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The Ulster Medical Journal

The Journal of the Ulster Medical Society. First published in 1932.
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THE ULSTER MEDICAL JOURNAL

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The Ulster Medical Journal, Volume 71, No. 1, pp. 1-9, May 2002.

Resuscitation in the past, the present and the future

Presidential Address delivered to the Ulster Medical Society on Thursday October 11, 2001

A A Jennifer Adgey, Royal Victoria Hospital, Belfast BT12 6BA, Northern Ireland

"O, that I could but call these dead to life!" King Henry VI, William Shakespeare.

"There is no malice in this burning coal; The breath of heaven has blown his spirit out . . . But with my breath I can revive it, . . ." William Shakespeare.

BACKGROUND

Respiratory System

One of the earliest recordings in Egyptian mythology of resuscitation was when Isis restored her husband Osiris by breathing into his mouth. The Bible has several accounts of resuscitation using the mouth or nostrils. In Genesis it was recorded that when forming Adam, God is said to have ". . . breathed into his nostrils the breath of life". In the first book of Kings, Elijah resuscitated the dying son of his landlady and we are told how he first prayed and then stretched himself along the sick child " . . . *and the soul of the child came into him again, and he revived*". In the second book of Kings it is recorded how Elisha, when summoned to a house where a child had died *"up and lay upon the child and put his mouth upon his mouth, and his eyes upon his eyes, and his hands upon his hands; he stretched himself upon him; the flesh of the child waxed warm and the child sneezed seven times, and the child opened his eyes"*.

When obstructed breathing is the cause of the collapse of the patient, varying attempts throughout the ages have been made to obtain direct access through the trachea. Dating back to 2000 BC, Egyptians are recorded as using reeds through a hole in the skin entering the windpipe and Homer in 356 BC described opening the trachea to relieve those choking. Even Alexander the Great when seeing a man choking from a bone lodged in his throat is said to have punctured the trachea with the tip of his sword.

Sudden Death

For many centuries, sudden death unrelated to trauma has been recognised as a clinical entity. But sudden death due to cardiac causes was first described about the first century AD. Pliny the Elder at this time in his work "Natural History" . . . studied many citizens of Rome – physicians, senators and businessmen – who had dropped dead. Since there were no post mortem examinations, these deaths were usually attributed to "an act of the Gods". Frequent records of sudden death were made throughout the middle ages and in the 17th and 18th centuries. Lusitanus in 1560 described "A reverend abbot from the Isle of Croma, one or two miles distant from Ragusa, when he was in good health and talking to several persons, said that he suddenly felt pain in his heart and with his hand moved rapidly toward the region of the heart, he fell, though slowly, to the earth and rapidly lost all his animal faculties. When called in I said he was dead. Not only was the pulse at the metacarpium, and the temples missing, but even no motion upon the heart could be perceived. In order to satisfy the assistants I brought to the nostrils a burning candle whose flame did not move at all. Also a bright mirror was advanced near the mouth and nothing of respiratory contraction was seen on it. We then applied a glass vessel filled with water upon the thorax but the water was unmoved".

Lancisi (1707) performed post mortems on citizens of Rome who died suddenly during 1705-1706.[1] He found a natural cause for death in every case and he referred particularly to diseases of the blood vessels with "obstruction therefrom of the free flow of blood".

Sudden deaths due to coronary artery disease still remain one of the greatest challenges in contemporary society. In 1971 Gordon and Kannel stated that "we are faced with a disease which is

extremely common and highly lethal, which frequently attacks without warning and in which the first symptoms are all too often the very last. Also, it is a disease which can be silent even in its most dangerous form".[2]

At present there are approximately 120,000 deaths from coronary heart disease in the United Kingdom per year. Each year in the United States approximately 800,000 individuals suffer an acute myocardial infarction, of whom approximately 550,000 die. More than half of the 550,000 deaths occur outside the hospital. Two thirds of the deaths from coronary artery disease of those aged less than 65 years are unexpected and occur outside hospital. More than one half are sudden and occur within one hour of the onset of the first symptom. Two thirds of sudden coronary deaths occur among patients who do not have previous clinical or electrocardiographic evidence of coronary artery disease. Death is more likely to be sudden in younger individuals and sudden coronary death is more likely in men than in women.

Sudden death and ventricular fibrillation

Sudden death and ventricular fibrillation are considered synonymous since in more than 90% of sudden deaths outside hospital, ventricular fibrillation has been documented. Sudden death need not be a manifestation of an acute myocardial infarction but may represent a brief ischaemic episode with a high tendency to recurrence.

The electrical storm of ventricular fibrillation was probably known to Vesalius but Hoffa and Ludwig in 1850 provided the first clear description.[3] Their investigations showed that electrical stimulation of the mammalian heart led to ventricular fibrillation and death. In 1887 the Aberdeen physiologist McWilliain [4] suggested that sudden death was due to ventricular fibrillation and in 1889 indicated there was a high probability that ventricular fibrillation was the cause of sudden death in patients with angina pectoris.[5] In 1911 Hoffman [6] was the first to obtain an ECG in a patient showing ventricular fibrillation and in 1933 Hamilton and Robertson [7] recorded ventricular fibrillation on the ECG during a fatal attack of angina pectoris in a patient. In 1939 Smith[8] and Miller [9] first documented ventricular fibrillation as the cause of sudden death in man following acute myocardial infarction.

Electric current applied to the heart and defibrillation

The application of electric currents to the heart using direct current derived from a Leyden jar commenced in the 18th century. Abildgaard in 1775, the Danish Veterinarian – Physician, recorded that chickens could be stunned and revived by electrical shocks administered to the head and to the heart. Benjamin Franklin in the United States at approximately the same time shocked goats and killed fowl with charges of static electricity.

Prevost and Battelli in 1899 successfully defibrillated the ventricles of a dog's heart by applying either DC or AC countershock directly to the myocardium.[10] In 1933 Hooker *et al* showed that internal cardiac massage and the direct application of AC shock to the ventricles corrected experimental ventricular fibrillation.[11] But it was not until 1947 that Beck and co-workers successfully corrected ventricular fibrillation by internal cardiac massage and direct application of AC countershock to the heart of a 14 year old boy undergoing thoracic surgery.[12]

Time had been shown to be a critical factor in determining recovery from cardiac arrest. In 1940 Weinberger *et al* looking at clinical recovery from cardiac arrest noted that if more than four minutes elapsed before resumption of an adequate cardiac output the chances for salvage without irreversible neurological damage were poor.[13] Thus the widespread application of resuscitative measures was limited.

Mouth to mouth respiration and external cardiac massage

In 1743 Tossach demonstrated the effectiveness of mouth to mouth respiration as a means of artificial ventilation by resuscitating a coal miner overcome by gaseous fumes.[14] The American physiologist James Elam was the first to prove that expired air was sufficient to maintain adequate oxygenation. During a poliomyelitis epidemic in Minnesota in 1946, Elam first carried out mouth to nose breathing on patients with acute bulbar poliomyelitis demonstrating their survival until transfer to mechanical ventilation.

The problem however that was still outstanding was extending the survival time of the collapsed patient in ventricular fibrillation until external defibrillation was available. In 1960

Kouwenhoven *et al* at the Johns Hopkins Hospital in Baltimore first showed that external cardiac massage with compression of the lower portion of the sternum during cardiac arrest maintained an adequate circulation thus lengthening the delay in effective resuscitation by more than four minutes and removing the feeling of uselessness when confronting a crisis in which a delay of four minutes was the limit for effective resuscitation.[15] They produced peak blood pressures of 80 mm Hg by closed chest cardiac massage. Thus by utilizing external cardiac massage and mouth to mouth ventilation, survival time to successful defibrillation was prolonged and ultimately the survival of the patient.

Defibrillation (internal and external)

In 1956 Reagan and co-workers[16] and Beck and co-workers[17] first reported successful resuscitation in hospital from ventricular fibrillation complicating acute myocardial infarction by internal cardiac massage and direct defibrillation of the heart. Yet in 1961 there were fewer than 20 reports of patients successfully resuscitated – not surprising since the chest wall required to be opened and access for defibrillation to occur. During this time sudden death was thought to be associated with very severe coronary artery disease and therefore resuscitation would be unsuccessful despite the pathological studies showing that the myocardial damage was not infrequently small. Despite the statement by Burns in 1809[18] "Where, however, the cessation of vital action is very complete, and continues long, we ought to inflate the lungs, and pass electric shocks through the chest: the practitioner ought never, if the death has been sudden, and the person not very far advanced in life, to despair of success, till he has unequivocal signs of real death", and the demonstration by several workers that experimental ventricular fibrillation could be removed by transthoracic countershock, essential application was delayed until 1956. In that year Zoll and co-workers[19] corrected ventricular fibrillation by an externally applied electric countershock to the thorax ie AC shock and in 1962 Lown and co-workers[20] introduced direct current shock (capacitor discharge) in the successful correction of ventricular fibrillation externally. Thus, resuscitative measures were available that could be rapidly applied by trained medical and auxiliary staff in the correction of ventricular fibrillation.

RESUSCITATION – THE PRESENT

Cardiac Arrest 1966 - 1969 (Belfast)

Looking at our first 193 cases of cardiac arrest outside hospital in Belfast from January 1, 1966 – December 31, 1969 where median onset of symptoms to arrest was 10 minutes, it was noted that when resuscitation was started within four minutes of the collapse and was efficient, of the 50 patients, 46 were in ventricular fibrillation of whom 40 (87%) were initially resuscitated.[21] However if no resuscitation took place within four minutes of collapse then the majority of the 106 patients were in asystole ie 85 and only 21 in ventricular fibrillation. Of these 21 in ventricular fibrillation, only one patient became a temporary survivor. Of the 193 cases of cardiac arrest outside hospital, in 139 the cardiac arrest took place in the patient's home. This is the most frequent area for cardiac arrest to occur and clearly the most difficult area to access with urgent medical care. In 106 of these 193 cases, the initial resuscitation was commenced by varying people including first aid workers and the family doctors. Fifty five of the 193 cases were initially successfully resuscitated outside hospital of whom 38 became longterm survivors.

Long term survivors

It was also important to show that survivors to leave hospital had a good outlook. In 1970 during a follow up period of 36 months we found that those who had ventricular fibrillation within 4 hours of the onset of symptoms were younger, usually had had a mild coronary attack and had the most favourable longterm prognosis in comparison with those in whom ventricular fibrillation occurred later.[22]

Initiation of ventricular fibrillation

The initiation of ventricular fibrillation which could have relevance to its defibrillation characteristics we first described in 1982.[23] This was a series of patients managed outside hospital and who developed ventricular fibrillation shortly after monitoring commenced. The most frequent initiating beat was an R on T ectopic ie on the peak of the T wave of the QRST of the patient there was a wide complex QRS (ventricular ectopic beat). Other methods of initiation but less frequent were a late cycle ventricular ectopic, ventricular tachycardia, ventricular flutter or idioventricular rhythm.

Ventricular defibrillation

Whilst ventricular fibrillation in a human rarely self-terminates, if the initiation of ventricular fibrillation is witnessed, a chest thump has a reasonable chance of success ie blow to the lower part of the sternum depressing it approximately a half an inch. However the majority of patients require external defibrillation in order to correct ventricular fibrillation.

The most important factor influencing survival is the delay to defibrillation. In the early days of ventricular defibrillation, the majority of studies advocated the maximum stored energy of the defibrillator ie 400 W seconds. From this stored energy most commercially available defibrillators delivered 270 to 330 W seconds through a resistance of 50 Ω. It was originally thought that depolarisation of every cell in the ventricles was necessary to terminate ventricular fibrillation. However it has been shown that successful defibrillation occurs when a critical mass of myocardium is depolarised.

Our earliest research in external defibrillation indicated that the position of the paddles/pads and their size ie circumference were essential in ensuring first DC shock success. For the anterior approach the upper paddle/pad requires to be under the right clavicle and to the right of the sternum in approximately the second intercostal space and the apical paddle/pad requires to be placed over the region of the apex of the left ventricle otherwise defibrillation is unsuccessful. In 1987 we showed that the greater the overall pad diameter the higher the percentage successful defibrillation.[24] This was related to the transthoracic impedance which was lowest for the largest pads. Of the pads tested those producing the greatest percentage success with the lowest trans thoracic impedance measured 12 cms diameter.[24] The number of shocks to correct ventricular fibrillation at the time of the initial arrest averages 2.[25]

In 1975 the Americans felt that "For 7 out of 10 patients, the present defibrillators may be powerful enough. But more important, for 3 out of the 10 it may not be". We therefore addressed this in 1975 and found no difference in the percentage success rate to 200 W S (stored) DC shocks for ventricular fibrillation for those in the heavy weight ranges ie > 90 kgs in comparison to those < 90 kgs.[26] A single 200 W S shock was associated with a 85% initial first shock success.[27] The energy used was half that previously proposed and is now standard for DC defibrillation (damped sine wave).

Since the majority of cardiac arrests occur in the patients' home, the automatic detection of cardiac arrest rhythms was crucial, with either semi-automatic or automatic defibrillation availability. In 1986[28] using a Microprocessor-based ventricular fibrillation detection system, ventricular fibrillation was detected and a shock advised. This advice only took a matter of seconds. Thus public access defibrillation was initiated. We looked at other techniques for defibrillation using even lower energies for defibrillation thus reducing the size of the defibrillator capacitor. In 1989 we explored the oesophageal access route for defibrillation and showed ventricular fibrillation initiated in the Electrophysiological Laboratory was corrected by 50 joules delivered transoesophageally.[29]

Trans-telephonic defibrillation

In 1987 to improve further accessibility to defibrillation we tested the world's first trans telephonic defibrillator where the detection circuitry for ventricular fibrillation was carried in a briefcase and after two pads had been placed on the chest wall the ECG could be transmitted by digital telephone to a central station where the ECG rhythm could be viewed by trained personnel and defibrillation or not advised.[30]

Impedance cardiography

There are many rhythms associated with cardiac arrest – some shockable and some not. To ensure that the rhythm is shockable it is imperative that the rhythm disturbance is associated with a low or no cardiac output. Whilst public access defibrillation is commendable there have been reports of the inappropriate delivery of direct current shocks to patients without ventricular tachyarrhythmias. The use of automatic external defibrillators by minimally trained personnel who lack the skills to differentiate cardiac arrest from other causes of collapse will increase the potential for inappropriate defibrillation. Clearly, the inclusion of a non-ECG haemodynamic sensor in an automatic external defibrillator device could increase its specificity.

Impedance cardiography is a non-invasive method for measuring cardiac output, and parameters derived from the impedance cardiogram have been used as indices of myocardial contractility

and aortic blood flow.[31] The impedance of the thorax (Z) can be recorded by passing a high frequency low amplitude current between two electrodes and recording the resulting voltage. Ejection of blood into the aorta causes small fluctuations in this impedance (ΔZ). The impedance cardiogram is a recording of the first time derivative of ΔZ (ie dz/dt) against time.

Traditionally the impedance cardiogram has been recorded using four circumferential band electrodes. The upper voltage electrode is placed around the base of the neck and the lower voltage electrode around the thorax at the level of the xiphisternum. The two outer current electrodes are placed at least 3 cm away from the voltage electrodes. Clearly it was not practical to employ such an electrode configuration in the cardiac arrest setting. Thus, a system was developed in which the impedance cardiogram could be recorded through two ECG/defibrillator pads, one placed at the second right intercostal space to the right of the sternum just beneath the clavicle and the other placed over the fifth left intercostal space in the mid-clavicular line.

The purposes of this research were firstly, to compare the impedance cardiogram recordings using a traditional four band electrode technique with the novel two ECG/defibrillator pad technique and secondly, to determine if one or more of the impedance cardiogram parameters, recorded through two ECG/defibrillator pads, could act as a haemodynamic sensor for an automated external defibrillator. The impedance cardiogram was recorded in 20 male subjects in sinus rhythm using sequentially the traditional four-band electrodes and the new two ECG/ defibrillator pad technique.

Over a 14-month period, simultaneous recordings of the ECG and impedance cardiogram were made at 116 cardiac arrest calls in 110 patients. The baseline characteristics age, sex, site of arrest, delay to cardiopulmonary resuscitation and delay to intensive care were documented for each of the patients. There were 39 females and 71 males. The age of one out-of-hospital arrest patient was not known. Of the remaining 109 patients the mean age was 66 years (range 38-87 years). Sixty cardiac (5 1.7 %) arrest calls were attended by the mobile coronary care unit outside hospital and 56 (48.3 %) were inside the hospital.

In the control subjects the ECG, impedance cardiogram and baseline impedance (Z) were recorded using a prototype device. This device could use either the four-electrode technique or the new two ECG/defibrillator pad technique. It passed a high frequency (64kHz) low amplitude constant AC current (1 mA RMS) between two electrodes (ie the outer two band electrodes in the four electrode technique and the two ECG/ defibrillator pads in the two electrode technique) and recorded the impedance cardiogram through two electrodes (ie the inner two band electrodes in the four electrode technique or the two ECG/ defibrillator pads in the two electrode technique). The signals were digitized and stored on a portable computer for subsequent analysis using a commercial software package.

The circuitry for the two ECG/defibrillator pad technique was then incorporated into a portable ECG/impedance cardiogram recording unit and hardware was added to protect the device from high voltage direct current shocks. This unit could be connected to each portable defibrillator using a locking plug. Again this unit passed a high frequency (64 kHz) low amplitude constant AC current (1 mA RMS) between the two ECG/ defibrillator pads. The ECG and impedance cardiogram were detected and the signals simultaneously digitized and stored on memory cards for analysis off-line.

Immediately on arrival at a cardiac arrest patient, cardiopulmonary resuscitation continued or was initiated by the junior doctor manning the out-of-hospital mobile coronary care unit or attending the in-hospital cardiac arrest and ECG/ defibrillator pads positioned as for cardiac arrest management.

The impedance cardiogram waveform has A, C and O waves and contains B, X and Y points (figure 1). The A and C waves occur during atrial and ventricular systole, respectively, and the O wave corresponds with ventricular filling. The B point has been related to aortic valve opening and the X and Y points to aortic and pulmonary valve closure, respectively.

