast. Dr Samuel Barron made

little reference to the new NHS in his presidential address on "Changing outlooks in Preventive Medicine" apart from a comment on education of the public. In the RVH Opening Address by Mr Frank MacLaughlin, FRCS on "The Patient and his Doctor" there is only a brief paragraph on the state medical service, "I have no doubt that in time modifications and changes will cause the wheels to run smoothly and efficiently . . .". Perhaps Dr J G Johnston in his presidential address to the Northern Ireland Branch of the British Medical Association got closest to the point in his remarks on "The Country Surgeon" – "we are at present passing through a great, new, transitional stage. The bad, old, poorly-equipped days are happily gone".

By 1972, when the Northern Ireland Hospitals Authority was abolished and four Area Boards appeared, Sir John Henry Biggart was still writing; this time on the origins of Hippocratic medicine in a scholarly comparison of the schools of Cnidos and Cos, and contributing to the introductory description of the new Northern Ireland Council for Postgraduate Medical Education. Dr J A McVicker, a distinguished family doctor in Belfast, could reminisce that general practice had always been an exacting way of life, and looked back with concern at the diminishment in the family doctor's role which took place after 1948; this was only gradually redressed, notably by the founding of the College of General Practitioners. In the same year a group of family doctors met at a management course at Ballygally Castle and looked forward with remarkable prescience to the community care team and the health centre concept.

But no-one foresaw a theoretical purchaser-provider split, or the concept of a fund-holding general practice, or a junior doctors' hours-of-work contract which threatened to close hospitals. If you read this issue carefully from cover to cover you will find a few phrases which show how we really feel about the present changes. But mostly we continue to record the unusual case, or the good medical care of a group of common diagnostic problems. *Plus ça change, plus c'est la même chose.*

D R HADDEN

Acute appendicitis in young children in the Belfast urban area: 1985 – 1992

D Wilson, S Sinclair, W A McCallion, S R Potts

Accepted 31 December 1993

SUMMARY

Eighty-one cases of acute appendicitis in children aged less than six years were identified in the Belfast urban area between 1985 and 1992. Appendiceal perforation, found in 43%, was related to symptom duration but not to age at presentation. Prolongation of symptoms was related to parental delay in seeking medical advice (52% > 36 hours), delayed or inappropriate general practitioner referral to hospital (19%) and diagnostic delay following surgical consultation (12% > 12 hours). Diagnostic delay in hospital was usually the result of nonspecificity of symptoms and signs and was therefore largely unavoidable. Delayed referral from general practice did not contribute unnecessarily to appendiceal perforation, and given that an individual general practitioner will see a case of preschool appendicitis once in 30 years, diagnostic accuracy was remarkably high.

INTRODUCTION

Appendicitis is the most common indication for laparotomy in childhood. In young children symptoms are often non-specific and initial assessment by accident and emergency staff or general practitioners is notoriously difficult. Therefore diagnosis may be delayed and morbidity increased^{1,2}. In this paper we review appendicitis in children aged less than six years in the Belfast urban area over a 7 year period and highlight factors contributing to diagnostic delay.

METHODS

The hospital records of all 100 children aged less than six years who underwent appendicectomy for suspected appendicitis in the Royal Belfast Hospital For Sick Children, Belfast City Hospital and Ulster Hospital between 1985 and 1992 were surveyed retrospectively. Symptom duration, referral pattern, investigations and post-operative complications were assessed. Discriminant function analysis was used to determine which symptoms and signs discriminated between children with perforated appendicitis, non-perforated appendicitis and those in whom the appendix was found to be normal. The specificity, sensitivity, positive

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and negative predictive values of groups of symptoms and signs were determined. A *t* test was used to compare symptom duration in children with perforated and non-perforated appendicitis.

RESULTS

Of 100 children undergoing appendicectomy for suspected appendicitis 62 were male. The mean age was 49 months (range 11 to 70 months). All were examined histologically and acute appendicitis was found in 81 cases. No seasonal variation was noted. Presenting symptoms and signs are shown in table 1.

TABLE 1
Symptoms and signs of acute appendicitis in young children.

<i>Symptoms/ Sign</i>	<i>Non-perforated appendicitis n=43</i>	<i>Perforated appendicitis n=35</i>	<i>Normal appendix n=19</i>	<i>Discriminant function analysis</i>
Right iliac fossa pain	37(86%)	26(74%)	16(84%)	NS
Generalised abdominal pain	5(14%)	9(26%)	3(16%)	NS
Involuntary guarding	37(85%)	30(85%)	6(32%)	$p<0.05$
Vomiting	30(69%)	29(83%)	13(64%)	NS
Pyrexia (>37.5°C)	29(67%)	35(100%)	10(52%)	$p<0.05$
Rebound tenderness	17(33%)	23(65%)	4(20%)	$p<0.05$
Diarrhoea	6(14%)	7(20%)	1(5%)	NS
Sore throat	2(4%)	1(3%)	4(20%)	$p<0.05$
Constipation	2(4%)	0	3(16%)	$p<0.05$
Dysuria	0	2(5%)	1(5%)	$p<0.05$
Headache	0	0	1(5%)	NS
Cough	0	0	2(10%)	$p<0.05$
Chest pain	0	0	2(10%)	$p<0.05$
Rhonchi/ crepitations	0	0	2(10%)	$p<0.05$

Using three-group discriminant function analysis, involuntary guarding, rebound tenderness and pyrexia were significantly more common in children with perforated or non-perforated appendicitis than those in whom the appendix was normal ($p<0.05$). Conversely cough, chest pain, sore throat and constipation were more common in children without appendicitis ($p<0.05$). Table 2a shows the sensitivity and specificity of these symptoms and signs in differentiating between the three groups of patients. The sensitivity for detecting appendiceal perforation was 50% and for non-perforated appendicitis 72.1%. The specificity

(correct normal prediction) was 52.6%. By combining the perforated and non-perforated groups (table 2b) the sensitivity for detecting appendicitis improved to 96.3% although the specificity remained unchanged. The positive predictive value was 89.7% and the negative predictive value 76.9%.

TABLE 2

Diagnostic predictions based on presenting symptoms and signs: (a) to distinguish between perforated and non-perforated appendicitis; (b) to distinguish between both types of appendicitis and the normal appendix group.

Actual diagnosis	Cases	Predicted diagnosis		
		perforated appendicitis	non-perforated appendicitis	normal appendicitis
(a)				
Perforated appendicitis	38	19(50%)	18(47.4%)	1(2.6%)
Non-perforated appendicitis	43	10(23.3%)	31(72.1%)	2(47%)
Normal appendix	19	3(15.8%)	6(31.6%)	10(52.6%)
(b)				
Appendicitis (all types)	81	78(96.3%)		3(3.7%)
Normal appendix	19	9(47.4%)		10(52.6%)

Fifty eight patients had been assessed initially by a general practitioner; acute appendicitis was suspected in 39 of these and was later confirmed in 36. Five patients who had been provisionally diagnosed as having gastroenteritis and were admitted to the Regional Infectious Diseases Unit were confirmed to have appendicitis. Fourteen children not referred to hospital at the first consultation by a general practitioner had non-specific symptoms for appendicitis; diarrhoea (5), dysuria (4), wheeze or cough (2), constipation (2) and sore throat (1). Five of these were reviewed within 24 hours and then referred for a surgical opinion; four had acute appendicitis. The nine remaining children were all "self-referred" to hospital and three had acute appendicitis.

The appendix had perforated in 35 cases. This was not related to age at presentation (Table 3). The mean delay from onset of symptoms to surgery in the perforated group was 77 hours compared with 45 hours in the non-perforated group ($p < 0.05$). Factors contributing to diagnostic delay in the perforated group included parental delay in seeking medical advice (52% more than 36 hours), delayed or inappropriate referral by the general practitioner (19%), and diagnostic delay following surgical consultation (12% more than 12 hours).

TABLE 3

Age at presentation and appendiceal perforation.

<i>Age</i>	<i>Number of cases of perforated appendicitis</i>
1 year	2(6%)
2 years	6(17%)
3 years	7(20%)
4 years	10(28.5%)
5 years	10(28.5%)

Abdominal radiography was performed on 50 children. An appendolith was demonstrated in one, and there were features of localised ileus in eight; in all these nine cases acute appendicitis was found. Urinary microscopy revealed pyuria in 14 of 95 children tested, four of whom had a bacteriologically proven urinary tract infection; three of these had concomitant acute appendicitis. The white cell count was elevated ($>11,000/\text{ml}$) in 32 children (92%) with a perforated appendix, 38(89%) with non-perforated appendicitis and 16(85%) of those operated upon where the appendix was shown to be normal.

Antibiotic therapy was used in all cases. Cephuroxime and metronidazole, given intravenously at induction of anaesthesia, was continued post-operatively for 24 hours in those with non-perforated appendicitis and for five days in those with perforated appendicitis. Wound infection occurred in five and an intra-abdominal abscess developed in a further four patients. Of these nine patients, seven had a perforated appendix.

The mean length of hospital stay in patients with perforated appendicitis was 5.7 days, compared with 3.7 days for non-perforated appendicitis and 3.2 days for those in whom the appendix was normal. If wound or intra-abdominal sepsis developed the mean length of stay was 8.6 days. All 100 children were reviewed once within 6 weeks of surgery and no further complications were noted.

DISCUSSION

Appendicitis in children aged less than six years is uncommon; only 81 cases occurred in the Belfast urban area in seven years in a population of 44,294 children at risk³. This area is served by 314 principal general practitioners, 22 assistants and 15 trainees⁴, who could thus expect to see one case every 30 years. The main factor contributing to appendiceal perforation is diagnostic delay, which results in increased post-operative morbidity, length of stay and treatment cost. It is no surprise that in over half the cases parents delayed for more than 36 hours before seeking medical advice, and such delay may be unavoidable. However, given the low incidence of the condition the diagnostic accuracy of the primary health care team was remarkably high, 92% of children referred at the first consultation being correctly diagnosed. In the 19 cases where delay was attributed to the family doctor, all had non-specific symptoms or signs for appendicitis. In this group only 21% perforated, compared to 49%

in those referred early following the initial consultation. Thus diagnostic delay outside hospital did not contribute unnecessarily to appendiceal perforation.

This study also confirms that clinical examination is the principal diagnostic tool. Abdominal pain radiating to the right iliac fossa with involuntary guarding, rebound tenderness and pyrexia remain the most common presenting features in young children with acute appendicitis. Using these criteria the sensitivity for diagnosing acute appendicitis in children in this age group is high (96.3%); however the ability to distinguish between perforation and non-perforated appendicitis is poor (sensitivity 50% and 72.1% respectively). Similarly, the ability accurately to predict that a young child presenting in this manner will have a normal appendix is also poor (specificity 52.6%). Computerised scoring systems are of no additional benefit in improving diagnostic accuracy⁵ and investigations such as urinalysis, radiography and ultrasonography are of doubtful value. Leucocytosis is sensitive but not specific, although assessment of acute phase reactants may improve specificity⁶. Diagnostic laparoscopy may have a role in cases with atypical symptoms or signs, particularly in the young age group.

This paper confirms that diagnostic delay is the main contributing factor to appendiceal perforation in pre-school children. Much of this delay is probably unavoidable. The diagnostic accuracy of general practitioners is high and any delay is usually a result of atypical presentation; delay in these patients does not add significantly to the risk of perforation.

We thank Mr V E Boston and Mr S Brown for permission to report their patients.

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Uvulopalatopharyngoplasty for snoring: the Belfast experience

Ruth Capper, I Gleadhill, M J Cinnamond

Accepted 25 January 1994

SUMMARY

We have studied thirteen patients to assess the efficacy of uvulopalatopharyngoplasty on snoring and on oxygen desaturation during sleep. Pre- and post-operative overnight pulse oximetry studies were performed and the patients were divided into snorers and those with obstructive sleep apnoea on the basis of the preoperative test. Uvulopalatopharyngoplasty did not result in a significant change in the number of oxygen saturation dips in either snorers or those with the obstructive sleep apnoea syndrome. Subjectively, 85% (11/13) of patients reported good or excellent improvement in snoring following surgery.

INTRODUCTION

Snoring is a common problem in adults, being habitual in 24% of men and 14% of women¹. It is more common in the elderly and in those who are obese. A small subgroup of snorers suffer from the syndrome of obstructive sleep apnoea in which complete obstruction of the upper airway occurs after the onset of sleep resulting in arterial hypoxaemia. These episodes of arterial oxygen desaturation are spontaneously terminated by waking, but when sleep resumes the cycle is repeated. This sleep disruption may result in daytime somnolence and intellectual decline. More importantly, hypertension, cardiac arrhythmias and cor pulmonale are also recognised as sequelae.

The initial treatment of snoring and obstructive sleep apnoea is weight reduction, limitation of alcohol consumption and bedhead elevation, but adequate weight reduction is seldom achieved and the other measures have limited success². Other conservative methods of management include chin and head straps and tongue restraining devices. Nasal continuous positive airway pressure ventilation is very effective but has to be used each night indefinitely and many patients or their partners find it unacceptable. Drug therapy has been disappointing. Surgical treatment, including uvulopalatopharyngoplasty³, mandibular advancement, hyoid elevation and

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tracheotomy⁴, has been described; the first of these has found popularity. We describe the results of this operation in a series of patients treated at the Belfast City Hospital.

PATIENTS AND METHODS

All patients undergoing uvulopalatopharyngoplasty for snoring or sleep apnoea 1989-91 were studied prospectively. There were 12 males and one female. Pre-operative weights ranged from 59kg to 133kg (mean 84kg). One patient was hypertensive. Twelve patients underwent uvulopalatopharyngoplasty, four also had trimming of the inferior turbinates and one had submucous resection of the nasal septum. One patient had a staphylectomy (removal of the uvula) only, with trimming of inferior turbinates, but this procedure was considered similar enough to include him in the study.

Overnight pulse oximetry (Ohmeda Biox 3700) was performed on all patients, pre-operatively and again no sooner than three months after surgery. The number of oxygen saturation dips of 4% or greater were counted and compared statistically using the Wilcoxon test.

TABLE I

Comparison of the number of oxygen saturation dips of 4% or greater in pre- and post-operative recordings.

Patient	No. of saturation dips	
	Pre-operative	Post-operative
Snorers	1	1
	2	20
	3	4
	4	13
	5	29
	6	8
Obstructive sleep apnoea	7	225
	8	54
	9	373
	10	43
	11	43
	12	125
	13	123

For the total group, using the Wilcoxon test for non-parametric data $p = 0.25$

For the snorers, using the paired t-test, $p = 0.42$

For the obstructive sleep apnoea group, using the Wilcoxon test, $p = 0.31$

Patients and their partners were also asked for a subjective assessment of the improvement in snoring at surgical follow-up using a simple score (0 = no improvement, 1 = mild improvement, 2 = good improvement and 3 = excellent improvement). Grades 0 and 1 were regarded as failed surgical intervention and grades 2 and 3 as successful.

RESULTS

The number of oxygen saturation dips in the pre- and post-operative tracings are shown in table 1. Analysis using the Wilcoxon test showed no significant difference at $p=0.05$. The patients were then sub-divided into those who were uncomplicated snorers and those with obstructive sleep apnoea (those with more than 30 desaturations overnight). Comparison of the number of desaturations in these two sub-groups pre- and post-operatively showed no significant difference in either case.

The patients' and their partners' combined assessment of improvement in snoring is shown in table 2. Eleven out of thirteen reported a good or excellent result, a success rate of 85%. One of the failures continued to have frequent apnoeic episodes during sleep and is being considered for tracheotomy.

TABLE II
Changes in snoring after surgery.

	<i>Success</i>	<i>Failure</i>	<i>Total</i>
Snorers	5	1	6
Obstructive sleep apnoea	6	1	7
Total	11 (85%)	2	13

Acute complications of surgery included three secondary haemorrhages and one epistaxis. There were two cases of subsequent nasal regurgitation during eating, one had settled completely after eight months and the second failed to attend for follow-up.

DISCUSSION

Uvulopalatopharyngoplasty has been reported as successful in the treatment of snoring in 90%-100% of cases^{5, 6, 7} and in 50% of cases of obstructive sleep apnoea⁵. The operation was first described in 1981 by Fujita et al³ and since then has achieved widespread acceptance as a method of treating these conditions when conservative management has failed. The tonsils are removed along with the anterior tonsillar pillars and the redundant posterior edge of the soft palate, including the uvula. The rationale is the appearance of a 'crowded pharynx' in these patients, with the combination of large tonsils, a narrow pharyngeal isthmus and a long soft palate and uvula^{3, 8}. Observation through the nasendoscope shows 'pharyngeal collapse' during performance of the Muller manoeuvre where the patient tries to inspire with the mouth and nostrils closed.

Improvement in patients with obstructive sleep apnoea can be quantitatively measured by polysomnography or, less invasively, by overnight pulse oximetry (the 'mini sleep study')⁹. Assessment of snoring is more difficult. The duration and intensity (loudness) of the snore can be recorded on an overnight audio tape recording but this may not reflect the social problem, and a subjective measurement of improvement should be considered in assessing success or failure of surgery. Gordon *et al*⁷ graded snoring from 0 (no snoring) to IV (obstructive sleep apnoea) before and after surgery and found a universal improvement in a series of eleven patients undergoing uvulopalatopharyngoplasty. They excluded patients with polysomnographic evidence of obstructive sleep apnoea.

The patients reported in this paper were assessed by overnight oximetry alone and the group included those with uncomplicated snoring as well as those whose tracings were suggestive of obstructive sleep apnoea (more than 30 dips overnight). In this mixed group, all but two reported good or excellent subjective results in improvement in snoring. Our findings confirm the reports of other investigators who showed that uvulopalatopharyngoplasty is a successful operation for the relief of snoring but is not as successful in improving the hypoxaemia of obstructive sleep apnoea.

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Guidelines for lumbar spine radiography in acute low back pain: effect of implementation in an accident and emergency department

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SUMMARY

Guidelines for lumbar spine radiography were agreed by consultation between staff in the radiology, accident and emergency and neurosurgical departments of a large teaching hospital. Study of 322 consecutive patients over an eight month period showed that the proportion of patients referred for radiography was reduced from 48.4% to 27.2% following introduction of the guidelines ($p=0.0002$). Successful use of such guidelines requires cooperation between clinical and radiological staff and frequent review of performance.

Low back pain is one of the commonest causes of attendance at accident and emergency departments. Many of these patients are referred for radiographic examination of the lumbar spine, but in most cases no useful information is provided¹⁻⁵. Guidelines for such referrals have been published⁶ and their use has been recommended by the National Radiological Protection Board⁷. The purpose of this study was to develop and introduce our own more detailed guidelines, as compliance is most likely to be achieved when staff are responsible for their development and introduction⁸.

METHODS

Details of patients presenting with low back pain to the accident and emergency department over the preceding six months were retrieved retrospectively from the departmental computer. For the next two months the records of all patients presenting with acute low back pain were retained prospectively by the clerical staff. The junior medical staff were not made aware of either this or the preliminary data retrieval described above. The aim was to establish the practice of the current junior staff in the department and to use this data as a baseline for the subsequent study.

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TABLE I
Criteria for lumbar spine radiography

<i>Criterion</i>	<i>Number to be recorded on request form</i>
Trauma	1
Possible serious pathology:	
Night pain worse than day pain	2
Constant pain unrelieved by bedrest (>2 weeks)	3
Thoracic pain	4
History of malignancy	5
Weight loss	6
Pyrexia	7
Kyphosis (not long standing)	8
Age <20 years or >55 years	9
<i>(NB 2-9 Consider sedimentation rate !)</i>	
Orthopaedic referral	10
Other (specify)	11

The guidelines were defined by the authors and based on the known natural history of low back pain and the results of investigation (table 1) ^{1-5, 9, 12}. Two further criteria were included, one for patients being referred to the orthopaedic clinic (which was not participating in the study) and one for any specific reason which the medical staff felt would justify radiography. At a meeting of the authors and all the junior medical staff in the accident and emergency department, the results of the preliminary retrospective six month review of current practice were presented. This was followed by a teaching session which covered history taking and examination of patients presenting with low back pain and interpretation of lumbar spine radiographs. The importance of minimising exposure to radiation was also stressed. The proposed guidelines and their method of introduction were then explained and any queries answered.

The guidelines were then prominently displayed throughout the accident and emergency department. All doctors were required to justify requests for lumbar spine radiography by recording the number of the applicable criterion (or criteria). In the case of criterion 11, the reason for referral was recorded on the patient's record. The radiographers were instructed not to accept a request for radiography if these details were not provided. The five months of the study comprised months 2-6 of the junior doctors' six month attachment to the department in order to ensure continuity of staff throughout. The results were presented to the accident and emergency staff at the end of the study period. The study was continued for a further three months in order to gauge acceptance by a different set of junior doctors.

TABLE II

Radiographic findings in patients presenting with acute low back pain: retrospective six month review.

	<i>Number</i>	
Patients presenting	445	100%
Referred for radiography	336	75%
Normal	221	50%
Degenerative changes	77	17%
Fracture	26	6%
Lytic or sclerotic lesion	4	1%
Spondylolisthesis	8	2%
Other (spondylolysis, transitional vertebra congenital anomalies)	0	0%

RESULTS

Over the six month period prior to the studies 336 patients with low back pain (75%) were referred for radiography (table 2). Twenty-six patients were referred because of trauma and had a fracture. Other significant abnormalities were found in only twelve patients, eight with spondylolisthesis and four with lytic or blastic lesions: these represented 1.8% and 0.9% respectively of all patients. Purely degenerative changes were considered not significant in view of their poor correlation with symptoms and lack of impact on patient management^{3, 5, 13, 14}.

TABLE III

Radiographic findings before and after introduction of guidelines.

	<i>Before</i>	<i>After</i>
	<i>Number (%)</i>	<i>Number (%)</i>
Patients presenting	128 (100%)	184 (100%)
Referred for radiography	62 (48.4%)	50 (27.2%)
Normal	38 (29.7%)	35 (19.0%)
Degenerative changes	15 (11.7%)	9 (4.9%)
Fracture	9 (7%)	4 (2.2%)
Lytic or sclerotic lesion	0	1 (0.6%)
Other (see table 1)	0	1 (0.6%)

The results of introduction of the guidelines are presented in Table 3. During the initial two months of the study, 48% of patients were referred for radiographic examination. Following introduction of the protocol, only 27% were referred. This reduction was significant (X^2 with Yates' correction = 13.9, $p = 0.0002$). The majority of male patients were aged 21-54 years, and female patients more than 55 years. Closer analysis suggested that the number referred had already started to fall during the initial two month period before the guidelines had been introduced, and that in the last month of the study (month three of the second group of doctors studied), the referral rate rose to virtually its pre-protocol level.

If trauma is excluded, the incidence of radiological findings suggestive of tumour or infection was less than 1%. Only one such case had been seen during the formal prospective study period. Spondylolisthesis was seen in 1.8% of patients during the initial six month period but it is unlikely that this finding influenced acute patient management.

DISCUSSION

Most cases of acute low back pain are mechanical in aetiology and symptoms will resolve with simple conservative measures¹⁵. Suspected prolapsed intervertebral disc should be investigated using myelography, CT or MRI if surgery is being considered⁹. When there is no history of trauma, the role of plain radiographs in initial management is to exclude the presence of metastatic or inflammatory disease which may require more active intervention^{9, 15-17}. A detailed history, sedimentation rate and isotope bone scan are much more discriminating than straight X-rays in this context²².

There is a low incidence of such abnormalities on lumbar spine radiographs in this group of patients. Liang calculated a 0.2% chance³ and Nachemson a 1 in 2500 chance¹³ of detecting significant pathological change. Waddell described criteria for identifying these patients based on clinical findings⁹ and Deyo successfully applied guidelines to 621 patients without missing any cases of significant spinal disease⁵. More recently, the Royal College of Radiologists have provided guidelines for patient selection for radiographic examination⁶. Adoption of such guidelines could achieve both financial savings and a reduction in population exposure to ionising radiation^{18, 19}. A large proportion of patients fall into the 20-55 year old age group, many of whom would not be referred for radiography using our guidelines.

We decided to base the indications for radiography on the clinical history and symptoms rather than on physical signs. The history has long been recognised as the most important discriminator in this context^{12, 20} and intra- and inter-observer variation is less likely²². The criteria were derived from a simultaneous study by one of the authors on the management of low back disorders²⁰. The junior doctors found the guidelines easy to use and particularly appreciated the tutorials which were given at their launch.

The initial fall in referral for radiography which occurred before the guidelines were brought into use was felt to be due to news of the survey leaking out despite our attempt to prevent this. It is also notable that the effects of the guidelines began to reduce especially during the period of duty of the second set of junior doctors. This problem has been encountered by others and highlights the need for constant reinforcement²¹. Referral rates can be easily recorded over further

short periods and should be discussed in combination with practical teaching as in our study.

Success in reducing referrals for radiography must not be at the cost of loss of diagnostic sensitivity. If trauma is excluded, less than 1% of findings were likely to affect acute management, so it is not possible to assess the sensitivity of our guidelines in the detection of these abnormalities. A very large study would be required to achieve statistical validity. Deyo, using clinical guidelines did not miss any significant pathology in 621 patients⁵. Good communication with patients has been shown to be more important than special investigations in achieving patient satisfaction with medical care¹¹. Guidelines based on simple findings in the clinical history can significantly reduce referral rates for lumbar spine radiography, but regular reinforcement is required to maintain their effects.

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Prostaglandin E₁ in the medical management of erectile dysfunction in a genito-urinary medicine clinic

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SUMMARY

Fifty consecutive patients with erectile failure who had previously proved refractory to papaverine and phentolamine intracavernosal therapy or were inappropriate candidates for such treatment were treated with intracavernosal prostaglandin E₁. Forty patients (80%) achieved an erection sufficient for sexual intercourse and after a mean follow-up period of 5.9 months, 32 patients were continuing to use treatment successfully. The average dose was 14 micrograms (range 2.5 to 30 micrograms). There were no cases of priapism or cavernosal fibrosis and no systemic side effects. A low incidence (8%) of local discomfort was reported. We conclude that prostaglandin is a safe and effective vasoactive agent for the treatment of erectile failure in a genito-urinary outpatient clinic.

INTRODUCTION

The use of intracavernous vasoactive agents has been shown to be effective in the medical treatment of erectile dysfunction. Virag¹ originally described the use of the smooth muscle relaxant papaverine while Brindley² demonstrated the effectiveness of the alpha adrenergic receptor blocker phenoxybenzamine. A combination of papaverine plus phentolamine (an alpha-blocker) was subsequently shown to be more effective than either agent alone^{3,4}. Ishii⁵ has described the use of prostaglandin E₁, and studies have since demonstrated its efficacy in association with a reduced incidence of serious side effects^{6,7,8}. We are unaware of reports of the use of this drug in a genito-urinary clinic, and describe our experience.

PATIENTS AND METHODS

Patients with erectile dysfunction were referred to the Genito-Urinary Medicine Clinic, which provides a weekly clinic for erectile dysfunction, from their general practitioners or from consultant staff within the Northern Ireland hospital system. After a detailed sexual and medical history a full physical examination was performed and blood was taken for haemoglobin concentration, erythrocyte sedimentation rate, plasma glucose, liver function tests, testos-

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sterone and prolactin measurement. Intracavernous Prostaglandin E₁ was first used in this clinic in November 1991, and this paper describes the first 50 patients. Those selected fulfilled one or more of the following criteria:

- (1) Previous failure to achieve satisfactory erectile response to papaverine 30 mg plus phentolamine 1 mg.
- (2) Previous priapism associated with papaverine plus phentolamine treatment or
- (3) Patients with a history of serious ischaemic heart disease but who were currently stable.

The latter group of patients were assessed by a consultant cardiologist to ensure that treatment for their impotence was appropriate.

Intracavernous injection of 10 µg of prostaglandin was given with a fine bore needle (26 gauge) into the lateral aspect of one of the corpora cavernosa at a site 1-2 cms proximal to the coronal sulcus. It was not our routine practice to use a constricting band at the base of the penis at the time of injection. The drug was supplied in 1 ml ampoules containing 10 µg prostaglandin E₁. These were individually prepared at the pharmacy of the Royal Victoria Hospital from 500 µg ampoules (Upjohn). The initial dosage was 10 µg with appropriate titration according to response up to a maximum of 30 µg. Once an erection sufficient for sexual intercourse was achieved the patient was instructed in the technique of self-injection and supervised to ensure that their technique was correct. A supply of needles, syringes and prostaglandin E₁, was then provided for home use with advice that the injection should not be used more than twice per week; the patient attended on a regular basis to monitor effectiveness, side effects and to provide new supplies. Those who did not achieve an erection sufficient for sexual intercourse despite maximal dosage of 30 µg were assessed for a mechanical suction device.

RESULTS

Fifty patients satisfied the criteria for treatment between November 1991 and September 1992. This represented approximately one third of patients on intracavernosal treatment. Their average age was 52.5 years (range 25-74) with a mean duration of impotence of 5.7 years (range 6 months – 30 years). The aetiology was organic in 44 cases, psychogenic in 3 cases and uncertain in three cases (Table 1). Five patients had had previous episodes of priapism.

TABLE 1
Aetiology of impotence

<i>Aetiology</i>	<i>Number of patients</i>	<i>(%)</i>
Vasculogenic	31	(62)
Diabetes	6	(12)
Neurgenic	5	(10)
Psychogenic	3	(6)
Idiopathic	3	(6)
Alcohol-related	2	(4)

Forty patients (80%) achieved an erection sufficient for sexual intercourse; ten failed. In those treated successfully the average dose was 14 µg (range 2.5-30), the average duration of erection being 80 minutes (range 20 minutes–4 hours). Of the original 40 patients with a satisfactory response 32 are still attending and regularly using injection therapy after a mean follow-up period of 5.9 months (range 1-11 months). Eight patients have failed to continue to attend for unknown reasons.

Four patients complained of local pain in the penis, usually burning in nature and associated with the erection. The aetiology of erectile failure in these cases was vasculogenic in two, diabetic in one and psychogenic in one. In the diabetic case local pain necessitated reduction of the dose from 10 to 5 µg. His erectile response was still satisfactory at the lower dose. To date there have been no systemic side effects and no cases of priapism or corporeal fibrosis.

DISCUSSION

Prostaglandin E_1 is an endogenous prostaglandin whose mode of action has yet to be fully elucidated. It acts as a powerful smooth muscle relaxant leading to dilatation of the cavernosal arteries and relaxation of the cavernosal sinusoidal smooth muscle. Its efficacy has been well documented, with erections sufficient for sexual intercourse reported in 68-86% of patients in unselected series^{5,9,10}. The response rate is highest in those of psychogenic and neurogenic origin^{7,8}, reaching almost 100% in some series^{7,8}. A significantly lower rate of positive response occurs in cases of vasculogenic or diabetic impotence^{5,11}. Our own series was a selected group in terms of aetiology in that failure to respond to papaverine plus phentolamine tended to favour patients with a vasculogenic aetiology and this subgroup formed 60% of the total patient population. The aetiological diagnosis was presumptive on the basis of the clinical history, the presence of coexisting or previous significant medical conditions and thorough physical examination. Angiography was not available for further assessment of presumed vasculogenic cases and it is probable that there was some overlap in the categories, most notably in diabetic cases where both vasculogenic and neurogenic components are commonly present. The idiopathic group were patients in whom no overt organic risk factor for erectile dysfunction could be identified but who at the same time demonstrated no clear evidence of psychological problems. More intensive psychological and physical assessment might allow a more accurate classification of such patients. In this study the overall response rate of 80% demonstrates the superior efficacy of prostaglandin E_1 in the treatment of vasculogenic impotence. In the ten cases where treatment was unsuccessful the presumed aetiology was vasculogenic in seven, idiopathic in two and diabetic in one.