Impedance cardiogram recordings are sensitive to motion artefact and electrical interference and thus subjected to ensemble averaging. Analysis software was written and the peak of the R wave of the ECG was identified and used as a reference point. The ECG and impedance cardiogram signals were digitally sampled over five cardiac cycles and synchronized with the R wave. The synchronized cycles were digitally summed and

Figure 1

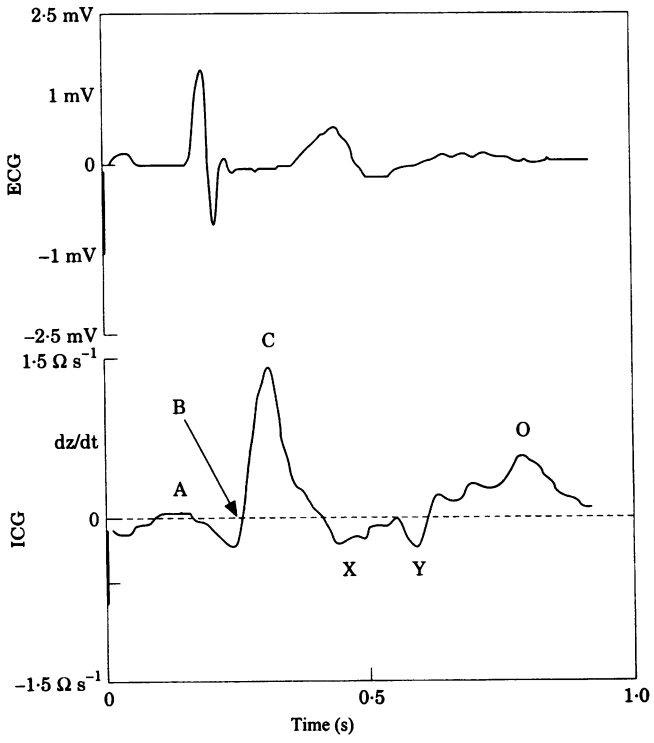

Fig 1. Impedance cardiogram with simultaneous ECG recording at 25 mm/s during sinus rhythm. A=A wave representing atrial systole, B=B point corresponding with aortic valve opening, C=C wave representing ventricular systole, X=X point corresponding with aortic valve closure, Y=Y point corresponding with pulmonary valve closure and O=O wave representing ventricular filling. ICG= impedance cardiogram.

averaged to provide the ensemble averaged complex. In the cases of ventricular fibrillation no R waves were present and ensemble averaging was performed using the peaks of the fibrillatory waveform that were greater than a threshold value (0.2 mV) as reference points. Similar amplitude criteria are employed in the detection algorithms of current automatic external defibrillators. In agonal rhythm, the peak of the ECG complex was used as a reference point. In asystole no reference point was available and averaging was performed at second intervals over a 5 s period.

Using the same analysis software, features of the ensemble averaged complex were manually extracted. These features included Peak dz/dt (the peak of the impedance cardiogram measured from the line dz/dt=0 Ωs^{-1}), Peak-trough (the peak-to-trough measurement of the impedance cardiogram Ωs^{-1}), Area 1 (the area under the C wave of the impedance cardiogram above the line dz/dt=0 mΩ) and Area 2 (the area under the impedance cardiogram 50 ms on either side of the Peak and above the line dz/dt=0 mΩ) (figure 2).

The analysis software also measured the R-R interval enabling a heart rate to be calculated. No R-R interval exists in either asystole or ventricular fibrillation. In agonal rhythm the interval was measured between the peaks of two consecutive complexes.

In the control group, Peak dz/dt measured using the two-electrode technique was correlated with the four-electrode technique. Baseline impedance (Z) and Peak dz/dt in the two groups were compared using the paired t-test.

The arrest rhythms encountered were divided into two groups: Group 1 contained rhythms associated with haemodynamic collapse ie no pulse – asystole, ventricular fibrillation, agonal rhythm and electromechanical dissociation or

Figure 2

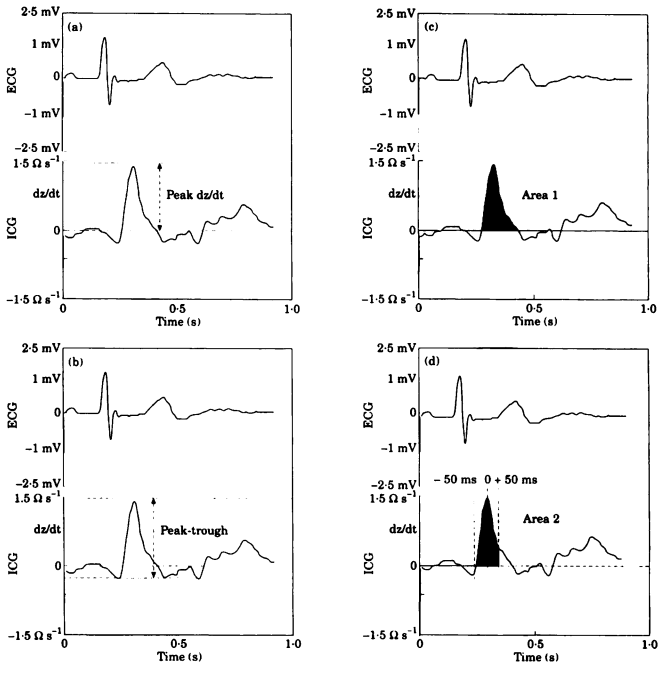

Fig 2. The impedance cardiogram derived parameters: (a) Peak dz/dt, i.e. the maximum value of the impedance cardiogram measured from the line dz/dt=0; (b) Peak-trough, i.e. the peak-to-trough measurement of the impedance cardiogram; (c) Area 1, i.e. the area under the C wave of the impedance cardiogram above dz/dt=0; (d) Area 2, i.e. the area under the impedance cardiogram curve 50 ms on either side of the peak and above dz/dt=0.

shockable ventricular tachycardia as defined by ventricular tachycardia associated with loss of consciousness, pulselessness or a systolic blood pressure of less than 80 mm Hg. Group 2 contained rhythms of patients where a cardiac arrest call was initiated but on arrival with the patient sinus rhythm was present in five (respiratory arrest) and in 20 with non-shockable ventricular tachycardia the patient was conscious with a pulse.

There was a significant correlation between Peak dz/dt measured using the four-band electrode technique and the two ECG/defibrillator pads method ($r=0.61$, 95% confidence interval 0.43 to 0.83, $p<0.01$) However, the two ECG/defibrillator technique resulted in significantly greater values of Peak dz/dt and Z ($1.540 \pm$ SD 0.649 vs $0.908 \pm$ SD 0.192 Ωs^{-1}, $P < 0.001$ and $65.7 \pm$ SD 13.9 vs $22.8 \pm$ SD 2.8, $P < 0.001$ respectively).

Of the 116 recordings, nine were rejected because of severe motion artefact and/or electrical interference. No recordings were rejected as a result of other adverse physical circumstances. Of the remaining 107 cardiac arrest calls, the rhythm initially recorded was: asystole in 19 (17.8%), ventricular fibrillation in 14 (13.1%), agonal rhythm in 20 (18.7%), electromechanical dissociation in 22 (20.6%), shockable ventricular tachycardia in 7 (6.5%), non-shockable ventricular tachycardia in 20 (18.7%) and sinus rhythm in five (4.7%). For each impedance cardiogram parameter there was a progressive fall in the mean value from sinus rhythm to non-shockable ventricular tachycardia to shockable ventricular tachycardia to each of the pulseless rhythms (ie electromechanical dissociation, agonal rhythm, ventricular fibrillation and asystole).

There was no significant difference between Groups 1 and 2 with regard to age or sex. There were significantly more out-of-hospital arrest calls in Group 1 and a significantly greater delay to cardiopulmonary resuscitation and intensive care. The mean initial heart rate, where assessable, was significantly greater in Group 2 and each of the impedance cardiogram-parameters was greater in Group 2 (ie Peak dz/dt, Peak-trough, Area 1 and Area 2).

Using multiple logistic regression the variables age, sex, heart rate, Peak dz/dt, Peak-trough, Area 1 and Area 2 were removed in a stepwise fashion until statistical significance was reached. The two parameters which best predicted a low or absent cardiac output (Group 1) were Area 1 and the Peak-trough measurement. Using these two parameters 78 of 82 (95.1%) patients in Group 1 and 20 of 25 (80%) patients in Group 2 were correctly classified. In particular the higher the value of the peak-trough of the impedance cardiogram the less likely is the rhythm to be shockable. This should help confirm the decision making process where the lay public alone are using the defibrillator.

Follow-up

In 1991 we looked at a 20 year follow up of our out-of-hospital cardiac arrest patients with ventricular fibrillation.[32] The major factors contributing to in-hospital mortality were cardiogenic shock after defibrillation, coma on hospital admission, age ≥ 60 years and ≥ 4 shocks to correct ventricular fibrillation.[33] After five years follow-up, 41% were alive.[32]

Aetiology of cardiac arrest in the community

Whilst ischaemic heart disease is the commonest cause of cardiac arrest, nevertheless there are other causes. One that is increasing in frequency is that seen following substance abuse and drug overdose. In this city two 16 year old males have survived resuscitation from cardiac arrest associated with either butane gas inhalation or glue sniffing. It is well known that the mortality from volatile substance abuse in the United Kingdom has its highest incidence in those aged 15-19 years. The most frequent solvents commonly encountered in abuse related deaths are fuel gases – cigarette lighter refills (butane), propane and gasoline, and typewriter correction or dry cleaning fluids or that contained in fire extinguishers. Others less frequently inhaled are adhesives (toluene and aerosol propellants ie Halons and/or Butane). The mechanism of cardiac arrest from substance abuse can be either a cardiac arrhythmia (major risk), or anoxia with respiratory depression and vagal stimulation, or aspiration of vomit or trauma or a combination of all three.

It is estimated that 220 out-of-hospital cardiac arrests occur among 500,000 people each year and with present resuscitation facilities 30-40 individuals should leave hospital alive. Ventricular fibrillation despite being a chaotic rhythm has a peak frequency and this peak is higher the shorter the time from onset of ventricular fibrillation to successful defibrillation.[34]

RESUSCITATION – THE FUTURE

Defibrillators for out-of-hospital use are getting lighter with the minimum of controls for the lay public. One of these is now produced in Belfast (Samaritan Defibrillator) and is shown in Figure 3 where after the two electrode pads are placed in the appropriate positions on the chest wall and the monitor turned to on, and following the advice to defibrillate for ventricular fibrillation the shock can be delivered by pressing the third button. There is a facility to download the information on arrival in hospital and thus a hardcopy write out can be obtained.

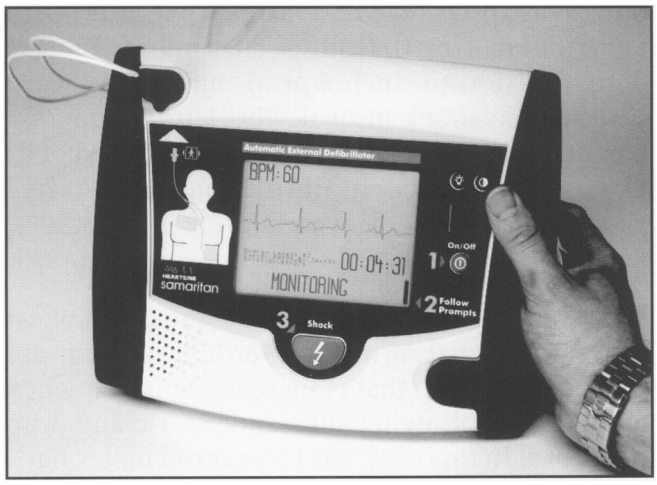

Fig 3. The Samaritan Defibrillator.

CONCLUSIONS

When ventricular fibrillation is corrected by a DC shock and the heart restarts, this equates to the pendulum movement restarting the clock. Each minute that passes with the patient in cardiac arrest decreases the chance for a successful outcome.

The fundamentals of cardiopulmonary resuscitation and instructions for cardiopulmonary resuscitation are available on the internet at http://www.learncpr.org and the skills of advanced cardiovascular life support can be obtained from http://www.cpr-ecc.org. Automatic external defibrillators have now been available for over a decade in airplanes, airports, shopping malls, casinos, stadiums, exercise facilities, office buildings and other public locations such as train stations. Public-access defibrillation has now come of age. A few trained personnel with the necessary equipment can bestow the greatest of all benefits – the saving of a human life.

In the words of Hilaire Belloc (1870-1953) *"For a Sun Dial" – Loss and possession, death and life are one, there falls no shadow where there shines no sun.* Both death and life are one in the process of resuscitation and the sun still continues to shine casting a shadow pointing to newer developments with the potential to improve the longterm survival for victims of cardiac arrest.

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A survey of diabetes care in general practice in Northern Ireland

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SUMMARY

We aimed to describe some key features of diabetes care carried out in primary care settings in Northern Ireland using a descriptive postal questionnaire survey sent to every general practice in Northern Ireland. 252 (70%) of practices responded. Of these 92% of practices have active registers of people with diabetes, identifying 1.9% of their population as having diabetes and 85% of practices use these registers for call/recall visits. Seventy five per cent of practices held diabetes clinics run by the general practitioner and nurse (63%) or a nurse alone (32%). Only 47% of practices felt they received adequate support from the acute diabetes team; with 29% meeting with them this team regularly and only 19% having a shared care protocol. Overall practices provided most of the routine care for 60% of their diabetic patients. The majority of GPs and practice nurses had received some diabetes education in the previous year. There has been a considerable change in the delivery of routine diabetes care in Northern Ireland. A large proportion of diabetes care now takes place in the community, much of it delivered by practice nurses. The organisational infrastructure necessary for the delivery of care is in place. Many practices have special interest in diabetes but the survey highlights a need for better communication and cooperation with secondary care. General practitioners recognise their educational needs in diabetes. They should also be aware of their practice nurses' needs, which should be addressed. There should be initiatives to improve the primary-secondary care interface in Northern Ireland.

INTRODUCTION

We report the outcome of a survey of the organisation of diabetes care in general practice in Northern Ireland. This survey follows on from one reported in 1991 in Northern Ireland [1] and uses a similar method to a survey undertaken in England and Wales reported in 2000.[2] From the previous study undertaken in Northern Ireland we know that by the late 1980's the focus of care for people with diabetes, especially those with Type 2, had begun to shift from hospital clinics to general practice. The authors of this study [1] sent a questionnaire to every practice in Northern Ireland and visited those practices which expressed an interest in further contacts.

The survey in England and Wales was undertaken approximately ten years after the Northern Ireland survey, and showed that a large proportion of diabetes care was being delivered in the community, much of it delivered by practice nurses. In the light of recent proposals to reform primary care in Northern Ireland it was considered that it would be important to discover if there was a similar pattern of care in Northern Ireland.[3]

Systematic review of studies comparing standards of care delivered to patients with diabetes in primary and secondary care have shown that primary care can equal secondary care, but only where general practitioners (GPs) have a special

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interest in diabetes, and the care is well organized.[4] There have been many published reports of successful area-wide initiatives.[5-8] These reports were all based in mainland UK and because of the enthusiasm of the individuals involved may give an over-optimistic impression of diabetes in primary care.

The aim of the current survey was to detail the degree of involvement in diabetes care reported by general practice and to identify the prevalence of the following key features of GP service provision in Northern Ireland: protected time for diabetes care; disease registers; practice nurses with some knowledge of diabetes: and written protocols agreed with local diabetologists. In 1997 the British Diabetic Association BDA (now Diabetes UK) and Primary Care Diabetes (PCD) UK recommended these key features for effective general practice diabetes care.[9]

METHOD

Refining the questionnaire

The authors (C.K., M.P.) were involved in the questionnaire development for the 2000 study.[2] This questionnaire was developed via iterative consultation with members of the PCDUK Steering Committee. As this questionnaire had been validated by this study it was decided to apply the same questionnaire in our study. It was decided to add two questions about problems and barriers to diabetes care to the previous questionnaire in order to identify problems particular to Northern Ireland. These questions were graded on a scale of 1 to 5 (1 no problem, 5 significant problems). The modified questionnaire was piloted in 20 practices in August 2000.

The questionnaire included:

- Practice demographic information
- Organization of care patients within the practice
- Educational experience of the primary care team
- Interaction with local secondary care

The final questionnaire on primary care diabetes was sent to all 358 Northern Ireland practices addressed to named GPs. The covering letter specified that if the addressee was not involved in diabetes care it should be passed to a more appropriate partner. Non-responders were telephoned within one month and invited to complete the questionnaire on the telephone. Remaining non-responders were sent a second mailing in November 2000.

RESULTS

Seventy percent of practices (252/358) responded. The characteristics of the responding practices are shown in Table I. Practices responding to the questionnaire were similar in list size and numbers of practices to those of Northern Ireland as a whole. However all 69 training practices in Northern Ireland responded to the survey. Training practices are over-represented amongst the responders.

Involvement of the practices in diabetes

Table 2 shows the involvement of the practices in diabetes care. It also details key features of the organization of that care within general practice.

TABLE I

Characteristics of the responding practices

		n
Practice list size (mean)	5,647	252*
Number of principals per practice (mean)	3	252*[a]
List size per principal	1912	252*[b]
Number of training practices responding	69(27%)	252*[c]

* Number of practices that participated in survey

[a] Mean number of principles per practice in Northern Ireland is 3

[b] List size per principal in Northern Ireland is 1882

[c] There are 358 practices in Northern Ireland in total of which 69 are training practices

TABLE II

The Organisation of diabetes care

	Yes(%)	*n*
Would you describe your practice as having a special interest in diabetes?	169(71%)	242
What is the total number of people with diabetes in the whole practice	108 (mean)	252
What percentage of these patients are having most or all of their routine diabetes care in general practice	151(60%)	252
Do you have an active register of patients with diabetes in your practice	232(92%)	252
Is it used for call/recall?	214(85%)	252
Is it fully computerised?	166(66%)	252
Do you have dedicated time for diabetes-only clinics in the practice?	141(75%)	188
How frequently are these held?		185
Weekly	35(19%)	
Fortnightly	55(30%)	
Monthly	75(41%)	
Other	20(10%)	
Who runs the clinic?		186
GP and nurse	117(630%)	
Nurse alone	59(32%)	
GP alone	10(50/o)	
Median number of patients seen per clinic	8	

TABLE III

GPs and practice nurses attendance at courses/meetings in diabetes

	*GPs**	*Nurses***
Courses duration half a day	85(40%)	21(11%)
Course duration one day	72(34%)	56(29%)
Course duration more than one day	38(18%)	103(53%)
Duration not known	19(9%)	14(7%)

* 214 practices answered this

** 195 answered this

Almost three quarters of GPs stated that their practice had dedicated time for diabetes-only clinics. Over one third of practices see ten or more patients per clinic whereas, 18% see less than five patients per clinic. Most commonly GPs and nurses run the clinics together (62%). Nurses run 32% of such clinics alone. Clinics are seldom run by GPs alone (5%).

Most of the respondents would be keen to receive extra help to facilitate the clinics (68%). Of the percentage who volunteered what help might be most useful, forty percent of GPs stated that the presence of a dietician would be most useful with other types of assistance required including a chiropodist, more nursing staff and clerical hours, administrative support and a specialist diabetic nurse.

Education and training and professional contacts

Table III shows GPs and practice nurses attendance at courses and meetings on diabetes. The majority of GPs (85%) had attended a PGEA approved diabetes course or meeting within the last three years. The majority of the courses (73%) lasted for either a day or half a day, but 18% had attended a course that lasted for more than one day. In three quarters of practices, a practice nurse had attended a diabetes-training course within the last three years. Only 14% had not. Over half (53%) of these courses lasted for more than one day and 40% lasted for either one day or half a day.

Relationships with secondary care

These are detailed in Table IV. Less than half of the respondents considered that they received adequate support from the acute diabetes team. Only 29% of GPs or their practice nurses meet regularly with a member of an acute diabetes specialist team. The frequency of these contacts is detailed in Table V.

Over three quarters of practices do not operate a shared care protocol (79%). Only 19% operate this form of protocol, although there were a number of variations on how it operated. These positive respondents were asked to comment on how this operated. Eighteen percent of these said they 'followed local diabetes shared care guidelines'. Fifteen percent said they were 'sharing with local hospital'. The remainder used

TABLE IV

Relationship with secondary care

Statement	*Yes(%)*	*n*
Do you operate a formal shared care protocol?	47(19%)	252
Do you or your practice team meet with any members of an acute diabetes specialist team?	74(29%)	252
Do you feel the practice receives adequate support from the acute diabetes team?	119(47%)	252

Table V

Frequency of contact with an acute specialist team

Frequency of contact with an acute specialist team member	*Percentage*	*n*
Weekly	4(5%)	74
Monthly	16(22%)	74
Three monthly	12(16%)	74
Six monthly	10(14%)	74
Less often	32(43%)	74

TABLE VI

Problems and barriers to care

Problems or barriers to care identified	*Percentage of respondents who found the problem significant (graded 4 and 5)*
Getting patients to alter lifestyle	75%
Lack of time	52%
Communications with secondary care	30%
Patient non-compliance	21%
Non-attendance of patients	18%
Inadequate chiropody services	29%
Inadequate ophthalmology services	17%
Lack of access to hospital consultants	16%

less widely used processes such as the patient being seen by a consultant, and the GP providing on going care. A few patients had a co-operation card and juvenile and insulin dependant patients were principally referred to hospital care only.

Relationships with other external diabetes agencies

The GPs were asked whether there was a Local Diabetes Advisory Group. Seventeen per cent said there was no advisory group and 34% replied that there was. Almost half (49%) of respondents did not know. Only 30% of practices belonged to Diabetes UK.

Challenges to high quality primary diabetes care

GPs were asked to score problems experienced in providing care to individual diabetic patients on a scale one to five (5 equated to a major problem.) The most commonly reported major problems were getting patients to alter their lifestyles, lack of time, communication with secondary care, and inadequate chiropody services (Table VI).

When barriers to individual practices proving good diabetes care were considered, lack of time (reported as a major problem by 57% of GPs), under funding (57%), lack of space (26%) and keeping up to date (23%) all were scored between 4 to 5 on the 1-5 scale. As for problems with individual patients 26% considered lack of space, facilities and gadget as important. Keeping up to date with protocols was deemed a significant problem for the practice by 23% of GPs.

Problems were also identified in terms of specific areas of service provision. 29% of GPs considered that inadequate chiropody services presented barriers to the practice in providing diabetes care and inadequate chiropody and ophthalmology services were considered a problem by 16% and 17% of GPs respectively. A further problem identified by 16% of GPs was lack of access to hospital consultants. Other problems that were documented by GPs included having no diabetologists, a lack of dietetics, and lack of communication between hospital and GPs. Some GPs reported not being confident about the eye examination for diabetes.

DISCUSSION

Diabetes-related activity

An important result is the amount of diabetes-related activity that practices have reported. Allowing for the significant number of small or medium sized practices in Northern Ireland, the typical practice has 100 registered patients with diabetes. This concurs with the previous study done in England and Wales [2] and lies within the range of prevalence estimates of known diabetes registers (1.5%-2.08%),[9,10] suggesting that practice registers across Northern Ireland are successful in recording known diabetes. This shows a considerable improvement from the 1988 N.I. survey when only 7% of practices could obtain numerical results from the computer.[1]

Seventy one percent of the responding practices

described themselves as having a special interest in diabetes. These practices are delivering all or most of the routine diabetes care to 60% of their diabetic patients within a general practice setting.

This shows a considerable change in the delivery of care from the 1988 survey, when only 45% of the surveyed practices did diabetes care.[1] Other localized studies have addressed the percentage of patients who are fully managed that is have their annual diabetes review in general practice (40%-50%).[10,11] A system of Chronic Disease Management was introduced throughout the UK in 1993, and we know claim that approximately 90% of general practices in N.I. claim chronic disease management payments. The requirements under this system are to ensure that reviews are taking place, and not to necessarily carry out the reviews within the practice.

Organisation of care

92% of practices in N.I. have an active register of people with diabetes. Chronic Disease Management of diabetes requires practices to keep a disease register. 85% of practices use this register for call/recall visits. This would suggest that these registers are kept for active reasons and the database of people with diabetes in Northern Ireland is held within general practice.

Over two thirds of practices have a fully computerised active register although one third do not. In the study reported in 1988 only 43% of practices had a practice computer, so this shows a considerable improvement.

Clinics

This study showed that diabetes clinics are the most common method of providing diabetes care in general practice. Most held monthly clinics. This is a considerable change from 1988 when only 15% of practices had special arrangements for diabetic patients. Most of the literature on 'best practice' assumes a clinic-based model.[12] This model has potential problems. It may lead to those not involved in the clinic becoming deskilled and disruption of doctor-patient relationships unless avoidance strategies are employed.

Moreover the clinic-based strategy may be inappropriate for some practices. 25% of the practices in the study did not have diabetes clinics. Typically the clinics in this study had approximately eight patients per clinic and were usually run jointly by the doctor and the practice nurse. These findings concur with the survey in England and Wales,[2] suggesting that this is the most popular method of delivering care.

Role of the practice nurse

The study underlined the significance of practice nurses to the delivery of diabetes care in general practice. They were involved in running almost all the clinics either jointly with the GP or alone – 32% of GP clinics were run by the nurse alone. This emphasises the importance of providing adequate support for the practice nurses. In the 1988 survey less than one third of practices identified a practice nurse with an interest in diabetes. It is not clear from our survey whether GPs were also carrying out an annual review as recommended by Diabetes UK.

Education

Given this high percentage of diabetes care being delivered in general practice it is encouraging that most GPs were engaged in further training and recognised the importance of attending diabetes courses. The value of the educational experiences of these courses to the doctors and nurses is unknown and it should be recognised that many will have been supported by the pharmaceutical industry. The fact that most had attended a full day of PGEA – approved activity in the past three years reflects the reasonable provision of such courses in Northern Ireland.

This may be also borne out by the fact that the GPs reported less educational activity on the part of their nurses, with only three quarters attending course in the past year. This does not concur with the England and Wales study and presents an unrecognised need on the part of practice nurses for further training or initiatives supported by the boards. Diabetes UK holds at least one annual primary care orientated meetings locally. Unfortunately only 30% of practices locally are members of Diabetes UK. This is disappointing given the amount of patient and professional support that can be accessed through this charity.

Relationships with secondary care

There would appear to be a difference in our study and the England and Wales study in the amount of professional contact with secondary care. In the England and Wales 80% of practices received adequate support from secondary care and 60% had regular contacts. In Northern Ireland 29% had support and only 22% had regular contacts. This may reflect the either the relative dispersal of diabetes teams, or the rural nature of

general practice in Northern Ireland. They may feel that they can manage without support or they have a low expectation of support from secondary care.

Whilst podiatry and dietetics cover both secondary and primary care the respondents felt that they had better support from these. This shows encouraging support from these services locally, with a much higher percentage of practices feeling better supported by these services, than secondary care services.

Limitations of the study

As this was a postal survey, this study could only examine a limited number of aspects of diabetes in general practice. It also did not address the issues of standards of care in general practice.

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Smoking in pregnancy – the size of our challenge

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SUMMARY

Reducing the prevalence of smoking in pregnancy is a priority target for health care. We administered a semi-structured questionnaire to mothers in an inner city general practice who were given brief anti-smoking advice during routine antenatal care. Of a cohort of 113 mothers, 52(46%) reported smoking at the start of pregnancy. Six(12%) of these 52 smokers reported no change in smoking habit during pregnancy; 24(46%) cut down; 12(23%) stopped; 10(19%) increased their cigarette consumption. Of the 52 smokers, 41(79%) believed smoking was harmful to an unborn baby, yet 30(73%) of these women continued smoking. Almost all recalled having been given anti-smoking advice by the GP and/or hospital. There is an urgent need to identify more effective methods of reducing smoking in pregnancy.

INTRODUCTION

While the overall prevalence of smoking is decreasing,[1] its prevalence among women, compared to men, is increasing, especially among teenagers.[2] Health inequality is increasing[3] and smoking is more prevalent in the lower socio-economic groupings.[4] Smoking in pregnancy has adverse effects on the mother's health and carries health risks for a fetus.[5, 6]

A reduction in smoking in pregnancy is a priority for health care.[1] Some women stop smoking without assistance when they become pregnant but cessation may be enhanced by advice from a health professional.[7, 8] Much of the evidence that health professionals could do more to promote smoking cessation comes from a research environment.[7, 9, 10]

This study aimed to determine, within an inner city general practice, the extent of self-reported efforts to quit smoking, after brief anti-smoking advice was given during routine antenatal care and to examine levels of knowledge in terms of patients' reported perceptions of harm and recall of advice. Brief anti-smoking advice involved asking the patient if they smoked and, if they did, if they would consider stopping. For those who wished, further help was available and was tailored to the individual.[8] Details of help provided were not recorded for the purposes of this study. A poster was displayed in the waiting room and information leaflets were available. It was the practice policy to mention the subject of smoking on a regular basis, thus reinforcing advice through repetition, with care being taken not to alienate patients from future consultations.

METHOD

This study was carried out within an inner city practice in a socially deprived area of Belfast, by a final year medical student with the supervision of a GP partner: research ethical committee approval was not sought.

In December 1999 computer records were used to identify mothers of all children aged under 18 months. Those who had not attended the practice for antenatal care and those who were known to have personal circumstances such that questioning regarding smoking might have caused distress were excluded.

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Patients were contacted by telephone by the medical student who invited their participation in a questionnaire survey of smoking habits. House calls were made if attempts at telephone contact failed. The student read out the questions from a piloted questionnaire and recorded responses. Those who reported not smoking or smoking less than one cigarette per day just before their last pregnancy were not classified as smokers. Interviews lasted less than ten minutes. Responses to open questions were reviewed by two researchers independently and those relating to reasons for changing their smoking habit were categorized into themes. No difference in attitude was noted between those contacted by telephone and others where a house call was made.

The sample size was arbitrary. The practice partners had been trying to promote smoking cessation among antenatal patients for two years prior to the study by giving brief advice: they wished to include approximately 50 patients.

Anonymous data were entered on to SPSS: statistical calculations of interrelationships of variables were inappropriate.

RESULTS

From the practice records 152 mothers were identified but 15 were excluded: 12 had not attended the practice for antenatal care; three had relevant problems. Of the remaining 137, 117 were successfully contacted but four declined to participate. The smoking status of these 24 mothers is unknown. Of the 113 who participated, 52(46%) reported smoking immediately prior to their last pregnancy. If the non-participants were non-smokers, the population's smoking prevalence would be lower (52/137; 38%).

These self-reported smokers ranged in age from 18 to 43 years (mean and median 27 years).

Changes reported in smoking habit during pregnancy

Smoking prevalence fell during pregnancy to 35% (40/113). Twelve of the 52(23%) smokers reported stopping; 24(46%) cut down; 6(12%) reported no change and 10(19%) reported increasing cigarette consumption.

The reason which was most frequently stated for cutting down or stopping was concern for the unborn baby (29/36; 81%) (Table I). Reasons for increasing cigarette consumption were not specifically sought but many told of their "craving" for cigarettes while being pregnant and others blamed the stressful prospect of having another child. Most changes in smoking habit occurred in the first trimester (Table II).

TABLE I

Main reasons for cutting down or stopping smoking during pregnancy (N=36)

Reason	*N (%)*
Concern for unborn baby	29 (81)
Encouragement by family	2 (6)
Advice from hospital	2 (6)
'Went off' cigarettes	3 (8)

Table II

*Smoking Habit Change during pregnancy by trimester**

	Cut Down n%	*Stopped n%*	*Increased n%*
1st Trimester	20(83)	10(83)	6(60)
2nd Trimester	4(17)	2(17)	4(40)
3rd Trimester	0	0	0
	24	12	10

* Note: N=52; 6 did not change their smoking habit in any trimester

TABLE III

Categories of smokers' perceptions of possible harmful effects of cigarette smoking (N=52)

Categories of possible harmful effects	N (%)
May affect unborn baby, child and adult	40 (77)
May affect unborn baby and child	1 (2)
May affect child and adult	6 (12)
May affect adult only	2 (4)
No harmful effects	3 (6)

Perceptions of harm of smokin

A belief that smoking was harmful to the unborn baby was reported by 41 of the 52 mothers (79%), yet only 11 of these stopped and 30 continued smoking. Variable beliefs regarding possible harmful effects were reported (Table III). Three mothers, who all continued smoking, reported

believing that smoking was not harmful to anyone. Of the 11 who did not believe that smoking harmed the unborn baby, one stopped and four cut down their consumption.

Recall of advice given on smoking during pregnancy

The majority recalled being given advice about smoking during pregnancy by the GP (43/52; 83%) and/or hospital (50/52; 96%). One denied having received advice from either the GP or hospital; she believed that smoking was harmful to the unborn baby, child and adult and stopped smoking during pregnancy. Nine of the 11 mothers who denied believing that smoking harmed an unborn baby recalled being given advice by the GP.

Postpartum resumption of smoking

Seven of the 12 mothers who stopped smoking during pregnancy resumed smoking afterwards (58%); those who remained stopped were three, eight, nine, eleven and eighteen months postparturn at the time of interview. Of the 24 who cut down, 17(71%) had resumed or increased their previous level of consumption.

DISCUSSION

These results indicate that 46% of women in an inner city population are smoking at the start of pregnancy, and 35% continue smoking, but they are based on findings in one general practice only. These figures are somewhat higher than those currently reported for the general population but smoking prevalence is higher among economically inactive women in the unskilled manual socio-economic grouping.[4] The study participants were largely economically inactive. They lived in an area of socio-economic deprivation (approximately 3 miles radius) within the city of Belfast. It is suggested that the sample is representative of the wider population of pregnant women presenting to inner city general practices.

The reported prevalence of smoking in pregnancy may have been even higher if mothers had been interviewed during pregnancy and a measure of biochemical validation had been included. Accurate disclosure of smoking status is a fundamental problem in research and is related to the possible consequences of disclosure but inaccuracies in self-report are more likely to be conservative than to over-represent the size of the problem.[11, 12, 13] Mothers of young children who are aware of possible harmful effects of cigarettes may not disclose their smoking and may over-report their attempts to comply with advice from health professionals.

The researcher did not detect any differences in responses or attitudes to questioning between patients who were telephoned and those who were visited in their homes. Formal comparisons, unfortunately, were not possible since the type of contact for each patient was not recorded specifically at the time of study. On reviewing the data, it was estimated that approximately two thirds of contacts were by telephone and one third by visits.

The 24 non-participants' smoking status is unknown. If these non-participants were nonsmokers, the study sample's smoking prevalence would be lower (52/137; 38%). However, information gained in trying to establish contact did not suggest that they differed from participants in socio-economic status or economic activity. Difficulties in contact included changed telephone numbers and addresses and different surnames of child, mother and father. It is considered unlikely that there was bias in recruiting participants in respect of their smoking habits.

The cessation rate of 23% during pregnancy falls short of government targets.[1] Encouragement may be derived from the 'cut down' rate of 46% but this strategy is unlikely to lead to cessation.[14] Reasons for increasing smoking during pregnancy included the stress associated with the prospect of having another child. In promoting smoking cessation it must be recognised that smoking is perceived by the socially disadvantaged to relieve pressures associated with hardship, poor housing and single parenthood.[15]

The level of cessation reported by patients in this study was disappointing but the reported level of recall of advice having been given (83%) surpasses previous reports of primary care activity: of smokers attending hospital antenatal clinics only 34% reported having received GP advice.[10] It may be suggested that the current responses are biased because the observer was identified with the practice but she was not known to the patients nor involved in their care: it is considered that they accurately reflect the practice's active policy in promoting smoking cessation.