The use of papaverine has two principal complications, priapism and corporeal fibrosis. With the introduction of a combination of papaverine plus an alpha-blocking agent the dosage of papaverine required to induce an erectile response was significantly lowered, but despite this priapism and fibrosis remain important clinical side effects. Ten percent of our patients were commenced on prostaglandin E_1 because of previous priapism associated with papaverine and phentolamine treatment.

Prostaglandin E_1 is a physiological agent partially metabolized locally within the cavernous tissue, and approximately 70% eliminated in a single passage

through the lungs¹². It is this rapid elimination which is believed to account for the absence of systemic side effects even in the presence of venous leakage. Many reports on its clinical use have shown a notable absence of priapism or fibrosis^{5, 8, 9}. Some authors, however, have documented priapism requiring treatment with metaraminol¹⁰; the most vulnerable group being those with a non-vasculogenic aetiology. Cases of sustained erections of up to 11 hours have also been described where spontaneous detumescence ultimately occurred^{6, 10}. In our own series there were no cases of priapism or sustained erection and this may be related to the selection of patients with vasculogenic disease. Corporeal fibrosis and fibrotic thickening of the tunica albuginea have been reported with papaverine injections and may be related to a number of factors including repetitive needle trauma, organization of haematomas associated with vascular puncture, or a local toxic reaction to papaverine solution which is of low pH¹³⁻¹⁶. We found no cases of corporeal fibrosis although the period of follow-up at present is relatively short.

In previous studies the most commonly described side effect of prostaglandin E₁ is the occurrence of localized pain in the penis, varying in intensity from mild discomfort to a severe burning sensation prohibiting sexual intercourse. The reported incidence varies from 11% up to 75%⁶⁻¹⁰, but was a complaint in only four patients (8%) in our own series. In only one was a dose reduction required to ameliorate this problem. Localized pain appears to occur more commonly in those individuals whose impotence is non-vasculogenic in origin¹⁰, which may explain the low incidence of this series. Intracavernous prostaglandin E₁ has proved an effective and safe alternative agent for the treatment of erectile failure with particular application to those patients where treatment with papaverine and phentolamine had been ineffective or inappropriate.

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Initial experience with an electronic CT image transfer system

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SUMMARY

An electronic image transfer system for computed tomographic images links the CT scanner in Altnagelvin Hospital, Londonderry with the regional neuroradiology department in the Royal Victoria Hospital, Belfast. In the first 13 months of operation, scans of 100 patients were transferred; 49 scans were taken in acute neurosurgical emergencies, and 51 were non-acute sent for a specialist neuroradiological opinion. Potentially hazardous inter-hospital transfer was avoided in 21 cases of acute neurosurgical emergency, and more efficient and appropriate referral was achieved in the cases whose scans had been sent for sent for radiological second opinion. We believe that the system has substantially improved the diagnosis and management of patients with neurosurgical problems in both hospitals.

INTRODUCTION

The availability of computerised tomographic (CT) scanning in the United Kingdom has increased substantially over the past five years¹ and Northern Ireland is no exception. CT facilities are now available in seven hospitals and all but one of these provides an emergency service. The regional Neuroscience unit is located in the Royal Victoria Hospital, Belfast and a specialist neuroradiology service is provided on this site. Neurosurgical emergencies in other hospitals are usually transferred to the Royal Victoria Hospital for investigation and assessment, but the patient's condition often makes transfer hazardous and in multiple trauma cases it is recommended that CT scanning is carried out at the base hospital². On other occasions a neuroradiological opinion is sought when there are unexpected findings on cranial or spinal CT imaging. Transfer of patient and scans by ambulance, or the scans by post, to the regional unit may lead to unacceptable delays.

In 1990 Lee et al, in Oxford³ published the results of a study on electronic image transfer in head injured patients. This system was described at a symposium in the same year. Following favourable reports on the use of the system elsewhere in the United Kingdom, and an expression of interest by Altnagelvin Hospital, Imlink systems (Electronic Imaging, Oxford) were purchased by the Royal Victoria and Altnagelvin Hospitals in 1991. We describe our first year's experience.

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METHODS

The Imlink image transfer system is a personal computer based system for acquisition, transmission and display of either CT or MRI images. These are captured from the video output of the scanner, and are stored on a hard disc with capacity of up to 750 images. The images are then transmitted through a modem to other Imlink users via standard telephone dial-up lines. Transfer times depend on the image content and on the quality of the telephone line, typically 6-8 minutes for 20 head images.

Patient identification and a brief clinical history can be recorded as part of the file and transferred with the images. We undertook a retrospective review of the first 100 cases in which image transfer took place. Patient data was obtained from the Imlink files and information regarding outcome was obtained from case records and by direct inquiry from clinicians.

RESULTS

Scans of 100 patients were transferred during the first 13 months of operation. There were 60 male and 40 female, aged from 9 days to 87 years, average age 43 years. There were 49 acute neurosurgical emergencies (head injury or spontaneous intracranial haemorrhage) and 51 cases where the scans were transferred for neuroradiological advice.

In the emergency group the scan images were transferred for assessment by both the neuroradiology and by the neurosurgical staff. Advice regarding the most appropriate management (transfer to Belfast or otherwise) was sought. The images in the second group were transferred for a radiological second opinion.

TABLE 1
Emergency cases: diagnosis leading to image transfer

Trauma	26
Spontaneous intracranial haemorrhage	15
Tumour	5
Other	3

The underlying diagnosis of the emergency patients is summarised in table 1. Of the 26 trauma patients there were 23 head injuries, two facial fractures, and one spinal fracture. Of the 15 patients with spontaneous intracranial haemorrhage 11 had subarachnoid haemorrhage, one an intracerebral haematoma, and three had subdural haematoma with no history of recent trauma. The five intracranial tumours were diagnosed radiologically as meningioma, glioma, colloid cyst of the third ventricle, cerebellar haemangioblastoma, and medulloblastoma. All presented as acute emergencies due to the mass effect associated with the tumour, or with acute hydrocephalus. Of the remaining three cases, one was considered to be normal, one had acute hydrocephalus with no obvious underlying lesion and the third an arachnoid cyst.

TABLE 2

Emergency patients: outcome following CT image transfer

<i>Diagnosis</i>	<i>Emergency transfer</i>	<i>Elective transfer</i>	<i>No transfer</i>
Trauma	3	15	8
Intracranial haemorrhage	0	9	6
Tumours	0	5	0
Other	0	2	1
Total	3	31	15

The immediate outcome of the emergency patients is summarised in Table 2. Three patients, all with severe head injuries, were transferred to the Royal Victoria Hospital, Belfast as emergencies for immediate neurosurgical intervention. Thirty-one patients were transferred electively, in working hours on the following day or once a bed became available. The remaining 15 patients were not transferred: five because it was felt that neurosurgical intervention either was unnecessary or was unlikely to improve the outcome in view of the clinical status and radiological appearances, and nine who were considered unfit for transfer due to the clinical condition or the severity of other injuries (Two of these had emergency treatment locally for acute extradural haematoma). Five of these nine patients subsequently died.

TABLE 3

Underlying diagnosis in 51 cases where the CT images were transferred for a neuroradiological opinion

Intracranial Tumour	22
Congenital lesion	7
AV malformation	4
Infarct	5
Demyelination	2
Normal	4
Spinal Lesion	4
Other	3

The underlying diagnosis in the patients whose scans were transferred for a neuro-radiological opinion is summarised in Table 3. None of these patients were transferred as an emergency, eight were transferred electively and 16 were referred to outpatient clinics at the Royal Victoria Hospital. Four of the

eight cases were transferred electively for further neuroradiological investigation (usually angiography), and three of these were shown to have intracranial arteriovenous malformations. The others were transferred for treatment of lesions such as intracranial tumours. Sixteen patients were referred as outpatients to either the neurosurgical or neurological clinics in Belfast. One patient was referred for an MRI scan in Oxford but was managed in Altnagelvin Hospital.

As a result of image transfer, a total saving of 21 emergency ambulance journeys from Altnagelvin Hospital to the Royal Victoria Hospital was made. The cost of an emergency transfer is calculated from mileage and personnel. The total saving for these 21 journeys avoided was £5197 (150 miles at 65p per mile = £187 : two ambulance crew at £6.50 for four hours = £60: total charge for each emergency transfer = £247).

DISCUSSION

As a result of image transfer from Altnagelvin hospital to the neuroradiology department at the Royal Victoria Hospital, patients presenting as neurosurgical emergencies have been managed in a more efficient and cost effective manner. The relatively modest cost of installation of the Imlink system (about £7500) was almost covered by the saving in unnecessary emergency ambulance transfers in the first year of operation. This finding is in common with other authors^{1,4}. An appreciable number of scans sent for second opinion have resulted in referral of the patient to either the neurosurgical or neurological departments. These referrals have been made more appropriately as a result of consultation between the radiologists and clinicians and some inappropriate referrals have been avoided.

Some difficulties have been encountered when scans are transferred out of normal working hours, when the neurosurgeon on call does not have access to the neuroradiology department where the Imlink unit is housed. At present this is overcome by the neuroradiologist on call coming in to read the scans. In other units terminals have been installed in the radiologists homes, and a portable Imlink device is now available which may provide the solution to out of hours image transfer to both radiologists and clinicians.

The educational aspects of the system have not been addressed in this paper, but there is a benefit to both the referring clinician and radiologist, and to the regional neuroradiology department in terms of experience. A successful teaching programme has been developed by another Imlink user in the UK. Overall we feel that the installation of this system has been of benefit to patients, radiologists and clinicians and our experience may be useful in other areas.

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Patients' perception of day case surgery

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SUMMARY

A postal questionnaire was used to assess patient compliance with instructions, post-operative sequelae and general practitioner workload resulting from the day case unit of Daisy Hill Hospital, Newry. Compliance with instructions was good. There was little post-operative pain but there was a high incidence of other side effects. Few patients needed to see their general practitioner in the week following surgery.

INTRODUCTION

Recent years have seen an increasing amount of surgery performed on a day case basis. This study was designed to assess patient compliance with instructions given, the incidence of post-operative sequelae and the extra workload for general practitioners as a result of this change in practice.

METHODS

Over a three month period all adult patients who had had general surgical and gynaecological operations performed under general anaesthesia on a day case basis in Daisy Hill Hospital were sent a questionnaire. (Table 1) This was timed to arrive one week after surgery and a stamped addressed envelope was enclosed. The anonymity of answers was stressed. Local medical ethical committee approval for the study was obtained.

RESULTS

Of 143 patients, 103 returned the questionnaires (72%). Of these 71 had gynaecological surgery and 32 had general surgical procedures. Their ages ranged from 20 to 70 years (61 aged 20-39 years, 32 aged 40-59 years and 10 aged 60 years or over). Post-operative pain experience was generally good – 21 (20.4%) patients had no pain, 42 (40.7%) only mild pain, 38 (36.9%) had moderate pain and only 2 (1.9%) had severe pain.

The operations performed included routine gynaecological procedures (Dilatation and curettage, colposcopy, cervical biopsy etc (46); laparoscopic tubal ligation (16), diagnostic laparoscopy (8), cystoscopy (10) and drainage of a Bartholin's abscess (1). Surgical procedures included vasectomy (8), breast lump removal (3), other minor excisions (4), anal stretch (4), circumcision (2) and laparoscopic liver biopsy (1).

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TABLE 1

<i>Please circle how you were after your operation</i>	
1 How did you get home?	Car passenger Car driver Taxi Walked Bus
2 Did you drive that night?	Yes / No
3 Did you take any alcohol that night?	Yes / No
4 Overall how would you describe the pain at home that first night?	None Mild Moderate Severe
5 Did you take any painkillers?	No Paracetamol Aspirin Other, please give its name _____
6 Did you need to contact your family doctor that night?	Yes / No
7 Why did you need to contact him/her?	For pain relief For nausea/vomiting Bleeding Undue drowsiness Worried, if so about what? _____
8 Were you actually seen by the doctor?	Yes / No
9 How did you feel that night? (Circle any answers that apply)	As usual Drowsy Confused Clumsy Drugged Dizzy Headache
10 When did you feel ready to go back to your usual daily routine ?	_____
11 Were you admitted to hospital that week? If so, why?	Yes/No _____

Over half of the patients (52) took no analgesic following discharge from the day procedure unit; 32 took paracetamol 500mg tablets, 13 took a proprietary compound of paracetamol 500mg and codeine phosphate 30mg (Tylex, Cilag); 6 patients took other preparations including co-codamol (paracetamol 500mg, codeine phosphate 8mg), co-proxamol (paracetamol 325mg, dextropropoxyphene HCL 32.5 mg), mefamanic acid 500mg or chlorpromazine.

The patients self-assessment of their wellbeing on the night of discharge (question 9) is shown in table 2. Thirty-four felt normal but the remainder reported various symptoms, the commonest being drowsiness or headache (Table 2).

TABLE 2.

Patients perceptions of well being on the night of discharge.

Normal	34	33.0%
Drowsy	44	42.7%
Headache	40	38.8%
Dizzy	20	19.4%
Confused	8	7.8%
Drugged	7	6.8%

Four patients drove home and a further three drove a car later that night. One went home in a taxi. The remainder were accompanied home as instructed. Two male patients took alcoholic drinks on the night following surgery.

Five patients were seen by their general practitioner in the week following surgery. Only two asked to see their doctor on the night of operation — both these were requests for analgesia, one from a patient who had had a laparoscopy and the other a vasectomy. The general practitioner for one of the breast lump biopsy patients called to see her on a routine visit. On the day after surgery one patient who had had an anal stretch went to see his doctor because he felt "sore all over" perusal of his anaesthetic chart revealed that he had been given suxamethonium. On the fifth post-operative day the patient with the Bartholin's abscess went to see her doctor because of persistent pain and bleeding, and was treated with antibiotics.

There was a wide distribution in the time to recovery to full normal daily activity, ranging from the day of operation in four patients, one to two days in 45, three to five days in 33 and six days or more in 21 patients (20.4%).

None of those surveyed was readmitted to hospital in the first post-operative week. Review of records in the day case unit revealed that during the study period a further six patients had an unplanned admission for overnight stay. Three of these had had laparoscopies performed — one was admitted because of persistent vomiting, one who underwent laparoscopic sterilisation because of hypotension, and the third who had a laparoscopic ventrosuspension required admission for analgesia. Two patients were admitted post-cystoscopy due to haematuria. One patient had a cervical polyp removed but bled in the recovery ward; she required intravenous fluids, and a further examination under anaesthetic was performed.

DISCUSSION

There has recently been an increase in the numbers of surgical procedures performed on a day care basis and it has been estimated that 40-50% of operations could be done in this way¹. Procedures suggested as suitable by the Audit Commission include, in addition to those detailed in this survey, hernia repair, varicose vein ligation, endoscopy, manipulation of fractures and arthroscopy². Many patients having hernia repair and varicose vein surgery prefer to be treated as an in-patient³ and such cases are not operated on as day procedures in this hospital, except for paediatric hernia repair.

Compliance with post-operative instructions was on the whole good, but there were a number of worrying aspects. All patients admitted to the day case units are advised of the necessity of being accompanied home, and to avoid driving for 24 hours. Sensitive choice reaction times have been shown to be impaired for as long as one to two days after hernia repair under halothane anaesthesia⁴, which would make making driving unsafe; despite warnings to the contrary four patients drove home. While the failure of seven patients to comply with instructions not to drive is disturbing, it represents a considerable improvement on Ogg's figures from 1972 which showed that 9% drove home and 73% had driven within 24 hours⁵.

One of the fundamental requirements in the selection of day cases is that operations where post-operative pain is severe are excluded⁶ and it is gratifying to find that only two of our patients described their post-operative pain as severe. Indeed for 61% of patients the pain was mild or non-existent, and half the patients required no analgesia. Only one third felt as normal on the night of operation with headache in 39%; and drowsiness in 42%. The incidence of these minor side effects is higher than in Ogg's series and may reflect the fact that his patients had had more minor surgery. Laparoscopy in particular has been associated with a high incidence of post-operative side effects^{7,8}.

By the second post-operative day 48% felt ready for work which is comparable with Miller's findings⁹ (range 33% – 59% depending on anaesthetic technique) but he included only minor surgical cases. We found that laparoscopic sterilisations and diagnostic laparoscopies tended to be associated with longer recovery times than other cases, with only 28% ready for work by day two and 44% taking six or more days to reach this level of activity — these findings are in direct contrast to Edwards' study of day case diagnostic laparoscopies and laparoscopic sterilisations where the average time to return to normal activity was 36 hours⁸.

On the basis of this survey the increasing use of surgical day case facilities has not led to an onerous increase in the general practitioners' workload as has been suggested¹⁰. However we did not examine community nursing workload where the true transfer costs from hospital to community may lie¹¹. The unplanned admission rate following day surgery was 5.8%, which is fairly typical, a wide range of figures being quoted (0.2% to 6.3%)^{12,13}. The fact that no patients were readmitted following discharge is a measure of the appropriateness of patient selection and the discharge criteria.

This postal questionnaire has shown good compliance with post-operative instructions, low post discharge pain and a very small demand for general practitioner services after discharge from the day procedure unit. The incidence of minor side effects of anaesthesia is however relatively high and may reflect the significant proportion of laparoscopic operations performed.

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Review:

Current ethical issues in organ transplantation

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Ethics in a medical context have been defined by Professor Gordon Dunstan¹ as “the obligations of a moral nature which govern the practice of medicine”. Ethics are expressed in the language of duties : the duty in general to serve and protect the interests of patients in ways consistent with the corporate ethics of the profession, and the moral values held in common with society. These duties, referred to as Hippocratic, must be worked out in particular cases by moral reasoning.

The great majority of transplants world-wide are kidney transplants. The kidney is duplicated and until recently it was the only solid organ which could be transplanted from a living donor. However it is now possible to transplant a lobe of liver or lung from a living donor, though as yet this is rarely done. I will deal mainly with the ethics concerned in renal transplantation as my own experience lies there.

Over the past two decades, particularly since the introduction of continuous ambulatory peritoneal dialysis (CAPD), the number of patients receiving treatment for end-stage renal failure has increased rapidly. What follows applies to westernized countries, but in the Third World the outlook for sufferers with end-stage renal disease has not improved and most still die.

A Renal Replacement Programme is made up of the dialysis population and those who have received a successful transplant. Together these make up the stock of patients, expressed per million population. The dialysis population contains the patients accepted for treatment in the current year, estimated at about 80 new patients /million/annum. This estimate resulted from two recent British surveys, but the studies were based on mainly Caucasian populations. Where the population contains significant numbers of Asians and Blacks the incidence of renal failure is two to three times higher than in Caucasians, due mainly to increase in Type 2 diabetes mellitus and hypertension. It may be as high as 90 to 140 /million, according to the age specific demography of the population. In 1992 only a few UK dialysis centres accepted as many as 80/ million and some as few as 50/million, despite populations containing substantial numbers of the ethnic minorities.

The incidence of renal failure rises sharply with age. The table shows the age specific acceptance rates in the Thames Regions for Whites, Blacks and Asians, the rates for Whites being regarded as 1. The rapid rise in incidence with increasing age is apparent.

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FIGURE I

Average annual age specific acceptance rates onto renal replacement therapy in the Thames Regions in different ethnic groups 1991-2.

	White	Black	Asian
<i>Age years</i>			
<i>16-54</i>			
Rate per million	52.5	160.0	158.1
Relative rate (95% CI)	1.0	3.05 (2.30 – 4.04)	3.01 (2.31 – 3.94)
<i>55-64</i>			
Rate per million	114.4	623.3	830.7
Relative rate (95% CI)	1.0	5.46 (3.62-8.24)	5.99 (4.5-7.99)
<i>65+</i>			
Rate per million	119.1	922.7	952.0
Relative rate (95% CI)	1.0	7.76 (4.81-12.50)	8.01 (5.18-12.4)

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The Dialysis Programme must provide treatment for patients remaining from previous years. About 75-80% of all patients survive for at least three years after treatment is commenced so that after a short span of years large numbers of patients accumulate. Added to these are patients whose renal transplant has failed. A "successful transplant" may not function for the remainder of the patient's life – though some function well for many years. The patient with the longest surviving cadaver kidney graft in the world, still functioning well after 28½ years, came from Belfast. Patients needing a second or even a third or fourth graft must be added to the accumulating numbers of patients on dialysis.

Patients exit from the Renal Replacement Programme by death, but this accounts for only 20-25% of patients by three years. The death rate of older, particularly diabetic patients is higher, perhaps 50% by three years. Voluntary withdrawal from dialysis was very rare in the UK until the past decade. It now accounts for some 5% of deaths on dialysis programmes, and recent data from both Canada and the Europe suggest that as many as 25% of deaths may be due to this cause. Exit by transplantation in the UK accounts for up to 38/million/population/year. It is commonly supposed that there is a ceiling on cadaver grafts available at about 40/million.

The ethical problems of transplantation begin as soon as a patient is diagnosed as having progressive, or near end stage renal failure. Each patient for whom the need for renal replacement can be foreseen must be given a clear understanding of the treatment to come. The benefit of rescue from death is

obvious, but the arduous discipline needed for success, and the fact that it may be for life, must be pointed out. Some may receive a successful transplant, but this may not be available for the older and more disadvantaged patients. The patient must appreciate the risks and the fact that the graft may fail. Before entrance to the dialysis programme the patient must be fully informed. If a transplant is planned, again a full explanation of all that is involved is needed.

Public confidence is essential for the development of a successful transplant programme. The public must be satisfied that the procurement of organ donors is ethical and that the distribution of organs is fairly carried out. For example the development of organ transplantation in Japan was delayed by more than 25 years by the circumstances surrounding a heart transplant carried out in Japan soon after Professor Barnard's first heart transplant. The transplant failed and the public seem to have been left with deep suspicion of the propriety of the diagnosis of death of the donor and the suitability of the recipient for transplantation. Partly though not entirely as a result of this case, brain stem death is not accepted as real death in Japan despite extensive discussion by the public and by a series of committees to examine the question. Three years ago a conference was held in Copenhagen to debate the issue of brain stem death, followed by yet another Governmental Commission which reported in favour of accepting brain stem death. However the bar council objected and the issue is not yet resolved.²

Kidneys and virtually all other solid organs used for transplantation, come from recently dead cadavers. This accounts for the vast majority of donations. Kidneys, much more rarely lobes of liver or lung, may be taken from living related donors. Living unrelated persons become organ donors much less frequently, the organ almost always being a kidney. A "domino" graft is an organ which has been removed from a patient, as part of his/her own treatment, which becomes available for transplantation into another patient. The heart removed from one patient before a heart-lung transplant may become a "domino graft" transplanted into a second patient, or the heart valves may be used in the same way. Even an eye may be removed as part of therapy and the cornea used for another patient. "Domino" organ grafts have become quite common. These procedures produce many ethical problems which need consideration.

In the UK the removal of human tissue for transplantation was governed by the Human Tissue Act³ of 1961, until the passage of the Human Organ Transplant Act⁴ in 1989. The donor of cadaver kidneys was dead in the traditional sense that heart beat and circulation had ceased. The time that elapsed from the cessation of heart beat until perfusion of the organs with cold perfusion fluid, known as the "initial warm ischaemia time", was long, often 60 minutes or more. Such kidneys did not produce urine for 10 days or longer, but their long term function was often very good. The initial warm ischaemia time was 30 minutes or longer for 53 of the patients transplanted in Belfast 1968-1978. 90% of the grafts functioned, including all 20 of those in whom it was 60 minutes or longer.⁵ However long warm ischaemia is clearly undesirable – kidneys with short ischaemia function sooner, some with long ischaemia never function at all. Very short initial warm ischaemia time is essential for heart, lung and liver transplants, which are damaged by even short periods of anoxia.

As knowledge of the management of patients in intensive care increased it became apparent that when the brain stem ceases to function, spontaneous respiration and the circulation cease within a short time. When these functions are replaced by a ventilator the organs of the body continue to be perfused and their function is maintained. Brain stem death is now almost generally accepted as equivalent to true death, except in Japan. Criteria for brain stem death are now established. Diagnosis of the cause of coma, exclusion of other causes of deep coma – depressant drugs, primary hypothermia, metabolic and endocrine disturbances, and specific tests of brain stem function are necessary before “permanent functional death of the brain stem” can be diagnosed, while respiration and circulation are being maintained. Further artificial support is then fruitless and should be withdrawn. These criteria were not established by law, but were described in detail in the Code of Practice⁶ for the removal of cadaveric organs for transplantation drawn up by a Working Party on behalf of the Department of Health in 1979 and revised⁷ in 1983. The timing of the withdrawal of artificial support is discretionary, and allows time for finding and informing relatives. If the circumstances are suitable, discussion may take place about transplantation. Permission for removal of organs may be requested. If consent is forthcoming, simple blood tests are carried out and the transplant team is mobilized. Ventilation is continued right up to the time of surgery for removal of the organs. Under these circumstances initial warm ischaemia approaches zero. Many kidneys obtained under these circumstances function immediately, and heart, heart-lung and liver grafts may be obtained. Corneas will tolerate very much longer ischaemia and may be harvested many hours after death.

Consent for the use of cadaver organs came to be regarded as the “Gift of Life” as Sir Roy Calne⁸ called it in his admirable book of that title in 1970. Virtually all cadaver donors occur in NHS hospitals where the organs are taken following the Code of Practice already mentioned. This has been accepted as ethical by the transplant profession generally, including the British Transplantation Society⁹ and the international Transplantation Society.¹⁰

During the late 1970s and 1980s a small number of cadaver kidneys were imported into the UK from USA as being surplus to their requirements. The arrangements were made by surgeons in this country directly with one or other of the recognised US transplant organ agencies, which were presumed to be following a similar code of practice. Almost all of these kidneys were used for private patients, usually of foreign nationality, who were not eligible for kidneys taken from NHS patients. The cost of these imported kidneys was too high for the NHS even although the cost was supposedly restricted to that of removal and transport of organs, plus a small contribution to the kidney retrieval organization. Later this source of kidneys, already diminished to a very few, was brought under the supervision of UKTS.

The Codes of Practice^{6, 7} ensure that all reasonable enquiries are made to ensure that the wishes of the deceased are carried out. The wish to become a donor may be clearly expressed by the carrying of a donor card and informing the next-of-kin. If this is not available the next-of-kin is asked if the deceased had expressed a view on organ donation. “All reasonable enquiries” must be carried out to consult the next-of-kin. If such a person cannot be found the

representative of the hospital may be empowered to give permission for donation, but this is done very rarely in practice, and it is considered good practice not to use such donors and risk being labelled “vultures” by the media. The view of the spouse or co-habiting partner is of the greatest importance, but other relatives may be contacted and their opinion obtained, as in particular cases this may be very important to the family. In one case in which I was involved, the young husband whose wife died as a result of a road traffic accident followed the wishes of his mother-in-law, upon whom he would depend for caring for their young infant – this in spite of the fact that he knew that his wife had highly approved of organ donation. In another case the husband of a very recently married couple died. The wife wished to follow the view against donation expressed by the man’s parents. In neither case did I make any effort to persuade the next-of-kin to allow donation. To do so would have been unethical.

The great majority of live donors are genetically related. Following the demonstration of successful drug immunosuppression by Calne and Murray¹¹ in Boston in 1962 most kidneys were taken from living related donors. The kidney can be obtained under ideal circumstances from a healthy donor who is not hypotensive before the organ is removed; the period of ischaemia is very brief and urine is usually produced almost immediately, often during surgery. In most early cases relationship was close and of the first degree. Only ABO matching was available, but it was known that other antigens must be of importance and might be expected to match when grafts were exchanged between closely related individuals, especially between siblings. The use of living related donors was extensive in the US and in some European countries. They were not used extensively in UK, and their use has diminished progressively during the past decade as numbers of cadaver kidneys have slowly increased. In Belfast living related donors have been used for only 54 of our total of 762 kidney grafts. Living donors are still used quite frequently in Scandinavia and some other European countries. Westlie et al.¹² stated recently that the use of living related donors is still an integral part of the Norwegian national programme for treating end stage renal disease.

In the past the use of a living genetically related donor has been accepted as ethical almost without question. Doctors have accepted naively that blood relationship ensures that donation is voluntary and altruistic, and that coercion does not occur. Perhaps they have been wilfully blind on this issue ! Donation from a parent to a child is usually truly altruistic, but it may be otherwise. One such “volunteer” donor was the father of a 28 year-old man. Both of the man’s parents were alive and there was one brother, a priest. All three were interviewed together, and all expressed willingness to give a kidney, but the mother said she had high blood pressure and a bad heart. She and the brother had a different ABO group to the patient, which would have excluded them in any case, but the father’s group was similar. When the father was admitted to hospital for full work-up, he confided that during his youth he had nearly died under anaesthesia when undergoing appendicectomy. He had been told that he would not survive another anaesthetic, and believed he would die during the operation for donation of a kidney. The situation was complicated by the fact that he was a Protestant who had married a Roman Catholic and the sons had been brought up in the Catholic faith. He felt that his wife would attribute his failure to give

a kidney to his son to the religious difference, and would never forgive him. He preferred to risk death he regarded as certain and go ahead with the donation. I arranged a intravenous pyelogram and led the father to believe that his kidneys were unsuitable. The ethics of this you can decide for yourself ! There was a good ending, as a cadaver graft was found which was a long term success.

The use of a sibling donor greatly increases the chance of an identical HLA match, and all available siblings are often matched with the recipient. This assumes that they are all true volunteers. I have known of several cases where a member of the family had emigrated many years before to USA or Australia, and there developed renal failure. The doctors responsible for treating the far-away patient, contacted the siblings in Ireland with the request that their blood group and tissue type should be done to see if they matched their patient. In some cases the recipient had not seen the family nor even written frequently for long periods. There were the wives and children, sometimes still young, to be considered. In one such case, there was a sister who was an identical match, who had recently become engaged to be married. After lengthy discussions on at least five occasions, sometimes with the fiancé present, in spite of the man's objection the sister went to the USA to see her brother. I never heard the outcome ! In the case of a patient in Australia, there were three brothers and a sister here who all offered to give a kidney. Interviewed separately, the sister was apparently very anxious to give her kidney, but each of the brothers said she must not be the donor as she was effectively a single parent responsible for four young children, while her husband served a long jail sentence. In fact she could not be the donor as she was hypertensive, weighed 20 stone, and had a different ABO group. The three brothers were each HLA and ABO identical with the patient in Australia. They drew straws as to who should be the donor, but only on condition that their brother should travel to Belfast for surgery.

Other family members may be chosen by the family to become the donor. A maiden aunt or cousin without dependant relative may be thought very suitable by the other family members. "Aunt Jane" is in fact being coerced into donation, unable to refuse to rescue the patient. In other cultures they may be offered money or a bribe in kind. Close enquiry must be made to ensure that family donation is truly altruistic. The really difficult situation arises when a living unrelated donor is proposed. The events which led up to the Human Organ Transplant Act in 1989 are very relevant here.

By the early 1980s most doctors accepted brain stem death as somatic death, but a vociferous few did not. Also the transplant profession became worried about rumours that donors had been brought from poor countries where renal replacement therapy was not available, and paid paltry sums to undergo surgery for the benefit of wealthy patients. It was alleged that London was a centre for this illegal trade, which was condemned by both the British Transplantation Society and the Transplantation Society. The British Transplantation Society became worried that these rumours of commercialism in live donation might have some foundation in fact. In 1985 the Society published its own guidelines⁹ on the use of living donors in the United Kingdom. The General Medical Council signified its approval of the profession's effort to regulate its own affairs. The British Transplantation Society asked also for a Register of all transplants to be set up, but in spite of much pressure by their Ethical Subcommittee, the Department of Health refused further legalisation.

This was said this was not to be necessary, and would erode the freedom of doctors.

These negotiations with the Department of Health were still continuing when in January, 1989, the media published details of kidneys which were purchased from Turkish donors and transplanted in the Humana Hospital in London. This was followed by the hasty passage of the Human Organ Transplant Act at the end of July, 1989.

Under the Act ⁴ it is an offence to make or receive payment for the supply, or the offer of the supply, of an organ which has been or is to be removed from a dead or living person, and is intended to be transplanted into another person whether in Great Britain or elsewhere. Payment is defined as payment in money or money's worth. The cost of removing, preserving and transporting the organs, and expenses or loss of earnings which may be directly attributed to supplying the organ from the donor's body are allowed. Advertisements for the supply of organs are prohibited. The Act expressly permits donations of organs from persons within defined degrees of genetic relationship, and specifies the ways in which the relationship is to be established. A person is genetically related to his natural parents and children, his brothers and sisters of the whole or half blood, the brothers and sisters of the whole or half blood of either of his natural parents, and the natural children of his brothers and sisters of the whole or half blood of either of his natural parents (i.e. genetic relationships are acceptable only as far out as first cousins). Donations from donors more distantly related than those permitted under the Act may be permitted with certain restrictions. Proposals for such donations must be referred to a new statutory body, the Unrelated Live Transplant Regulatory Authority, known as ULTRA, for approval. This Authority has 11 or 12 members, appointed by the Government, its Chairman being a medically qualified person not engaged in transplantation. The Authority reports regularly to the Secretary of State for Health.

The Act is given effect by a series of detailed regulations. The Authority has prepared a booklet giving advice to clinicians about referral of proposals to it, and has revised the booklet in the light of their experience of difficulties brought up in individual cases. The Act also established a Register requiring a record of all transplants carried out to be kept. The Register is currently maintained at UKTSS, and is periodically reviewed. Prosecutions under the Act shall be instituted by the Director of Public Prosecutions. The Act came into effect for England and Wales in 1989, and by Order in Council, in Northern Ireland in December, 1990. Cases must be referred to ULTRA if the genetic relationship claimed is not confirmed by testing, if the relationship claimed is outside that allowed by the Act, or if the donor is unrelated.

Experts in tissue typing are not satisfied with the tests for genetic relationship defined in the Regulations. At present the tests must be personally carried out by recognised testers registered on an official list. The tests prescribed are now out of date, cumbersome and no longer in regular use in most laboratories, and many of the recognised testers no longer perform them. Moreover such tests cannot prove relationship, only suggest that it is likely. I may say that Government has recognised that the Regulations for testing genetic relationship are inadequate and that revision is needed.

Cases may also be referred to ULTRA because the donors are claimed to have a genetic relationship less close than the full cousin relationship defined in the Act. The tests prescribed are of no value in these circumstances. These cases have not been British Nationals, and in the Third World “cousin” may be interpreted very liberally! Evidence of a lasting emotional relationship is sought, but it is very difficult to obtain satisfactory evidence. For practical purposes they have to be regarded as essentially similar to unrelated living donors.

The last category covered by the Act is the unrelated donor. The most frequent unrelated donor is the spouse or live-in partner of the recipient. If the relationship concerned is a true life partnership, this donation is almost always truly altruistic. The emotional bonding is deep and lasting, the donor has much to gain if the sick partner is returned to health – their life style often improves greatly. However it is necessary to make certain that the marriage or relationship is not one of convenience made for the purpose of procuring a donor. In this country it is easy to ascertain the duration of the relationship, but this may be less easy when a patient comes to the UK for the purpose of the transplant, accompanied by a spouse donor. Families from the Third World sometimes come here with a “family friend”. This type of donor is very difficult to evaluate. Payment in money or kind may seem to be very likely, especially when the donor and recipient belong to different social classes. Our purpose is to prevent exploitation of the donor, but our understanding of their world is incomplete. One of the ULTRA members has worked in Africa and his opinion is often valuable. He has suggested that there may have been the hidden exchange of a “bride price”, which may have been the only way a poor young man may obtain a wife – while providing a life-line to a wealthy member of his tribe. Bedouin arabs regard the members of their own tribe as blood brothers, and although fully informed of risks inherent in transplantation, say if they die in the procedure it is Allah’s will and a Passport to Paradise. India is different again and there have been many reports of exploitation of the poor in Bombay and Calcutta.

There have been occasional donors who were not known personally to the recipient. One such case was that of a much loved bishop in an African country.¹³ When his almost end-stage renal failure was known in his church, a number of young men volunteered to give a kidney, and one was selected to be the donor. He came to London with the recipient and although previously not known to him lived as a member of the family while awaiting transplantation. This occurred before the Act, but the Ethical Committee of the British Transplantation Society was very uneasy about the almost hysterical enthusiasm these circumstances had generated.

Lastly, in the USA kidneys were occasionally taken from convicts serving long sentences. It was alleged that there was no remission of sentence or other payment. These procedures were later admitted to be unethical. More recently there have been reports of the use of organs taken from executed criminals in China,¹⁴ which must be regarded as unethical.

These case histories show why it has become necessary to require a report made by an independent third party who has interviewed both the donor and recipient, each being interviewed separately. The independent third party is

acting in an altruistic capacity to protect the interest of the prospective donor. The report must be sent direct to ULTRA, not via the clinician making the proposal. The third party must be acceptable to ULTRA for this purpose, and must be an NHS consultant physician, surgeon or psychiatrist, or someone of equivalent professional status, who is not otherwise party to the transplant proceedings nor a close associate of one who is. He or she should not be practising in renal medicine or renal transplantation.

ULTRA reports directly to the Secretary of State for Health. Over the last two years ULTRA has approved nearly 500 applications, the over-whelming majority being "domino grafts", mainly hearts and heart valves, with a few corneas. Kidney cases account for less than 10 per year. Each application is sent to the Administrative Secretariat of ULTRA at the Department of Health, who ensures that the documentation is complete, then forwards it to a panel of three members, led by one of the clinicians on ULTRA. Every effort is made to process the applications quickly. Very rarely it is necessary to hold over a decision until a meeting of the Authority, though each case is reviewed at the next meeting. On the whole the Act has regulated effectively the transplantation of solid organs. Bone marrow grafts are not included.

As well as being satisfied that donor organs are obtained in an ethical way, the public must be satisfied that available organs are distributed fairly. This is not covered by the Human Transplant Act, and is a matter for doctors to regulate. A perfect system for this does not exist. In UK and in most developed countries where transplantation is a regular procedure, patients with information of their blood group and tissue type are entered on a computerised recipient list. When organs become available details of the donor, including blood group and tissue type are reported, nowadays by Fax, to the organ distribution centre. The best recipient match or matches are found by computer. When the tissue type is a common one there may be a number of well matched, even identically matched, possible recipients. In this situation, or if there are only less good matches where the tissue type is a poorer prognostic tool, other principles must be invoked. Apart from ABO group and tissue type match, the principles which may be used are as follows:¹⁵

- * Give organs to those most in need – the "rescue principle" – not a good idea unless there is reasonable chance of a good outcome.
- * Give organs to those have had a failed transplant – the "fidelity principle".
- * Allocate by random choice – the "lottery".
- * Priority to the longest on waiting list – "first come, first served" – seen as just by patients but may ignore important clinical points.
- * Allocate by ability to pay -- not acceptable to us but is the main principle in countries where mandated health insurance is not backed by government.
- * Allocation by other parameters of social worth – the system used to allocate dialysis in the 1960s – unjust.
- * Lobbying by press and media – also unjust, but often used.
- * Allocation by tissue match grade – accepted by the public as just.

There are no simple solutions for the ethical dilemmas which ensue. There is also the hidden agenda concerning the fair distribution of organs between centres. Rules to ensure this were set up by the Management Committee of United Kingdom Transplant Service and modified many times over the years. The United Kingdom Transplant Support Service Authority which succeeded the Management Committee, is faced with the same difficulty in trying to agree principles which would ensure "fair shares for all".

France had a similar non-profit organisation run by doctors, with its own guidelines for collecting organs, managing the national waiting list, and allocating organs according to tissue compatibility and other parameters. They ran into difficulties recently when the French Inspectorate General of Health noted that a large number of organs were allocated to non-resident foreigners, especially Italians. Some irregularities in the collection of organs were also reported. This has resulted recently in a plan to place transplantation in France more firmly under state control. Their Minister of Health, Dr Douste-Blazy,¹⁶ has said that there is no question of placing transplant physicians under finicky restrictions (his words) but controls were necessary to guarantee equal access to organs for all patients.

The one type of organ that remains to be considered is the xenograft. No other human is involved, avoiding many of the ethical objections which have been outlined, but some may object to receiving tissues from an animal on religious grounds. Unfortunately when an animal tissue is grafted into a human the body rapidly destroys the graft, even if taken from a closely related primate species such as the baboon. In 1965-66 Reemtsma, then working in New Orleans where he had access to the Louisiana chimp research centre, transplanted a chimpanzee kidney into a woman. The kidney survived for over nine months, of course with heavy immunosuppression. As he pointed out at the time, this was not a breakthrough – the chimpanzee is an endangered species very difficult to breed in captivity. Baboon kidneys were tried then with no success and recent attempts using improved immunosuppression have not fared better.

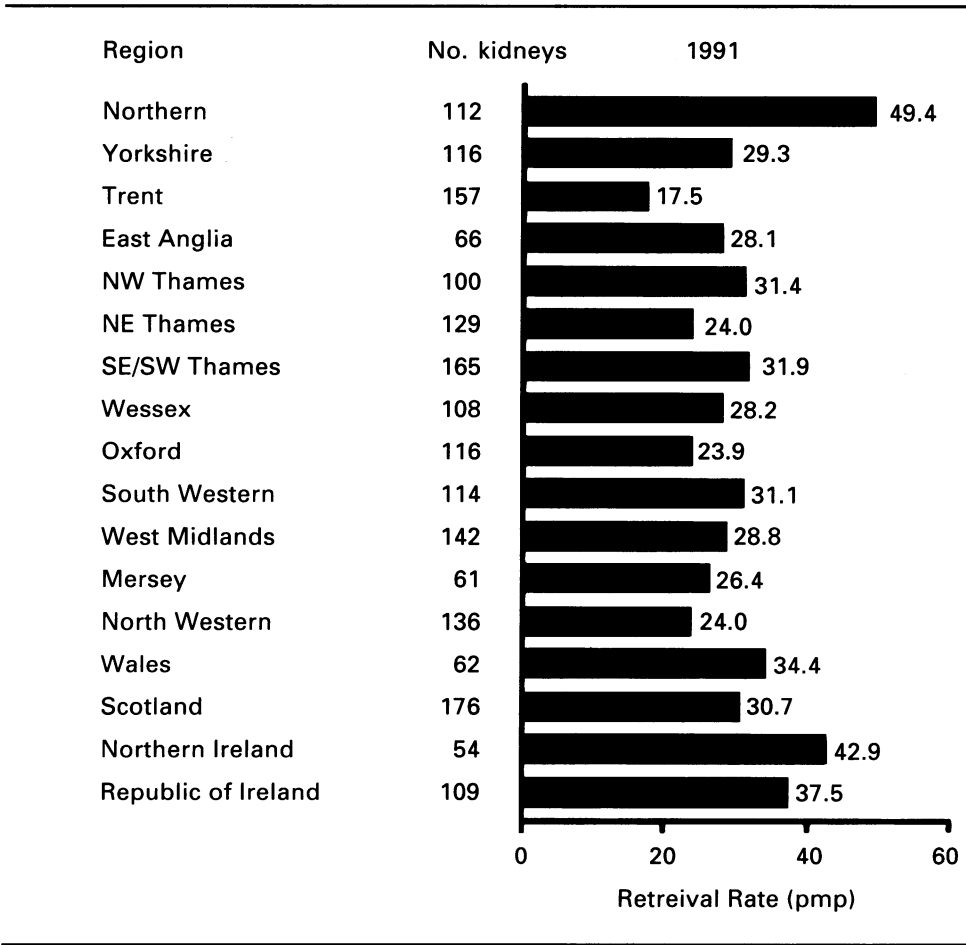
Although attempts to transplant these closely related, so called concordant species have not been successful, much effort is now being put into the possibility of using pig organs. The pig kidney is about the right size and the animal is easy to breed and matures quickly, but is genetically far removed from the human. In such discordant species rejection of transplanted tissue is immediate and catastrophic. The rejection is mediated by complement. Much research has centred on the idea that human anti-complementary proteins can be injected into the pig genome to produce transgenic pigs. There are immense difficulties still to be overcome before it becomes possible to use transgenic pigs as a source of organs for human transplantation. It is not known how they would function in a different species. Calne¹⁷ stated recently that he believes that clinical xenografting will become possible, but he and other eminent transplanters think that this development is at least a decade away.

In the 1993 Audit of Renal Transplantation¹⁸ (UKTSS) the UK national rate for kidney transplantation is 29/million/year. Two centres, one being Northern Ireland, reached 38/million/year in 1992. The figures included a small number of living related grafts and two spouse grafts, amounting to a maximum of about 50 out of the approximately 1900 grafts performed in the year.

Figure 2 shows the number of kidneys per million population obtained by each region in 1991, the range being 17.5 to 49.4. Only five of the 18 regions exceeded 30 per million. This wide variation between centres makes it probable that the remaining 13 regions could obtain more donors.

FIGURE II

Cadaveric kidney regional retrieval rates per million population reported to UKTSSA.²¹



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The Exeter study by Feest and colleagues¹⁹ has shown that some patients dying outside intensive care units could be used as donors. My own view is that kidneys can be harvested from non-heart beating donors. It is more difficult to organize the team for this, and post-transplant dialysis is usually necessary – but this source served us well until we began to use heart-beating donors in 1976.

Every effort must be used to increase the contribution of transplantation to the treatment end-stage renal failure. Organs for donation are a national resource and must be used wisely. Meticulous observance of ethical principles is essential to ensure public confidence. Informed use of the knowledge bought by experience in matching kidneys with donors, and well judged pre-transplant assessment of patients with renal failure are essential. The Holy Grail of the perfect method of immunosuppression has yet to be found^{20, 21}. We can hope for better, and the immunosuppression available at present must be used with great care. I personally would be reluctant to search for more live donors.

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Review:

Adjuvant therapy for colorectal cancer – is there a place for a Northern Ireland study ?

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SUMMARY

Survival from colorectal cancer has not improved over the last four decades despite advances in surgery and anaesthesia. The answer to the question whether adjuvant chemotherapy and radiotherapy will improve survival from the disease can only come from randomised, controlled trials. In the future, immunotherapy and gene therapy may be of benefit but these are still many years from the clinical arena. We believe that current evidence suggests that patients with Dukes' B and C colorectal cancer should be entered into trials of adjuvant therapy. This evidence is reviewed below along with estimates of the impact that adjuvant therapy would have on the outcome from this disease in Northern Ireland.

There are approximately 600 new cases of newly-diagnosed pathologically proven colorectal carcinoma in Northern Ireland annually.¹ This disease accounts for an average of 440 deaths yearly in our community.² Colorectal cancer is the second most common cause of death from malignancy in adults in this population. The Northern Ireland colorectal cancer register has found that the proportion of tumours using Dukes' staging was as follows: Dukes' A 4%, Dukes' B 50%, Dukes' C 28%, Dukes' D 18%.

These figures were calculated using the Astler-Collier Modification of Dukes' staging:³ A – mucosal (ie intramucosal and submucosal), B – into or through the colonic muscle wall, C – one or more lymph nodes involved, and D – distant metastases present. Survival figures for colorectal cancer have not improved over the last few decades despite advances in medical care. Using the above version of Dukes' staging, five-year survival figures⁴ are: A – virtually 100%; B – range 30%-85%, average 70%; C – range 30%-60%, average 45%; and D – under 5%.

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Potentially curative surgery is possible in around 75% of new cases of colorectal cancer, but long-term follow-up reveals that around half of these "cured" patients will develop incurable recurrence of colorectal cancer.⁵ There is no indication for adjuvant treatment in Dukes' A colorectal cancer. The hazards of currently available therapies outweigh the benefits in a disease with 98-100% five-year survival. Equally, patients with Dukes' D or incurable disease cannot receive adjuvant therapy but may benefit from additional therapy after palliative surgery. This may result in improvements in both survival time and quality of life.⁶

There are approximately 600 cases in Northern Ireland annually. From the stage distribution above we expect there to be about 470 cases in the Dukes' B and C groups. Estimates of five year survival applied to the projected 470 cases per annum in Duke's B and C would give a five year mortality overall of 40%.

We believe that patients with Dukes' B and C colorectal cancer should be enrolled in a randomised, controlled trial of adjuvant therapy. This would entail treatment arms of modulated 5-fluorouracil chemotherapy for colon cancer and radiotherapy and chemotherapy for rectal cancer. Statistical calculations show that a trial of 520 patients (260 per treatment group) will have 80% power to detect a statistically significant 30% relative reduction in mortality with adjuvant therapy ($P < 0.05$; two-tailed). This would represent a mortality in the treatment groups of 28% compared to 40% and is approximately equivalent to the long term survival of one in every eight patients who currently die within five years.

Although some Dukes' B and C stage patients are currently offered adjuvant therapy in Northern Ireland, this remains a very small proportion (<10%) of the total. Northern Ireland is an ideal area for a trial of adjuvant therapy in colorectal cancer as we have one of the highest incidences of this cancer in the world¹, and our population has low rates of immigration, emigration and mobility compared to the rest of the United Kingdom, allowing excellent follow-up; clinical trials are possible without dissipation of patients between health authorities, hospitals and regions because of our small size, and easy communication between consultants. At present adjuvant therapy is not often offered to suitable patients.

It is anticipated that the necessary sample size of a minimum of 520 patients could be accrued in Northern Ireland within three years. A larger multicentre trial would greatly increase the number of patients and a national study is currently being proposed by the United Kingdom Co-ordinating Committee on Cancer Research which will have multiple arms of varying chemotherapy regimens. However, recent experience has shown that local recruitment from Northern Ireland into national studies in colorectal cancer such as the AXIS trial of intraportal chemotherapy and the Medical Research Council trial of chemotherapy in advanced colorectal cancer is very low.

Chemotherapy

Previous trials have shown that 5-fluorouracil, either singly or in combination with other agents is the most effective adjuvant systemic chemotherapeutic agent.⁷ This substance is a prodrug which is metabolised in place of uracil or

orotate in the de-novo or salvage pathways of generation of uridine nucleotides producing a cytotoxic insult through effects on translation, transcription, mitosis or DNA synthesis.⁸ Folinic acid in combination with 5-fluorouracil is more effective than 5-fluorouracil alone due to inhibition of thymidylate synthetase.⁹ A combination of 5-fluorouracil and folinic acid would be administered according to the 48-hour infusion regime used by the ICRF medical oncology department at St Bartholomew's Hospital.¹⁰ Chemotherapy should commence at two weeks postoperatively unless there are wound or other postoperative complications and must occur within six weeks of surgery. Folinic acid is administered at 200mg/m² (maximum dose 350mg) by intravenous infusion in 250ml normal saline over two hours. This is followed by an intravenous bolus of 400mg/m² 5-fluorouracil in 100ml normal saline over 15 minutes followed by an intravenous infusion of 400 mg/m² 5-fluorouracil in 1000ml normal saline over 18 hours. The above regimen is given on two consecutive days as an in-patient and repeated every two weeks for a total of eight courses (sixteen days of in-patient stay over four months).

The original report of this regimen showed a low incidence of toxicity. In 64 patients with advanced adenocarcinoma, none had toxic effects greater than WHO Grade II, 9% developed mucositis, 12% diarrhoea and 3% significant neutropaenia. No dose-reduction was necessary and 97% of treatments were given as planned. It is expected that these figures will be even better when given in an adjuvant setting, as has already been the experience in the Northern Ireland Centre For Clinical Oncology. When this regimen was used in Belvoir Park Hospital as adjuvant treatment for colorectal cancer, gastrointestinal upset occurred in under 10% of cases and significant neutropenia has not occurred. The 48 hour infusion schedule results in much lower toxicity and emergency hospital admissions than schedules using daily bolus injections.

Data from Austria from a randomised trial on the use of modulated 5-fluorouracil in advanced disease suggests that chemotherapy often results in mild to moderate gastrointestinal symptoms⁶ but does not result in a decrease in quality of life scores. Indeed, in patients with poor quality of life from symptoms of their disease before treatment, there was an improvement with chemotherapy.

Radiotherapy

The area most at risk of local recurrence of rectal cancer below the peritoneal reflection is the posterior pelvis. Radiation enteritis is avoided by using fields limiting high radiation doses to this volume. Prone positioning to prevent irradiation of loops of small bowel will also decrease complications. The treatment fields should centre on the site of the resected tumour and include the lateral pelvic nodes. The postoperative radiotherapy should commence as soon as possible but must be within six weeks of resection. The dosage ranges suggested are 40-50 Gy delivered in 20-25 daily fractions over a four to five week period and may precede or run concurrently with chemotherapy.

Summary of Previous trials

One half of patients with colorectal cancer die with distant disease.⁵ The disease is systemic and occult micrometastases are commonly present in patients who have undergone apparently complete tumour resection. Dissemination often occurs before the primary tumour becomes clinically apparent and this

characteristic has prevented improvements in cure rates despite advances in surgical and anaesthetic techniques. In order to improve the prognosis by eliminating micrometastases, a number of investigations have studied adjuvant chemotherapy but its value in colorectal cancer remains unclear. Many trials have taken place, with great variation in the use of randomisation, patient numbers, particular chemotherapeutic regimens and the duration of follow-up.

Chemotherapy trials

Chemotherapy trials in colorectal cancer using 5-fluorouracil alone have demonstrated it to be the best single agent. However, large studies by the Veterans Administration Surgical Adjuvant Group¹¹ and Central Oncology Group¹² demonstrated only minor activity. Overall, single agent chemotherapy with 5-fluorouracil has given a reduction in mortality of 10% at best. The Veterans Administration Surgical Adjuvant Group later administered low-dose intravenous 5-fluorouracil plus oral lomustine.¹³ They demonstrated prolonged disease-free survival in Dukes' C patients but no improvement in overall survival. The Gastrointestinal Tumour Study Group¹⁴ studied the use of 5-fluorouracil plus lomustine with or without BCG immunotherapy against BCG alone, and against controls. They found no improvement in survival and the further problem that lomustine was associated with increased risk of leukaemias. The South West Oncology Group¹⁵ compared 5-fluorouracil and lomustine with or without BCG against controls and found no survival benefit at seven years. The National Surgical Adjuvant Breast and Bowel Project (NSABP)¹⁶ compared adjuvant 5-fluorouracil, lomustine and vincristine against BCG and controls, and demonstrated an 8% improvement in survival after five years.

Windle et al¹⁷ compared adjuvant 5-fluorouracil with levamisole against levamisole alone and controls. After eight years, they found improved survival in Dukes' C patients with combination chemotherapy. Levamisole is an anti-helminthic drug with immunostimulatory properties and has been used as adjuvant cancer treatment in the last two decades either alone, or with radiotherapy or chemotherapy,¹⁸ but with unclear results on survival. The European Organisation for Research and Treatment of Cancer group demonstrated recently that by itself it has no adjuvant effect in colonic cancer,¹⁹ although it is standard practice in the USA to combine levamisole with 5-fluorouracil in treatment of colorectal cancer. The mechanism of action of levamisole is unclear and 5-fluorouracil alone may be responsible for the observed effects on survival in trials on the combination of 5-fluorouracil and levamisole.²⁰

The North Central Cancer Treatment Group (NCCTG)²¹ compared 5-fluorouracil plus levamisole against levamisole and controls. They also showed increased survival with combination chemotherapy in Dukes' C patients. A larger intergroup study was performed to confirm these results and enrolled three time more patients.²² They showed that this combination chemotherapy increased survival in Dukes' C patients by 33% and decreased recurrence by 41%. Levamisole alone was no better than the untreated controls. There was no clear benefit in patients with Dukes' B disease. The addition of folinic acid to 5-fluorouracil resulted in improvements in response, quality of life and survival in the NCCTG study in advanced colorectal cancer.²³ There is also considerable discussion on the best route for administering adjuvant chemotherapy –

intrahepatic, intraperitoneal, intraportal or intravenous. Of these, the latter two are of most current interest. Hepatic metastases are the commonest cause of failure following surgery for colorectal cancer and these presumably arise from haematogenous spread via the portal vein. Portal infusions are an attempt to target the chemotherapy to the liver and to limit toxicity. These are usually given in conjunction with heparin for a short period of about a week. The treatment is well tolerated without significant hepatic toxicity²⁴ but results have been very conflicting. Taylor et al²⁵ showed significant improvement in survival following portal vein infusions of 5-fluorouracil particularly in Dukes' B lesions. The NSABP conducted a similar, but much larger trial of seven day portal vein infusion of 5-fluorouracil versus no postoperative adjuvant treatment in Dukes' A, B and C disease.²⁶ They observed an 8% improvement in survival with intra-portal 5-fluorouracil but no reduction in clinically detectable hepatic metastases. The Large Bowel Cancer Project failed to reveal any improvement in survival or incidence of liver metastases with intra-portal 5-fluorouracil and heparin infusion.²⁴ There is no evidence currently that portal-vein infusion is superior to systemic intravenous administration. The NSABP recently reported a trial designed to evaluate the efficacy of folinic acid-modulated 5-fluorouracil in adjuvant therapy of Dukes' B and C colon cancer.²⁷ They found that folinic acid and 5-fluorouracil treatment significantly prolongs disease-free survival with a 32% reduction in mortality risk compared to a control group randomised to receive lomustine, vincristine and 5-fluorouracil. Further evidence that modulated 5-fluorouracil may be beneficial came in a meta-analysis of nine randomised prospective clinical trials with 1381 patients with advanced colorectal cancer; this demonstrated a 23% objective response rate with folinic acid and 5-fluorouracil.²⁸

Radiotherapy Trials

The object of adjuvant radiotherapy is to prevent the further growth of cancer cells not removed at the time of surgery. Radiotherapy results in cytotoxicity principally by damaging DNA, thereby interfering with the ability of cells to reproduce. It was initially thought that adjuvant radiotherapy after surgery for rectal cancer would reduce the risk of local recurrence and thereby improve survival rates. The incidence of pelvic recurrence is variable, with figures of 10% to 40% commonly quoted.²⁹ The risk of recurrence increases with worsening Dukes' stage.³⁰ The first site of recurrence found at re-operation is often the general area of the primary cancer³¹ and studies have also shown that prevention of recurrence in the area of the primary tumour is associated with a decreased incidence of distant metastase.³² Pelvic recurrence may be associated with both microscopic extension of tumour to the lateral resection margins³³ and metastases in unresected pelvic wall lymph nodes.³⁴ The following studies examined the outcome after curative surgery with or without postoperative radiotherapy in Dukes' B or C colorectal cancer. The Gastrointestinal Tumor Study Group³⁵ showed a 9% increase in five year survival and 4% reduction in both local and extrapelvic recurrence with adjuvant radiotherapy. The National Surgical Adjuvant Breast and Bowel Project³⁶ showed a 3% decrease in five year survival, 9% improvement in local recurrence and 5% worsening in extrapelvic recurrence with radiation. The Denmark study³⁷ showed that radiotherapy caused no change in five year survival, a 2% decrease in local recurrence and a 2% increase in extrapelvic

recurrence. The Netherlands study³⁸ showed a 10% decrease in five year survival, 9% improvement in local recurrence and 12% worsening in extrapelvic recurrence. Overall, these studies have shown that radiotherapy as the sole adjuvant therapy, given either pre- or post-operatively, will reduce pelvic recurrence but not markedly influence either survival rates or extrapelvic recurrence.²⁹ Reduction in pelvic recurrence is worthwhile as this is often difficult or impossible to control, and symptoms are often severe and result in a very poor quality of life.

Combined radiotherapy and chemotherapy trials

The failure of adjuvant chemotherapy to lower pelvic recurrence and of adjuvant radiotherapy to lower extrapelvic recurrence or mortality rates has resulted in establishment of trials of adjuvant combination therapy. The following studies examined the outcome after curative surgery and post-operative radiotherapy with or without chemotherapy in Dukes' B and C colorectal cancer. The Gastrointestinal Tumor Study Group^{35, 39} trial had five year survivals of 43% with surgery alone, 52% with adjuvant radiotherapy and 59% with combination radiotherapy and chemotherapy. The local recurrence rates were 24%, 20% and 11% respectively and extrapelvic recurrence rates 34%, 30% and 26%. The NCCTG trial⁴⁰ had five year survival of 47% for adjuvant radiotherapy and 58% for adjuvant combination therapy. The local recurrence rates were 25% and 14% respectively, and extrapelvic recurrence rates 46% and 29%. Another study,⁴¹ however, showed no significant improvement in survival with combination chemotherapy and radiotherapy over one or other of the adjuvant modalities alone. The combinations of radiotherapy and chemotherapy used in the trials described were fairly well tolerated. The risks of serious late morbidity such as enteritis and treatment-related mortality were broadly similar to those of patients treated with radiotherapy alone.

Conclusion

Previous trials of adjuvant therapy in colorectal cancer have suggested a modest survival benefit. Recent evidence shows that modulation of 5-fluorouracil with folinic acid results in greater efficacy with acceptable toxicity. We believe that a local, randomised, controlled trial can accrue sufficient patients to allow us to demonstrate whether adjuvant therapy of colorectal cancer using modulated 5-fluorouracil provides worthwhile improvement in survival in this common disease.

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Historical Review:

The legacies of Sir William Whitla

R G Shanks

Presidential Address to the Ulster Medical Society – October 1993

How many of us think of Sir William Whitla when attending events in the Sir William Whitla Hall? How much do we know about him or his benefactions to Queen's, to the Ulster Medical Society and other organisations in Belfast?