Current findings in relation to post-partum resumption of smoking are in keeping with previous work.[16] Approximately 80% of those who reduced or stopped during pregnancy did so because of concerns regarding the unborn baby. The absence of this motivation after childbirth may be a factor in restarting smoking.[17]

The apparent contradiction that many women continued smoking despite believing that it was harmful to the unborn baby supports the observation that knowledge of risk does not appear to be a major determinant of maternal smoking.[10] Statements such as: *"It's never done myself or the kids any harm"* and *"I know they've got asthma (the children) but it runs in the family "* may help to explain why women, who say they believe it is harmful, continue smoking. If personal experience contradicts advice imparted by health professionals, beliefs of harm may be held weakly and personal threat may not be perceived. There is variation in beliefs held by pregnant women regarding different possible harmful effects of cigarettes.[18] Haslam has suggested that a targeted health care approach to maternal smoking cessation should be combined with wider community initiatives.[19]

Consistent with previous reports, most changes in smoking habit, regardless of type, were reported in the first trimester. Thus, maximal efforts to promote smoking cessation should be made early in pregnancy.

The difficulties in initiating contact with patients illustrate problems encountered in trying to provide preventive care for this population. The workload involved may often be greater than that recognised when planning health care delivery. It is essential that the efforts of health professionals in attempting to achieve government targets among socially disadvantaged communities are adequately resourced.

CONCLUSION

This study gives an indication of the size of the challenge facing those involved in helping antenatal patients stop smoking – almost half of those presenting within an inner city practice are likely to require this help. The outcomes are those of routine clinical care rather than of a research environment. Knowledge of the risks of smoking together with anti-smoking advice and recall does not necessarily result in an appropriate behavioural change. There is an urgent need for the best efforts of health professionals to be informed by further research regarding methods of achieving smoking cessation in routine clinical practice.

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Laparoscopic managment of common bile duct stones: our initial experience

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SUMMARY

The management of choledocholithiasis has changed radically since the introduction of laparoscopic cholecystectomy. However, perceived technical difficulties have deterred many surgeons from treating common bile duct stones laparoscopically at the time of cholecystectomy. This has lead to reliance on endoscopic retrograde cholangiopancreatography followed by endoscopic sphincterotomy to deal with common bile duct stones. We retrospectively reviewed the charts of patients who had laparoscopic common bile duct exploration at Downe Hospital between December 1999 and August 2001. Among 149 laparoscopic cholecystectomies done by our group in this period, 10 patients (6.7%) underwent laparoscopic CBD exploration, three by the transcystic technique and seven by choledochotomy. Three patients (2%) had unsuspected stones found on routine per- operative cholangiogram. The mean operative time was 2.34hrs (range 1.50-3.30hrs). The mean hospital post- operative stay was 3 days (range 1-6 days). Post-operative morbidity was zero. Stone clearance was achieved in all cases. We conclude, laparoscopic exploration of the common bile duct is relatively safe and straightforward method. The key skill required is the ability to perform laparoscopic suturing with confidence.

INTRODUCTION

The incidence of choledocholithiasis in patients with cholelithiasis is reported at 5%-10%, with 4% to 5% incidence of unsuspected choledocholithiasis when routine cholangiography is performed.[1-4] During the era of open cholecystectomy the management of choledocholithiasis was relatively straight forward but with the advent of laparoscopic cholecystectomy the treatment of common bile duct (CBD) stones, whether recognised pre-operatively or per-operatively remains controversial. Treatment options include selective pre-operative endoscopic retrograde cholangiopancreatography (ERCP); conversion to open choledochotorny,[5] post-operative ERCP with endoscopic sphincterotomy (ES) and a one-stage laparoscopic clearance of CBD stones.[6] Many surgeons performing laparoscopic cholecystectomy remain uncomfortable with laparoscopic exploration of the common duct, and therefore, ERCP with ES is commonly used to treat choledocholithiasis. There are several disadvantages with ERCP. Selective pre-op ERCP for suspected CBD stones results in a large number of negative studies[7] and it also fails to address the issue of unsuspected CBD stones found at per-operative cholangiography. Conversion to open surgery after positive cholangiography adds its own morbidity. Post-operative ERCP with ES for those stones discovered at surgery has a clearance rate of around 90% in experienced hands.[8] It also places the patient at risk of the complications of sphincterotomy including pancreatitis, perforation and bleeding.[9-12] The morbidity of ERCP with ES has been described as around 10% and the mortality around 1- 2%.[8] Laparoscopic CBD exploration can be the option for choledocholithiasis, as it is possible to solve the problem in a single procedure. It also has the advantage of leaving the sphincter of Oddi anatomically intact and avoids the morbidity

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associated with laparotomy. This study presents our initial experience of laparoscopic CBD exploration over a period of eighteen months in a small district general hospital.

PATIENTS AND METHODS

We reviewed the charts of 10 patients who have undergone laparoscopic CBD exploration between December 1999 and August 2001. Prior to this period patients with suspected CBD stones had ERCP/ES, and patients with CBD stones found on routine per-operative cholangiography during laparoscopic cholecystectomy were usually subjected to immediate laparotomy and choledochotomy. Since December 1999 laparoscopic CBD exploration has been carried out in ten patients. The exploration of the common bile duct requires some additional instruments: a 30° telescope, per-operative cholangiogram cannula (we use a Steriseal Homer 1530 per-operative cholangiogram cannula set) 3mm and 5min flexible choledochoscope/cystoscopes with a second light source, processor and monitor as well as some means of retracting a floppy duodenum. A per-operative cholangiogram is routinely performed in all patients (not just in patients with suspected stones) using an image intensifier in real time. We have found that the best position for the cannula is between the epigastric and mid clavicular ports.

The appropriate method of exploration of the duct is decided.

A) *Via the cystic duct.* [3mm'scope] Small stones can be cleared either by extracting them with a Dormia basket or flushing/pushing them through the papilla, thus avoiding opening the common bile duct.

B) *Direct exploration of the common bile duct.* This involves exposing the anterior wall, making a small transverse choledochotomy and inserting the 5mm 'scope. Stones are easily identified and removed by a dormia basket (size 5.5F). Large stones are best located in the mesh of the basket before extending the choledochotomy to prevent leaking of irrigation fluid. After stone clearance, the choledochotomy wound is closed with a 4-0 continuous absorbable suture.

RESULTS

During a period between December 1999 and August 2001, a total of 149 patients underwent laparoscopic cholecystectomy and ten of these patients (6.7%) had laparoscopic CBD exploration. There were eight female and two male patients with an age range between 21-81 years (average 54.8 years). At the time of surgery, three patients had no evidence to suggest the presence of CBD stones. Of the other seven, three were jaundiced and four had a history of jaundice. Pre-operative ultrasound revealed stones in the common bile duct in five patients, (three of whom had known failed ERCP removal of stones) but in two patients the duct was reported as dilated without any obvious stones. The routine per-operative cholangiogram showed apparent filling defects in all ten cases, but subsequently stones were found only in nine.

Exploration via the cystic duct (3)

In one patient there was a stricture found at the lower end of the common bile duct following sphincterotomy four years previously. This was clearly identified using the 3mm scope via the cystic duct and needed no treatment. One patient had a small stone flushed into the duodenum, and the third patient had the stone extracted using a dormia basket thus avoiding any need to open the common bile duct.

Direct exploration of the CBD (7)

Through a 5mm transverse choledochotomy, stones were extracted using a Dormia basket, with the initial choledochotomy extended in two patients to remove very large stones. The choledochotomy wound was closed with a continuous 4-0 absorbable suture. In the first case there was a stent already in situ so the common bile duct was closed with a degree of confidence, a simple quarter inch drain being placed in the sub hepatic space. In the next patient it seemed logical to insert a stent via the 5mm scope. There was no bile leak in either of these two patients. In the following three cases the common duct was closed around a T-tube (technically easier than anticipated) and there was also no bile leak in these patients. As we gained confidence in the suturing technique we reverted back to placement of a simple drain and closure of the duct without a T-tube or a stent; in last two patients again there was no bile leak.

There were no intra or post-operative complications. The mean operative time was 2.34hrs (range 1.50hrs- 3.30hrs). The post-operative mortality rate was zero. The mean post-operative stay was 3 days (range 1-6 days); the patients with T-tubes being allowed home with

the tubes clamped and returning on day eight for out-patient removal after a T-tube cholangiogram.

DISCUSSION

Several different ways have been described for treating CBD stones, which are diagnosed during laparoscopic cholecystectomy. It would seem logical that the best treatment should be a one-stage technique, with the least discomfort for the patient and with low morbidity. Laparoscopic trans-cystic or trans-choledocic exploration requires superior surgical dexterity [13] and the time required to carry out the procedure is significantly lengthened. Most authors therefore stress the need to perform ERCP as part of the treatment of the common bile duct stones. Some patients certainly require an endoscopic trans-duodenal approach, because of acute suppurative cholangitis, ampullary stone impaction, severe biliary pancreatitis or severe co-morbidities, but the rapid expansion of transduodenal techniques has reopened debates concerning the most appropriate management.[14] The use of ERCP and ES in competent hands gives important benefits to high-risk patients; decreasing morbidity and mortality and at times avoiding a major surgical procedure in carefully selected patients.[15] Benefits need to be balanced against the high incidence of failure rate reported variously between 3%-27% and the serious complications such as bleeding or pancreatitis in the early stage as well as and late stricture or recurrent stone formation.[9-12]

Laparoscopic CBD exploration provides an alternative therapeutic approach which is cost-effective and permits early recovery with a reduced period of short-term disability.[12] The results of a multi-center study reported by Cuschieri *et al* suggest that a single stage laparoscopic treatment is a better option.[7] When the laparoscopic approach for CBD exploration is selected, choices still exist. A trans cystic approach avoids opening the CBD but is limited in usefulness, requiring the cystic duct to be of sufficient size and shape to permit instrumentation and the stones to be small. Direct laparoscopic exploration allows the surgeon to perform a more complete and direct visual exploration of the duct system. As a consequence there is lower incidence of residual stones.[16] we have found the cystic duct approach to be useful in 3 out of 10 cases.

The key to this technique is having confidence to perform laparoscopic suturing, with the magnified image enabling an almost leak proof continuous suture line to be achieved as experience progresses. A simple sub hepatic drain is sufficient in most cases but if there appears to be any narrowing at the lower end of the duct, T-tube placement or even per-operative stenting from above are useful techniques to keep in mind.

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Otolaryngology consultations by real-time telemedicine

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SUMMARY

We aimed to assess the value of real-time telemedicine using low cost videoconferencing equipment for otorhinolaryngology consultations. A general practitioner, using low cost videoconferencing equipment, presented patients to an otorhinolaryngologist. After history taking and clinical examination, investigations were requested if required and a diagnosis and management plan formulated. The patients were then seen, by the same otorhinolaryngologist, for a conventional face-to-face consultation. Differences in the history, clinical examination and investigation requests were reported. The accuracy of diagnosis and correlation of management plans between the two consultations were analysed. Forty-three patients were admitted to the study but one, a young child, refused examination either by tele-link or the conventional approach and had to be excluded. There were thus 42 patients with 55 diagnoses included in the trial, 26 (62%) females and 16 (38%) males. Age range was 5 months to 70 years. There was no difficulty with any of the patients in obtaining an accurate history and ordering investigations, if required, via the tele-link. Clinical examination during the tele-link consultation was inadequate for eight out of the first 20 patients, resulting in a wrong diagnosis in three patients and a missed diagnosis in five patients. All of the next 22 patients had a correct diagnosis and management plan. Comparison of data from the two types of consultation showed that a correct diagnosis and management plan was made in 34 patients. Low cost real-time telemedicine is a useful technique, providing reliable otorhinolaryngology consultations in a general practice setting. However initial difficulties due to inexperience in using the equipment need to be overcome.

INTRODUCTION

Real-time telemedicine as a means of gaining expert advice is fast gaining recognition as a viable alternative to the traditional referral system. Clinical areas such as cardiology and dermatology have demonstrated its value and effectiveness as a diagnostic and management tool.[1-2]

Previous studies have used medium to high bandwidth transmission and have shown that the quality of tele-otorhinolaryngological images are highly acceptable for remote diagnosis.[3-6]

There are no reported formal studies of tele-otorhinolaryngology consultation effectiveness at low bandwidth.

This study aimed to evaluate the diagnostic, investigative and clinical management decisions of otorhinolaryngological conditions using real-time low-cost equipment at low bandwidth transmission.

METHOD

Basic rate ISDN lines at 128kbits/s were connected between two adjacent rooms in a teaching hospital in Belfast. Low cost videoconferencing units (VC7000, BT) were installed in both rooms; one for the general practitioner and patient, the other for the otorhinolaryngologist.

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A video camera with a Storz rigid endoscope (Endovision Dx-cam 20230001) and light source (CLS 150-2, Rimmer Brothers) were connected to the videoconferencing unit in the general practitioner's room to enable transmission of close-up images to the otorhinolaryngologist. The endoscopic camera had a resolution of 752x582 pixels.

Patients with a range of otorhinolaryngological conditions requiring a specialist referral were invited to participate in the study by their general practitioner. All such patients consented to take part in the study and were referred to a pre-arranged tele-otorhinolaryngology clinic.

Conditions such as dysphonia, dysphagia and others requiring indirect laryngoscopy or fibre-optic laryngoscopy were excluded as the general practitioner did not feel proficient in examining these areas and did not have the necessary equipment. Uncooperative patients, who refused examination via tele-link or by conventional approach, were also excluded.

The general practitioner obtained a full, medical history and conducted an examination, which was observed via tele-link by an otorhinolaryngologist situated in an adjacent room. A three-way interactive consultation ensued and the otorhinolaryngologist recorded a history, clinical examination, diagnosis, and management plan. Any investigation required, such as audiometry, was requested during the tele-link consultation.

Following the tele-consultation the patient was seen for a conventional consultation by the otorhinolaryngologist to confirm the history, examination, diagnosis and management plan.

RESULTS

A total of nine tele-otorhinolaryngology clinics was arranged. Forty-three patients attended the above clinics, 27 females and 16 males, with an age range from 5 months to 70 years. One child refused examination during both the tele-link consultation and the conventional consultation and had to be excluded from the study.

Table I lists the range of otorhinolaryngological conditions presenting to the clinic.

Eleven patients presented with two or more symptoms.

There was no difficulty in obtaining an accurate history or ordering investigations, if required, during the tele-link consultation. Twelve patients were referred for audiometry or tympanometry, and two patients were referred for allergy testing. Clinical examination via the tele-link was inadequate in eight patients resulting in a wrong diagnosis in three and a missed diagnosis in five patients.

TABLE I

Presenting conditions	*Number of patients*
Nasal obstruction	14
Hearing loss	13
Recurrent sore throats	7
Tinnitus	4
Otalgia	4
Dizziness	2
Otorrhoea	2
Prominent ear	2
Snoring	2
Aural fullness	1
Facial palsy	1
Nasal trauma	1
Nasal bone deformity	1
Epistaxis	1
Total number of diagnoses	55

TABLE II

Diagnostic accuracy of tele-link consultation compared to conventional consultation

Diagnosis	*Number of patients*
Correct	34
Missed	5
Wrong	3

Thus a correct diagnosis was made in 34 patients (Table II). All eight patients with an incorrect diagnosis were within the first 20 patients assessed. In three patients there was an inadequate view of the tympanic membrane resulting in glue ear being missed and a wrong diagnosis. In five patients it was difficult to obtain adequate nasal views via the tele-link resulting in a deviated nasal septurn (two patients), hypertrophy of inferior turbinates (two patients) and a nasal septal bleeding point (one patient) being missed.

TABLE III

Level of agreement between tele-link consultation and conventional management plans

Correlation	*Number*
Correct	34
Sub-optimal	1
Incorrect	7

All of the next 22 patients assessed had a correct diagnosis.

Table III shows the level of agreement between the tele-link consultation and conventional consultation management plans. There was no agreement in the management plans for seven patients because of an inadequate view using an endoscope during the tele-link consultation. In five of these patients there was difficulty in obtaining an adequate view of their nasal cavities as described above, resulting in a missed diagnosis and subsequent inappropriate management plans. Two patients had glue ear misdiagnosed, again due to inadequate visualisation of the tympanic membranes resulting in inappropriate management plans. Another patient with a history of recurrent otalgia and hearing loss was documented as having normal tympanic membranes by the tele-link consultation but had glue ear confirmed at the conventional consultation and by tympanometry. The management plan for this patient was broadly similar at both consultations, though the level of agreement was recorded as sub-optimal.

All eight patients with less than optimal level of agreement between the two consultations were from the first 20 patients assessed.

TABLE IV

Outcome of conventional face-to-face consultations

Clinical outcome for patients	*Number of patients*
No action needed	19
Review with General Practitioner	5
Surgical waiting list	6
Review at otolaryngology clinic	12

Table IV outlines the outcomes of the conventional face-to-face consultations. Nineteen patients needed no further action to be taken and were discharged. Five patients were referred back to their general practitioner. Six patients required surgery and were placed on the otorhinolaryngology waiting list. Twelve patients were requested to re-attend an otorhinolaryngology clinic for further review.

DISCUSSION

Telemedicine allows consultations between primary care centres and specialised hospital clinics by use of low cost videoconferencing equipment and in real-time. It not only gives access to expert advice, but also has an educational role for the general practitioner [7] and otolaryngologist.

As a health care system develops to meet the needs of patients, expert advice can be easily sought by the use of telemedicine. Patients and general practitioners can receive faster and more efficient advice resulting in a higher quality of health care.

Telemedicine also enables distant case discussion between specialist and sub-specialist, and inter-hospital case discussion between different specialities.[8]

Once a telemedicine link has been established between two centres it allows more efficient use of specialist time and will hopefully reduce the number of unnecessary referrals.

The results of this study demonstrate that the diagnostic, investigative and clinical management decisions of a range of otorhinolaryngology conditions are possible via real-time tele-link consultations using relatively cheap low bandwidth transmission lines.