Whitla was one of the outstanding graduates of the Queen's University of Ireland; he had both national and international reputations and was an intellectual giant amongst our predecessors, being a pharmacist, physician, politician, Shakespearian scholar, medical author and benefactor. Unlike other distinguished graduates, his contribution to Northern Ireland has continued to develop through his generous legacies so that his name, although not the man, is probably more widely known now than at the time of his death. I thought that it might be of interest to examine some aspects of the influence of Sir William Whitla on the University and this Society since his death. I do not intend to cover the biographical details of his life extensively as these were admirably described by Dr Cecil Kidd in his Presidential Address to the Ulster Medical Society in 1962. ^{1, 2, 3, 4, 5}

Sir William Whitla

William Whitla was born on 13 September 1851, at the family home in the Diamond, Monaghan where his father was a pawnbroker and woollen draper. William spent his childhood in Monaghan, a country town recovering from the effects of the famine. He attended the Model School and left at the age of 15 when he was apprenticed to his eldest brother, James, a pharmaceutical chemist with a shop on the Dublin Road, Monaghan – still a chemist's shop. Here he served his time and learned the rudiments of his profession. Two years later he moved to Belfast, where he continued his apprenticeship with the leading firm of dispensing chemists in the city – Messrs Wheeler and Whittaker of 37 High Street. About this time he decided to make medicine his career, and in 1870, while still employed by Wheeler and Whittaker, he matriculated and embarked on his medical curriculum at Queen's College, Belfast. The transition from pharmacy to medicine was very common in those days and in Whitla's case, it clearly influenced his subsequent medical and literary career. In 1873 he obtained by examination the double licences of the Royal College of Physicians of Edinburgh and of the Royal College of Surgeons of Edinburgh and was appointed Resident Medical Officer at the Belfast General Hospital, Frederick Street for one year.

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On completing his year in the General Hospital he apparently sought to extend his medical education and experience and it is probable that he went to England and attended in some capacity St Thomas' Hospital, London. Here he met Miss Ada Bourne, a friend of Florence Nightingale, and a member of the Salvation Army. She was a Ward Sister in St Thomas' Hospital and in 1876 she married William Whitla. They set up house at 41 Great Victoria Street, and Whitla commenced general practice. In the following year – 1877 – he obtained his higher qualification – Doctor of Medicine in the Queen's University of Ireland, with gold medal and first class honours and commendation.

In the same year he was appointed assistant physician to the Belfast Charitable Society, which at that time held an important place among the few institutions which provided medical care in the city. This was not a very lucrative appointment, even for those days. He was required to provide all medicines to the house, as well as his medical services, for £40 per annum. He continued to hold this post until 1882 when, at the age of 31, he was appointed physician to the Belfast Royal Hospital in Frederick Street. He was to remain a full member of the visiting staff of this hospital, and later of the Royal Victoria Hospital, until 1918.

He developed a large and superior medical practice, numbering among his patients many important and influential families and soon became an active and dynamic member of the medical community of the city. In 1884 he moved from Great Victoria Street to a more appropriate dwelling at 8 College Square North, Belfast. This locality could be described as the Harley Street of Belfast at this period, and this large Victorian terrace house provided him with an appropriate if gloomy consulting suite, together with suitable rooms for the entertainment of his guests and the essential coach houses and stabling in the rear – greatly improved accommodation and address for a young ambitious physician. In this period it became clear to him – and here his pharmaceutical background must have had its influence – that there was no adequate textbook which met the joint needs of medical students, dispensing chemists, and medical practitioners. In his spare time he tried his hand at medical authorship and his best selling classic “Elements of Pharmacy, Materia Medica and Therapeutics”, published in 1882, was the result.

Whitla was appointed in 1890 to the chair of Materia Medica in Queen's College Belfast on the resignation of Professor Seaton Reid. It is said that he soon breathed new life into the teaching of this hitherto dry and dull subject. His book was naturally an asset to his teaching and his appointment did nothing to diminish its increasing circulation. In 1902 he was knighted in the Coronation Honours list. He was now 51 years old – active and energetic, and with a wide variety of extra-curricular interests. He bore himself with dignity and aplomb, and he was the inevitable selection of the profession for the presidency of the British Medical Association for the annual meeting held in Belfast in 1909. His hospitality on this occasion was notable and he presented each member attending with the two volumes of his recently published book – “Dictionary of Treatment”.

He was President of the Ulster Medical Society on two occasions – 1886-87 and 1901-02. In December 1918 he was elected with a large majority as the first representative of The Queen's University of Belfast in the Westminster

Parliament. His re-election in November 1922 was unopposed and he retired from Parliament in 1923. In 1919, the year of his retirement from his Chair in the University, he was appointed Honorary Physician to the King in Ireland and subsequently Pro-Chancellor of the Queen's University. In the previous year – 1918 – he had retired from the Royal Victoria Hospital. This severed his active connection of 36 years with the hospital. As he was now 67 years old he retired from active practice, to live in Lennoxvale House. He died there at the age of 82 years on 11 December 1933 four years after a stroke. Two days later, on a miserable winter's day he had a civic funeral with much pomp and circumstance. He was buried in the City Cemetery after a funeral service in University Road Methodist Church attended by representatives of government, university, the medical profession and many religious organisations. Lady Whitla had died 18 months before her husband.

Sir William Whitla had not only been one of the most outstanding members of the medical profession in Northern Ireland, but also a distinguished Professor of Queen's with an international reputation as a medical author. However, it was the publication of his will in 1934, that confirmed that he would be one of the most generous benefactors Queen's would have in its first 150 years. Even before his death he was known as a generous person, having built the Medical Institute in College Square North for the Ulster Medical Society and also presented the Good Samaritan stained-glass window to the old Royal Hospital in Frederick Street in 1887. This beautiful window was removed to the out-patients' waiting hall of the Royal Victoria Hospital in 1903 and later was transferred to its present site at the end of the Royal corridor.

As Sir William and Lady Whitla had no children, the residue of his estate of almost £90,000 was left to the university.⁶ This amount in 1934 is probably equivalent to seven or eight million pounds today. Whitla made his fortune in three ways – from his medical practice, from the publication of his books, and from astute investment in the stock market, especially in the new area of oil stocks at a time when his contemporaries were still buying stock in the Belfast and County Down Railway.

The Whitla Hall, Methodist College, Belfast

Sir William was appointed to the Board of Governors of the College in 1906, when there was much uncertainty about the future of the school which like many voluntary schools was in financial and administrative difficulties.^{7,8} It was at this time that the Royal Belfast Academical Institution had to sell the plot of land as a site for the Belfast Technical College which they now probably regret. Sir William was regarded as the most influential of several new governors appointed in 1906 and played a major role in the development of the school, not only in the refurbishment of buildings and the introduction of technical education with properly equipped laboratories, but in the appointment of a scientist, E I Lewis as the headmaster. These innovations were to provide the foundation for the reputation that Methodist College now has as one of the country's leading grammar schools. Whitla remained a Governor of the school until his death. In his will he bequeathed to the College £10,000 free of duty to found a library or chapel or hall. The Governors decided to build an assembly hall which was opened by Lord Craigavon in December 1935.

The Sir William Whitla Hall, Queen's University of Belfast.

The greatest memorial to the generosity of Whitla was the provision of the assembly hall, which now bears his name, for the Queen's University. It stated in his will "all the rest residue and remainder of my property, I devise and bequeath to the Governing Body of the Queen's University Belfast to be devoted towards the fund for the erection of a Hostel for male students attending the University or for the erection of a ceremonial or common hall to be erected within the said building".⁶ The university received about £35,000 for this building and, after much discussion the Senate decided to build a hall on a site in the south west corner of the grounds beside University Road.⁹ The site had to be cleared of wooden huts which accommodated the Departments of Geology, Commerce, Education and Law. The foundation stone was laid by the Chancellor, Lord Londonderry, in July 1939. The architect was John MacGeagh from Belfast and the main contractor F B McKee and Company. The tender price was £44,390. The outbreak of war brought many problems which were eventually overcome and the building was completed, except for internal fittings, in 1942 when it was requisitioned by the Ministry of Commerce to provide accommodation for American forces.¹⁰

With the end of the war in 1945, the university set about completing the building to the original plans but there were major difficulties in obtaining materials for curtains, wood flooring, panelling and seating. Although incomplete, the building was used as an examination hall. It was finally completed "by dint of great effort and much ingenuity" and opened by Sir Henry Dale on 19 February 1949. Dale – a most distinguished pharmacologist – was chosen to perform the ceremony as a "person distinguished in Sir William Whitla's subject of Medicine". The opening was attended by several surviving relatives of Sir William and by many civic dignitaries. The event was unfortunately overshadowed by the death, a few days previously, of the Chancellor of the University, Lord Londonderry but the only part of the celebration to be cancelled was the evening ball.

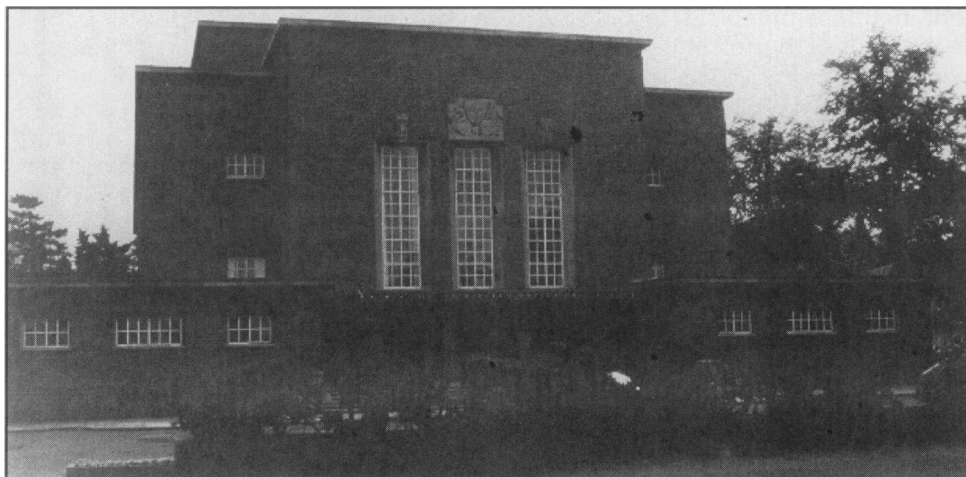


Fig. 1 The Sir William Whitla Hall, The Queen's University of Belfast. Finally opened by Sir Henry Dale in 1949.

The Sir William Whitla Hall is a most impressive building and blends in with the older Lanyon buildings of the University. (Fig. 1) There is seating accommodation for 1,500 people on the ground and gallery levels. The platform will accommodate a further 100 seats, for choir, orchestra or other gatherings. The Mitchell Organ, which had been in the Great Hall in the Lanyon Building was transferred to the new building, modernised and extended by the further benefactions from the Mitchell Family. It is a splendid instrument and is encased in an excellent chamber behind an oak screen at the rear of the platform. The plan form, section and constructional features of the interior are on traditional lines. Columns support the narrow side galleries and clerestory walls of the auditorium. The side galleries follow the English tradition for convocation seating and mark the processional way to the platform. The high level windows of the clerestory admit abundant natural light for examination work on the hall floor.



Fig. 2 Bust of Sir William Whitla by Gilbert Bayes, RBS, on the west wall of the Sir William Whitla Hall.

There are interesting external features including a bronze bust of the benefactor placed in a stone niche on the west wall, overlooking a stone paved terrace and the university road. (Fig. 2) The carvings to the heads of the triple windows to the forecourt include the University coat of arms, supported on a globe and flanked by figures of Aesculapius and the Scribe, depicting Whitla's services to humanity and learning. Carvings on the keystones to the heads of the tall windows of the east facade depict the trade and commerce of the province, whilst those of the west facade depict

the faculties of the University. The bronze bust is by Gilbert Bayes RBS, of London, and the carved stonework is by the same sculptor working in conjunction with Morris Harding RHA, of Belfast. The low relief plaster panels on the walls of the entrance hall depict Music and Drama, and are also by Bayes.

The Sir William Whitla Hall has been the centre of the Belfast Festival at Queen's for the past 30 years, and has contributed to the enjoyment of the arts by many of the citizens of Northern Ireland. If the university had not received this generous bequest it is unlikely that Queen's would have been able to provide the funding for a hall of this size and quality, which today would cost at least three million pounds. Whitla's request that his endowment be used to provide a building was a shrewd decision which may not be fully appreciated unless by consideration of the effects of inflation on the value of scholarship endowments.

The Vice-Chancellor's Lodge

Since 1934, the Vice-Chancellors of Queen's have been provided with a most elegant and comfortable residence in Lennoxvale, off the Malone Road. It is said to be one of the most desirable of all Vice-Chancellor's residences in the British Isles. Vice-Chancellors originally lived in the main University building, but in 1913 moved to Elmwood House in Elmwood Avenue. When this ceased to be

occupied by the Vice-Chancellors, it housed several university departments until demolished in the early 1960s to provide space for the new Students' Union.

In his will Whitla bequeathed Lennoxvale House (Fig. 3) to the governing body of the Queen's University of Belfast with the earnest wish that the house and grounds be used as a residence for the Vice-Chancellor.⁶ The first Vice-Chancellor to occupy the Lodge was Professor Ogilvie and it has been used by all his successors. The house was built by John Ward, an artist and Egyptologist, in 1876.¹¹ He was the owner of the firm of Marcus Ward and Co, Dublin Road, Belfast, which had a world class reputation for high class colour printing and the artistic production of illuminated addresses, Christmas cards, calendars and books (including Vere Forster's copy books). It was built in Scrabo stone for the sum of £2,850. Ward lived in the house until 1906, when he sold it on the death of his wife, Grace and moved to Kent where he died in 1912. Sir William Whitla bought the house in 1906 and used it as his residence until his death in 1933.

The Lodge has been well maintained by the University and while there has been little change to the outside, there have been internal alterations over the years as the requirements of the occupants have changed with time. An interesting feature are the carvings of small animals carved in the headings of the ground floor windows. In the extensive and beautiful gardens is a summer house to which Whitla retired to write his books when his wife had her Salvationists in the main house. The grounds contain two lakes – now known as the Vice-Chancellor's lakes – which are about an acre in size. These lakes – in reality the Strand Mill dam – were constructed in 1808 by the Belfast Charitable Society who, at that time were the authority for supplying water to Belfast.



Fig. 3 The Vice-Chancellors Lodge, Lennoxvale, in 1993.

The lakes formed part of a system consisting of a number of dams including Lyster's Dam, near the second locks on the Lagan at Deramore and an open conduit passing through what is now Botanic Gardens, Agincourt Avenue, University Street and Conduit Street to a reservoir situated close to the junction of Adelaide Street and Ormeau Avenue (beside the old Ormeau Baths). This water system was little used after 1848 and the Strand Mill dam was sold to the owners of the adjoining lands after 1884. The lakes are still present but little used.

Galileo

Sir William Whitla was a great traveller, visiting many countries including Russia, Palestine, Italy, France and Canada. On his travels he collected many different items and in particular pictures and pieces of sculpture, amongst them the statue of Galileo (Fig. 4) which he purchased on a trip to Italy, apparently as a present for his wife who was not with him. When the statue arrived in Belfast, it was too large for the house and was initially placed in the garden

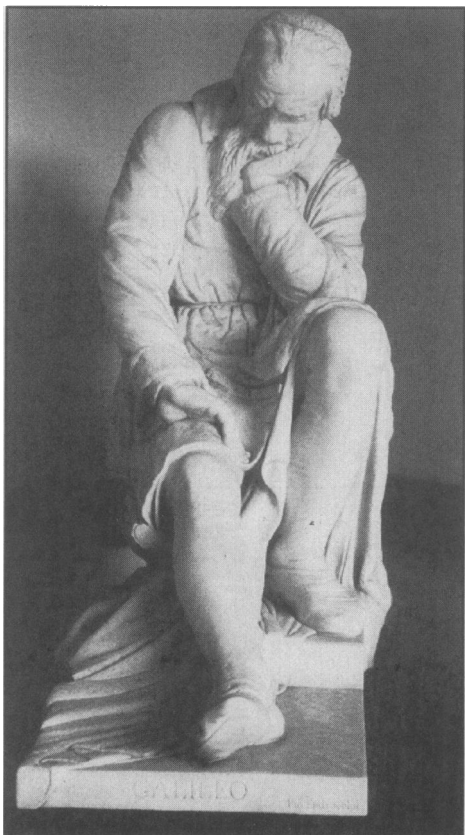


Fig. 4 Statue of Galileo, by Pio Fedi, now in the Medical Biology Centre, QUB.

before being presented to the Ulster Medical Society in 1915.¹² It was also too large for the Medical Institute and was given a temporary home in the Belfast Public Library in Royal Avenue before being taken to the new Museum and Art Gallery on the Stranmillis Road. After 65 years the Museum decided that they no longer wished to house the statue and asked the University to have it removed. The only suitable location was in the north end of the foyer of the Medical Biology Centre where it has been since 1980. The sculptor was Pio Fedi, one of the most distinguished Florentine sculptors of the nineteenth century, some of whose work is still displayed in the main square in Florence amongst statues known the world over. The celebrated astronomer is represented in the prison of the Inquisition sitting on a stool; a map of the world and rolls of paper lie on the ground. It may seem strange to house the statue of such a famous astronomer in a medical building but Galileo matriculated as a student of medicine in the University of Pisa in 1581.

The Chain of Office of the President of the Ulster Medical Society

Sir William Whitla was President of the British Medical Association when its annual meeting was held in Belfast in 1909. His colleagues marked the occasion by presenting a presidential badge and chain of office in gold and enamel to Sir William Whitla.¹³ In turn, he presented this to the Ulster Medical Society as the presidential chain which has since been used by all Presidents of the Society, with their names engraved on small medallions attached to the chain.

The Whitla Medal

On 5 January 1953, a British European Airways Viking crashed at Nutt's Corner after a flight from London.¹⁴ Twenty-seven people were killed including four Queen's students – Naomi Brudno, Clive Mishon and Jeffrey Wilks, students in the Faculty of Medicine and Leonard Rees, a research student in the Faculty of Science. (Fig. 5) Naomi Brudno was in my year at Queens having started in 1951. All four were members of the Literary and Scientific Society (Literific), which was founded by a group of young men for the purpose "of affording students of the Queen's College and others an opportunity of improving themselves, by writing papers on literary and scientific subjects, to be read and

discussed before the Society”.¹⁵ The Society rapidly rose from these small beginnings to a position of great importance in the social life of the College with regular meetings being held during the academic year in the Great Hall of the University. These arrangements continued until the 1960s when the society withered away.



Fig. 5 The Belfast Telegraph, Jan 6th, 1953: report of the air crash at Nutt's Corner the previous day.

A fund was launched by undergraduates to commemorate the four students killed in the air crash and £630 was raised. The organising committee allocated £250 to the "Literific" to endow a medal for the best debater and £355 to the Faculty of Medicine to endow an annual prize in a subject to be designated by the Dean of the Faculty. The subject was to be such that as large a number as possible of the students in the faculty could be eligible, and it was agreed – "that the fund given to the Faculty of Medicine by the Aircrash Memorial Fund Committee be used to fund a medal, to be known as the Whitla Medal to be awarded annually to the most distinguished student in Therapeutics in Final Part 1 and to carry with it a prize of £4, with a prize of £3 to the student judged second".¹⁶ The first recipient of the Whitla Medal in June 1955 was David L Freedman. Many subsequently distinguished graduates of the Medical School have been awarded the medal. The Whitla Medal was not a legacy of Sir William Whitla, but the Faculty of Medicine used this opportunity to mark his contribution to the subject of therapeutics.

The Whitla Medical Institute

Sir William Whitla was president of the Ulster Medical Society for the second time in the session 1901-02. The annual dinner of the Society was held in the Prince of Wales Hotel, Victoria Street, Belfast, at which 84 were present on the 21 November 1901.¹⁷ In his after-dinner speech, Sir William apologised for reducing the number of afterdinner speeches to four and stated that this was not

done in order to provide him with a longer period for his own speech. In the course of his speech he talked about the future of the Society and particularly emphasised the importance of drawing members of the Society more closely together into a compact brotherhood whose chief aim would be "the advancement of those great principles of which true progress, honour and dignity of our noble and self-denying profession depends". He believed there was widespread conviction that this would be accomplished by bringing the entire local profession under one roof and that this roof should be their very own. He understood that two schemes had been considered for providing accommodation for the Society but the only one that had hitherto been considered feasible by those members who had given thought to the subject "is to look around for a

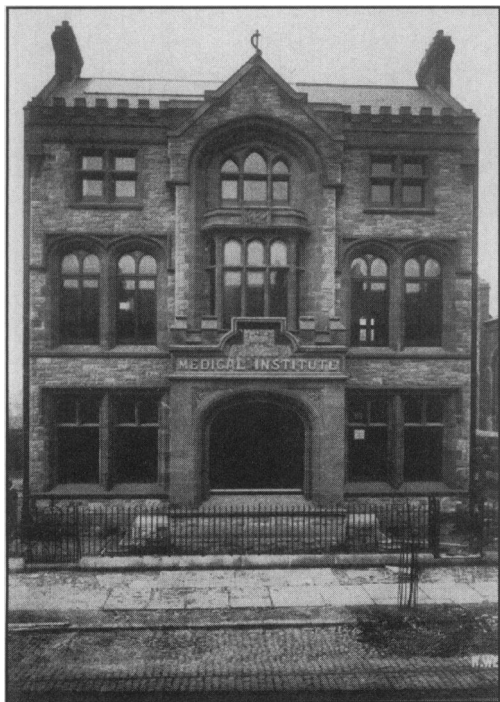


Fig. 6 The Medical Institute photographed soon after completion, dated 1902. The name Whitla was not carved until after his death in 1933.

large empty house in some district where rents had fallen and to secure on a long lease a derelict property upon which we could spend a large sum of money in such structural alterations as would be essential for our purpose." He condemned this plan and stated that the only scheme seriously worth considering "is to procure a plot of ground in a conveniently central position and erect upon it a building suitable to our pressing needs and requirements." He suggested that it should be called a Medical Institute. He then asked the members to look at the problems which would arise in running such an institute. He spent some time working out the cost of the upkeep of such a building and the ways in which the subscriptions of members of the society should be increased in order to cover the running expenses. He rapidly disposed of the ways in which capital would be found to provide the Institute. "Since I have been your President fifteen years ago, it has

been a dream of my life that one day I should be able to leave behind me when that day comes, enough money to build for you a suitable institute. I feel that I am able to do this now and I don't want to be deprived of the joy that I shall have for the remainder of my days – be they short or long – in seeing you, the Ulster Medical Society housed in a home of your own." He continued "if you tell me gentlemen that you are determined to keep up the building, I will erect it, furnish it and hand it over to you or to trustees acting on your behalf. Before I ask some pledge of you to maintain this building, I shall give you some idea of what sort of a structure it should be and to what uses I should like to see it put." He then proceeded to describe the frontage of the building, the size of the hall, the number of rooms and their size and the uses to which they could be put.

Clearly he had gone to a great deal of trouble to plan the building and the accommodation that it should contain. Finally, he disclosed that he had twice within the past six weeks thought he had secured a site on College Square North which would be suitable for the project but on each occasion he had not been successful.

This must have been one of the most memorable and unusual speeches ever made by a president of the Ulster Medical Society at its annual dinner. Within a short time, a plot of land at College Square North was rented from the Governors of the Royal Belfast Academical Institution for the yearly rent of £60 for the purpose of erecting the Medical Institute. The foundation stone was laid by Professor Redfern on 12 April 1902 and on 20 November 1902 it was declared open by the Earl of Dudley, the Lord Lieutenant of Ireland.¹⁸ (Fig. 6) It was described as a handsome, commodious building, built of rough hewn stone with doors and windows relieved by red sandstone in a gothic manner.^{19, 20}

The ground floor contained a library and committee rooms. The fireplace in the library on the ground floor had been so designed that a space above the mantelpiece contained a large stained-glass window. The previous winter there had been a serious outbreak of typhus fever on the island of Aranmore off the west coast of Donegal. As the local fishermen would not help the doctor from Burtonport to attend the victims, Dr William Smyth rowed himself to the island in a leaking boat with food and medical supplies and then was joined by Dr Brendan McCarthy. Eventually together they conveyed patients to the mainland but Dr Smyth contracted the disease and died on 19 November 1901. The glass window was a memorial to this event and of Dr Smyth's death. On the staircase was a window from Sir William's own house representing a scene from "As you like it" in which Sir William himself appeared in the guise of Corin. (Fig. 7) On the first floor was a large hall which would seat 200 and dine 120, but alcoholic beverages were only to be supplied on the occasion of the annual dinner. This meeting room was fitted with double windows to deaden outside noises. The building cost £8,000 and was handed over to seven medical men to hold in trust for the Society. In his will, Sir William bequeathed a further sum of £500 to purchase the ground rent of the Institute.

The indenture establishing the Institute stated that it was to be called The Medical Institute and immediately after the death of Sir William Whitla, it shall be called "The Whitla Medical Institute and such name shall be cut in stone in a space at the front of the building to be left vacant for that purpose." The



Fig. 7 Scene from "As you like it", with portrait of Whitla as Corin on the right.

Medical Institute was for many years a focus of medical activity as it provided a place in which the Society could keep its possessions, pictures and library and where Fellows and Members could meet both socially and for scientific business. Until the 1940s College Square North was a fashionable area of Belfast. In the late 1940s use of the Institute declined except for the social gathering before and after scientific meetings and it was no longer the club it had been in the pre-war years. The abolition of petrol rationing and greater availability of motor cars increased traffic congestion and made it increasingly difficult to park near the Institute. A greater problem was deterioration in the fabric of the building when cracks appeared in the walls and dry rot was discovered. It was reported that the seating in the main assembly hall was dangerous and the Society was advised that the room was no longer safe for use. By March 1954, Council found it impossible to insure anyone against the risk of damage from falling plaster and decided to close the premises temporarily until repairs were carried out. The Whitla Medical Institute was refurbished and opened for the 1957-58 session but before long it was realised that the income of the Society was not covering the cost of upkeep of the building, and ever-decreasing use was being made of the premises. The Society was loath to sell the premises because the trust deed stated that the trustees were to commit the building to be used for the purposes of the Ulster Medical Society and in the event of the Society omitting or declining to observe these conditions, the trustees had the power to sell the property and hand over the proceeds in such share as they thought fit to the Royal Victoria Hospital for the endowment of a ward and to the Queen's University of Belfast for the endowment of a chair for original research in pharmacology. Clearly a very difficult situation for the Ulster Medical Society because if it did not continue to use the Whitla Medical Institute, then the proceeds would not be to its benefit.

On 2 June 1965 Council informed the trustees officially that they had defaulted and were vacating the building. Subsequently the Institute was sold to the Governors of the Royal Belfast Academical Institute, the ground landlords, for £13,500 and after attending to certain expenses, this left a disposable sum of £13,082 4s 6d. These proceeds could not be used to provide alternative accommodation for the Society but were to be divided between the Royal Victoria Hospital and the Queen's University. However, previously to this, on 17 April 1964, the solicitors for the trustees of the Whitla Medical Institute had written to the University appraising them of the situation and enquiring if the University would formally consent to the sale of the Whitla Medical Institute. The Secretary of the University subsequently wrote to the Dean of the Faculty of Medicine, Professor Biggart, to ask his advice.²¹ In his reply Biggart wrote:

'I do not see that the University can refuse to accept the bequest as it can easily use the money to endow further the Department of Pharmacology and Therapeutics and indeed one of the posts down for this quinquennium is a Lectureship in Experimental Pharmacology, and as the Wellcome Trust have given us £35,000 to build this laboratory it is obvious that the Faculty will be seeking to fill this post. No matter where one's sympathies would lie it would therefore be legally impossible for us to advise the Trustees that we could not meet the terms of the bequest. However, we should do our best to preserve the life of the Ulster Medical Society, and if in the process of building the New Wing for Pharmacology etc. on the pre-clinical site, one

²¹ The Ulster Medical Society, 1994.

or two Committee rooms could be set aside for the Ulster Medical Society and lecture room facilities given to them I think this would be much appreciated by the medical profession in the area’.

Discussions continued between Professor Biggart and Mr Miller Bell who was the Honorary Secretary of the Society at that time. The solicitors for the trustees of the Institute were informed that the University would be prepared to apply such funds as the trustees handed over from the sale of the Institute for the purposes specified in the Declaration of Trust. They were also informed of the possibility of incorporating appropriate accommodation for the Ulster Medical Society in the proposed new buildings. The Senate of the University accepted the following proposals in 1965 – that £500 be paid to the Royal Victoria Hospital for the naming of a bed in memory of Sir William Whitla and the balance remaining – amounting to just over £12,500 – would be paid to Queen’s for the further endowment of the existing Chair of Therapeutics and Pharmacology and the provision of rooms for the use of the Ulster Medical Society.

Fortunately, at that time the university was planning to build an extension to the Medical Biology Centre to accommodate the university departments of anaesthetics, therapeutics and pharmacology and mental health and planned new departments of cancer studies and geriatric medicine. In 1965 the trustees of the Society accepted that the rooms for the use of the Society would be provided in the proposed new clinical extension to the Medical Biology Centre. The Ulster Medical Society indicated to the University the type of accommodation that would be required and the University agreed that it could use certain lecture rooms in the Medical Biology Centre for lectures and discussions by members of the Society or the general public in furtherance of the objects of the Society. As it was realised that it would be some years before this new accommodation would be available, the University agreed that other facilities would be available in the meantime to the Ulster Medical Society. The University also agreed to release the trustees from all further obligations under the original Declaration of Trust dated 30 October 1902 and to regard the same Trust as discharged and fully performed.^{21, 22}

These proposals were accepted by the trustees of the Ulster Medical Society and by the Senate of the University. The construction of the new building, now known as the Whitla Medical Building, began in 1974 and was completed in January 1976. (Fig 8) It contained accommodation for the university departments of geriatric medicine, anaesthetics, oncology, mental health and therapeutics and pharmacology. In addition, it contained a meeting room, council room and additional storage and catering facilities for the use of the Ulster Medical Society. However, because of some difficulty over the Trust that was signed between the University and the Ulster Medical Society in 1966, it was not until 1982, that the final deed between the two parties was signed and accepted by both parties.²²

During the planning phase (1972 - 76) of this new building it was referred to as the “clinical extension” to the Medical Biology Centre but this term was not acceptable to the heads of departments which were to be housed in the new building. The meeting of the Faculty of Medicine on 25 November 1975 considered a letter signed by Professor Shanks for the heads of the departments and by Dr D A D Montgomery (President of the Ulster Medical Society)



Fig. 8 The Whitla Medical Building, opened in 1976 by Professor Owen Wade.

suggesting that the building be called “The Whitla Clinical Research Centre”.²³ After discussion there was agreement on the use of “Whitla” and alternatives to clinical research centre were suggested, for example, Whitla Medical Building. The Dean proposed to write to the University indicating these views. At the next meeting of Faculty on 27 January 1976, the Dean reported that the Standing Committee of Senate had suggested the name “Whitla Medical Wing” as an alternative to those proposed by Faculty but after discussion Faculty accepted the name “Whitla Medical Building”.²⁴ The building was opened in May 1976 by Professor Owen Wade who had been instrumental in planning the accommodation not only for his own department but for the other departments in the building. This building has been a most successful addition to the accommodation provided for the clinical departments in the Faculty of Medicine and appears to have served the Ulster Medical Society well since they vacated the Whitla Medical Institute in College Square North.

Clearly there is a marked difference between the old Whitla Medical Institute in College Square North and the new Whitla Medical Building. The former was a stone building, the latter a modern steel-framed building with concrete cladding. Accommodation for the Ulster Medical Society is not of the same range that was available in the Institute, but, the Society has been provided with accommodation which meets its current needs and it has been possible to house some features of the old Institute in the new building. The stonework containing the title “Whitla Medical Institute” was removed and stored and has now been installed in the ground floor of the Whitla Medical Building. The four carved heads of Dr Henry MacCormac (Professor of Medicine), Professor Thomas Andrews, (Professor of Chemistry, 1849-1879), who Whitla selected as the two most distinguished professors when the medical school was in R.B.A.I., and Professor Peter Refern (Professor of Anatomy and Physiology, 1860-1893) and Professor Alexander Gordon (Professor of Surgery, 1849-1886) considered by Whitla as

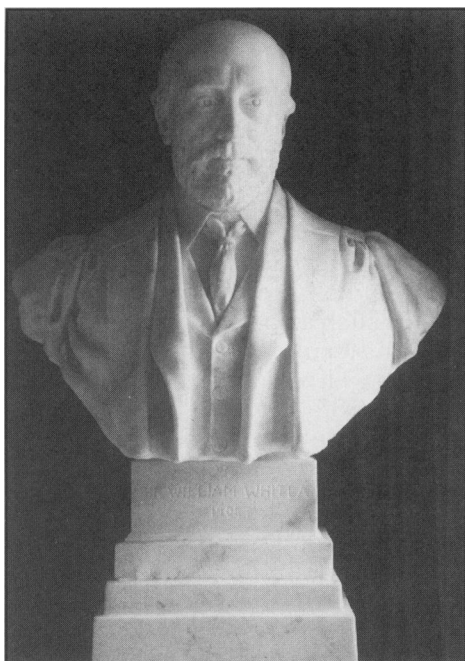


Fig. 9 Bust of Sir William Whitla presented in 1904 by the members of the Ulster Medical Society in recognition of his generosity in founding the Medical Institute.

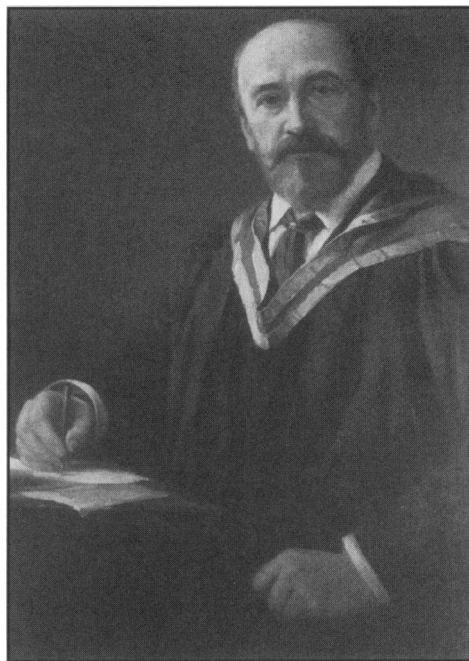


Fig. 10 Portrait of Sir William Whitla painted by Frank McKelvey (1938), and presented to the Society by Professor W W D Thomson.

the two most distinguished professors from the Queen's College era, that were a feature at the front of the Institute were re-erected within the new building. The stained-glass windows (including the Smyth window and the scene from "As you like it") all found a home in the new building which also houses the bust of Whitla presented to him in 1904 by the members of the Society in recognition of his generosity in funding the Medical Institute, (Fig. 9) and the posthumous portrait by Frank McKelvey of Sir William Whitla presented to the Society in 1938 by Professor W W D Thomson. (Fig. 10) The bust had been ceremonially handed over by Sir Lauder Brunton, Professor of Therapeutics in St Bartholomew's Hospital and the discoverer of the use of amyl nitrate in the treatment of angina pectoris.²⁵

Professor Biggart lost no time in acknowledging the legacy that had been received by the University, as the Faculty of Medicine at its meeting on 25th April 1967 accepted his proposal that the 'Chair of Therapeutics and Pharmacology' should be known as the 'Whitla' Chair of Therapeutics and Pharmacology.²⁶ This was a most appropriate way to perpetuate the name of one of the most distinguished holders of the Chair of Therapeutics and Pharmacology in this University. Owen Wade, who had been appointed to the Chair of Therapeutics and Pharmacology in 1957, became the first 'Whitla Professor' in August 1967. Thus two of Whitla's main interests – the Ulster Medical Society and the Department of Therapeutics and Pharmacology – came together in a building which bears his name.

Whitla's legacy as a medical author

In 1882, at the age of thirty-two, Whitla published his first book "Elements of Pharmacy, Materia Medica and Therapeutics". The book consisted of 524 pages, and was written primarily for students of medicine as Whitla believed that it was impossible for a practitioner to write a scientifically constructed recipe unless he had some knowledge of pharmacy, but he also stated that for a pharmacist to compound a recipe, he had to have knowledge of materia medica. There were five sections in the book based on his philosophy of the importance of different aspects of prescribing, pharmacy, materia medica, therapeutics, the administration of medicines, and pharmacopoeial reactions and tests. Whitla was ideally qualified to produce such a book as he had training in pharmacy, knowledge of materia medica and experience in therapeutics from the practice of medicine. The book was very well received and was a great success, 11 editions being published between 1882 to 1922; about 50,000 copies were sold. Further editions were published by a number of authors after his death but these were not as well received.

The success of the first book encouraged Whitla to provide a second one. He at first thought of producing a "Therapeutic Index or Index of Diseases" to be appended to his first book and that it would consist of 50-60 pages. However, he felt that a mere enumeration of the drugs suitable for the treatment of each condition would be of little value unless the list was accompanied by 'some expression of opinion regarding the relative value of each drug, and of the different methods by which it might be employed'. Instead of a supplement of 60 pages, he produced a volume of nearly 1,000 pages – a tremendous performance that must have required an immense amount of work by one man with a busy clinical practice. In the book various diseases and many symptoms, not diseases in themselves, were alphabetically arranged, each with full details as to treatment; it started with "abortion" and ended with "yellow fever". He generally described his own favourite treatment first and then those of other writers. It would appear that Whitla not only wrote the book but was responsible for its printing, publication and distribution.

The book was an immediate success. At the beginning of this century the regulations of the Merchant and Royal Navies decreed that all ships with a crew of greater than 100, had to carry a doctor. All ships with a crew of less than 100 had to carry a copy of Whitla's 'Dictionary of Treatment' to be consulted by the captain when a member of the crew became ill. When the size of these two navies at the beginning of this century is calculated, the potential market for Whitla's books can be appreciated. Dr David Duncan-Main, a missionary of the Church Missionary Society in China, was so impressed with the dictionary that he translated it into Chinese. The second and third editions were both published in Hangchow in China. In the fourth edition which appeared in 1894, Whitla received help from Mr A B Mitchell and Dr Cecil Shaw who provided sections on surgery and diseases of the ear, nose and throat. Whitla was responsible for the publication of seven editions, the last of which appeared in 1923. The "Dictionary of Treatment" had been a most successful book, apparently greatly appreciated in many countries. Further editions of the "Dictionary" were published after Whitla's death but did not enjoy the same success; the last edition in 1957 was edited by Dr Sidney Allison and Dr Howard Crozier with 26 contributors from Belfast Medical School.

Whitla published a third book -- "A Manual of the Practice and Theory of Medicine" in 1908. He regarded this as an introduction, even though it consisted of 1900 pages in two volumes, to his Dictionary of Treatment. In this book, each article contained a description of the aetiology, pathology, symptomology, diagnosis and a brief resumé of the treatment of each medical condition. Unfortunately, this book did not become as popular as Whitla's first two books, but to have two best sellers out of three was an outstanding achievement. While several organisations have benefited from the legacies resulting from these books, no one has attempted to maintain the standards achieved by Whitla and the last edition of his Dictionary appeared in 1957. Nevertheless, there has been a determined effort to improve the drug treatment of disease by staff of the Belfast Medical school. Owen Wade, Whitla Professor of Therapeutics and Pharmacology, emphasised the importance of the adverse effects of drugs in his book "Adverse Reactions to Drugs" and the Northern Ireland Faculty of the Royal College of General Practitioners has provided a "Practice Formulary" which provides simple and appropriate treatment for the vast majority of patients presenting the more common conditions. Its 100 pages do not compare with the volumes produced by Whitla but it should have an important role in improving drug prescribing.

The development of Therapeutics and Pharmacology in Queen's

Materia Medica was one of the foundation chairs when the Belfast Medical School was established in the Royal Belfast Academical Institution in 1835. The first holder of the chair was James Drummond Marshall.²⁷ With the move to the new Queen's College in 1849, Professor Marshall was retired with a gratuity of £250 – his salary for five years – clearly, premature retirement schemes with compensation were introduced before the 1980s. Thomas O'Meara was appointed to the chair in 1849 but resigned shortly after his appointment, when Dr Horatio Agnew Stewart was appointed. Professor Stewart was more a surgeon than an authority on drugs. He was succeeded in 1857 by Dr James Seaton Reid who was visiting physician to the Union Fever Hospital for almost half a century and held the chair for 33 years. His contribution to the university was to give a lecture course in materia medica – the description of remedies. At this time materia medica was not the most popular subject. Dr Charles Darwin said "that he looked back upon the hours spent in attending the materia medica lectures as the most inexpressibly dreary experience of his life". The situation was not helped by the fact that Seaton Reid was apparently "a most terrible lecturer".^{28, 29} The students created such an uproar in his classes that he had to appeal for help and protection to the President of the College, Dr Henry, who stationed an additional porter in Professor Reid's class to help preserve order, but apparently with little success.

After Professor Reid retired Whitla applied for and was appointed to the chair in 1890. His application which was printed and bound in leather, contained testimonials from an impressive list of experts. He was eminently qualified for the appointment with the wide acceptance of his textbook, 'Elements of Pharmacy, Materia Medica and Therapeutics'. Whitla appreciated the enlightening effect of therapeutics to materia medica, and of greater significance the importance of the development of pharmacology in the latter part of the last century. Whitla's role was to link these subjects together in his teaching,

lectures and textbooks. He developed pharmacology in Queen's through his teaching but realised that research was important.

Sir William devoted at least three important public lectures to these subjects. The first was his presidential address to the Ulster Medical Society in 1886 which was entitled "The present position and prospects of the domain of therapeutics, with a glance at its relations to the neighbouring sciences";³⁰ the second was his presidential address to the Section of Pharmacology and Therapeutics at the annual meeting of the British Medical Association in Dublin in August 1887; his address was entitled "Progress of Therapeutics";³¹ the third occurred when the Medical Society of London appointed him their orator for 1913, the title of his oration being "The Trend of Thought in Recent Pharmacological Research".³² In this lecture he gave a learned discourse on the importance of linking the structure of a chemical (drug) to its action using as examples substances that had been evaluated at that time.

William Whitla did not have the opportunity to carry out observations on the effects of drugs on man but clearly felt that this was important because he referred several times to the work of Lauder Brunton in the discovery of the use of amyl nitrite in the treatment of angina pectoris. In 1867 Lauder Brunton published a paper in the *Lancet* entitled "Use of nitrite of amyl in angina pectoris",³³ which he described experimental work in animals and in man showing that amyl nitrite lessened the arterial tension. On the basis of such experiments he tried the drug in a patient whose severe angina pectoris had been relieved by bleeding – an effect attributed to the diminution in arterial tension. Brunton thought that as amyl nitrate had the same effect, it might be effective in the relief of angina. Subsequently, he gave the patient with angina pectoris five or ten drops of nitrite on a cloth and stated that 'the physiological action took place in from 30-60 seconds and simultaneously with the flushing of the face, pain completely disappeared and generally did not return till its wanted time next night'. Brunton later became the first external examiner in materia medica in Queen's and provided the first testimonial for Whitla on his application for the Chair. Unfortunately, it was to be many years before Whitla's expectations for the study of drugs in man would materialise in Belfast.

Whitla was succeeded by John Elder McIlwaine in 1921 when the title of the chair was changed to Materia Medica and Therapeutics. Dr McIlwaine was a consulting physician in the Royal Victoria Hospital. He had a degree in Engineering and was the first to engage in electrocardiography in Ireland but he had essentially a clinical approach to medical problems. He retired in 1928 and it was largely on his recommendation that the title of the chair was again changed to Pharmacology and Therapeutics. Dr E B C Mayrs was appointed to the re-named chair in the same year. Mayrs had been educated in the Methodist College Belfast and the Queen's University, graduating in medicine in 1914. His ambition was to become a surgeon but in 1916 he lost his left arm, had to leave the RAMC and eventually turned to pharmacology. He had some training in pharmacology in Edinburgh before returning to Queen's as a lecturer in pharmacology in 1923. By the appointment of Mayrs, the University recognised the growing importance of the discipline of pharmacology but unfortunately Mayrs made few contributions to the subject and did little to advance the ideas of his illustrious predecessor Sir William Whitla. Mayrs is more remembered as a collector of antiques not only in his University department but in his own

house. He kept and handed on successors in the Department a set of beautiful early nineteenth century pharmacy jars amongst other items.³⁴

The first person in Queen's to become interested in the scientific study of the effects of drugs in man was Henry Barcroft who was appointed to the Dunville Chair of Physiology in 1935. He joined the staff in the same year as Douglas Harrison was appointed to the Chair of Biochemistry and both professors were "indoctrinated" into Queen's by the medical students on the same day. Harrison remained in Belfast giving great service to Queen's for over half a century. Barcroft had had a distinguished undergraduate career at Cambridge and after qualifying in medicine at St Mary's Hospital Medical School, became a lecturer at University College London for three years before his appointment to the Dunville Chair at the very early age of 30. The Barcrofts were a well-known family and Henry Barcroft's aunts lived in a large house known as "The Glen" on the Dublin Road out of Newry. He had been a regular visitor to this house before he was appointed to the chair.

Henry Barcroft, with great vigour and skill, initiated research into human physiology at Queen's and introduced the technique of venous occlusion plethysmography using the water-filled temperature control plethysmograph to measure blood flow to the arms and legs.³⁵ The plethysmographs constructed by Barcroft are still used in the Department of Physiology. He and his colleagues studied the effects of a variety of substances including adrenaline, noradrenaline, histamine and acetylcholine on the peripheral circulation, but it was the effects of adrenaline which appeared to interest them most as it was difficult to explain

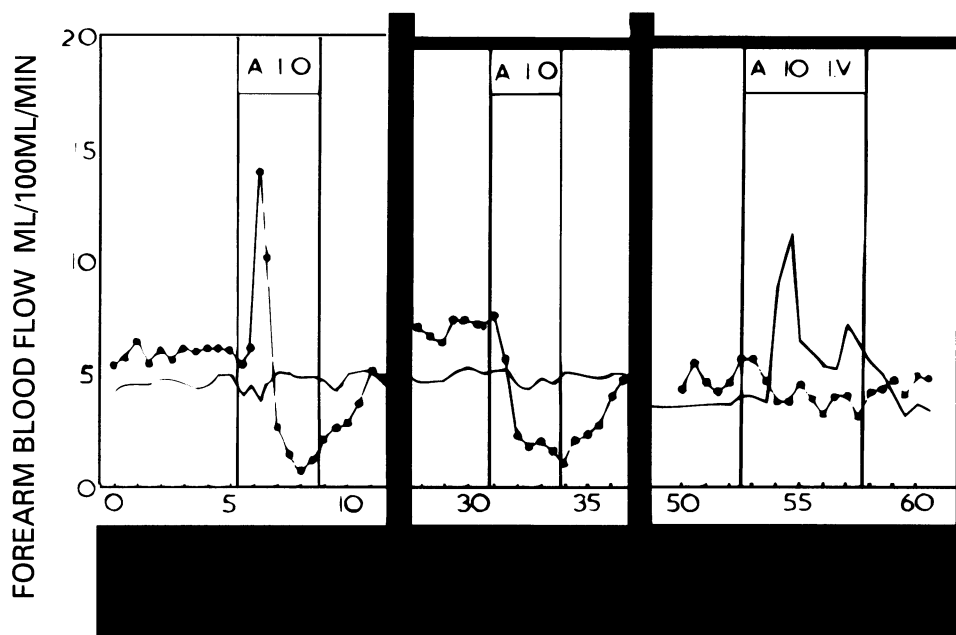


Fig. 11 The response of forearm blood flow to intra-arterial adrenaline (1.0 ug/min) and to intravenous adrenaline (10 ug/min). DCI 0.05 mg/min was infused intra-arterially during the time represented by the black line at the top of the Figure (i.e. from 20 min). — control side; •• side receiving arterial infusion (Modified from reference 39).

the nature of the response to this drug.³⁶ The infusion into the brachial artery of a small amount of adrenaline produced a marked increase in forearm blood flow followed by a rapid decline to below the pre-drug level where it remained during the period of drug infusion. In contrast, when adrenaline was infused intravenously, there was the rapid initial increase in flow followed by a decline in flow but to a level higher than the pre-drug level. Barcroft and his colleagues could not understand why adrenaline first produced a transient increase in blood flow with both intra-arterial and intravenous administration, followed by a decline, but to different levels, depending on the route of administration. (Fig. 11)

Barcroft resigned from the chair in Queen's in 1948 on his appointment to the chair of physiology in St Thomas' Hospital Medical School in London. He has continued his association with Queen's through regular visits to the Department of Physiology and was last in Belfast attending the meeting of the Physiological Society in September 1990 when he met two of his successors to the Dunville Chair of Physiology, David Greenfield and Ian Roddie, both of whom have now retired. Barcroft will be 90 in 1994.

In 1948 Raymond Ahlquist, Professor of Pharmacology in the Medical College of Georgia in Augusta, Georgia, USA, published a paper entitled "The classification of adrenotropic receptors" in which he suggested that adrenergic receptors could be divided into two groups, alpha and beta.³⁷ Ten years later his classification of receptors was confirmed by the demonstration in animals that dichloroisoprenaline (DCI) selectively blocked only those responses attributed to stimulation of beta receptors.³⁸ A D M Greenfield, who had received his medical training in St Mary's Hospital, London, succeeded Barcroft in 1948. He and his colleagues continued to investigate the factors controlling the peripheral circulation in man and they elucidated the nervous and humeral control of the peripheral circulation in man. During this time the Physiology Department developed an international reputation for their studies. Greenfield's colleagues – John Shepherd, Bob Whelan and W E (Darty) Glover left Belfast on their appointment to important posts elsewhere while Ian Roddie succeeded Greenfield to the Dunville Chair in 1964. They continued to study the action of adrenaline on the peripheral circulation but did not make any further significant advances until 1960 when a supply of dichloroisoprenaline was obtained from the United States by R G Shanks. As the drug had never been given to man, the first human subject had to be selected. David Greenfield – the head of the department – volunteered and became the first person to be given a beta blocking drug. In a series of experiments in healthy volunteers in which DCI was infused into the brachial artery, it was shown to block the increase in forearm blood flow produced by the intra-arterial infusion of isoprenaline thus demonstrating blockade of beta adrenergic receptors in the blood vessels in the human forearm.³⁹ In a forearm treated with DCI the subsequent infusion of adrenaline into the brachial artery only reduced blood flow. The intravenous infusion of adrenaline produced a normal response in the control (untreated) forearm but in the DCI treated arm there was only a reduction in flow. Thus the transient increases in forearm flow produced by adrenaline given by both intra-arterial and intravenous routes and the sustained increase in flow after intravenous infusion were abolished by DCI indicating that these effects were due to stimulation of beta adrenergic receptors in forearm blood vessels.

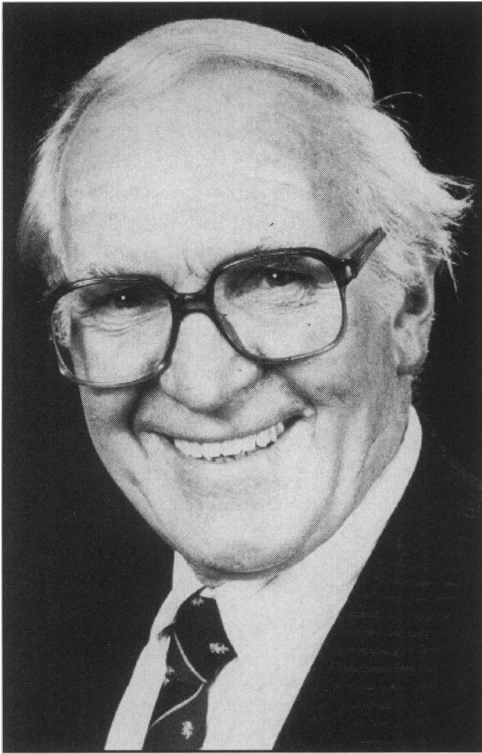


Fig. 12 Sir James Black

Unknown to the Belfast team another physiologist was interested in the properties of dichloroisoprenaline. He was James Black – now Sir James Black – probably the most successful discoverer of new drugs in this country. (Fig. 12) Black graduated in medicine from St Andrews in 1946 and after war service was appointed to a lectureship in physiology in the Veterinary School in Glasgow where he became interested in the treatment of angina pectoris, after the death of a close relative. At that time the current view on the pathophysiology of angina was that exercise increased cardiac work and if coronary blood flow could not increase to supply an adequate amount of oxygen to the myocardium, ischaemia would develop in poorly perfused parts of heart muscle and anginal pain would occur. The only available therapy at that time (late 1950s) was glyceryl trinitrate taken sub-lingually, which had been introduced in 1867 by Lauder Brunton. It reduced arterial tension (blood pressure) one of the

main determinants of cardiac work and as a result, myocardial oxygen demand would fall and a balance restored between the supply and demand of oxygen, and anginal pain would be relieved.

Studies in the 1950s had shown that glyceryl trinitrate increased coronary blood flow in animals with healthy coronary arteries, and thus it was assumed, erroneously as we now know, that it had the same effect in patients with ischaemic heart disease.

Black was interested in developing new drugs for the treatment of angina pectoris and put forward a hypothesis that was derived from Brunton's much earlier work.^{40, 41} At that time the drug treatment of angina pectoris was directed towards coronary vasodilation to increase the supply of oxygen to the ischaemic myocardium and it was thought that glyceryl trinitrate worked in this way.⁴² Black speculated that the treatment of coronary artery disease would be advanced by reducing cardiac oxygen consumption rather than trying to increase coronary blood flow. As increased catecholamine secretion during stress leads to an increase in cardiac demand for oxygen without an increase in supply, Black hypothesised that it might be possible to develop a new approach for the treatment of coronary artery disease through blockade of the action of adrenaline in the heart. He began to look for anti-adrenaline drugs that would selectively block the beta adrenergic receptors which had been described by Ahlquist. He approached the Pharmaceuticals Division of Imperial Chemical

Industries for help. After a visit to their new laboratories at Alderly Park in Cheshire he could not resist the attraction of the splendid new facilities to develop his new ideas and went to work there in 1957. He now had the resources to look for his “anti-adrenaline” drug. At this time Moran and Perkins (1958) had shown that dichloroisoprenaline (DCI) selectively blocked beta adrenergic receptors but did envisage a therapeutic role for a drug of this type.⁴⁰ Black began his studies at ICI investigating the properties of DCI, unknown to him that it was also being studied in Belfast. Black confirmed that DCI blocked the cardiac effects of adrenaline and isoprenaline and of stimulation of the sympathetic nerves to the heart in animals. DCI increased heart rate in animals and as a result it was realised would not be suitable to treat patients with angina. Incidentally the same effect had been noted in the first experiment on Greenfield, who developed a tachycardia, and as a result smaller doses were used in subsequent studies.

Black and his colleagues began to synthesise derivatives of DCI and the first one selected for study in man was pronethalol. It blocked beta adrenergic receptors in man and was shown to be effective in the treatment of angina.⁴³ However in toxicity studies in animals, pronethalol was found to be carcinogenic and studies in man were stopped.⁴⁴ Black and his colleagues continued to test derivatives of pronethalol for blockade of beta adrenergic receptors. One of the compounds tested in 1962 was ICI45520 which was to become propranolol. This compound was shown to be at least ten times more potent than pronethalol in blocking beta receptors, to be devoid of a stimulant effect on the heart, and not to be carcinogenic in mice.⁴⁵ Within a short time, propranolol was shown to reduce resting heart rate and exercise tachycardia after oral administration in healthy volunteers. It was realised that propranolol had the potential to be developed for the treatment of patients. These hopes were realised when studies in patients demonstrated that propranolol was effective in the treatment of angina pectoris.⁴⁶

The results of these studies were presented at a symposium in Buxton, Derbyshire, in 1965, which brought together many of the investigators who had been working with propranolol.⁴⁷ The drug was launched for the treatment of angina at this meeting, which was the first symposium to be held on the subject of beta blocking drugs. It was a remarkable achievement to complete all the studies required to register a new drug in three years from the time it was first tested in animals – today it would take at least ten years. The programme for the first session of this symposium contained three contributions from medical graduates of Queen’s. The first paper describing the pharmacology of propranolol was given by the present author. Ian Roddie and his colleagues had continued with the study of the peripheral vascular effects of beta blocking drugs and described the effects of propranolol on the peripheral circulation. In Ballymena the late Dr R J Kernaghan had become interested in the use of these drugs in the treatment of patients with angina, and was a co-author of the first paper to be presented and later published describing the beneficial effects of propranolol in angina.⁴⁸

At last the Belfast Medical School was making contributions to the pharmacology, clinical pharmacology and the therapeutics of new drugs. These activities have continued to develop in several departments in the Faculty of Medicine in Queen’s University and hospitals in Northern Ireland. During the past twenty-

seven years the properties of many beta blocking drugs have been investigated by the staff of the University Department of Therapeutics and Pharmacology. These studies have been facilitated by the development of novel methods to investigate these properties, including selective blockade of beta one and beta two receptors, partial agonist activity, duration of action, frequency of dosing, and pharmacokinetics. Many people have contributed to these studies which have resulted in many publications in scientific journals and established an international reputation for the department. (Fig.13)

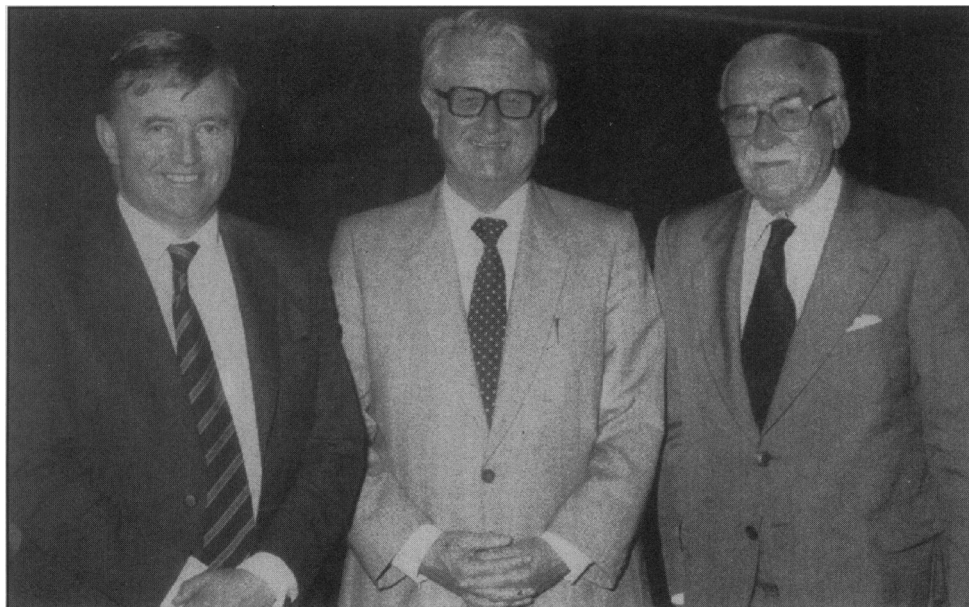


Fig. 13 Professor Ian Roddie, Professor David Greenfield and Professor Henry Barcroft: Belfast 1990.

Studies on the therapeutic value of beta blocking drugs have also been carried out in Belfast. The most important of these established for the first time in controlled therapeutic trials that propranolol was of value in controlling the signs and symptoms of thyrotoxicosis.⁴⁹ Propranolol was shown to be of particular value as an adjunct to treatment with radio-active iodine and in neonatal thyrotoxicosis.⁵⁰

The generous legacies of Sir William Whitla have been of undoubted value to many organisations in Northern Ireland but his legacy of the importance of scholarship, teaching and research in Therapeutics and Pharmacology, which has developed in Queen's in the last 30 years, has been of interest and value to a much larger audience.

Acknowledgement

I very much appreciate the generous help of many colleagues in the research activities within the Department of Therapeutics and Pharmacology in Queen's University and their help in the preparation of this lecture and paper.

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Historical Review:

A Corridor to the Past

Annual Oration at the opening of the 1993-94 teaching session at the Royal Victoria Hospital

R S J Clarke

A primary purpose of this opening address for the winter session of the Hospital is to welcome the new students. I sometimes hear of medical students in mid-stream wondering whether they have chosen the right profession or more definitely stating that they have made a mistake. This often arises from exhaustion by the scientific pressures of the first three years, and I can only say that it is rarely a complaint in the final years. In fact, my advice to the clinical students would certainly be to enjoy your ward work to the full. As a student one has time to talk to patients which is never available so freely again as House Surgeon or Registrar, and this is what makes medicine interesting. The patients are available in the wards not, as is sometimes feared by outsiders, as victims to be preyed on by the students, but as people who love to talk about themselves and hear other more or less informed views on their condition.

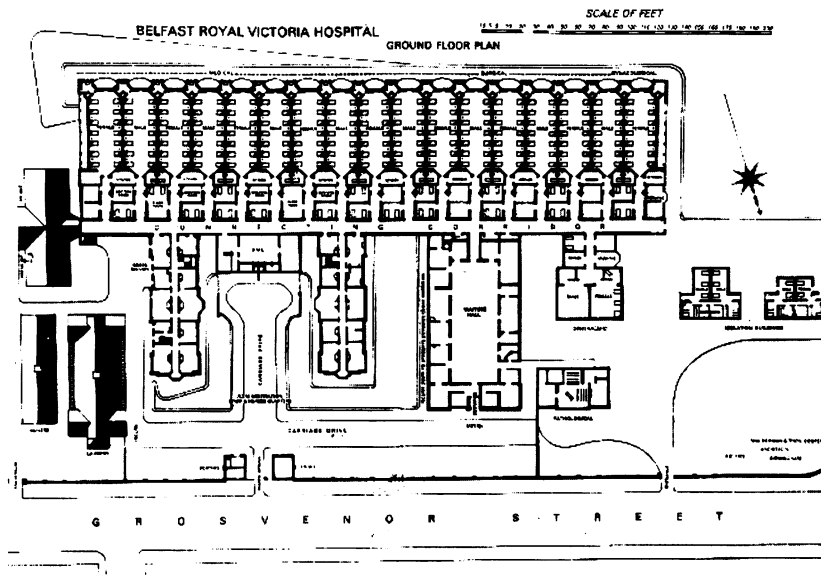


Fig. 1 Original plan of the Royal Victoria Hospital with its 17 Wards and "connecting corridor". To the left can be seen the intake of the plenum ventilation system, the boiler house and laundry. The east and west wings are not joined on the north side as at present and the "waiting hall" as shown is now a kitchen and serving area.