There is a learning curve in mastering the technique of endoscopic examination with the main difficulty occurring in the correct focusing of the endoscope. However this difficulty can be quickly overcome, as shown in the results of this study. Out of the first 20 patients, examination was inadequate in eight resulting in an incorrect diagnosis and management plan with the tele-link consultation, whereas examination was adequate in the remaining 22 patients.

We feel that using low-cost videoconferencing equipment at a low bandwidth transmission provides satisfactory images. Once the

practitioner acquires the necessary skills and expertise to operate the equipment, accurate diagnosis and clinical management decisions can be made.

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Duodenal stents for malignant duodenal strictures

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SUMMARY

Duodenal obstruction may be caused by inoperable malignant disease. Symptoms of nausea and vomiting have been traditionally palliated by surgery. The aim of the study was to determine the efficacy of the endoscopic placement of metal self expanding duodenal stents for the palliation of malignant duodenal obstruction. Four patients with malignant gastric outlet obstruction are described. One patient had a history of oesophagectomy for oesophageal adenocarcinoma and presented with further dysphagia. At endoscopy the recurrent oesophageal tumour and an adenocarcinoma involving the pylorus were both stented. In the other three patients there was a previous history of colonic carcinoma, cholangiocarcinoma and oesophageal adenocarcinoma respectively. All four patients were successfully stented with good palliation of their symptoms. Duodenal Wallstents are a useful alternative to surgery in patients with inoperable malignant duodenal obstruction or those who are unfit for surgery.

INTRODUCTION

Duodenal obstruction may be caused by inoperable malignant disease. Symptoms of nausea and vomiting have been traditionally palliated by surgery although surgical gastrojejunostomy is associated with significant morbidity and mortality.[1] An endoscopic alternative to surgery, employing the placement of self-expanding metal stents across strictures, has previously been described for malignant gastric outlet obstruction.[2-6] However the number of patients described in the literature is relatively small and it is not routine practice in many institutions.

We describe the efficacy of the endoscopic placement of metal self-expanding duodenal stents for the palliation of malignant gastroduodenal obstruction in four patients.

METHODS

We used self-expanding metallic stents (Wallstent Enteral, Boston Scientific, Microvasive, UK) 22mm in diameter and 60-100mm in length. These stents are constructed from a woven stainless steel superalloy and have a larger diameter than the commonly used biliary stents. Before deployment, these stents are constrained by a transparent plastic membrane (Unistep System) onto a delivery system of outer diameter 10Fr and overall length of 230cm. This long thin delivery system allows the insertion and deployment of stents through the accessory channel (diameter 4.2mm) of an upper gastrointestinal endoscope.

Stents were placed under endoscopic and fluoroscopic guidance. After identification of the stricture, we passed a standard 0.035-inch Zebra guidewire (Boston Scientific, Microvasive, UK) through it using a standard ERCP catheter. We determined the length of the stricture by the distance the catheter travelled over the guidewire

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under fluoroscopic monitoring. The Wallstent Enteral was advanced over the guidewire so that the ends of the undeployed stent were equidistant from the ends of the stricture. We assessed the adequacy of stent placement at the conclusion of each procedure using endoscopy and fluoroscopy.

RESULTS

We carried out the placement of metal self-expanding duodenal stents in four patients with malignant gastroduodenal obstruction. All four patients were unsuitable for surgical treatment in view of their advanced disease as assessed by their attending gastroenterologist and surgeon.

A 57-year old man with a previous history of distal oesophagectomy and proximal gastrectomy in 1996 for adenocarcinoma presented with further dysphagia. At endoscopy a 5cm malignant lesion was evident in the distal oesophagus. A 10cm length 22mm diameter Wallstent was inserted in good position. In addition an infiltrating biopsy-proven adenocarcinoma involving the pylorus was found and two 7cm length 22mm diameter Wallstents were inserted successfully in tandem across the stenosis. The first stent was deployed too distal to the stricture and the second stent was deployed more proximally in good position across the stricture with the distal portion overlapping the first stent. At 2-month follow-up he was eating normally and gaining weight. He died from progressive disease four months following stent insertion.

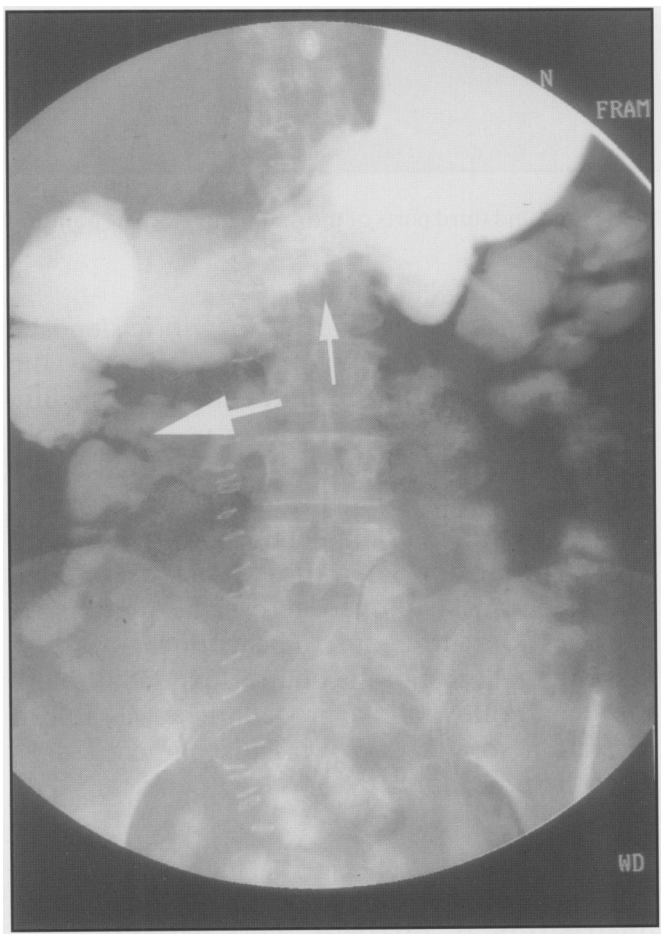

Fig 1. Barium meal demonstrating obstruction between the second and third parts of the duodenum (thick arrow; the thin arrow demonstrates the gastroenterostomy).

A 65-year old lady with previous right hemicolectomy for carcinoma of the colon was admitted with features of duodenal obstruction due to local recurrence resulting in extrinsic compression between the second and third part of the duodenum. An initial attempt at endoscopic placement of a duodenal stent was unsuccessful due to equipment incompatibility. A bypass gastroenterostomy and anterior gastrostomy were performed. The former was complicated by retrograde intussusception of the efferent loop and resulted in further vomiting and a large gastric aspirate (Figure 1). Repeat endoscopy confirmed extrinsic compression between the second and third part of the duodenum and a 6cm length 22mm Wallstent was successfully placed across the extrinsic compression with resolution of her vomiting and a marked reduction in the amount of gastric aspirate (Figure 2). The anterior gastrostomy was then allowed to close over once the duodenal stent had been inserted successfully endoscopically. She was discharged home after a six-week admission and had a two-month period of good symptom control before being re-admitted with symptoms due to an obstructed stent caused by tumour ingrowth. An unsuccessful attempt was made to insert a further stent in tandem in order to relieve the obstruction and co-existent distal small bowel obstruction on contrast studies was also noted at that time. A defunctioning percutaneous gastrostomy was performed for symptom palliation. She died a short time later.

A 64-year old man had a history of inoperable cholangiocarcinoma and was palliated two years previously by means of a hepaticojejunostomy. He presented with recurrent vomiting and Barium meal demonstrated a stricture due to extrinsic compression as a result of recurrent tumour in the second part of the duodenum with no flow of contrast beyond. A 9cm 22mm Wallstent was inserted across the stricture and provided good symptomatic relief. Following endoscopy routine

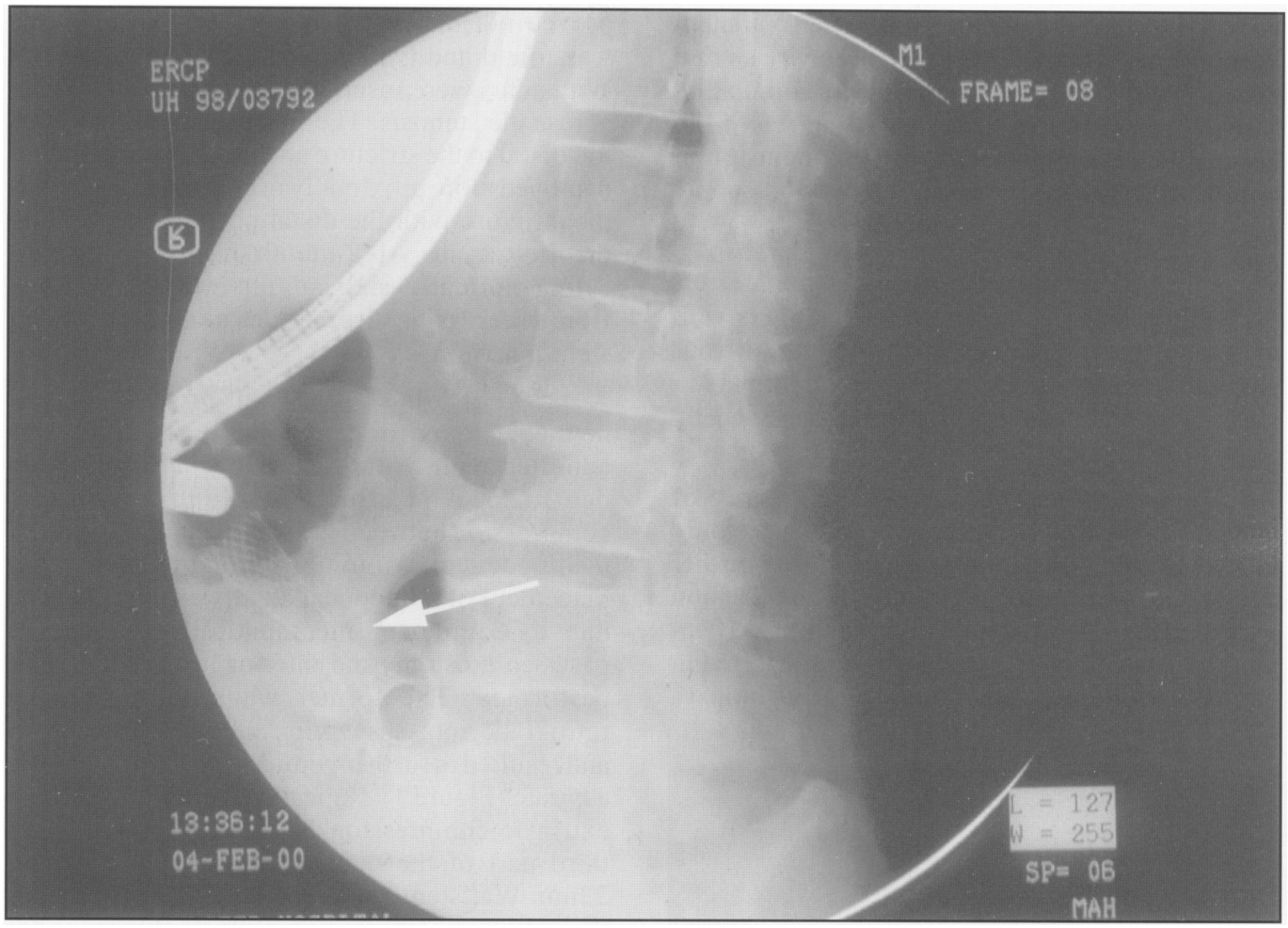

Fig 2. Endoscopic deployment of the duodenal stent between the second and third parts of the duodenum (arrow pointing to duodenal stent).

Gastromiro meal was suspicious of a small contained perforation in the proximal part of the second part of the duodenum. He had no symptoms and was treated conservatively with intravenous antibiotics, parenteral nutrition and was fit for discharge after 1 week. He subsequently tolerated a light diet and remained well for four months at which time he developed ascites and died one month later.

A 56 year old man with adenocarcinoma arising from the gastro-oesophageal junction had undergone oesophagectomy 14 months earlier. He presented with vomiting, abdominal pain, weight loss and cachexia. CT scan of his abdomen showed soft tissue around the aorta in the diaphragmatic crus and soft tissue adjacent to the duodenal loop. There was abdominal ascites. Barium meal showed delayed gastric emptying from a narrow pyloric channel. While in hospital he was noted to have significant vomiting and was unable to keep any fluids down. At upper gastrointestinal endoscopy, there was a large amount of gastric residue due to pyloric stenosis, probably from tumour infiltration, and the duodenum could not be entered. A therapeutic duodenoscope (Olympus) was used. A Zebra guidewire (Boston Scientific) was inserted across the pyloric stenosis under fluoroscopic guidance. A 9cm long, 2.2cm diameter uncovered enteral Wallstent (Boston Scientific) was passed through the scope and deployed across the pylorus. A routine post procedure Gastromiro swallow showed that most of the contrast passed through the stent. Following the procedure he was able to tolerate a soft diet. He was discharged 2 days after the procedure.

DISCUSSION

The management of malignant gastroduodenal obstruction is difficult. Our patients were unsuitable for surgery in view of their advanced disease. Whilst supportive care is commonly used, it neither relieves nausea or vomiting, nor allows an adequate food intake. Surgical options include

gastrojejunostomy or antral gastrectomy, although these are associated with significant morbidity and mortality.[1] Other treatment options, including chemotherapy and radiotherapy, are not helpful in relieving symptoms. The combination of a surgically placed jejunostomy for feeding purposes and a defunctioning percutaneous endoscopic gastrostomy has been used, but is often unsatisfactory.[7] Endoscopic dilatation only provides transient relief of symptoms and carries a significant risk of perforation.

We have found that the placement of self-expanding metallic Wallstents is a safe and effective alternative to surgery in patients with inoperable malignant duodenal obstruction. The slim and flexible delivery system allows stent placement into the angulated parts of the upper gastrointestinal tract without prior dilatation. The larger diameter of these stents allows patients to resume a normal diet. This advantage has also been confirmed in one of the largest studies to date.[8] Twelve patients with malignant gastroduodenal obstruction were followed up, of whom 6 were able to resume a regular diet, three could eat pureed food, in two patients the procedure was unsuccessful due to technical reasons and one patient had coexistent distal small intestinal obstruction.[8] One of our patients may have had a small contained perforation. An estimate of the incidence of perforation related to the placement of duodenal stents is limited by the small size of the studies. In one study of 31 patients, one perforation occurred, representing a complication rate of 3%.[9] An alternative to endoscopic placement is stent placement under fluoroscopic control.[10]

The use of Wallstents for the relief of malignant gastric outlet obstruction is more cost-effective than surgical gastrojejunostomy.[11] In addition, stenting can be expected to provide a greater quality of life and there is less time required for convalescence. In one study, the median survival time for patients who underwent enteral stent placement compared with those who underwent surgical gastrojejunostomy was 94 and 92 days, charges were $9,921 and $28,173 ($p=<0.005$) and duration of hospitalization was 4 and 14 days ($p=<0.005$), respectively.[11]

In conclusion, recent studies suggest that the endoscopic placement of enteral stents provides a feasible and effective means of the palliation of obstructive symptoms due to malignant gastroduodenal obstruction and may be preferable to surgery although confirmation of this is awaited from randomised controlled trials.

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Successful colonoscopy; completion rates and reasons for incompletion

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ABSTRACT

Factors such as poor bowel preparation or obstructing colonic disease may confound the reporting of colonoscopy completion rates, as these factors are outside of the control of the endoscopist performing the procedure. By adjusting for these factors when calculating a colonoscopy completion rate, it may be possible to make a more accurate assessment of a unit's or individuals' competence.

Details of two thousand two hundred and sixteen colonoscopies performed by four consultants and their trainees between 1993-2000 were analysed retrospectively from a prospective endoscopy database. Crude (all cases) and adjusted (excluding poor bowel preparation and disease as causes of incompletion) rates were recorded for each sex, and by age according to cause.

Overall crude and adjusted completion rates were 77.9% and 85.0% respectively. There was a significant difference between male and female completion rates due to a difference in the incidence of excess looping and intolerance of the procedure (adjusted rate 88.9% in males vs. 81.6% in females, $p<0.05$). There was a non-significant trend to lower completion rates in patients over 75 years of age compared to younger patients. Completion rates were significantly higher following bowel resection (adjusted rates 93.5% vs. 82.8%, $p<0.05$). There was no significant difference between completion rates for inpatient and outpatient referrals ($P=0.36$).

Reporting colonoscopy completion rates by adjusting for factors such as poor bowel preparation and obstructing colonic disease allows for direct comparisons of completion rates reported by different units. Reporting completion rates in this way also highlights the effect of inadequate bowel preparation on successful colonoscopy.

INTRODUCTION

Colonoscopy remains the gold standard for investigation of most colonic disease. However the number of incomplete examinations limits its usefulness especially in the investigation of suspected colonic malignancy where full examination of the bowel is mandatory. Published completion rates vary widely from 55-98.8%.[1-3] Our aim was to examine colonoscopy completion rates in our unit over a seven year period and to try to identify the impact of disease and inadequate bowel preparation on the caecal intubation rate.

METHODS

Details of all colonoscopies performed by four consultants and their, trainees in a single unit between 1993-2000 were analysed retrospectively from a prospective endoscopy database. Bowel preparation was achieved with Klean-Prep (*Norgene*), and 165cm Olympus endoscopes were used in all cases. Patients were sedated with intravenous benzodiazepines (diazepam or midazolam) and pethidine if required. All patients were routinely monitored for heart rate and oxygen saturation. Fluoroscopy was not used in any case.

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Routine manoeuvres and change of patient's position were used as necessary to facilitate forward movement of the colonoscope. Crude (all cases) and adjusted (excluding poor bowel preparation and disease as causes of incompletion) rates are reported as described by Church.[18] Complete colonoscopy was defined as visualisation of the caecum, confirmed by identification of the ileo-caecal valve and tri-radiate fold, or by performing terminal ileoscopy. Details of the endoscopist, referral source, patient sex, indications for colonoscopy and previous surgery were noted. Student's t-test was used to detect differences between completion rates; significance was achieved when $p<0.05$.