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Fig. 2 Window given by Dr William Whitla to the Belfast Royal Hospital in 1886. It was transferred to the new Royal Victoria Hospital in 1903.

One might well ask cynically “why is an anaesthetist telling us this when he only sees patients asleep?” This a misconception for it is part of an anaesthetist’s duties to talk to the patient pre-operatively to explain about the anaesthetic, pain relief and the pros and cons of general or local techniques. In the process he cannot avoid hearing about the problems of getting in the hay crop, or carrying the shopping up the hill in Ligoniel. The more intelligent comments he can make on these points, the more he will impress the patient and enjoy the interview.

Learning communication skills should begin as a student and nowhere better than in the big old-fashioned wards of the Royal. I come therefore, to sing the praises of this Institution as it is, to remind you of its past benefactors and to suggest what lessons we may learn from their efforts.

The corridor of the Royal Victoria Hospital is well known to all medical graduates of Queen’s University, and members of the staff of the hospital, as a place where one is bound to meet friends and colleagues over the day (Fig. 1). However it also has a number of tablets above the wards and nearby, commemorating donations to the hospital and, in view of the changes in the hospital under discussion, it seemed appropriate to record systematically the source of the donations and the inscriptions.

Even more striking than the tablets is the Good Samaritan window at the east end of the corridor (Fig. 2). It shows of course the Samaritan helping the man who had been beaten up 2000 years ago – an image as common now as it was then, while the Priest and the Levite walk past with the thought – “It’s not my problem”. The four coats of arms highlight the early history of the Hospital and its partner the University. (1) The Belfast Royal Hospital founded in 1792 as the General Dispensary and later as the Belfast General Hospital, only becoming the Belfast Royal Hospital in 1875. The roundel shows the Royal Arms and those of the City of Belfast. (2) The Queen’s University in Ireland. (3) The Queen’s College, Belfast. (4) The Royal University of Ireland.

The window was originally given to the Belfast Royal Hospital in Frederick Street in 1886 by Dr William Whitla. With the erection of the new Royal Victoria Hospital which opened in 1903, the window was transferred to the new “Extern Hall” where it was situated at a high level above the entrance door. Then when this large hall was split horizontally in 1947 the window was moved to its present position. We are fortunate that this window has survived the moves of over 100 years as a fitting reminder of this great physician and teacher. The career of Dr (later Sir William) Whitla is fully documented elsewhere ¹ and it should only be stated here that he was one of the “Olympians” of the Belfast General Hospital ² and a benefactor also of the Queen’s University, the Ulster Medical Society and Methodist College Belfast.

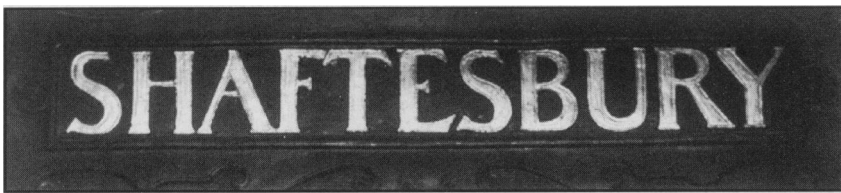
Immediately below the window is a tablet to James Girdwood which was also transferred here from the Belfast General Hospital. (Fig. 3) The tablet reads “This memorial is erected by the late Mr Girdwood’s numerous friends who have deeply mourned his removal from their midst, to record their high estimation of him as a citizen and his sterling worth as a friend. Also to testify their admiration for his indefatigable energy and invaluable services on behalf of this Institution for a period of eighteen years”. He was born on 23 January 1823 and



Fig. 3 Bust of James Girdwood, honorary treasurer of the Belfast Royal Hospital, 1854-1873.

owned a carpet, damask and wallpaper warehouse at 44 High Street, Belfast.^{2,3} He must have been well organised to be able to leave his business to run itself in 1854, when he was only 31, and devote himself to the unpaid task of Hospital Treasurer. Again and again it was said that the hospital's growing prosperity was due to his far-seeing and shrewd handling of the finances. James Girdwood was married, with a family, and died on 14 September 1873, being buried in Knockbreda Parish graveyard. A bust by S F Lynn, ARHA and C B Birch was completed in 1876 and erected in the Board Room of the General Hospital and under it was the inscription "So long as the Hospital exists his name will never cease to be associated with it". It is now in the King Edward Building.

In turning to the named corridor wards, one must admit that the headings above them are somewhat cryptic and deserve to be better understood. Even the doctors and nurses who pass under the bronze plaques would admit to total ignorance of the people commemorated and this is only a little helped by the additional marble tablets in the wards themselves. It must be stressed that the sum represented by a named ward was considerable – a minimum of £10,000 in 1900 or about £250,000 in modern terms. On the other hand, the less prosperous could name a bed for £500 and most donations to the Hospital came from church collections, Saturday street collections and gifts from all the workpeople of Belfast – sums like 3/6d from the carpenters in the Belfast Ropeworks or £4.5.6d. from the tug boat and barge men of the Belfast Harbour.



Ward 1 The name Shaftesbury commemorates Anthony, eighth Earl of Shaftesbury (1831-1886),⁴ son of the noted philanthropic seventh Earl who had been involved in redressing the great social evils of the Victorian era (including the exploiting of little children as chimney sweeps). His connection with Belfast was his marriage in 1857 to Harriet, daughter and heiress of the third Marquis of Donegall.⁵ Her only brother, the Earl of Belfast, who died of scarlatina in Naples in 1853 had been a popular and romantic figure in Belfast social life, and is commemorated by a rather beautiful statue in the City Hall. The third Marquis built Belfast Castle c 1868 to replace Ormeau House and

when he died in 1883 his wealth and the castle passed to Harriet and her husband. They and their son, the ninth Earl of Shaftesbury (1869-1961), continued the family interest in the Belfast Royal Hospital and in 1889 sealed this with a gift of the ground in Frederick Street on which it was built. When the General Hospital moved they extended this gift and a tablet in the ward records that "This ward has been called the Shaftesbury Ward in grateful recognition of the generous action of Harriet, Countess of Shaftesbury, and her son Anthony Ashley-Cooper, the ninth Earl of Shaftesbury, in allowing the site of the old Royal Hospital in Frederick Street to be sold free of rent for the benefit of the endowment fund of this Hospital". The ninth Earl of Shaftesbury became Lord Mayor of Belfast in 1907 and first Chancellor of the newly created Queen's University of Belfast in 1908. He gave Belfast Castle and grounds to the City in 1934.



Ward 2 This ward is named after the Riddel family of Beechmount in the Ballymurphy area, and specifically with the donation of Eliza and Isabella Riddel in memory of their father John, a successful hardware merchant. Their brother Samuel Riddel, who died in 1903, was a bachelor and having inherited from others in his family left nearly £500,000 in investments throughout the British Isles, USA and elsewhere, much of it in railway stock.⁶ The sisters donated £10,000, as the ward tablet states "In memory of John Riddel and family of Beechmount, 1904", and also undertook to bear the cost of the construction of a house for the Medical Superintendent, then Colonel Andrew Deane.⁷ The family in the same year also established a Demonstratorship in Pathology (for £5,000) and in 1912 gave a total of £45,000 to build and endow a hall of residence for women students at Queen's.⁸ Riddel Hall was opened in 1915 and for the next 50 years was well-loved by the women students, as well as being one of the great social centres of the University. It was not actually the property of the University and became difficult to manage financially; in 1975 it was bought from the trustees by Queen's University for £232,000 and closed as a hall of residence. The building and grounds were subsequently occupied by the Arts Council of Northern Ireland.



Ward 3 This ward commemorates Ruby Gallaher, a daughter of Thomas and Robina Gallaher of Ballygoland, Whitehouse. Tom Gallaher, the founder of the tobacco firm was born in 1840 near Eglington and opened a shop at 7 Sackville Street, Londonderry. The business prospered and in 1870 he moved to much larger premises in Hercules Street (now Royal Avenue), Belfast. In spite of opposition from such unlikely people as the poet Swinburne, smoking received

support from the Prince of Wales and indeed almost everyone at that time. Tom Gallagher opened two factories in London, and in 1896 moved his main factory in Belfast to 138 York Street, converting it to a limited company with a capital of £1 million. He died on 3 May 1927 aged 87 and his share of the business passed to trustees.⁹ Robina died on 30 October 1930, specifically leaving £10,000 in her will to the Royal Victoria Hospital. The tablet in the ward records that "This ward has been named by the late Mrs R M Gallagher of Ballygoland, Whitehouse, in memory of her daughter Ruby. This tablet was erected in 1931".

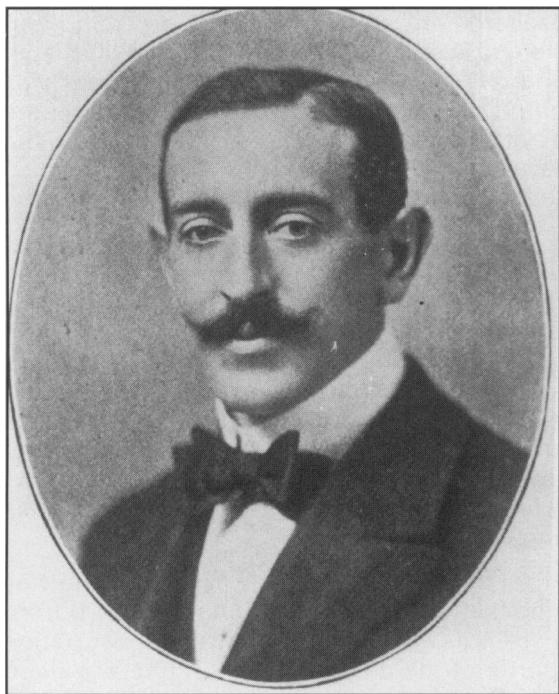


Fig. 4 Sir Milne Barbour, Bt, president of the Royal Victoria Hospital, 1939-1951.

Ward 4 This ward is named after Sir Milne Barbour, Bt. notable as head of the largest linen thread company in the world at Hilden. This company was founded by John Barbour at Plantation, near Lisburn, c 1784, and in 1823, to obtain better water-power to drive his machinery, he moved it to Hilden to a 45 acre site with over 500 houses for mill-workers.¹⁰ The company gradually swallowed up such firms as Dunbar, McMaster (Gilford), F W Hayes (Seapatrick), and Robert Stewart (Lisburn) and was chaired in succession by John Barbour's son William Barbour and later by the latter's son John D Barbour.^{11,12} It became the Linen Thread Company in 1900 and John Milne Barbour (1868-1951)¹³ of Conway, Dunmurry was its chairman for

most of the first half of this century. (Fig. 4) He was also Minister of Finance in the Northern Ireland Government, but his connection with the Royal Victoria Hospital was as President of the Hospital from 1939 until his death. He was created a Baronet in 1942 and died on 3 October 1951 leaving 3 daughters and no surviving son. He was on the governing bodies of many other hospitals and schools and was president of the Royal Ulster Agricultural Society, a body in which he had a special interest.



Ward 5 The name Pirrie above Ward 5 is of course firmly associated with shipbuilding history in Belfast but it has an older connection with the Hospital. The first of the family in Belfast, William Pirrie had been born in Wigton in Scotland in 1780, travelled much as a ship's captain and settled in Belfast in the 1820s.¹⁵ He was elected to the Ballast Board in 1827 which was responsible for improving Belfast Harbour by cutting across the curves at the lower end of the Lagan. He was later appointed one of the first Harbour Commissioners and opened the new Victoria Channel in 1849 by pouring a bottle of whiskey into the water.

William Pirrie married in 1810 Elizabeth Morrison and had four sons and four daughters. One of these, John Miller Pirrie studied medicine at Trinity College, Dublin, graduated MB in 1845 and MD in 1848, and in the latter year was appointed one of the physicians of the Belfast General Hospital.¹⁶ He became senior attending physician in 1857 at which time he was also secretary to the medical staff and retired as honorary consulting physician in 1865. He died on 16 July 1873 in Liverpool at the early age of 48.¹⁷

Another son of William Pirrie was James Alexander Morrison Pirrie who was born in Belfast in 1822 and died in 1848 of cholera in Quebec.¹⁸ He married (1849) Elizabeth Montgomery, niece of the Rev Henry Montgomery of Dunmurry, leader of the Non-Subscribing Presbyterians. His son William James Pirrie (1847-1924) after an education at the Royal Belfast Academical Institution entered the newly established firm of Harland & Wolff as an apprentice in 1862.¹⁵ Twelve years later, when only 27, he became a partner and eventually its Chairman. William Pirrie was not only an Instonian but married Margaret Montgomery Carlisle (a first cousin) whose father John Carlisle was head of the English School there. Instonians will remember the pride the school still takes in this distinguished family, naming a house after him.

The plan to build the present hospital began in 1896 when William Pirrie was Lord Mayor of Belfast and he started the funds with donations of £5,000 from himself and £2,000 from his wife.¹⁹ He was made chairman of the construction committee and was a strong supporter of the design by the architect William Henman, which became famous for its overhead window lights and plenum ventilation system. In this he had the support of the medical staff, notably Professor Cuming (medicine) and Professor Byers (gynaecology). The scheme was designed to supply clean, humidified air at a comfortable temperature throughout the hospital. It must be remembered that when it opened it was simply a corridor with 17 wards one side, together with East and West wings for staff quarters and administration, an Extern Department (where the kitchens now are) and an ophthalmic ward. Beneath the corridor is a great tunnel with an enormous fan which keeps the whole system of air moving, though the scares about Legionnaire's disease in the 1980s led to the abandonment of the simple humidifying mechanism.

William James Pirrie received honorary degrees from various universities and was created Baron Pirrie in 1906. He died on 27 August 1924 and was buried in the City Cemetery with a fine memorial which has recently been taken to Harland and Wolff Limited for safe keeping. Lady Pirrie was involved in all his philanthropic schemes and probably even more involved in this hospital.²⁰ She not only raised the £10,000 for the naming of Ward 5 but collected over £100,000 for the naming of beds. Her bust (by Mr A Bertram Pegram) is displayed facing the front entrance in the corridor (Fig. 5) and her full-length portrait hangs beside her husband's in the City Hall, an unusual distinction. She was in fact President of the hospital from 1914 until her death in 1935. The Marquis of Dufferin and Ava described her as "the most charming and most popular Lady Mayoress who ever sceptered a city or disciplined a husband".²⁰

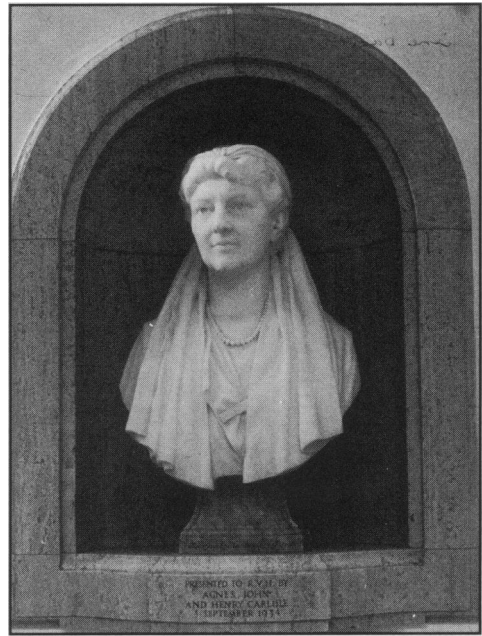
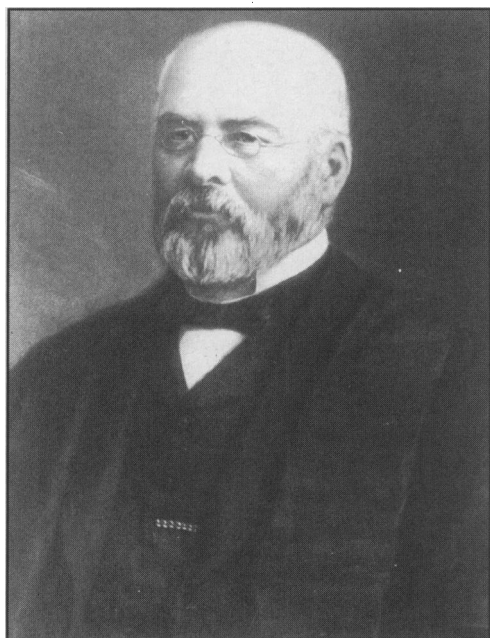


Fig. 5 Bust of Margaret, Lady Pirrie, benefactress, fund-raiser and president of the Royal Victoria Hospital, 1914-1935.

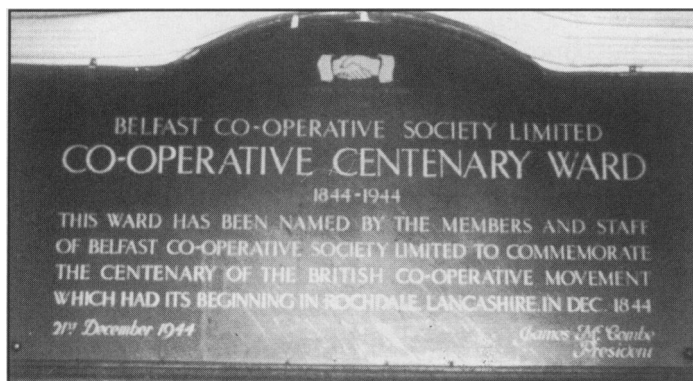


Ward 6 This is named after Professor James Cuming (1833-99) who was one of the leading physicians in the Belfast Royal Hospital. He was born in Markethill, County Armagh, and trained in medicine at Queen's College, Belfast, 1849-56, graduating MD in 1855 and MA in 1858.²¹ He was a fluent linguist and travelled throughout the continent, studying particularly the diseases of the nervous system and attending clinical demonstrations in the Salpêtrière, Paris, by such figures as Professor Charcot. James Cuming was only 25 when he was elected to the staff of the then Belfast General Hospital, where he remained attending physician until his death, becoming Professor of Medicine at Queen's College, Belfast, in 1864.²² (Fig. 6) He lectured with enthusiasm on conditions like tabes and disseminated sclerosis, but he had lost all faith in any form of therapeutics and he seemed even to question whether diagnosis was possible.



Professor Cuming lived in Wellington Place but died at his country home in Greenisland of influenza on 25 August 1899, being buried in Milltown Cemetery.²³ He was enormously loved and respected and took an active part in the planning of the present Royal Victoria Hospital. For this reason particularly, Lady Pirrie undertook to collect £10,000 to name Ward 6 in his honour. There was an attractive bust of him in the ward but, like so much else, it was lost during refurbishment a few years ago.

Fig. 6 Professor James Cuming, consultant physician in the Belfast Royal Hospital and Professor of Medicine at the Queen's University of Belfast, 1864-1899.



Ward 7 The Belfast Co-Operative Society, along with so many other organisations in the City, took a keen interest in our hospital but specifically we have to thank James McCombe from the Braid valley area, a president of the Belfast branch of the Society, for the idea of endowing a ward. He was first a school teacher but entered the Customs and Excise Service at the Custom House, Belfast, in 1895 to work there for 40 years.²⁴ He pioneered the Belfast Co-Operative movement, joining its Board of Management in 1901 and becoming President in 1937. He was a prime mover behind the establishment of a Co-Operative Dairy in 1913 at a time when pasteurisation of milk was a new idea in Belfast. The Co-Operative movement had been founded in 1844 and in 1944 the members and employees joined to raise the necessary £10,000 to mark its centenary; in fact they raised £13,750 and sums were also given to the Mater Infirmorum and Royal Maternity Hospitals.²⁵



Ward 8 The title “Our Day” over Ward 8 is particularly obscure to us now but it harks back to the middle of World War 1 when the British Red Cross Society and the Order of St. John had a massive fund-raising effort. Between 1916 and 1918 Ulster raised a total of £146,000 for the “Our Day” effort and until well after the war the Hospital had many wounded soldiers as patients. In 1920 the joint committee of the societies decided to give the sum of £10,000 to name a ward in recognition of Belfast’s contribution to the welfare of the armed forces.²⁶



Ward 9 This was named in 1953 in recognition of the Honorary Medical Staff. We must remember that from inception of the hospital in 1792 until 1948 the senior doctors gave their services free and only the house physicians and house surgeons were paid.²⁷ Of course, they did not spend as much time as consultants spend now in the hospital, for they had to live by their private practice and might only visit the hospital twice a week to see the cases which the house doctors brought to their attention. Nevertheless, they carried the responsibility for running the hospital, and when there were problem cases, were always available for help. This system came to an end in 1948 and now the term Honorary Medical Staff or Consulting Staff is confined to our retired colleagues.



Ward 10 With the Sinclair Ward, we are back with a family remembered for its support of the General Hospital in Frederick Street. The firm of John and Thomas Sinclair Ltd was in business as provision merchants in Tomb Street, Belfast from the 1830s, being involved in bacon curing and the pig trade generally.²⁸ Thomas Sinclair, JP, of Hopefield House, Belfast, had married

Sarah Archer, and eventually died on 2 January 1867 aged only 56. He was buried in the so-called New Burying Ground in Clifton Street,³¹ and his ornate classical memorial has managed to survive the vandalism there. In recognition of his public contribution a public subscription in his honour raised the sum of £2,287.10s.4d which was given to the hospital as the Sinclair Memorial Fund.²⁹ As a result, the first accident ward in Frederick Street was renamed with a tablet reading "1869. Sinclair Memorial Ward", followed by a list of 40 subscribers. The family continued to support the hospital – for instance, we read in the minutes of 1882 "that the best thanks of the Board of Management are due to the members of the Sinclair Family for the excellent work they have done in completely renovating and supplying with all modern requisites the Sinclair Memorial Ward . . ." ³⁰

The family business was continued by his son the Rt. Hon. Thomas Sinclair, MP (1838-1914) who was noted as a Liberal and Liberal Unionist, twice President of the Belfast Chamber of Commerce, first Chairman of the Convocation of Queen's University and an Honorary D Litt.²⁸ Yet another Thomas Sinclair (1857-1940) of the same family was the second Professor of Surgery. He was a Queen's graduate winning many honours and was appointed Assistant Surgeon to the Belfast General Hospital in 1885, becoming Professor of Surgery in the following year.³² He served in the army during World War I and is noted as having performed the autopsy on the German air ace Baron Von Richthoven.³³ He retired in 1923 at the age of 65 and was elected a Pro-Chancellor and Unionist MP for the University, dying in 1940. The name Sinclair was also perpetuated by the first Thomas Sinclair's grandson, Mr T Sinclair Kirk, a surgeon in the Belfast Royal and Royal Victoria Hospitals from 1896 to 1935, who died in 1940.³³



Ward 11 The name Charters is associated with benefactions to three of our great institutions – The Royal Belfast Academical Institution, the Belfast Charitable Institute and the General Hospital and once again we are dealing with a wealthy and generous business man.³⁴ John Charters (1795/6 - 1874) of Ardmoulin House, Falls Road, and later of Craigavad was proprietor of the Falls Flax Spinning and Weaving Company, which was one of the largest linen mills in the country. (Fig. 7) In 1865 he decided, following the example of Andrew Mulholland two years earlier, to finance the building of a complete surgical wing to the Hospital costing about £2,000, to be named the Charters Wing. He also paid for the building of a waiting room for visitors and for putting new railings and stone entrance gates in front of the hospital. He was appointed a Life Governor of the Hospital from 1864 until 1873 and died on 13 August 1874, being buried in the New Burying Ground³⁵ with a memorial fixed to the wall near the gate. There is a bust of him in Ward 11 with a tablet reading: "This bust was formerly in the Royal Hospital in Frederick Street, Belfast and was removed to



Fig. 7 John Charters, benefactor of the Belfast General Hospital and other institutions of the city

this position in the Royal Victoria Hospital to perpetuate the name of Charters so honourably associated by munificent generosity with this and many other charities in this City. Just after his donation to the General Hospital, he made a similar gift to the Poor House (now known as the Belfast Charitable Institute or Clifton House) so that a whole wing was erected in 1868 behind the main block.³⁶ These were later to be supported by the connecting wings of Edward Benn to form the unit of Clifton House which is still active today.

John Charters married and left several children, one of whom Anna Boomer Charters gave further donations to the hospital and endowed four scholarships at the Royal Belfast Academical Institution (1875).³⁷ Yet another daughter Katherina Maria married Dr William MacCormack, then a young and

impoverished Belfast surgeon, as Sir Ian Fraser has recorded in his 1968 address.³⁸ Both families had originally disapproved of the match but it was apparently very happy. In 1864 William MacCormack was appointed Visiting Surgeon to the General Hospital but in 1871 he moved to Harley Street and was very glad to borrow £4,700 from the Charters family to finance this ambitious step (a debt which incidentally he paid back in full). Plainly, John Charters came round to the marriage for it was only a few years later that he made his great donation to the General Hospital, influenced by his son-in-law. William McCormack achieved experience and fame in the Franco-Prussian and Turco-Serbian wars, was appointed to the staff of St Thomas' Hospital in 1871, given a Baronetcy in 1897 and died in 1901.

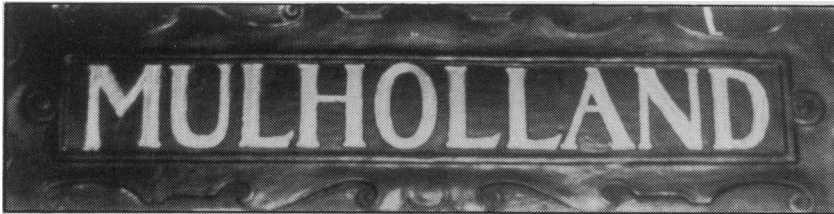


Ward 12 It was dedicated to Sir William James Pirrie in 1903 and has a commemorative tablet in the ward which stresses his particular contribution: "This hospital owes its origin to the Rt Hon W J Pirrie and his wife Margaret M Pirrie of Ormiston, Belfast, who not only contributed largely to its construction and equipment, but by their untiring efforts in connection with its erection, furnishing and endowment, enabled it to be opened free of debt and made it an



efficient medium for the relief of the sick and the suffering poor. To perpetuate the memory of their many deeds of kindness to, and interest in this hospital, and to encourage others to do likewise, this ward bears the name W J Pirrie."

Fig. 8 Sir William James Pirrie, benefactor and chairman of the Construction Committee for the building of the Royal Victoria Hospital, 1896-1903.



Ward 13 The Mulholland family commemorated here were children of Thomas Mulholland (died 1821) a Belfast merchant, who had four sons including Andrew and St. Clair Kelburn.³⁹ In 1816 they erected a cotton mill in Winetavern Street and as it prospered moved in 1822 to a "green field" site in what is now York Street.⁴⁰ Then on Sunday 10th June 1828 the whole mill caught fire and was burnt to the ground. As a result of this the family decided to make a new start and switched from cotton to linen. They thus came in a little after John Barbour of Hilden and from the outset employed steam power for spinning and weaving of linen, which was then building up its world trade. Thomas and both sons were on the committee of the hospital from the 1820s and the sons were made Life Governors.⁴¹

Andrew, the elder of the two (1792-1866), built up the business into the York Street Flax Spinning Company which combined spinning and weaving of linen. It grew from 8,000 spindles in 1830 to 25,000 in 1856, bringing in huge profits even before the American Civil War (1861-5) cut off cotton supplies completely and helped it further. Andrew was elected Mayor of Belfast in 1845, built Ballywalter Park in 1846 and in 1865 gave the Ulster Hall the Mulholland organ.

His son took over the business and after 11 years as a Tory MP was created Baron Dunleath of Ballywalter.

St Clair Kelburne Mulholland (1798-1872) derived his distinctive name from the noted minister of the Third Presbyterian Congregation, the Rev St Clair Kelburn, who was imprisoned for 'seditious practices' before the 1798 rising. He was born in 1798 and as well as being involved with Andrew in the York Street Mill established his own company in Durham Street. He married in 1829 Margaret Wright and lived at Eglantine, Hillsborough, but his only son, also called St Clair Mulholland, died before him so the family business was wound up. It was St Clair Mulholland who in 1863 gave £2,000 in memory of this son to build the Mulholland wing of the General Hospital, a new ward of 30 beds at right angles to the main block.⁴² He was one of our great benefactors, and dying on 27 January 1872 was buried at Eglantine.⁴³

There are three tablets, side by side, in ward 13:

(1) A brass tablet transferred from Frederick Street, "In this ward which has been erected by a father's love to the Glory of God for the purpose of associating the memory of his only son St Clair Kelburne Mulholland, with the relief of human suffering, his mother and sisters have placed this tablet to record a hope full of immortality and stronger than sorrow through Jesus Christ Our Lord. Born June 9th 1830. Died at Sorrento, Italy, April 4th 1861".

(2) "This brass tablet was removed from its original position in the Frederick Street Royal Hospital and placed in this ward to continue and commemorate in this new Royal Victoria Hospital, the name of St Clair Kelburne Mulholland, Junior, son of St Clair Kelburne Mulholland, who was one of the original founders of the flax spinning industry in Belfast".

(3) "Epitaph. Thy body rests beneath the Italian sod,
Thy soul's inheritance is the light of God.
Yet here our hopes and memories of thee
Who sleepest well beside the far blue sea.
We twine, all fair and sunny as they are,
With other sights and scenes that differ far,
With sickness, mortal agony and tears,
Yet not reproach from thee affection fears
In anguish comforted and want sufficed
Thy spirit joy'd on earth, is now with Christ.

Written by William Alexander, DD, in 1862, Bishop of Derry in 1867, Primate of all Ireland in 1896".



Ward 14 The name Ismay is not as well known here, since the family did not live in Ireland and had only business connections. However, Thomas Henry Ismay really did contribute to the City by his support of our leading industry as well as by his Company's donation. He was born on 7 January 1837 in Maryport, Cumberland, the eldest son of Joseph Ismay, shipbuilder.^{44,45} He left school at the age of 16 and was apprenticed to the Liverpool firm of Imrie and Tomlinson, Shipowners. He subsequently started business independently and in 1867 at the age of 31 he acquired the White Star Line of Australian clippers. He went on to form with William Imrie the Ocean Steam Navigation Company (1869). From this time he decided to introduce iron vessels to replace the wooden ships of the past and it was this change that connected him with Belfast. The American route was clearly the important one for both passengers and cargo and in 1869 Ismay's company ordered from Harland and Wolff no less than six large transatlantic steamers to sail between Liverpool and New York.

It is calculated that over 30 years the White Star Line paid Harland and Wolff the sum of £7,000,000. The 'Oceanic' (launched in 1871) was the first of these and the new features included greater passenger comfort, especially for the first class in the centre of the ship, more powerful but economical engines for speed and stability, and greater cargo capacity. The order necessitated considerable enlargement of Harland and Wolff's shipyard and started a long lasting partnership with the White Star Line.

T H Ismay was given the Freedom of Belfast in 1898 in recognition of his contribution to the City's prosperity. In return, he gave £1,000 to the building fund of the Royal Victoria Hospital and after his death on 23 November 1899 the White Star Line gave £10,000 to dedicate a ward as a memorial to him.⁴⁶
⁴⁷ He lived all his life in the Liverpool area and is buried in the churchyard of Thurstanton, near Birkenhead. The commemoration tablet in the ward reads: "In memory of the late Thomas Henry Ismay, founder of the White Star Line, this ward bears his honoured name. A sum of £10,000 was generously voted by the shareholders in the Oceanic Steam Navigation Company Limited at their Annual Meeting held 1 May 1901, towards the funds of this Hospital, as a permanent memorial to one who was closely identified with the prosperity of Belfast and its charities". Below are approximately 100 names of shareholders.



Ward 15 This commemorates the Moore family, Eliza Jane and her brothers James and George L Moore, the latter being a solicitor from Limavady. George Moore graduated BA with honours at Queen's University, and was articled to a solicitor in Belfast where he practised for 20 years.^{48, 49} He seems to have been a particularly successful investor here and when he moved to Forest Hill in London to engage in other business interests, was estimated to have an income of over £1 million annually (in 1920). (Fig. 9) He gave £150,000 to create a large park in London but was equally generous in Ulster, giving much to Limavady and £20,000 for a ward in the Royal Victoria Hospital, also in 1920. His recipe for long life he declared to a News of the World reporter — "Temperance in everything . . . freedom from worry, and having sound sleep until three o'clock in the morning".

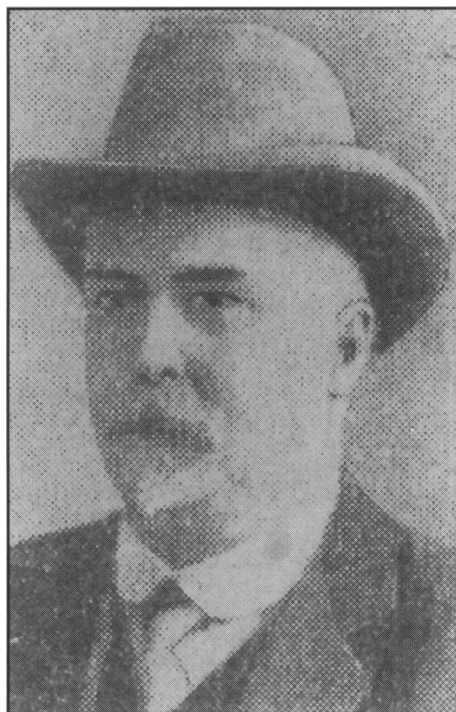


Fig. 9 George Moore, solicitor, and benefactor of the Royal Victoria Hospital, 1920.



Ward 16 Edward James Harland was born in Scarborough, Yorkshire in May 1831 and was the sixth son of Dr William Harland, a general practitioner there.⁵⁰ Interestingly, as well as his medical practice, Dr Harland was an enthusiastic amateur scientist. In his younger days he had patented a steam carriage with a multi-tubular boiler for quickly raising high-pressure steam. He was a close friend of George Stephenson of railway engine fame. Edward went

to school in Edinburgh and was determined, in spite of parental pressure, to be an engineer. As a result he was apprenticed to Robert Stephenson & Company of Newcastle-on-Tyne and, as well as working on the design of railway engines became involved in lifeboats and the design of iron ships. Thence he moved to Clydebank as a journeyman shipbuilder, then to Newcastle again and in 1854 at the age of 23 he was appointed manager of Robert Hickson's shipyard in Belfast.

When Edward arrived he strove to raise standards and to push for harder work and, in spite of financial difficulties and strikes from disgruntled workmen, he built up the firm. In 1857 he took on Gustav Wolff from a Hamburg Jewish family and in the following year they took over Hickson's old yard on Queen's Island as a going concern. In January 1860 Edward Harland married Rosa Wann, a Belfast girl related to the Gallaher family, and from then on we may say that he was firmly settled here. The success of Harland and Wolff Limited is fully chronicled in Moss and Hume's "Shipbuilders to the World".

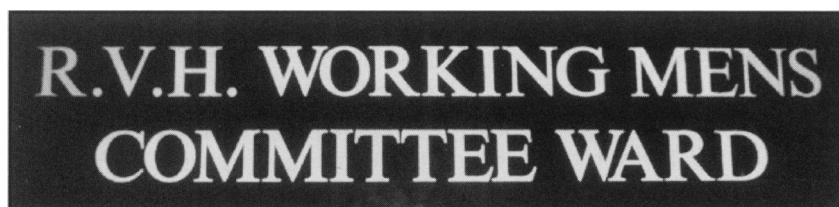
Edward Harland was elected Mayor of Belfast in 1885 and, having eased out of business by this time became heavily involved in politics against Home Rule.⁵⁰ He became a Unionist MP and retired to County Leitrim, when William Pirrie bought his Belfast house, Ormiston. Edward Harland concentrated on politics during his latter years being created a Baronet for this work, and died quietly at his home in Leitrim on Christmas Eve 1895. He was buried in the City Cemetery, Falls Road. His shareholding was divided between his brothers and his wife Rosa and she donated £10,000 to name a ward in his memory in 1903.⁵¹

Thus, four wards are named after leaders of the shipbuilding industry, Sir Edward Harland, Thomas Ismay and Lord and Lady Pirrie. The three men were well educated but moved from school to apprenticeship and thence quickly up the ladder in their chosen firm to the top. They all supported this hospital but it is ironical to note that their titles were given not for their work or for the generosity for which we remember them, but for "political services".

At this point the Titanic must be mentioned for there seems to be a strong belief connecting donations to the Hospital with it. However, the wards were named and the major donations given when the Hospital was opened in 1903, long before the launch and tragic sinking of the ship in 1912. The only connections are in the personalities, for Thomas Andrews, the chief designer was Sir William Pirrie's nephew. It was he who was last reported staying on the ship and throwing deck chairs to the survivors in the water though there was little hope for them in the freezing temperatures.⁵² His behaviour is certainly one of the inspiring legends to come out of the disaster. One of the survivors was Bruce Ismay who had inherited control of the Ocean Steam Navigation Company and the White Star Line from his father Thomas Henry Ismay. He apparently, after giving assistance to several passengers, found a half-full lifeboat being lowered, so he jumped in. There was no evidence at the inquiry that his presence prevented anyone else from getting in, so he was not officially blamed. Nevertheless, many felt that as owner of the ship and knowing that she was doomed he should not have left while many women and children were still trapped there (and inevitably most of these were the third-class passengers). However, all this is a digression for it occurred long after T H Ismay's donation to the Hospital, though still before much of Lady Pirrie's work for it.



Ward 17 When we hear the name Clarence we cannot help thinking of the unfortunate Duke who was drowned in a butt of Malmsey wine by order of Richard, Duke of Gloucester ("False, fleeting, perjured Clarence", as Shakespeare called him). In any case, this ward was not called for him. In fact, when the Hospital was opened on 27 July 1903, by King Edward VII and Queen Alexandra, they asked for a ward to be named after their eldest son, Prince Albert Victor, a later royal Duke of Clarence⁵³ as recorded in the tablet. He had been born in 1864 and in due course went into the army; he developed pneumonia in 1892 and died at the early age of 28. Albert had been engaged to marry Princess Mary of Teck and she subsequently married his brother George, the future King George V.



Ward 18 Wards 18-20 were an extension to the original part of the 1903 hospital, opened in 1924. Ward 18 was the last to be named and it was only on 9 September 1992 that the Hospital unveiled a plaque to honour the contribution of the Working Men's Committee. (Fig. 10) A history of this body is at present being written by Professor Leslie Clarkson following the centenary of its founding.⁵⁴

In 1887 the Truck Act was extended to Ireland making it illegal to deduct contributions from employee's wages. A committee was therefore formed in 1888 for "the increases of the Working Classes' subscriptions to the Hospital". With this role went the very necessary point of informing the subscribers of the work of the hospital and assuring them that it was efficiently and economically run. The committee therefore from the outset was in close touch with the matron and administration generally and took an interest in any complaints, which were then investigated. The table from the 1892 Annual Report shows the amount subscribed over the first five years and, perhaps more interestingly, the number of different places of work where subscriptions were collected.⁵⁵ The report stresses that although things are improving, the sums collected do not in any way cover the cost of running the Hospital – perhaps only about 25%. Other popular sources were, as stated earlier, church and street collections. Nevertheless, over the years to the present this body has collected more than



Fig. 10 Unveiling of Memorial plaque in ward 18 to commemorate the contribution of the Working Mens' Committee to the Royal Victoria Hospital (left to right: Sir Ian Fraser, FRCS, Mr W McCann, Miss F Elliott, Prof J Bridges and Mr J McKeown (photo courtesy of Wilfred Green, Photographer).

£1,000,000 for the Hospital. In their early years particularly, deputations went round most of the firms in Belfast asking to have a representative collector nominated there. To increase the pressure, they would be armed with information as to the number of employees from that firm treated (free of charge) in the hospital during the past year. Certainly the Working Men's Committee played a large part in keeping the hospital and the citizens of Belfast in touch.

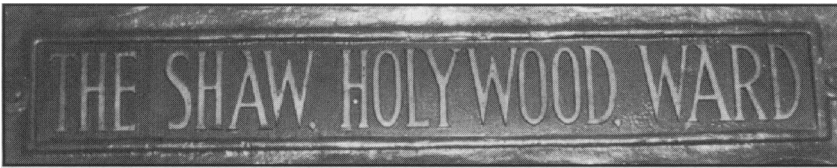
TABLE

Record of number of places of work and subscriptions collected by the Working Men's Committee 1888-1892⁵⁵

Year	Number of work-places	Amount subscribed £
1888	137	1,563
1889	146	1,601
1890	157	1,864
1891	190	2,083
1892	200	2,177



Ward 19 This is named after Thomas Gordon Herald who died in 1918. His father Samuel Herald of Windsor Avenue was Managing Director of the Irish Preserve and Confectionery Company at 178 Ormeau Road and when he died on 22nd August 1922 he left £20,000 to name a ward in the Royal Victoria Hospital for his son.⁵⁶ However Samuel Herald's widow Sarah had a life interest in the capital and the bequest did not come to the Hospital until she died on 2nd February 1943. The firm was carried on by a younger son, Robert Irwin Herald, and was still in business in the 1950s.



Ward 20 Ward 20 was also named following a bequest in 1943, this time by Mrs Hetty Hamilton Shaw of Holywood. Her husband William Shaw, JP, had been a partner in Messrs Shaw & Jamison, wholesale druggists of Townhall Street, Belfast. He had already left the Hospital £1,000 when he died in 1925.⁵⁷

The firm was founded c 1865 by Thomas Shaw and passed to his nephew William Shaw in 1882. William took on as a partner William Jamison and they erected a warehouse in Townhall Street at its junction with Musgrave Street. The description in an account of the Industries of Ireland published in 1891⁵⁸ gives us an example of Victorian hyperbole. "The magnificent five-storey warehouse, recently erected by the firm, has no equal in the trade in the City, is handsomely designed and offers the most commodious location imaginable for a wholesale business of great volume . . . A very convenient cart entrance, in Musgrave Street, admits the carts and runs right into the despatch department, where a powerful lift worked by a six-horse gas engine, expedites the despatch and receipt of goods. The variety of drugs, chemicals, patent and proprietary medicines and preparations is endless, while the list of general goods is no less exhaustive and complete. These include all the best lines in pickles, sauces, jams, jellies, marmalades, vinegars, meat extracts. The business, in a word, is one of marvellous extent and still rapidly expanding under the energetic direction of the enterprising proprietors".

BRYSON TABLET

Having covered the dedications of the 20 main wards in the Hospital, we should also note the Bryson tablet opposite ward 12 "This tablet is erected in memory of Surgeon Major Allan Bryson who died March 8th 1874, bequeathing to this hospital the savings of his lifetime." Surgeon-Major Allan (or Allen) Bryson was

born in Carrickfergus in 1832, was a student in the Belfast General Hospital and graduated MD in Glasgow.⁵⁹ He joined the army in 1854 and served as a regimental medical officer in the Crimea, being promoted Staff Surgeon in 1865 with the rank of surgeon-major (equivalent to Lieut Colonel). He made a will in 1873 by which he bequeathed money to the hospital and the legacy which became available in 1879 "to be expended as the Board saw fit," amounted to £2,975, the largest bequest received in the 19th century.⁶⁰ Allan Bryson died on the steamship "Indus" on his passage home from India aged only 48, and was buried at sea though he is commemorated in the old graveyard in Kilroot.

It so happened that at that time the Board was anxious to move the laundry from the space under the fever wards of the General Hospital and when a new laundry had been built with some of this money (£782) the hospital was able to take twice as many fever patients and genuinely isolate them in a building of their own.

CONCLUSION

I have stressed that the people of Belfast felt a real need for the General Hospital, the Royal Hospital and the Royal Victoria Hospital and a loyalty to them. The support for four wards came from shipping and shipbuilding, for three wards from linen, for one from property, for six from other businesses, for three from various organisations and two are dedicated to the medical profession. It came from right across the community – the very rich, the professionals and the working men. It must be said that people had to feel that they were getting good value for money, and the close contact with the Working Men's Committee is an example of this. Perhaps we need to again convince the citizens of Belfast and, indeed, of Northern Ireland that this is their hospital and is worth supporting, and perhaps we can then open a new "state of the art" building by the year 2003.

In concluding, I would like to express my thanks to Dr John Logan for many helpful discussions, and to Mr Norman McMullan and the staff of the RVH photographic department for so willingly taking the host of photographs.

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Case Report

“Sonic, Tonic, Clonic”: three cases of video game epilepsy

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Video games have become increasingly popular over the last five years and have rapidly become one of the biggest sellers in the market place. The first description of an epileptic seizure associated with a video game, was in 1981 by Rushton¹, when a seizure was described in association with a game of “Space Invaders”, the precursor of many of the video games available today. Video game epilepsy is considered to be due to an underlying photo-sensitivity in the individual involved^{2, 3}. Various stimuli in the games have been implicated, including flashing lights, shifting scenes and geometric patterns. Other factors that may be relevant in the production of seizures would include sleep deprivation, sitting too close to the television screen, playing in a darkened room, the level of excitement, and the length of time spent playing the game⁴. We report on three patients who recently presented to the neurological department with seizures after playing video games.

CASE ONE

A 13 year old boy had been in an excited state, having just purchased a “Sonic the Hedgehog” video game, for which he had been saving for some time. His mother, who witnessed the event, reported that he had only been playing the game for a few minutes, when he suffered a tonic/clonic seizure. He had no previous history of seizures and no family history of epilepsy. A full general and neurological examination was entirely normal on admission to hospital. A subsequent EEG recording showed paroxysmal features on photic stimulation, suggestive of a photo-convulsive response (figure 1). An EEG recorded while playing “Sonic the Hedgehog” on his Sega Mega Drive, consistently revealed similar paroxysmal features at a certain point in the game when balls flashed (figure 2). EEG recordings were performed on his non identical twin and on his mother and both proved to be entirely normal. Wearing dark glasses seemed to ameliorate the photo-convulsive response. Caution regarding the use of video games was advised. He was not started on any anti-epileptic drugs and no further seizures have occurred to date.

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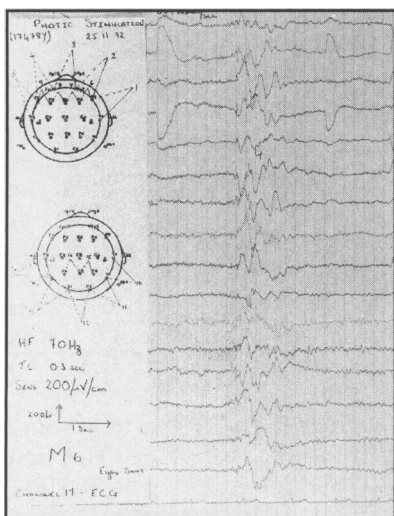


Fig 1. Case: EEG recording with photic stimulation demonstrating photo-sensitivity.

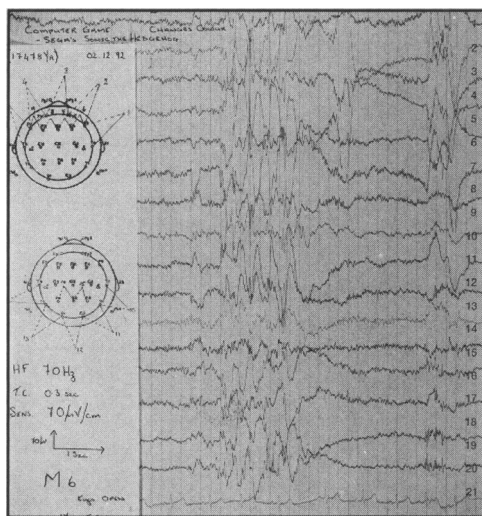


Fig. 2 Case 1: EEG recording while playing "Sonic the Hedgehog" demonstrating similar response.

CASE TWO

A previously fit and well 14 year old boy had been playing "Super Nintendo Street Fighter II" for about one hour. He had difficulty getting past one particular stage and had become totally engrossed in the game. He admitted he was sitting very close to the television screen in the room with the lights out. He said that he was aware that something was wrong and attempted to switch off the computer, but before he was able to do so, he lost consciousness. He was discovered a few minutes later by his mother who initially found him difficult to rouse, and subsequently to be drowsy and confused and complaining of headache. He reported that a few days earlier, while playing the game "Super Mario", he had felt dizzy and switched the game off. At that time there was no frank loss of consciousness. He had no significant past medical history; his mother suffered from epilepsy of a partial type. Examination was entirely normal. EEG recordings showed features of primary generalised epilepsy with a photo-convulsive response. He was not commenced on any anti-epileptic medication but was advised to take precautions when playing video games. No further seizures have been reported.

CASE THREE

A 13 year old girl had suffered a tonic/clonic seizure while using a computer in school and a second seizure whilst watching television at very close range. There was no significant personal or family history. Examination was entirely normal, but an EEG recording revealed a normal resting record which became rather unstable on photic stimulation. Following these two episodes she had been commenced on sodium valproate 200mgs twice daily and remained seizure free for a period of three years, after which her drug therapy was slowly withdrawn. Three months later, when she was playing "Super Nintendo Street Fighter" she suffered a further tonic/clonic seizure. She was recommenced on

sodium valproate and was advised about the relationship of the seizure and the video game. No further seizures have occurred.

DISCUSSION

Video game epilepsy is thought to be a form of photo-sensitivity. Photo-sensitive epilepsy occurs in response to flickering light stimulation and seizures may occur in day to day life when exposed to sunlight flickering through trees or flickering television screens. The prevalence of photo-sensitivity is not completely certain and estimates range from two to eight per cent in patients with epilepsy^{4,5}. Photosensitive epilepsy is said to have an age of onset between 8 and 19 years, females being slightly more affected than males⁵. Between 1981 and 1992, there have been a total of 17 case reports of video game epilepsy. The age of onset has ranged from 4 to 17 years (mean of 11.9 years), the male to female ratio is 4.7 to 1⁶. It is likely that the difference in the sex ratio, between pure photo-sensitive epilepsy and video game epilepsy is simply due to the fact, that video games are more often played by boys than by girls. Video games are thought to be more potent in provoking seizures than ordinary television because of the nature of the stimuli that are presented, with flashing lights and shifting scenes, and the children often sit very close to the screen, in darkened rooms, becoming totally engrossed in the activity on the screen. Because of concern regarding seizure production, Sega and Nintendo, the two market leaders, have recently issued a warning with their products, (figure 3).

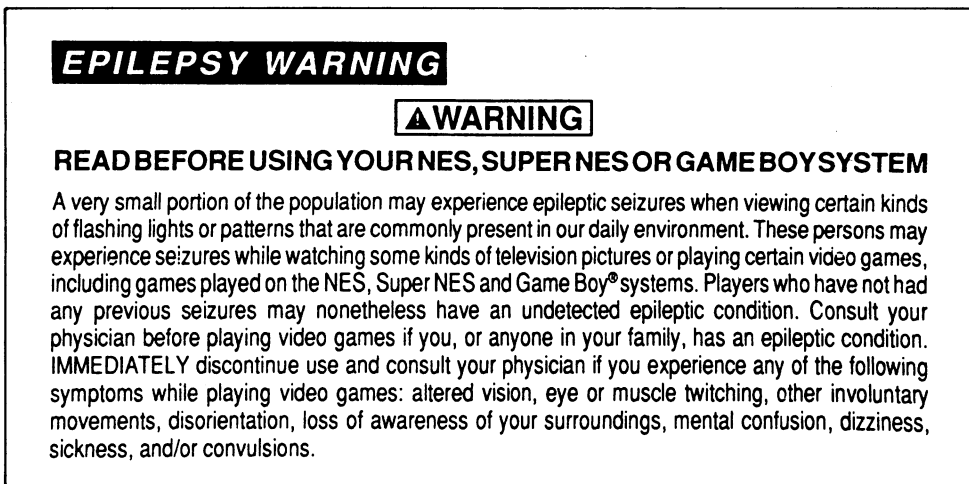


Fig 3. An example of the warnings now supplied by the video games manufacturers.

In only one of our patients was anti-epileptic medication prescribed and this was because of the history of seizures which had been provoked previously by lesser stimuli. Patients presenting with video game epilepsy should be advised of the relationship between the video game and the seizures, that they should avoid playing the games if possible, though this advice is not always readily received. If they continue to play the games, they should stay well back from the screen, in a well lit room. It has been shown that the wearing of a patch over one eye appears to abolish the photo-sensitive response, and in one of our

cases wearing dark sunglasses also seemed to ameliorate the photo-sensitive response.

Although the overall risk of photo-sensitivity is low in the total population, of the order of 1 in 4,000, but because of the continuing popularity and dissemination of video games, it seems likely that we will see further cases in which they have provoked seizures.

We thank Dr D P Nicholls who was the initial physician in one of the cases, the Departments of Neurophysiology in the Royal Victoria and Belfast City Hospitals, and Miss Brenda Magee for typing this manuscript.

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Case Report :

Malignant hyperpyrexia in an MDMA (“Ecstasy”) abuser

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Accepted 5 January 1994.

Malignant hyperthermia is a pharmacogenic disease and is manifest by a hypermetabolic crisis with tachycardia, ventricular ectopy, metabolic acidosis, and a rapid rise in body temperature. “Ecstasy”, 3,4-methylenedioxy-methamphetamine (MDMA), is a semisynthetic amphetamine, the recreational use of which has increased in recent years. Severe reactions to MDMA have been noted in the past, including hyperthermia, rhabdomyolysis and disseminated intravascular coagulation¹. Reports of overdose with MDMA are rare, but hyperthermia and rhabdomyolysis have been reported in association^{2,3,4}. Compounds such as MDMA are thought to cause hyperthermia by a central action at 5HT₂ receptors⁵. However dantrolene, a muscle relaxant acting peripherally, has been used apparently successfully in the treatment of MDMA overdose⁴. We report a case of acute perioperative increase in temperature, initially diagnosed and treated as malignant hyperpyrexia, in a patient who later emerged to be an “ecstasy” abuser.

CASE REPORT

A 23 year old man was scheduled for internal fixation of a two day old fracture – dislocation of the right ankle. He had suffered no other injury. He had a squint correction when 6 years old and repair of a Mallory-Weiss tear when aged 17. Both anaesthetics were uneventful, employing thiopentone, suxamethonium, pancuronium and halothane. He reported no medications or allergies, consumed 10-20 units of alcohol per week and was a moderate smoker. He was afebrile, and other vital signs were normal. Physical examination was unremarkable. He was premedicated with temazepam 20 mg.

On arrival in the anaesthetic room ECG, pulse oximeter and non-invasive blood pressure monitors were applied. An 18 sw gauge intravenous cannula was placed in a vein on the dorsum of the left hand and an intravenous infusion of Hartmann’s solution was commenced. Anaesthesia was induced with fentanyl 0.1 mg and propofol 150 mg. After induction, a size 4 laryngeal mask (Intavent)

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was inserted and anaesthesia was maintained with 66% nitrous oxide in oxygen and isoflurane 0.5-1.5%, by spontaneous respiration through a Bain breathing system. The patient was moved to the operating theatre where the same monitors were reapplied. A tourniquet was applied to the right thigh. No antibiotics were administered.

Surgery proceeded uneventfully for 45 min with an SaO_2 of 98% and an end-tidal CO_2 of 4.0-4.5%. It was then noticed that the patient's left shoulder was flushed, felt warm and the heart rate increased suddenly from 55 to 90 beats/min. At the same time there was a rapid rise in the end-tidal CO_2 to 8.5%. A nasal temperature probe was inserted which recorded a temperature of 38.9°C. The heart rate then increased to 120 beats/min. There was no cyanosis and the pulse oximeter continued to show a saturation of 98%. Masseter spasm and rigid upper limbs were noted. An arterial blood gas sample revealed pH 7.28, PO_2 17.2 kPa, and PCO_2 8.04 kPa. A presumptive diagnosis of malignant hyperpyrexia was made and treatment commenced.

Isoflurane administration was stopped and the patient was switched to a 'clean' anaesthetic machine and unused Bain breathing system. While dantrolene sodium was prepared, crushed ice and a cooling blanket were applied to the patient and he was sponged with iced water. A tracheal tube and an oesophageal temperature probe were inserted and the patient manually ventilated with 100% oxygen. The temperature continued to rise to 39°C. The Hartmann's solution was replaced with 0.9% saline. A 16 gauge cannula was placed in the left antecubital fossa and a 20 gauge cannula in the right radial artery. Dantrolene sodium 1mg/kg, pancuronium 4 mg, midazolam 10 mg and methylprednisolone 1000mg were administered. In spite of the cooling measures the temperature continued to rise to 39.1°C with a tachycardia of 150 beats/min. A double lumen central venous catheter was inserted through the right internal jugular vein and an ice cold 0.9% saline infusion commenced. A urinary catheter was inserted and 200ml mannitol 10%, was administered to prevent tubular necrosis.

The patient developed severe bronchospasm which responded to 250mg aminophylline by slow intravenous injection. The oesophageal temperature did not rise beyond 39.2°C. Repeat arterial blood gas samples at ten min. intervals showed normal pH. Serum potassium measurements remained slightly raised. Oesophageal temperature gradually decreased to 36.8°C over the next two hours and cooling was stopped at this stage. The patient was transferred to the intensive care unit, sedated with propofol and fentanyl infusions and ventilated overnight. All subsequent measurements of blood urea and electrolyte concentrations, liver function tests, arterial blood gases and clotting status were normal. He remained normothermic and maintained a good urine output over the next 24 hours. All laboratory investigations remained normal. The highest creatine kinase reported in that time was 235 $\mu\text{mol/l}$. The endotracheal tube was removed the next morning and he was discharged to the orthopaedic ward. He made a full recovery and was discharged home two days later with instructions on follow up. The patient later confessed to regular ecstasy abuse, the most recent episode being two days prior to the day of surgery. No relevant personal or family history was obtained and he was referred to and examined by a neurologist specialising in muscle disease. On his advice, confirmation of malignant hyperpyrexia as a diagnosis was not pursued.

DISCUSSION

Malignant hyperpyrexia is a rare, potentially fatal condition well recognised in anaesthesia. The true incidence is unknown, with estimates of up to 1:250,000 overall ⁶. The primary defect is not known, but is believed to involve an abnormally sensitive calcium-induced calcium release mechanism. As anaesthetists have become more aware of the condition the mortality rate has fallen, but concomitantly the number of dubious and aborted cases has risen. The commoner trigger agents are suxamethonium and halothane, but all volatile agents have been implicated ^{7,8,9}. Propofol has been studied *in vitro* and *in vivo* and is considered safe ¹⁰. Previous uneventful anaesthesia is not an indicator of nonsusceptibility, even if known trigger agents have been used ^{8,11}.

Malignant hyperpyrexia can be classified into four categories: the fulminant form, abortive malignant hyperpyrexia, masseter spasm and atypical presentations. The clinical diagnosis of malignant hyperpyrexia, especially when made early in the course of the crisis, can be difficult as the signs are non-specific at this stage and other conditions can mimic it to a certain extent. Muscle rigidity may or may not be present, and the predictive value of the most informative signs, when combined, is only 78% specific ¹². Though an increase in temperature of 1°C/hour is quoted as one of the diagnostic criteria in malignant hyperpyrexia, it may well be much faster ⁸. An increase in temperature is a relatively late sign, so capnography is of crucial importance at an early stage ¹³. Hyoglobulinuria and elevated serum creatine kinase are also indicative of malignant hyperpyrexia ¹².

Dantrolene, a drug which impairs calcium release from skeletal muscle sarcoplasmic reticulum, is recommended for treatment. It has also been used in the treatment of hypermetabolic states associated with theophylline overdose, the neuroleptic malignant syndrome, exertional heat-stroke, tetanus, toxic reactions to, γ -asperaginase, amphotericin-B induced rigors and delirium tremers ^{14, 15, 16}. It has been employed in the treatment of massive MDMA overdose ⁴.

In recent years the recreational use of the semisynthetic amphetamine, "ecstasy" has increased. Preparations of this substance may contain relatively pure methylene dioxyamphetamine (MDA, "Eve") or its N-methyl congener MDMA, and biotransformation of MDMA to MDA may occur ¹⁷. Clinically, MDA has been evaluated as an anorectic and antidepressant and as an adjunct to psychotherapy, though it has yet to find an acceptable place in the medical pharmacopoeia ^{18, 19}. MDA has been shown to be neurotoxic, destroying serotonergic nerve terminals in the brain ¹⁹. These substances induce a state of excitation of the central nervous system, with central autonomic hyperactivity, manifest as changes in mood (usually euphoric, sometimes depressive) and perception. Trismus, myalgia, tachycardia, hypertension and hyperthermia have been reported ^{20,21}. Studies in animals have shown MDA toxicity to parallel that of amphetamines and to produce mydriasis, profuse salivation, tachycardia, hypertension, hyperthermia, convulsions and death ¹⁹. These signs can develop several hours after Ecstasy ingestion; the prolonged duration of sympathomimetic action relates to the resistance of these substances to degradation by enzymes that metabolise catecholamines ²². The unpredictable hyperthermic response to MDA or MDMA in certain individuals may reflect an

underlying metabolic myopathy, with deregulation of mycoplasmic calcium ion homeostasis²³. The mechanism may involve a combination of direct effects of the drugs and a raised metabolic rate, dehydration or any cause of stress²¹.