RESULTS

2,216 colonoscopies were performed in the study period (1,079 males). Mean age was 53 years (range 15-94 years) and there was no difference in age between male and female patients. Overall crude and adjusted completion rates were 77.9% and 85.0% respectively. 144 procedures (69 in male patients) were abandoned because of inadequate bowel preparation and 14 procedures (8 in males) were incomplete because of obstructing lesions or severe colitis (Table I). 256 procedures (94 in males) were incomplete due to excessive looping and patient intolerance. This was more common in females (adjusted completion rate 88.9% in males vs. 81.6% in females, $p<0.05$), due to an increased difficulty in negotiating the female sigmoid colon (36.4% of failures occurred distal to the splenic flexure in females vs. 30.0% in males, $p=0.5$). Diverticular disease was the cause of incompletion in 29 males and 47 females (24.2% vs. 22.5% of failures for each sex, ns). Completion rates were significantly higher following bowel resection (adjusted rates 93.5% vs. 82.8%, $p<0.05$). Two hundred and nine colonoscopies were performed on patients over 75 years of age (Table II). The crude and adjusted completion rates were 71.8% and 80.9% respectively. Although there was a trend towards lower completion rates in older patients, there was no significant difference in

TABLE I

Causes of incomplete colonoscopy by gender

	Poor bowel preparation	*Obstructing disease or colitis*	*Excess looping/patient intolerance*	*Diverticular* disease
Overall	114	14	256	76
Male	69	8	94	29
Female	75	6	162	47

Table II

Effect of age on colonoscopy completion rates

Age (years)	*Total no. of procedures*	*Cause of incompletion*				*Completion rate (%)*	
		Poor bowel preparation	*Obstruction/ colitis*	*Looping/ intolerance*	*Diverticular disease*	*crude*	*adjusted*
All	2216	144	14	256	76	77.9	85.0
<75	2007	137	2	235	57	78.5	85.4
>75	209	7	12	21	19	71.8	80.9

adjusted completion rates between patients over 75 years of age compared to younger patients.

DISCUSSION

Colonoscopy is the investigation of choice for most colonic disease [4-7] though its usefulness is limited by the technical proficiency of the endoscopist.[1] Completion rates of over 90% should be attainable after 200 examinations,[8,9] though published completion rates vary widely from 55-98.8%.[1-3] The documentation of completed colonoscopy can be troublesome as identifying caecal landmarks can be difficult.[10,11] In addition, various factors have been shown to reduce the completion rate independent of the skill of the endoscopist such as prior pelvic surgery, and a long transverse colon.[12,13] However total colonoscopy is mandatory in the investigation of colonic disease particularly if neoplastic disease is suspected.

We have demonstrated the advantage of measuring colonoscopy completion rates by allowing for incomplete examinations due to obstructing lesions of the colorectum and inadequate bowel preparation. Reporting completion rates in this way allows fair comparison of the performance of an endoscopy unit and allows individuals to assess their own technical ability. The difference in completion rates between male and female patients is emphasised, as more examinations fail in the left than right colon in females than males.

It is well recognised that colonoscopy is difficult in particular groups of patients. It tends to be more difficult in women due to a longer more tortuous colon.[12,13] Failure in women most often tends to occur in the sigmoid colon as opposed to the ascending colon in males.[13] Several studies also suggest that previous abdominal surgery, especially abdominal hysterectomy, makes colonoscopy more difficult.[13] The roles of age, diverticular disease, peritonitis and pelvic irradiation are more controversial.[12]

Several means of improving colonoscopy completion rates have been proposed. The usefulness of judicious abdominal pressure is well established.[14,15] Gastroscopes or paediatric colonoscopes may facilitate passage of a stricture and have been used with considerable success,[16] and more recently the introduction of variable stiffness colonoscopes has proved helpful.[17] Fluoroscopy remains popular but has the disadvantages of being time-consuming and exposing endoscopy staff and the patient to radiation.[10,11] Recently real-time electronic imaging has been proposed as an aid to training and completion of difficult colonoscopy.[18] It has the advantage of being relatively inexpensive and easy to use, though it is not currently widely available. Improvement in the quality of bowel preparation would improve completion rates. There is little difference in the quality of currently available preparations, though patient compliance may be better with non-polyethylene glycol preparations, and in certain patient groups, for example the elderly, administering bowel preparation in hospital may improve compliance.[19,20]

In conclusion, completion rates in our unit are in line with current UK practice and our data highlight the difference in completion rates between males and females. The use of rates adjusted for disease and inadequate bowel preparation allow a fairer evaluation of colonoscopic ability. An improvement in bowel preparation would significantly improve the efficacy of colonoscopy and strategies to improve practice will be sought.

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Confirming congenital hypothyroidism identified from neonatal screening

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SUMMARY

All patients identified in the neonatal screening programme for congenital hypothyroidism in Northern Ireland between 1983 and 1993 were reviewed. 131 infants were recalled because of TSH elevation of whom 85 proved to have true permanent congenital hypothyroidism, while 44 had transient TSH elevation and 2 cases died before the diagnosis could be confirmed. TSH elevation at presentation was milder in the transient group and these infants were more likely to be unwell and/or suffering from congenital malformation.

INTRODUCTION

Congenital hypothyroidism (CH) is a largely preventable cause of learning disability.[1] In the United Kingdom, neonatal screening for this condition began in 1978 and by 1982 a national programme was established. Early results estimated the incidence at 1 in 3937 live births.[2] However, follow-up shows that some infants have transient abnormalities of thyroid function tests which do not require lifelong treatment. This study was performed to ascertain the incidence of permanent CH and transient neonatal abnormalities of thyroid function within a Health Service Region from January 1983 to December 1993 and to compare the clinical differences at presentation between these two groups.

PATIENTS AND METHODS

All infants in Northern Ireland from 1st January 1983 to 31st December 1993 were screened for congenital hypothyroidism at a recommended age between 6 and 8 days. Only patients born before 1994 were included as this allowed sufficient follow up, if necessary off treatment, to confirm the initial diagnosis. The number of live births was determined from the report of the Registrar General. Screening was performed by thyroid stimulating hormone (TSH) measurements from blood spots using Schleicher and Schuell No. 2992 filter paper cards. TSH was measured over the reported period using reagents supplied by Pharmacia UK (1983-1986) and EG&G Wallac Delfia TM Neonatal hTSH for the remaining period. The intra and inter coefficient of variation was <12% within the working range (10-250 mU/l whole blood) of the assays.

A whole blood TSH concentration of ≥10-25 mu/l was considered borderline and a second screening sample requested. Infants with a whole blood TSH >25 mu/l or a persistent borderline result were recalled for clinical assessment and venous blood sampling. Patients were considered to have permanent hypothyroidism if the serum TSH became abnormal (≤5 mu/l) after infancy while on treatment (indicating poor compliance or a need for an increase in thyroxine dosage) or if serum TSH increased to ≥5 mu/l on withdrawing treatment after the second birthday.

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Transient elevations in TSH were defined in the following three circumstances:-

1. a persistent mildly elevated whole blood TSH >10 mu/l on screening with a serum. TSH <5 mu/l at recall.
2. a serum TSH ≥5 mu/l at recall which returned to normal in infancy without treatment.
3. normal thyroid function tests (serum TSH <5mu/l) over a 6 month period after withdrawal of treatment.

RESULTS

Table shows the number of live births and number of positive TSH tests per year with 131 cases referred during the 11-year period. Two patients with mildly abnormal thyroid function tests at birth died in early infancy and could not be classified. Both were born preterm and one had Downs Syndrome and congenital heart disease.

There were no known patients with a late diagnosis missed on neonatal screening during this period.

The incidence of permanent CH from January 1983 to December 1993 inclusive was 28.7 per 10^5 live births or 1 in 3478 live births. The annual incidence as shown (figure) suggests that in 1991 and 1992 an unusually large number of babies with permanent CH were diagnosed. Of the 85 patients with permanent CH, the female to male ratio was 2.5:1. Two children were from the same family, 3 had congenital heart disease (1 of whom also had Downs Syndrome) and 2 were preterm. At first recall the mean serum free thyroxine was 6.5 pmol/l (median 4.4 pmol/l, range 0.4-23.3 pmol/l) and mean serum TSH 350 mu/l (median 267.5 mu/l, range 11.9-1490 mu/l).

The incidence of infants with abnormal screening tests but subsequently found to have transient abnormalities was 1 in 6720 live births. Of these patients, 30% had normal TSH concentrations of <5 mu/l at their first recall, 37% had mildly elevated serum TSH concentrations during infancy which returned to normal without treatment and 33% were started on thyroxine in infancy which could subsequently be withdrawn. All 12 infants with a raised blood spot TSH on screening but normal serum TSH (<5 mu/1) at recall remained clinically and biochemically euthyroid at follow-up. Of the 32 patients with raised serum TSH (≥5 mu/l) at recall, the male to female ratio was 1:1. Five siblings from 2 families were identified and the mother of another infant had developed hypothyroidism 1 year earlier.

TABLE

Live births and numbers of patients with transient abnormalities of thyroid function and permanent CH for each year 1983-1993.

Year	*Total live births*	*Recalled*	*Unclassified*	*Transient Abnormality TSH at recall*		*Permanent CH*
				5< mu/l	*≥5 mul*	
1983	27,255	11	0	1	3	7
1984	27,693	10	0	4	1	5
1985	27,635	9	0	2	1	6
1986	28,152	9	0	0	2	7
1987	27,865	10	0	1	2	7
1988	27,767	8	0	0	3	5
1989	26,071	11	1	1	0	9
1990	26,499	13	0	0	5	8
1991	26,252	19	0	2	5	12
1992	25,572	15	0	0	4	11
1993	24,909	16	1	1	6	8
1983-1993	295,670	131	2	12	32	85

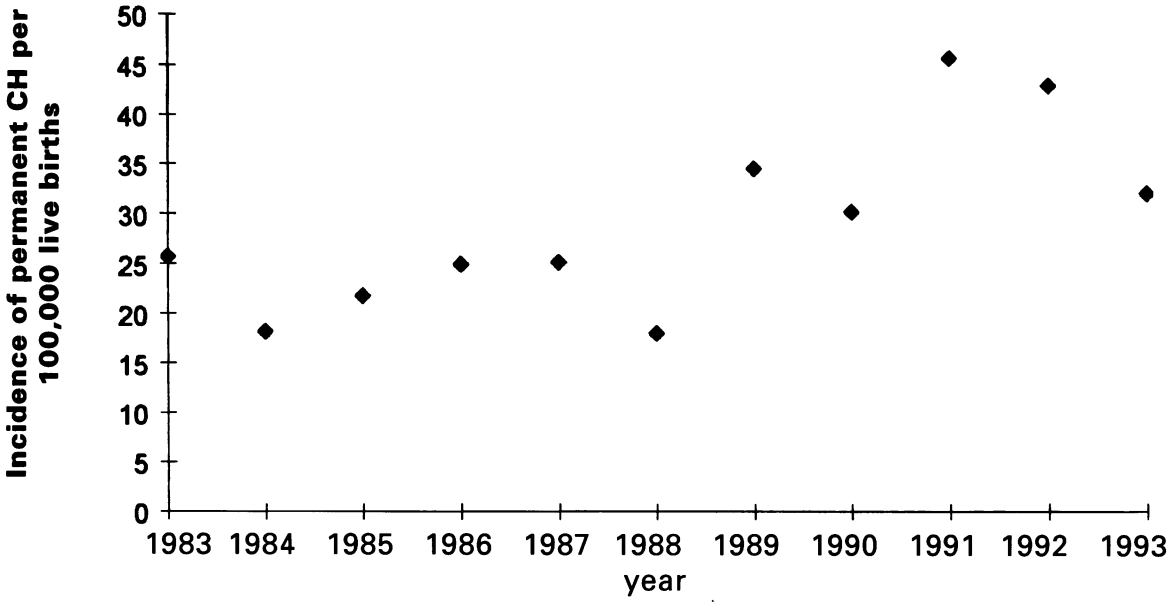

Fig. Annual incidence of permanent congenital hypothyroidism for each year 1983-1993

Myelomeningocele was present in 6 infants, congenital heart disease in 4, Downs Syndrome in 2 and prematurity in 2. Within this group, the median serum free thyroxine at recall was 19.1 pmol/l (range <2-28.4 pmol/l) and median serum TSH was 14.5 mu/l (range <5->320 mu/l).

DISCUSSION

The estimated annual incidence of permanent CH from 1983-93 in Northern Ireland was 1:3478 live births, slightly higher than the incidence of the 1982-1984 survey for England, Wales and Northern Ireland,[2] and 1979-1993 Scottish review.[3] Female preponderance is found in all 3 studies. A small rise in the annual incidence of permanent CH was observed in this study, but numbers were small. 33.6% of patients recalled turned out eventually to have transient disease, slightly higher than the Scottish figure of 25%.[3] The difference may be attributed to the lower screening TSH value used to recall patients in the present review. Approximately one third of this group had normal serum thyroid function tests at recall and remained clinically and biochemically euthyroid at follow-up. The remaining two-thirds of this group were more problematic because of persisting abnormalities of thyroid function at recall. In retrospect, a risk factor for transient TSH elevation was present in the majority of these patients from a history of maternal hypothyroidism or siblings with transient TSH elevation, possibly as a result of maternal TSH receptor-blocking antibodies,[4,5] Downs Syndrome and use of iodine either as an antiseptic for myelomeningocele,[6] prematurity[7] or in radiological investigations of congenital heart disease.[8] High incidence of congenital malformation associated with transient TSH elevation has been shown.[9] In addition, compared to infants with permanent CH, this group had an equal male to female ratio and a significantly higher free thyroxine and lower serum TSH level at recall.

All neonates who are started on thyroxine for CH and maintain normal thyroid function tests on follow-up should have their diagnosis confirmed by withdrawing treatment after 2 years of age and following up thyroid function. As previously shown [10,11] this is particularly relevant for ill or pre-term infants with less severe abnormalities of thyroid function before thyroxine replacement.

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A short history of the treatment of cancer in Northern Ireland

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SUMMARY

The development of cancer treatment has been discussed. The progressive provision of the service in the province is described with emphasis on the place of the Belfast City Hospital in the overall plan.

INTRODUCTION

Cancer is not a single disease with a single cause and a single cure. Rather, it is a family of closely related diseases and has probably been present from the beginning of life. Sarcoma has been found in the bones of dinosaurs, while cancerous tissues have been found in Egyptian mummies.

Celsus, one of the fathers of medicine, classified and treated breast cancer in 30 BC. His treatment was purgation and blood letting! Another famous pre-Christian doctor, Galen, is reported to have performed the first mastectomy for this condition. The first radical operation was performed by Cabrol in France in 1590. The radical operation which is still performed in some centres was originally described in 1867 by an English surgeon, C H Moore. He himself never performed the operation which was popularised during the 1890's by Halstead and Mayo in the USA, and by Bilroth in Germany.

At that time much progress was being made in medicine. In January 1896, Roentgen reported his discovery of x-rays, and in the following year x-ray therapy was used to treat skin cancer. In 1898, Pierre and Marie Curie discovered radium. In 1902, together with Dr. Bequerel who had recognised the radioactivity of radium, they were jointly awarded the Nobel Prize. In 1911, Marie Curie was awarded a second Nobel Prize for further work. This award had been given to her at a time of great personal distress.[1]

In 1903, Dr. Gernord in Montreal treated three patients suffering from breast cancer with x-rays. This treatment was soon used throughout the world but it was not until 1952 when Professor McWhirter of Edinburgh combined simple mastectomy with radiotherapy that the cure rate began to improve. Since that time better equipment has been provided. The x-ray machine was superseded by the deep x-ray machine which was followed by the Betatron and more recently the Cyclotron.

The third form of treatment was the use of cytotoxic drugs – chemotherapy. The discovery of the first of these drugs was made in unfortunate circumstances. Nitrogen mustard gas had been used during the First World War with devastating effect. It was not used during World War II, but an American cargo ship loaded with cylinders of the gas was bombed in the port of Barato, Italy. A few crew members survived the explosion but they were soon found to be suffering from leucopenia. In 1946, Gilman and Phillips began to treat cancer of the lymphoid tissues with a derivative of the gas.[2] A large number of newer chemotherapeutic agents is now available for use.

DEVELOPMENTS 1841-1921

The Belfast Workhouse opened in 1841. Three years later, Dr. Lamont wrote to the Board of Guardians from the General Hospital in Frederick Street informing them that the charge for treating one of their inmates suffering from breast cancer would be three shillings per week. There is no record of patients with cancer being treated in units on the Workhouse site. Dr. J. Lynas was appointed to the Union Infirmary in 1899 as its first surgeon.

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In the General Hospital (now the Royal Victoria) chloroform was first used as an anaesthetic in 1850.[3] Prior to that only a few surgical procedures could be carried out because of a lack of anaesthesia. In 1869, only 69 operations, including six for the treatment of cancer, were recorded. The first defunctioning colostomy was performed in 1884; the patient died. Five years later, in 1889, three such operations were performed and the patients survived.

In 1896, Mr. Forster Green donated £500 to provide a new wing in the Samaritan Hospital for cancer patients. The ward was opened on 28th May 1897 by Miss Benn, sister of the founder of the hospital, and Mrs. Forster Green. As there are no medical records, details of any treatment are not available. At that time gynaecological surgeons treated women suffering from cancer of the breast in addition to their other work (Armstrong MJ, personal communication).

PROGRESS IN TREATMENT 1921-1948

Northern Ireland was established as a state in 1921. In 1924, Dr. (later Sir) Frank Montgomery was appointed as a consultant radiologist to the Royal Victoria Hospital. He persuaded the Hospital Management Committee to purchase 0.75 mg of radium at a cost of £15,000. Patients were treated in the King Edward Building which then housed the x-ray department. The treatment was given by x-rays from the standard diagnostic machine or by the insertion of a radium needle. Cancers of the skin, tongue, breast, uterine cervix and rectum were treated by these means.

In 1941, Dr. Montgomery was also appointed as a Visiting Medical Officer to the Union Infirmary (now Belfast City Hospital).[4] At the request of the medical staff in 1923 a decision was taken by the Board of Guardians to build a new hospital for cancer patients and this was erected between the Workhouse and the Infirmary. The foundation stone was laid on 24th May 1923 by the Duchess of Abercorn who gave permission for the hospital to be named 'The Abercorn Hospital'.[5] There were 80 beds on two floors, the wards on the lower floor being used for the observation of patients while those on the upper floor were devoted to the care of cancer patients. The building had a flat roof so that patients would be able to enjoy the advantage of fresh air and views over the city roofs to the hills beyond! Mr. Andrews, then Chairman of the Board of Guardians, said he hoped that the Abercorn Hospital would assist in the great campaign being waged throughout the land in an endeavour to discover the deadly secret of the disease.

Unfortunately, his hopes were not to be realised as there are no records showing treatment of the disease. There were no operating theatres in the unit, nor was there a supply of radium. It would appear that this was a unit for nursing care only – either terminal or for postoperative management following surgery in the main Infirmary.

In 1929, Mr. T. S. S. Holmes, Visiting Medical Officer in Obstetrics, spent one month studying the use of radium in women in several of the London teaching hospitals. On his return, he persuaded the Guardians to purchase 1.0 mg of radium, pointing out that as time passed it would increase in value! The radium was stored in a safe in the basement of Ivy Cottage and was used in the treatment of the same forms of cancer as in the Royal Victoria Hospital.[6]

The Mater Infirmorum Hospital offered a limited service using both x-ray equipment and radium. The equipment had been purchased in 1932 by a partnership of the Board of Management and Mr. John O'Doherty, an honorary surgeon to the hospital (Gormley P., personal communication). In 1945, officials of the Ministry of Health carried out a survey of cancer treatment in the province. They found that some district hospitals had supplies of radium but stated that the quantity available was insufficient for major treatment and that the number of patients treated each year in any one of these hospitals must be small.

The stimulus for the development of the use of radium for the treatment of cancer in the province was directly due to events in Great Britain.[7] The Government had been concerned about the lack of treatment available to anyone with cancer. In 1929, King George V recovered from a serious illness and as a form of thanksgiving a national radium fund was established to receive donations from the public. Donations amounted to £150,000 and the Government gave £100,000 to augment this figure. Twenty grams of radium were purchased by the new National Radium Trust and distributed to those hospitals who agreed to treat cancer patients. A Royal Commission was later established to consider the problem. This led to the Cancer Act which was passed and became law on 29th March 1939 but was held in abeyance at the onset of World War II. The Act did not apply to Northern Ireland.

A Ministry of Health was established in the province in 1944. Officers of the Ministry and members of the Local Health Advisory Committee visited several cancer hospitals in England during 1945, and in 1946 published a memorandum entitled 'Treatment of Cancer in Northern Ireland'.[7] Their main recommendations were:

1. All patients suffering from cancer should be treated free of charge, the cost being borne by the County Council of the area in which the patient lived.
2. An administrative centre should be build at public expense in the grounds of the Royal Victoria Hospital.
3. One hundred and fifty beds should be provided for treatment – 100 for surgical treatment and 50 for radiotherapy. A new hospital should be built for this purpose but, in the interim, patients requiring surgery should be treated in the Royal Victoria Hospital and a radiotherapy unit should be located in the War-time emergency hospital built in Musgrave Park.
4. The care of cancer patients declared untreatable should form part of the cancer scheme. Both institutional and domiciliary care should be provided.

FURTHER ADVANCES 1949-2001

These recommendations were not carried out as preparations were being made for the introduction of a new free National Health Service which began on 5th July 1948. In 1949, the Northern Ireland Hospitals Authority advertised for a radiotherapist but there was no applicant. Medical staff at the world-famous Christie Holt Cancer Hospital in Manchester were approached to provide a service in the province on a rota basis but declined to do so. In 1950, Dr. Ralston Patterson from that hospital was invited by the Hospitals Authority to assess the needs for the treatment of cancer patients in the province. One of his proposals was that Corry's building (now part of the laboratory) on the City Hospital site should become a radiotherapy centre. As this was a very strong proposal the Chairman of the Hospital Management Committee, Mr. H. I. McClure, and the chief hospital engineer travelled to Manchester to study that hospital and to make recommendations to the Hospitals Authority for future development on the City Hospital site. Dr. John Millen was appointed to the vacant radiotherapy post in 1950.

Following much discussion and in view of the reduced need for 'fever' beds, the Hospitals Authority decided that, as a temporary measure, the new Radiotherapy Centre should be based in Purdysburn Fever Hospital. Two pavilions were converted into a 70-bed unit for inpatients and another as a treatment centre. This centre contained an operating theatre, four deep x-ray machines and one ordinary voltage machine. Conversion work began in August 1951 and the unit, named in honour of Sir Frank Montgomery, was opened in December 1952. All supplies of radium in the province were sent to the new unit in 1954.[8] Dr. Millen established outpatient clinics in the Royal Victoria and Jubilee Hospitals during 1953. Outpatient clinics were not held in Montgomery House.

In 1961 the Hospitals Authority took the decision to re-develop the City Hospital site and the final plans were produced in 1965. These included a Radiotherapy Hospital to be built on the site of Jubilee Maternity Hospital and adjacent to the proposed Tower Block. In passing, it is of note that the Jubilee Hospital was the brainchild of Mr. T. S. S. Holmes and he used the first radium implant in the City Hospital in the gynaecological theatre. The report of the Chief Medical Officer (1996)[9] confirmed that the City Hospital was to be the main centre for the treatment of cancer in the province. The hospital was to be supported by facilities provided in the Ulster Hospital, Dundonald, and the three area hospitals. As a first step forward, management of Belvoir Park Hospital was transferred to the City Hospital Trust in March 1998.

During this time further developments took place (Houston RF, personal communication) New equipment was installed in Montgomery House (later known as Belvoir Park Hospital). In 1962, the first megavoltage cobalt teletherapy units were installed, and a linear accelerator was provided in 1977. The first CT scanner in the province, purchased by funds provided by public subscriptions following an appeal by the late Dr. G. A. Lynch, was installed in 1983. Two more linear accelerators were installed in 1989. A Selectron remote after-loading device for the treatment of gynaecological cancers was installed in 1992. Many improvements and alterations to the buildings were carried out. The centre for the administration of chemotherapy was extended in 1989. Outpatient clinics for cancer patients were held in all the acute hospitals in the province.

In 1968, Professor J. H. M. Pinkerton established a gynaecological cancer unit in Jubilee Hospital, and a colposcopy service commenced in 1971. This unit was the regional centre for gynaecological cancer. Jubilee Hospital has recently been demolished.

A new chemotherapy unit under the charge of Dr. R. Atkinson was opened in Gardner Robb Hospital in 1976. This was transferred to the Tower Block in 1986 and was recently upgraded to meet the needs for modern therapy. The official opening of the unit was performed in 1998 by Dame Deirdre Hine, Chief Medical Officer for Wales.

Other aspects of cancer care mentioned in the 1946 memorandum[7] have not been neglected. These include education, prevention, early diagnosis, research, support and terminal care.

Cancer education had been made a responsibility of the County Medical Officers of Health when the Health Service was established. As the subject was 'taboo' among the general public and there were so many other pressing needs the education service to the public did not commence until the mid-1970's. Two cancer charities, the Ulster Cancer Foundation and Action Cancer, also provided speakers to attend meetings throughout the province. Some of this work has previously been described.[10]

Prevention has been tackled in two ways:

I. a) Education about the dangers of smoking which is the cause of most cancers of the lung, and b) the dangers of long periods of exposure to sunshine as a cause of skin cancer.

II. The finding of premalignant cells in tissue. This mainly involves the cervical smear service which has been available since 1963 to all women in the province over 35 years of age.

Early diagnosis involves the cervical smear service, mammography and self-palpation of the breasts, the use of radiological tests, and routine invasive procedures, eg colonoscopy. The introduction of the PSA test in the diagnosis of carcinoma of the prostate is also currently being urged by Action Cancer.

Research. In 1974, The Queen's University of Belfast appointed the first Professor of Oncology and now both Queen's and the University of Ulster have very active research units. Much of the funding for this work is provided by the cancer charities in the province. In addition to their many other activities fund-raising for research is a prominent part of their work. These charities include the Cancer Research Campaign, the Ulster Cancer Foundation, Action Cancer, the Malcolm Sargeant Fund and the Leukaemia Research Fund Group.

Part of any ongoing research is the epidemiology of the disease. A cancer register was established in 1949 but was abandoned in the mid-1960's because of failure by consultants to notify their findings to the officers of the Hospitals Authority. A new cancer registry has been established under the directorship of Dr. Anna Gavin and is being funded by Queen's University, the Ulster Cancer Foundation and the Department of Health.

Support for patients and relatives is most important and the majority of the cancer charities have phone-in help-lines. The Gerard Lynch Centre at Belvoir Park Hospital offers counselling to patients and relatives. Practical help to patients can be obtained from the Mastectomy Association,[11] the Laryngectomy Group and the Ileostomy Group, among others.

Terminal care recommended in the Memorandum[7] is unfortunately not a full part of the National Health service. This is provided by the hospice movement – the Northern Ireland Hospice and the Marie Curie Centre in Belfast, the St John of God Hospice in Newry and the Foyle Hospice in the city of Derry. In addition, an excellent domiciliary service is provided by MacMillan nurses who are based in various hospitals and health centres. All these facilities rely very heavily on the various charitable organisations.

THE FUTURE

Cancer is no longer regarded as the dreaded disease of the last generation. Despite a more open attitude to the disease, earlier diagnosis and better treatment, much work has still to be done. This is already taking place in the province. It is fitting that the new treatment centre is about to be built on the site of Jubilee Hospital where radium was first used in the City Hospital. In a modern 'high-tech' environment one can only wish the new unit every success and hope that it takes as its motto the words enscribed on the Jubilee foundation stone "Here at whatsoever hour you come, you will find light, and help and human kindness."[12]

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Changing Times

Annual Oration: Royal Victoria Hospital, Belfast, October 2001

James M Sloan

The great majority of these Orations have been delivered by men, but since 1995 the medical staff have to some extent redressed the balance albeit belatedly, and Professor, now Dame Ingrid Allen gave the Oration in 1995. Last ear Professor Jennifer Adgey gave the Millennium Oration. It gives me great pleasure to follow her as Orator and when I look down the list of previous Orators it makes me proud to join that distinguished company. At this moment it also makes me nervous.

Heraclitus was an ancient Greek; he was indeed a very ancient Greek. He lived in Ephesus around 500 BC but he was a man ahead of his time, and he is reputed to have said "there is nothing permanent but change". I have chosen the theme of "Changing Times" for this Oration and would like to discuss some aspects of changes which have taken place in recent times in this profession and in my own specialty.

The first of these is the effect of recent changes on Academic Medicine. I fear these have not been entirely beneficial. The late Gary Love, former Professor of Medicine in this Medical School, gave this Oration in 1988. It was entitled "Serving Two Masters". By that he meant serving two employers, the University and the National Health Service. As everyone knows it is difficult to serve two masters and recently these difficulties have been compounded. This is largely due to divergence which has arisen between the priorities and objectives of the University and those of the National Health Service. As Gary Love said, the cardinal aspects of academic medicine are patient care, teaching and research.

All medical staff, academic or otherwise are well acquainted with changes in patient care. The increasing complexity of modern medicine, the necessity for continuous up-dating and revalidation coupled with increasing expectation by the general public, is something which we are all learning to live with, not only in the medical profession but in nursing and professions allied there-to. Similarly teaching is not the prerogative of academic medicine. A great deal of undergraduate medical teaching is carried out by NHS staff. This hospital has a long and proud tradition of teaching which I will return to later. Nonetheless with the introduction of the new medical curriculum by the GMC three years ago, there was a switch away from formal lectures to problem-based learning and small group teaching. The jury remains out on the efficacy of this type of teaching but it certainly takes a great deal more time and many more personnel to deliver. In my own specialty, demands for teaching time quadrupled.

The most controversial aspect of recent change in academic medicine has been with regard to research and the institution of the Research Assessment Exercise. This is a peer-review system commissioned by the Higher Education Funding Council which assesses universities on their research performance and determines to a considerable extent their funding for the next five years. Thus it has assumed very high priority in university life. Teaching and in particular patient care have been forced into the background. Indeed the great majority of university departments have no responsibility for patient care. Thus it rates a very low priority.

Assessment is based on three factors, the number and quality of peer-reviewed publications, number of research support staff and, most importantly income from research grants. The implication is that expensive research is good research. Consequently clinical academic staff find themselves under unrelenting pressure to pursue research grants and bring in income. Combining this with a heavy clinical commitment and

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teaching is a formidable task and one which for many is losing its appeal.

A meeting of Professors of Pathology throughout the UK was held recently to discuss this matter. It was probably a crisis meeting. The report of this meeting[1] written by an eminent pathologist and research worker pulls no punches. It states "it was felt strongly that the Research Assessment Exercise had been singularly unhelpful if not destructive, especially in the sphere of academic surgical pathology." I think the same applies to many specialties well beyond surgical pathology.

The result of these recent policies is not difficult to predict and is shown in Table I. These figures have been compiled by the Council of Heads of Medical Schools [2] and thus I think it is safe to assume they are authentic. It shows the considerable number of vacant posts at various levels in academic medicine throughout the United Kingdom in October 2000 and the number which have been vacant for more than six months. Bear in mind that ten years ago these posts were considered highly desirable. The most ambitious, the brightest and the best medical graduates would have been competing fiercely for these positions. Now it appears they are walking away. I think the General Medical Council and the Higher Education Funding Councils need to take a long and urgent look at the consequences of their policies in academic medicine. If the drift from academic medicine continues, who will take responsibility for undergraduate medical education?

TABLE I

Summary of Vacancies in Academic Posts in UK Medical Schools (as at 1/10/2000)

Data collected by Council of Heads of Medical Schools

	Posts unfilled	*Posts unfilled for more than 6 months*
Professor	79	36
Reader/S Lecturer	145	81
Lecturer	177	98

I would now like to move on from that rather downbeat assessment to look at some of the changes that have taken place in my own specialty of tissue pathology in recent years. In a very different context Harold Macmillan coined the phrase "the winds of change". Sometimes it feels almost like a whirlwind of change. The practice of tissue pathology or histopathology includes autopsy practice. Morbid anatomy is the depressing term often applied. Within the past few months this practice has come under intense scrutiny over the practice of tissue retention for teaching and research and retention of small tissue samples for microscopical examination. What was not only accepted practice but best practice, carried out for decades, indeed for centuries, has now in some cases become unacceptable in the absence of detailed consent. This is not a suitable forum in which to discuss this matter and I do not intend to do so. However few people outside the department are aware of the amount of time and energy that this controversy has consumed and I would like to acknowledge the enormous amount of effort put in by many members of the Pathology department as a result of this matter. Since January of this year the department has received over 1200 enquiries. These have been dealt with initially by the secretaries within the department and then by Dr. Maureen Walsh, Dr. Meenakshi Mirakhur in Neuropathology and in particular by Dr. Claire Thornton. Dr .Thornton and her secretary, Mrs. Claire Preshaw, have themselves dealt with over 1000 enquiries. These require detailed reference to records, in some cases going back 40 or 50 years. In all instances these enquiries have been dealt with in a patient, polite and understanding fashion and I think this Trust owes a debt to the people involved, particularly Dr. Thornton. The Trust has provided help in the form of a telephone helpline and a great deal of assistance in dealing with psychological aspects has been given by Dr. Nicola Rooney. No help has been provided by Government agencies or Coroners, despite the fact that many of these autopsies were carried out at Coroners' request. This has been a stressful matter on all sides.

One of the major changes in histopathology practice over the past 30 years has been the change in emphasis away from autopsy work to surgical pathology, the examination of tissue from the living patient with a view to establishing the diagnosis and the extent of disease. Table II compares the number of biopsy and operative specimens examined in pathology laboratories in Northern Ireland in 1970 and in the year 2000. There has been a marked increase in this activity over 30 years. This takes no account of screening

and diagnostic cytology which have increased almost exponentially. The number of autopsies carried out has remained roughly the same or fallen slightly in that period. Personally I welcome this change of emphasis greatly. On the technical side the great advance has been the advent of immunohistochemistry (ICC) whereby a labelled antibody is applied to a tissue section in order to identify cell and tissue types, gene products etc – the applications are multitudinous. This technique was refined and improved by Ludwig Sternberger in the 1970s. Shortly afterwards Professor Cesar Milstein working in Cambridge described the production of highly specific monoclonal antibodies.[3] The application of these techniques has greatly increased and refined our diagnostic abilities.

Table II

Surgical Pathology in N. Ireland
Specimens Reported

	1970	*2000*
RVH	11150	23900
BCH	18050	18300
Altnagelvin	1850	11600
Antrim	–	13500
Craigavon	–	13000
Total	31050	80300

Now for a little bit of medical science. I would like to turn attention to some diseases in which I have had some interest over the years and in which there has been remarkable change in recent times. This change has been almost exclusively beneficial. The disease I would principally like to discuss is Peptic Ulcer Disease.

This term covers chronic gastric and duodenal ulcers. It is perhaps easy to forget how common this disease was even 30-40 years ago and how much misery, morbidity and not inconsiderable mortality it caused. It is still quite prevalent today especially in the elderly but the treatment and prognosis have changed completely. Surgery, which was a mainstay of treatment is now seldom necessary.

Reference to a prestigious textbook of Gastroenterology published in 1984 gives a variety of causes of chronic peptic ulcer disease.[4] Many of the listed causes were perfectly valid. Aspirin and other non-steroidal antiflammatory drugs are important causes of peptic ulceration particularly gastric ulcers and this has been increasingly recognised. Syndromes such as the Zollinger-Ellison syndrome and multiple endocrine neoplasia are also potent causes but account for only a very tiny proportion of cases; other causes listed are vague and not very relevant. Psychological stress was at that time considered very important. This may be so but it is not the basic underlying cause.