The cause of the sudden increase in temperature in this case remains uncertain. Initially the clinical impression was of a fulminant malignant hyperpyrexia, though the lack of progression suggested this not to be the case. It may have been an aborted or atypical form of malignant hyperpyrexia, though in view of the normal postoperative serum creatine kinase concentration this is unlikely. It may have been a delayed hyperthermic response to the MDMA alone, and purely coincidental with the hospital admission. As the interval between the last ingestion of "Ecstasy" and surgery was less than 48 hours it may have been a result of a combination of residual MDMA, due to its slow metabolism, and a combined factor of hospital admission, surgical stress, catecholamine release and the administration of anaesthetic drugs. A MDMA-induced Ca^{++} release myopathy leading to a deregulation of mycoplasmic calcium ion homeostasis would also be an explanation: as the final common pathway in the development of malignant hyperpyrexia is excessive mycoplasmic Ca^{++} , and hyperthermia with MDMA in certain individuals may reflect a deregulation of mycoplasmic calcium ion homeostasis, this case may represent an additional type of malignant hyperpyrexia.

The differential diagnosis of severe hyperthermia should include 3,4 methylenedioxymetamphetamine intoxication, and serum MDMA concentrations should be measured in young adults who develop hyperthermia during anaesthesia^{21, 22}. With the increasing abuse of MDMA and related compounds, the preoperative interrogation of the patient regarding recreational drug abuse should assume greater importance.

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Case Report :

Infective endocarditis due to *Gemella morbillorum* complicating hypertrophic obstructive cardiomyopathy

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Accepted 11 January 1994.

This report documents successful medical treatment of endocarditis caused by an infrequently encountered and recently renamed organism, occurring four weeks post-dental extraction in a patient with pre-existing hypertrophic obstructive cardiomyopathy.

CASE REPORT

A 29 year old woman with hypertrophic obstructive cardiomyopathy was admitted to hospital in July 1992 with a history of persistent lethargy. Three weeks previously she had suffered a flu-like illness with night sweats and dry cough. The sweats had subsided but she still felt unusually warm at night. A week prior to this episode she had developed a swollen and tender left knee which had quickly settled on a non-steroidal anti-inflammatory drug. Three months prior to admission extraction of two wisdom teeth had been performed under oral antibiotic prophylaxis: this had comprised three doses each of 3g amoxycillin; (1hr before, 3 and 18 hr post-operation). Recovery following this procedure had been uneventful. She had been taking propranolol 40mg four times a day to increase exercise tolerance, and thyroxine 50µg daily to induce shrinkage of a goitre. The day before admission her general practitioner had prescribed vitamin B₁₂ 1000µg and ofloxacin 400mg twice a day. On examination she had a small goitre, temperature 37.5°C, heart rate 100/min, blood pressure 90/60mmHg; there was a loud systolic murmur at the left sternal edge radiating to all areas. Dental examination was unremarkable. The erythrocyte sedimentation rate was 45 mm in the first hour, white cell count 8,200/µL. Electrocardiography showed marked left ventricular hypertrophy, and a trans-thoracic echocardiogram showed severe hypertrophic obstructive cardiomyopathy. No vegetations were seen.

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On the second day blood cultures grew an α -haemolytic, nutritionally variant gram-positive coccus growing in chains, requiring serum and vitamin supplements in order to grow; this was biochemically identified by the APIStrep identification system (BioMerieux, France) as *Gemella morbillorum*. Empirical treatment was started with intravenous benzylpenicillin 1.2g four times a day, and gentamicin 80mg three times a day. Both the minimum inhibitory concentration and the minimum bactericidal concentration of penicillin for the organism were subsequently shown to be less than 0.06 μ g/ml. The pyrexia resolved after four days. At this stage serological tests for Q fever, chlamydia, adenovirus, mycoplasma, legionella and brucella infection were reported to be negative. During the second week the patient gradually became lethargic, the erythrocyte sedimentation rate rose to 110mm in the first hour, her temperature rose to 38°C and a self-limiting left elbow arthralgia developed. She was thought to have become sensitised to penicillin and towards the end of the third week of treatment antibiotics were changed to oral erythromycin 500mg four times a day and oral rifampicin 900mg per day. The minimum inhibitory concentrations of the isolate were <0.25 and <0.5 μ g/ml respectively and in each case the minimum bactericidal concentration was equal to the minimum inhibitory concentration. Two days later her temperature had settled again. On day 26 a generalised itchy erythematous maculopapular rash developed which settled within 24 hours on oral chlorpheniramine. Treatment continued for a total of six weeks after which she was discharged. She remains clinically well to date.

DISCUSSION

Infective endocarditis is a rare complication of hypertrophic obstructive cardiomyopathy. Sixty-one cases were reported between 1961 and 1990.¹ The overall mortality rate of infective endocarditis associated with hypertrophic obstructive cardiomyopathy is reported as 39%, compared to 20-30% for other forms of endocarditis.^{2, 3} Antibiotic prophylaxis is given for dental or other procedures which may cause bacteraemia in patients with underlying heart disease predisposing to endocarditis.

The British Society for Antimicrobial Chemotherapy recommendations for oral antibiotic prophylaxis for patients who are not allergic to penicillin and who undergo general anaesthesia for a dental procedure are 3g amoxycillin orally four hours before anaesthesia followed by a further 3g as soon as possible afterwards.⁴ *Gemella morbillorum*, formerly known as *Streptococcus morbillorum*,⁵ is an anaerobic to aerotolerant gram-positive coccus whose taxonomic position has been uncertain. The natural habitat of the organism is the human intestinal tract. It is a rare but important pathogen and has been associated with endocarditis and suppurative infections.⁶ As the dental antibiotic prophylaxis given in this case can be considered adequate, and the causative organism was fully sensitive to penicillin, infective endocarditis may have resulted from a spontaneous bacteraemia of gastro-intestinal origin occurring at a different time from the dental extraction; most cases of infective endocarditis follow seemingly 'spontaneous' bacteraemia⁷. This case illustrates the unpredictable nature of bacteraemia which may result in infective endocarditis in predisposed individuals, and underlines the role of hypertrophic obstructive cardiomyopathy as a risk factor.

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Case Report

Liposarcoma of the colon

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Lipomas are frequently encountered in the gastrointestinal tract but liposarcomas in this location are extremely rare. We present the first reported case of primary colonic liposarcoma.

CASE REPORT: A 54 year old female presented with lethargy, abdominal discomfort, diarrhoea, and loss of 7 kg weight. She was clinically anaemic. A firm, irregular 6 cm mass was palpable in the right upper quadrant of the abdomen, and a 6.5 cm mass in the left breast.

Haemoglobin was 7.3 g/dl with microcytic hypochromic indices. Faecal occult blood tests were positive. Barium enema revealed a polypoid tumour in the colon just proximal to the hepatic flexure (Fig 1). Fine needle aspiration cytology confirmed the presence of a carcinoma in the left breast. Right hemicolectomy and left mastectomy operations were performed. There was no clinical, operative or radiological evidence of primary tumour at any other site.

Pathological examination revealed a 6 x 4 x 5 cm polypoid tumour projecting into the colonic lumen (Fig 2). It was largely covered by mucosa with only focal areas of surface ulceration. The cut surface showed multi-lobulated well circumscribed greyish yellow polypoid tumour of firm consistency with no gross evidence of haemorrhage or necrosis. Histological section showed the classical features of the pleomorphic variant of liposarcoma, including univacuolar and multivacuolar lipoblasts with bizarre forms, multinucleated giant cells and numerous mitotic figures (Fig 3). Immunohistochemical markers for epithelial, smooth muscle and neural antigens were all negative. Oil red fat stain was strongly positive. Electronmicroscopy confirmed the lipoblastic and lipocystic differentiation of the tumour cells. One enlarged mesocolic lymph node showed metastatic involvement with tumour cells similar to that of the primary colonic neoplasm

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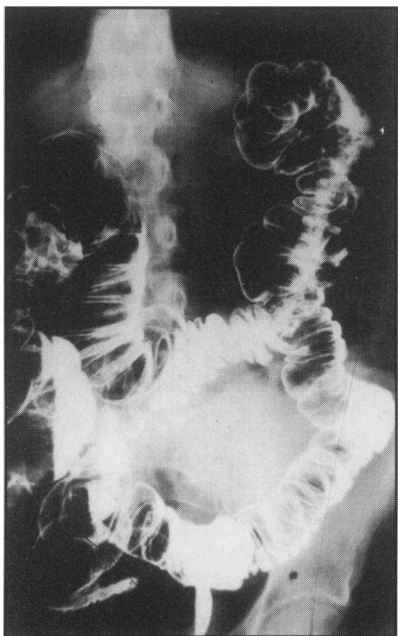


Fig 1. Barium enema showing a polypoid tumour projecting into the colonic lumen just proximal to the hepatic flexure.



Fig 2. Polypoid tumour removed at right hemicolectomy.

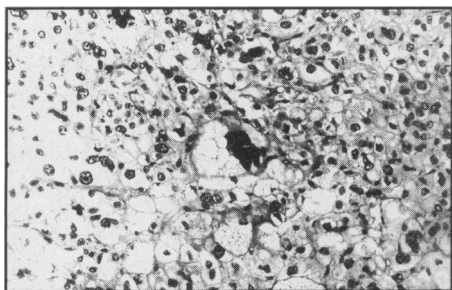


Fig 3. Histological section of the pleomorphic colonic liposarcoma, showing lipoblasts and mitotic figures (haematoxylin and eosin x 175).

The mastectomy specimen contained a 6.5 cm grade II infiltrating ductal carcinoma (type NOS) with extensive ductal carcinoma in situ, (comedo type). Further sampling revealed no areas of poorly differentiated, spindle shaped or metaplastic carcinoma. Three axillary nodes were replaced by tumour cells histologically similar to the breast primary lesion.

DISCUSSION: Liposarcomas most commonly involve the limbs and the retroperitoneum. Primary liposarcomas of the gastrointestinal tract are extremely rare. There have been cases reported involving the oesophagus¹, stomach², small intestine³, and ileo-caecal valve⁴, but liposarcoma arising in the large intestine has not been reported. In this case the histological appearances were unequivocally those of a liposarcoma. Physical examination revealed no palpable tumour in the extremities and CT scan showed no other retroperitoneal, intra-abdominal or intrathoracic masses. The involvement of an intra-abdominal regional lymph node suggests metastatic spread from the bowel lesion.

The infiltrating ductal carcinoma of the breast would appear to be an incidental finding, but may reflect an impaired immune status. Hadju studied a large series

of 242 patients with liposarcoma at various sites, and found a 12% incidence of a histologically different but co-existent primary tumour ⁵.

Preferred treatment for liposarcoma in any location of the body is complete surgical excision. The role of radiation therapy and chemotherapy is not established, but survival may be improved by adjuvant radiotherapy ⁶. The prognosis for liposarcoma is dependant on the location, size and histology of the tumour – no patient with pleomorphic variant survived more than five years in a large prognostic study in Scandinavia ⁷.

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Case Report

Strangulation of the appendix in a femoral hernia sac

C D Weir, S J Dolan, V Loughlin, T Diamond

Accepted 1 February 1994

The appendix is reported to be found in the hernia sac in 1% of femoral hernias, but strangulation of the appendix in this site is extremely rare¹. We report three unusual cases, in which femoral herniation and strangulation resulted in ischaemic necrosis of the appendix.

CASE 1. An 83 year old man presented with a 48 hr history of vomiting and constipation. He was pyrexial, the abdomen was distended, and a tender swelling was present in the medial aspect of the right groin, below the inguinal ligament. A diagnosis of incarcerated femoral hernia was made. Exploration through a McEvedy incision revealed strangulation and necrosis of a loop of small bowel and of the appendix in the hernial sac. Appendicectomy, small bowel resection and repair of the femoral ring were performed. He made an uneventful recovery. Histopathology confirmed appendiceal necrosis and focal necrosis in the small bowel.

CASE 2. A 60 year old woman presented with a painful lump in the right groin. She was pyrexial and there was an irreducible lump in the right groin with erythema of the overlying skin. A diagnosis of incarcerated femoral hernia was made. A McEvedy approach was undertaken and the hernial sac was found to contain omentum and a gangrenous appendix. Appendicectomy and repair of the femoral ring were performed. She made an uneventful recovery. Histopathology revealed congestion of the meso-appendix, with ischaemia and necrosis of the appendix.

CASE 3. A 77 year old woman presented with a two week history of a painful lump in the right groin. There was a tender, irreducible lump in the region of the right femoral ring with no cough impulse. The overlying skin was oedematous and inflamed. A McEvedy incision, extended inferiorly over the lump, revealed

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an abscess containing 30ml pus, adjacent to a femoral hernial sac which contained a perforated appendix. The abdominal cavity was entered through the upper part of the incision and the herniated appendix reduced. The mid-portion only had herniated, and was surrounded by a constriction ring which resulted in ischaemic necrosis. The distal tip, lying intra-peritoneally, was normal in appearance. Appendicectomy and repair of the femoral ring were performed and the lower half of the skin incision left open. She made an uneventful recovery. Histopathology revealed necrosis and perforation affecting the mid-portion of the appendix only, the distal portion being normal in appearance.

DISCUSSION

Strangulated femoral hernia is a common surgical emergency. The contents of the hernial sac commonly include omentum and small bowel, but occasionally strangulation of other organs such as Meckel's diverticulum, stomach, ovary or appendix may occur, resulting in unusual clinical presentations. The presence of the appendix in a femoral hernia was recognised as early as 1731², but the small number of cases reported since then indicate that this is an extremely rare presentation³.

The appendix has been found in other abdominal wall hernias, including inguinal, umbilical, obturator and incisional hernias^{4,5,6}. Although the majority of these cases have been reported as "appendicitis" it is difficult to determine from the reports whether the pathological process is one of primary visceral inflammation in the appendix, which could be described as appendicitis, or secondary strangulation and ischaemic necrosis. It is possible that an appendix which was situated in a femoral hernia could become primarily inflamed and then present with local signs in the hernial sac. This is the proposed pathological mechanism in the majority of reported cases⁷. It is also possible that the primary event which leads to presentation is irreducibility with subsequent strangulation of the sac contents⁸. This is supported by the operative and histological findings in our series, with ischaemia and necrosis of the appendix in each case. In addition, in one of our cases, only the mid-portion of the appendix was strangulated while the distal tip, lying intraperitoneally, was normal in appearance.

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Case Report

Nephrobronchocutaneous fistula

S A A Aly, B Cranley, A Todds

Accepted 12 February 1994

A fistula between the urinary tract and the lung is a rare occurrence. In 1949 Abeshouse reviewed the world literature and reported that among the abnormal connections between the kidney and other organs, nephropulmonary fistulae were second in incidence to renocolic communications.¹ We have found 70 published cases of nephrobronchocutaneous fistula but, only nine of these were after 1949, suggesting that most cases were from the pre-antibiotic era.

CASE REPORT

A 72 year old man presented with a discharging sinus in the left renal area of three years duration. He was otherwise well. On examination coarse crepitations were noted at the lung bases. There were no other abnormal findings. Apart from an elevated erythrocyte sedimentation rate (55mm/hr) laboratory tests were normal. Haemoglobin 12.2g/dl, white cell count 9.5, 10⁹/l, urea 5.1 mmol/l, sodium mmol/l, potassium 3.5 mmol/l. Midstream urine sample showed no abnormal cells or growth on culture and no acid-fast bacilli were identified. Chest X-ray was normal. The left kidney was non-functional on intravenous urography; ultrasound scan showed stones and this was shown to be pyonephrotic on CT scanning. A sinogram was carried out with a water soluble contrast; during the examination the patient started to cough and a nephrobronchocutaneous fistula was demonstrated. Repeated bacteriological investigations of his sputum failed to reveal any acid-fast bacilli. He refused to have treatment, either surgical or medical, and remains clinically well one year after presentation.

DISCUSSION

Calculus pyonephrosis, primary perinephric abscess and tuberculosis are the most common causes of nephrobronchocutaneous fistula. Other reported cases are shown in the table. The patient often presents with a cough and foul smelling sputum. Other symptoms include loin and chest pain, fever, weight loss and general malaise. The case we described had none of these features. The triad of an enlarged kidney, staghorn calculus and ipsilateral posterior basal pulmonary infiltrate should arouse the suspicion of the clinician². An anatomical explanation as to how a perinephric suppurative process extends

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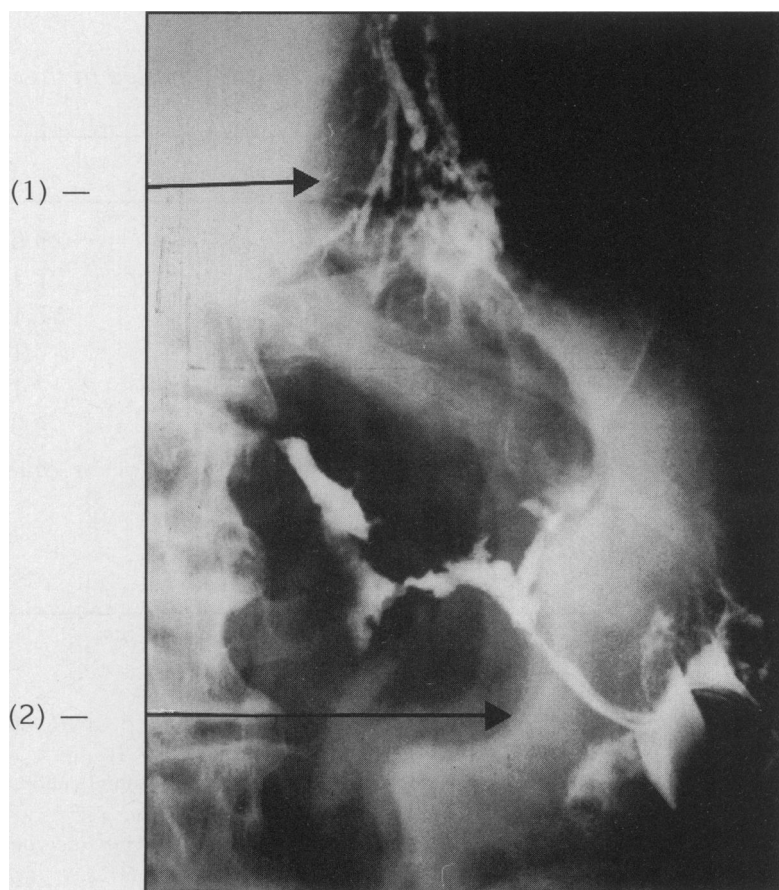


Fig. Sinogram demonstrating nephrobronchocutaneous fistula

(1) Bronchial part of fistula.

(2) Renal part of fistula.

up through the diaphragm is that the anterior and posterior perirenal fascial layers meet and are attached to the diaphragmatic fascia above the adrenal glands. The point of this attachment is usually the site of eventual perforation and communication with the pleural cavity and the lung ³.

Ultrasound scanning, intravenous urography and CT scanning are useful in establishing the presence of perinephric sepsis and of involvement of the diaphragm and ipsilateral lung. It is unusual for the fistula to be demonstrated radiographically unless there is also a cutaneous fistula. The surgical treatment of nephrobronchocutaneous fistula would necessitate removal of the involved kidney with drainage of the perinephric abscess and empyema. Sometimes however the fistula persists, and a transthoracic technique using a free graft of fascia lata to close the fistulous communication has been described ⁴. A case of nephrobronchocutaneous fistula has been successfully treated with antituberculous therapy alone, even though acid-fast bacilli were not isolated ⁵.

TABLE

Causes of nephrobronchocutaneous fistula in 70 cases reported in the medical literature.

<i>Causes</i>	<i>No.</i>	
Calculus pyonephrosis	20	28.6%
Prenephric abscess	19	27.1%
Renal tuberculosis	12	17.1%
Non-calculus pyonephrosis	5	7.1%
Echinococcal diseases	5	7.1%
Hydronephrosis	2	2.9%
Undetermined cause	3	4.3%
Pyelonephritis, rupture of dysplastic kidney, gunshot wound, ureterobronchial fistula after nephrectomy	1 each	

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Case report:

Coalition of the proximal row of the carpus

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Accepted 21 December 1993

The human carpal bones, as in most mammals, are usually eight in number, and develop from a common embryological origin by the eighth week of intrauterine life ¹. Failure of separation during this development leads to the phenomenon of carpal coalition. The prevalence of the anomaly is uncertain as it is usually asymptomatic ². Individual cases have been reported which have presented as unusual causes of wrist pain, through arthritis or fracture ³, or even tendon rupture ⁴. The case reported here shows bilateral lunate-triquetral coalition with unilateral synostosis of the pisiform and triquetrum.

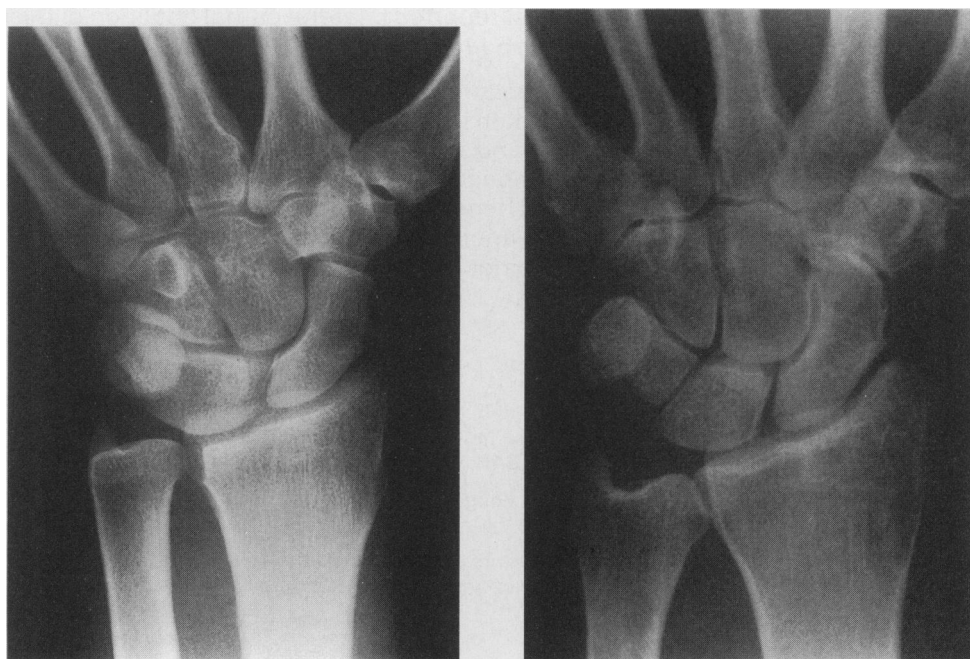


Fig. (a) PA radiograph of the left wrist showing lunate and triquetral coalition. The pisiform triquetral fusion was shown on lateral views. (b) Radiograph of normal carpal configuration for comparison.

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CASE REPORT. A 39 year-old white female presented with a dorsal pattern dislocation of the metacarpo-phalangeal joint of the right thumb. Radiographs showed a proximal carpal coalition (Fig) and comparative radiographs of the left wrist confirmed this to be bilateral. She had previously been asymptomatic and there was no history of other congenital anomalies affecting the patient or her immediate family. She made a full recovery following closed reduction of the dislocation and a period of splintage.

DISCUSSION

Lunate-triquetral coalitions have been classified into four types by Minaar in his study of 12 cases occurring in South African Bantu³. In this patient complete fusion of triquetrum and lunate on the right (Minaar Type III) is associated with a similar pattern on the left with involvement of the pisiform (Minaar Type IV). Minaar noted that the anomaly was much more widely reported in blacks and in particular American negroes. This is supported by the largest series of 36 cases recently reported by Delaney and Eswar². They investigated two hospitals for this anomaly, one serving a black population, the other a white population, and found a ratio of blacks to whites 11:1 and males to females of 5:1. We believe this case to be the first reported bilateral carpal coalition of this pattern to be described in a caucasian female.

None of the coalitions described by Delaney and Eswar was symptomatic, and each was identified on radiographs taken for other reasons. It is well recognised that the lunate rotates during ulnar and radial deviation of the wrist¹, and it might therefore be expected that impedance by attachment to other carpal bones would affect wrist function and hence produce symptoms. This does not appear to be the case, although these anomalies have not been followed up and the long-term effect on the carpus is not clear^{4,5}.

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Ulster Paediatric Society

Junior Members' Forum

The Junior Members' Forum provides opportunity for paediatricians in training to present scientific and clinical material of research interest. At the Annual Meeting in November 1993 Professor Sir David Hull, President of the British Paediatric Association, and Dr Paul Thomas, President of the Ulster Paediatric Society acted as judges. Prizes were awarded on the basis of the best scientific paper to Mr Bill McCallion for his paper "*Helicobacter Pylori* in children in Northern Ireland", and for the best presentation to Dr Fiona Stewart for her paper "Molecular Investigation of patients with Prader Willi syndrome".

Helicobacter Pylori in Children in Northern Ireland – Initial Impressions.

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Helicobacter pylori is a recognised cause of gastritis and peptic ulceration and has been implicated in the causation of gastric carcinoma. The prevalence of *Helicobacter pylori* among school-children in developed countries is 1 to 8%. Whilst peptic ulceration in children is uncommon, *Helicobacter pylori* is believed to be a cause of dyspepsia and possibly recurrent abdominal pain. The aim of this paper is to determine: (1) the prevalence of the infection in children in Northern Ireland, (2) the extent of intrafamilial clustering, (3) if prevalence is associated with social class, (4) if *Helicobacter pylori* causes recurrent abdominal pain, and (5) the effect of eradication on gastrointestinal symptoms.

367 children were investigated for *Helicobacter pylori*: 71 presenting with severe dyspepsia had oesophagogastroduodenoscopy, 50 siblings underwent a carbon-13 urea breath test, and 242 children attending for non-gastrointestinal daycase surgery had serological tests only.

	Patients				Social class						Intrafamilial clustering
	Overall	Dyspepsia	Sibs	Daycases	I	II	IIIN	IIIM	IV	V	
Prevalence %	37	45	58	30	0	29	27	47	44	42	96

Of 32 children with severe dyspepsia and *Helicobacter pylori* 2 had peptic ulcers. Following eradication, dyspepsia was cured in one third, persisted with some improvement in one third, and persisted with no improvement in one third. 20% of children with no *Helicobacter pylori* had recurrent abdominal pain compared with 28% of those with *Helicobacter pylori* (p=0.13).

The prevalence of *Helicobacter pylori* in children in Northern Ireland is significantly greater than in any other published report from the developed world. Prevalence is higher in lower social classes ($p=0.01$). Intrafamilial clustering is very common suggesting person-to-person spread. Most children with severe dyspepsia do not have *Helicobacter pylori*. Furthermore eradication of the organism does not alleviate symptoms in the majority recurrent abdominal pain more common in children with *Helicobacter pylori*. Given that peptic ulceration is uncommon despite a very high prevalence of *Helicobacter pylori*, its role as a significant pathogen in children is questioned.

Molecular investigation of patients with Prader Willi syndrome

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A study was undertaken of all patients in Northern Ireland with suspected Prader Willi syndrome from a clinical, cytogenetic, and molecular viewpoint. Where possible patients were examined clinically, and blood taken from the patient and both parents for cytogenetic and molecular analysis. Molecular analysis was carried out using two microsatellites 4-3R and GabaRB3 to look for deletions of the Prader Willi region of chromosome 15, or parental disomy.

Results are available on 12 patients: 8 have the typical Prader Willi syndrome diagnosed clinically, 2 have suspected Prader Willi syndrome; 2 have chromosome rearrangements involving 15q12.

Of the 8 patients, 4 showed a deletion on the paternally derived chromosome 15; 2 showed maternal disomy and 2 were uninformative. Of the 2 suspected patients, 1 showed evidence of non-paternity and the other showed no evidence of deletion or disomy. Of the 2 patients with chromosome rearrangements, 1 showed a deletion of 4-3R. Results on the second patient are rather unusual and further work on this sample is planned.

As only 50% of patients with Prader Willi syndrome show a visible cytogenetic deletion we feel that the use of microsatellites is very helpful in confirming the diagnosis – particularly in the newborn period when the clinical features may not be striking.

Book review

Mental Health and Politics in Northern Ireland. By Pauline Prior (pp 194. £32.50) Avebury, Ashgate Publishing, Aldershot. 1993. ISBN 1 85628 540 5.

Commonly, when chatting with visitors to Northern Ireland, or, when at meetings abroad, one is asked "... and how does the situation in Northern Ireland affect people's mental health?" One generally responds that it is a remarkable testimony to the human spirit that despite the trauma experienced by individuals, there is little hard evidence of adverse effects on the population generally. One will also refer to publications by Alex Lyons, Peter Curran and his group, and of course the work of Fraser, Cairns and Wilson, and others. Until now however, no-one has attempted to cover the whole gamut of relationships between mental health and politics in Northern Ireland.

The author of this study has scanned the range of available government records, and some of the research, from before the foundation of Northern Ireland, up to the present. She attempts to provide an overview of the changes in service provision, and gives an opinion on how these were related to and affected by the particular political developments of the day. Later she addresses the available research on the direct impact of 'the troubles' on individuals, and describes from case notes the histories of half a dozen patients whom she regards as illustrative, though not representative, of psychiatric patients during the period.

The result is very critical in tone, and while there are occasional acknowledgements of innovative developments, and credit given to a few who worked within the service, there is a general impression that those who established this political entity, and the various authorities who have held responsibility for mental health care over the years, have little of which to be proud. At times this finds expression in some remarkable phrases, as when the term 'legitimate target' (used in Northern Ireland by terrorists to justify certain murders) is applied to those who receive, or do not receive, mental health care from the service (p 115). One certainly would not come to the end of this book and know that training in psychiatry and the development of some specialist services is much more advanced in the North than in the Republic, or in Wales. The higher per capita spending in Northern Ireland until recent times gets little credit, and the advantages for hospital and community care of the integration of Health and Social Services in Northern Ireland, are not fully appreciated. The view to the future is similarly gloomy because it is informed largely by expenditure projections, rather than by close acquaintance with the service at the point of delivery.

There is a temptation in Northern Ireland to attribute such a partial and censorious critique to the local political propensities of the author. It is my own impression that the work has failed to reach its full potential because of the author's view of society generally. Instead of seeing a particular service in its proper historical context, or comparing a service in Northern Ireland with like services in the rest of the island, or similar areas elsewhere, and giving an objective assessment, she usually moves immediately to a critique whose justification is not well founded. A crowning example is the claim that the expansion and contraction of mental health service provision has had little to do with need. She seems to base much of this judgement on a crude bed count, which she rightly rejects as inadequate when used by others.

The greatest value of the book, and it is expensive for its size, lies in the extensive referencing and the bibliography. It is a very useful starting point for anyone wishing ready access to the literature, though again I note an absence of reference to Northern Ireland-based advances in the understanding of mental illness and mental health generally, as distinct from 'troubles-based' literature.

Sadly then, the author has chosen an important area of study, but has produced a text which will be useful for reference to the interesting facts and figures it brings together, rather than for the perspicacity of the conclusions drawn.

J T ALDERDICE

ERRATUM

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