The first major step forward in treatment of this disease came from the pharmaceutical industry when James Black, who at that time was working with Smith, Kline and French, developed the first H_2 receptor antagonist drug Cimetidine or Tagamet. He was subsequently knighted and received a Nobel Prize for this work and deservedly so. This was the first really effective drug to suppress acid secretion in the stomach. The old adage "if there is no acid there is no ulcer" proved to be true, and in many cases treatment with cimetidine allowed these ulcers to heal. However it was noted that once treatment was stopped, a depressingly high percentage of ulcers recurred and really we were no further on in understanding why the ulcers occurred in the first place.

Then two letters appeared in the Lancet under a single heading,[5] "Unidentified curved bacilli on gastric epithelium in active chronic gastritis." The letters came from Perth in Western Australia. The first was written by Dr. Robin Warren a pathologist and the second by Dr. Barry Marshall who was at that time a trainee gastroenterologist. They described the presence of bacteria on the surface of the gastric mucosa, the lining of the stomach. Such bacteria had been described before but had been dismissed as mere contaminants. Marshall and Warren observed the crucial association between the presence of the bacteria and active chronic inflammation of the underlying gastric mucosa. In addition, with a lot of help from the then Professor of Microbiology in Perth, Stewart Goodwin, Marshall also managed to grow the bacteria in culture. A year later Marshall and Warren made the additional connection between the presence of bacteria and peptic ulcer disease in a paper published in the Lancet.[6] Marshall is an articulate and flamboyant man who enjoys the limelight and is not one to hide his light under a bushel. Warren, on the other hand appears to be quiet and unassuming and seems happy to let others take the glory. You will I am sure,

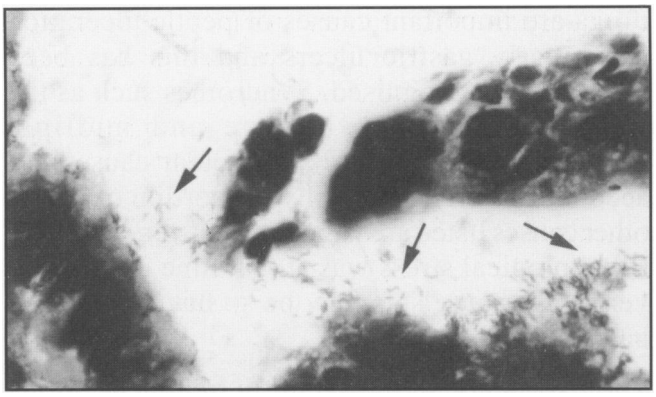

Fig 1. *Helicobacter pylori* organisms (arrows) on the surface of gastric mucosa in active chronic gastritis. Oil immersion. Giemsa.

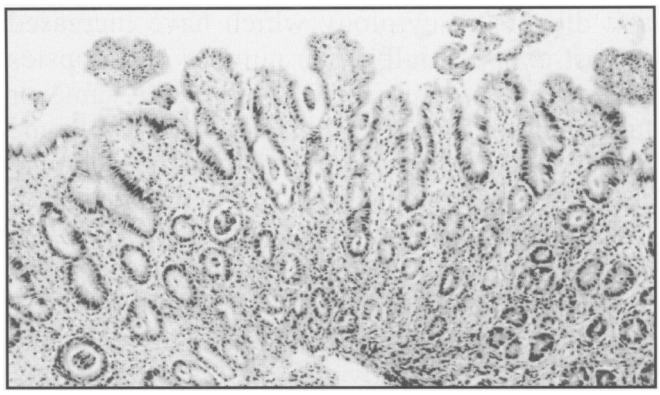

Fig 2a. Biopsy of gastric mucosa in *H pylori* gastritis. There is intense inflammation of the lamina propria with infiltration by polymorphs, plasma cells and lymphocytes. *H pylori* were present on the mucosal surface.

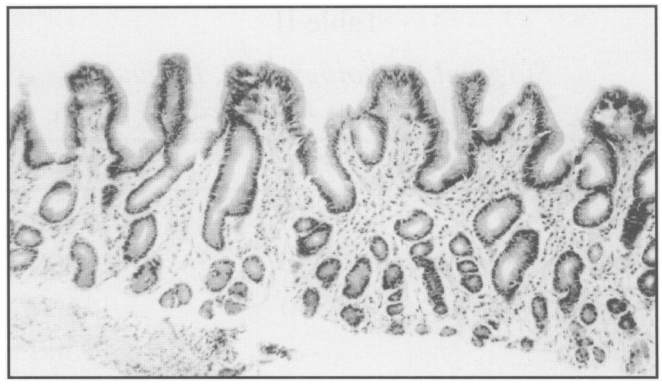

Fig 2b. Biopsy from the same patient 13 months after eradication of *H pylori* infection. The inflammatory infiltrate is much reduced. Polymorphs have disappeared and only small numbers of lymphocytes and plasma cells remain.

immediately recognise these as the characteristics of a typical pathologist.

There was considerable reluctance to accept Marshall and Warren's hypothesis that peptic ulcer disease might in most cases may be an infectious disease. This was treated with scepticism and in some cases with derision. It was considered that colonies of bacteria could not survive for any length of time in the hostile environment of the human stomach with very low pH levels but they can and they do. Fig 1 shows the surface of the mucosa and the curved or spiral- shaped organisms which Marshall and Warren described. Viewed under the scanning electron microscope at a magnification of about 4000 they can be clearly seen on the surface of the gastric mucosa. Microbiologists rapidly developed methods of growing the organism in culture which is difficult. Unfortunately for the rest of us they kept changing its name and the bacterium became known by a series of names. Eventually it was decided that it belonged to a separate genus and the name of *Helicobacter pylori* was adopted. This is quite sensible as it refers to the spiral-shape of the organism and the fact that it is found mainly in the pyloric antrum.

Subsequent work carried out over the next few years showed that this is an exceedingly common infection. In Western countries by the time we reach middle-age, 50 or 60% of the population have this infection, in the developing world the incidence is almost 100%. What was perhaps more relevant was the finding that in 95% of patients with duodenal ulcer and in around 60% of patients with gastric ulcer the infection is present. However as I said, the hypothesis that infection and subsequent gastritis may lead to chronic ulceration was difficult to prove and was accepted only slowly. The most convincing evidence in favour of this hypothesis came from therapeutic trials. Histology helps illustrate this with regard to gastritis (Fig 2a and 2b).

Similar work provided convincing evidence of the beneficial effect of eradication of the infection on peptic ulcer healing. Such work was pioneered in Dublin by Professor Colm O'Morain's group.[7] Similar findings are summarised in a later American study published in 1993.[8] In patients treated with acid suppression therapy and antibiotic therapy to eradicate the organism, ulcers recurred in only 2% after treatment was stopped. In patients treated with acid suppression therapy alone and in whom the organism was not eradicated, ulcers recurred in 85% of cases. That is fairly convincing evidence and it was evidence

of this type that finally convinced even the sceptics that this infection is the principal cause of peptic ulcer disease.

Because *H. pylori* inhabits the mucus layer covering the gastric mucosa it is not easily attacked by the body's immune system and thus in most cases patients who contract the infection have it for the rest of their lives unless suitable treatment is administered. It has long been known that long-term inflammation pre-disposes to development of cancer and soon epidemiological studies carried out in various different countries indicated that there is an increased risk of gastric cancer in patients who have *H pylori* infection. There is also an increased risk of malignant lymphoma of the stomach although this is much less common. Thus it became apparent that there are two principal outcomes to long-standing infection with *Helicobacter pylori.* In most cases (pathway 1), bacteria and subsequent gastritis are confined to the antrum. The chronic active inflammation eventually leads to atrophic gastritis and intestinal metaplasia in the antrum. This tends to be accompanied by increased levels of circulating serum gastrin, increased gastric acid and increased risk of peptic ulcer.

In the other pathway (pathway 2), the gastritis is more widespread and involves both the antrum and the acid-secreting corpus of the stomach i.e. a pangastritis. This gives rise to much more diffuse atrophic gastritis further diminishing the acid secretion and allowing the organisms to spread. Patchy change then takes place in the lining of the stomach whereby it comes to resemble the lining of the small intestine (intestinal metaplasia) and these patients are at slightly increased risk of developing gastric cancer.

In the past 10 or 15 years the morphological sequence of events, in other words the changes in the gastric mucosa which we can detect down the microscope have become fairly well defined. Everyone in whom the infection becomes established develops active gastritis. Most of these patients will develop some degree of atrophic gastritis and most will, over the years develop intestinal metaplasia. A small minority, especially among those in whom the disease process follows pathway 2, will go on to develop dysplasia which is a term for disordered growth and a significant proportion of those will develop carcinoma.

The question arises, can we interrupt this sequence of events before it reaches the dangerous stage. There is considerable debate about this but I believe that in the early stages this sequence can be stopped and perhaps reversed. Dr. Catherine Larkin carried out a study on the effect of eradication of *Helicobacter* on atrophic gastritis affecting the body of the stomach.[9] She measured gastric acid levels and serum gastrin levels and found that in most cases these revert to normal after the organism is eliminated. These are markers of atrophic gastritis and their return to normal levels indicates reversal or at least lack of progression of this process. Histology supports this. Biopsies taken at the start of the study showed patchy mild or moderate atrophic gastritis of the mucosa of the corpus of the stomach in most patients with *H Pylori* infection. Biopsies taken approx one year after eradication of the infection showed not only improvement of the active gastritis but in most cases partial regression of the atrophic gastritis. However none of the cases studied showed intestinal metaplasia on biopsy and it is likely that a point of no return is reached. Once intestinal metaplasia is established, it is doubtful if the mucosa will revert to normal.

The incidence of gastric cancer has been falling throughout the world quite dramatically which can only be good news. However there is a sting in the tail – there is always a sting in the tail. The sting is associated with Barrett's oesophagus. In this condition the normal lining of the lower oesophagus is replaced by patches or tongues of gastric mucosa which have moved upwards in a cephalic direction. It is thought to be due to reflux of acid contents in the stomach upwards into the oesophagus. In these circumstances the normal lining of the lower oesophagus changes to resemble that of the stomach. Barrett's oesophagus is usually fairly harmless. It causes heartburn and sometimes ulceration but in a small number of cases it progresses to adenocarcinoma of the lower oesophagus or the junction between the oesophagus and stomach as shown here. This tumour is highly aggressive and while incidence of cancer of the more distal stomach has declined considerably the sting in the tail is that adenocarcinoma of the lower oesophagus and upper end of the stomach has increased recently. This was first noted in the early 1980s and reported in 1991 and the trend has continued.

I had the pleasure of working with Dr. Catherine Gleeson when she did her PhD under the

supervision of Dr. Hilary Russell. In her PhD Kate studied the molecular biology of Barrett's oesophagus and related adenocarcinoma. She published a series of good quality papers and among other things identified chromosomal loci which may be involved in progression of Barrett's epithelium to cancer.[11] In addition her molecular studies supported the theory that there is a step-wise sequence leading from relatively normal mucosa to malignancy similar to that already described in the stomach.[12] This progression consists of replacement of the squamous epithelium of the lower oesophagus by columnar epithelium i.e. Barrett's oesophagus. The next step is development of intestinal metaplasia in Barrett's mucosa. In a tiny proportion of such cases Dr. Gleeson detected molecular changes at this stage similar to those in fully fledged cancer despite the fact that there was nothing alarming in the histology. In a small proportion of cases intestinal metaplasia proceeds to dysplasia and in a further minority to invasive adenocarcinoma.

I should state, in case I sound alarmist, that the risk of developing adenocarcinoma in Barrett's oesophagus is quite low. Earlier studies indicated that the risk was increased by approximately 40-150 times but Dr. Liam Murray has compiled a sizeable series of local cases which have been followed up for a considerable number of years. His findings indicate that the risk of cancer associated with Barrett's oesophagus is approximately fifteen times that of the rest of the population and considerably less than earlier estimates.[13]

The challenge in the future will be to identify the relatively small number of patients who are at risk of developing cancer well before they actually do so. At present histological detection of dysplasia remains the basis for this but histology in its present form is a fairly blunt instrument. Hopefully improved molecular biology techniques such as those used by Dr. Gleeson or perhaps computer assisted image analysis of biopsy material will identify potentially dangerous abnormalities within cells with greater precision than we have at present and will thus be able to identify patients at risk at an earlier stage long before cancer develops. That remains the goal with this particular cancer and indeed with most cancers.

Finally I would like to turn to the changes taking place on this site. They are quite momentous and are there for all to see. We are moving from the familiar but rather tired facade fronting onto the Grosvenor Road to a new building. More importantly we are moving from wards which have barely changed since the Edwardian era. Phase I of the new building is now complete and we have a pristine brand new hospital which will hopefully provide much needed improvement in facilities for patients, relatives and staff alike. I do hope that we can keep it in that pristine state of cleanliness. Unfortunately on this site, parts of the estate are in a very run-down condition. There is an abundance of litter, a dearth of litter bins and in some places fixtures and fittings are in a dilapidated state. Litter and vandalism are sadly endemic in this country and 20 years of under-funding on this site mean that there is little money left over for site maintenance after provision of clinical services. Hopefully with the opening of the new hospital things will change for the better.

It is of course very easy to blame management for everything. We all have our pet gripes. In Laboratory Medicine for instance, Haematology has been moved off this site and we find it difficult to understand how a hospital such as this, containing a major trauma centre, obstetrics and substantial cancer services can function optimally without the presence of Consultant Haematologists on site. It is however worth remembering that in the early 1990s there was a real danger that the Royal Victoria Hospital would be downgraded and that acute hospital services would be moved off this site. Instead it remains a centre point of hospital services and referrals for the Province and we have the first phase of the new hospital. To achieve this U-turn has required determination, intensive lobbying and involvement in politics at the highest level by our management team. Few of us are aware of the amount of effort involved particularly on the part of the past and present Chairmen of the Trust and our Chief Executive Mr. William McKee. The cost of phase I of the new hospital has been 47 million pounds. The completion was supposed to take place in 36 months. In fact it took 30 months. The builders also deserve great credit for completing ahead of schedule and for causing much less disruption to the everyday running of the hospital than many of us anticipated. Phase II will cost 67 million pounds.

The purpose of the Oration is not to give the Orator a chance to indulge himself. The purpose is to welcome new students to this hospital and I

bid you a very warm welcome. I have spoken briefly about the long and proud tradition of teaching in this hospital and I have no doubt it contributes to the high reputation of Queen's Medical School as a teaching centre. All aspects of professional life are now subject to scrutiny and assessment. Teaching is no exception. In the last Teaching Quality Assessment this Medical School was rated highly. In soccer parlance it is well in the top half of the Premiership division. The Dental School did even better, indeed it could not have done any better. It won the equivalent of the league and cup double. Such standards will be hard to maintain but as this hospital is in the forefront of teaching I am confident we can offer you a good medical and dental education. I wish you well in your careers. It will be demanding but hopefully rewarding. The care and welfare of your patients will be your first priority. I wish you well with your patients and also with the colleagues you will be working with.

There are a number of people I have to acknowledge with regard to this Oration. First, foremost and most importantly are the colleagues I have worked with for many years in the Pathology Department on this site. Very few people are as lucky as I have been in this respect with regard to colleagues at all grades and levels. To these colleagues I am exceedingly grateful. Most of them have a healthy sense of humour and I would recommend this as an essential ingredient for harmonious relations.

I would like to acknowledge the late Mr. Terence Kennedy and the late Mr. John Gibbons. They were both expert surgeons. Terence Kennedy specialised in surgery of the stomach and treated many cases of peptic ulcer and gastric cancer. In addition he was a skilled endocrine surgeon and together with Keith Buchanan and Teddy McIlrath raised treatment of neuroendocrine tumours in this Province to world-class levels. John Gibbons was a highly skilled thoracic surgeon and a marvellously friendly and sociable person. These men had very different personalities but had much in common. They were excellent surgeons with a busy workload. Not only did they have to treat everyday disease but for many years like all their surgical colleagues they had to treat horrendous trauma caused by terrorist activity. Lesser men might have wilted but they did the very opposite. They possessed sharp and enquiring minds and had the ability to see beyond the everyday routine. They were constantly sparking off ideas and research projects for younger colleagues. Many of us benefited greatly from knowing them.

There are several colleagues outside pathology, too numerous to mention individually in this article whom I gratefully acknowledge. They include gastroenterologists, endocrinologists, surgeons, radiologists, epidemiologists, molecular biologists and computer experts. A few have retired, others are at the peak of their careers and some are starting out. It has been a pleasure and an education to work with them. They have all contributed greatly to the work of this hospital and if we can continue to recruit and retain people of this calibre – and we will have to work at it – then the future of this hospital is assured.

While on the subject of change one final piece of mild black humour – "If you are in a bad situation, don't worry, it'll change. If you are in a good situation, don't worry, it'll change".[14]

James M. Sloan
Date: 4 October 2001.

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Case Report

Ortner's syndrome: a radiological diagnosis

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Ortner's Syndrome is a rare clinical entity, first described in 1897.[1] It describes left recurrent laryngeal nerve palsy resulting from identifiable cardiovascular disease. For this reason it is also known as cardiovocal syndrome.[2] The various underlying conditions includes mitral stenosis, septal defect, mitral valve prolapse and aortic aneurysm.[3,4,5] We present a case of left vocal cord paralysis secondary to a large thoracic aortic aneurysm.

CASE REPORT An 81-year-old man attended ENT outpatients with a 4-week history of hoarseness. Clinical examination and laryngoscopy revealed paralysis of the left vocal cord, but was otherwise unremarkable. The patient was a non-smoker and had no other related symptomatology. Contrast-enhanced computed tomography (CT) of the neck and thorax was performed on a helical CT scanner (Siemens Somatom Plus S, Siemens, Erlangen, Germany). Data was acquired using a 10mm slice, 14mm feed, pitch 1.4, algorithm. This demonstrated a large aneurysm of the thoracic aorta, measuring 70 x 70 mm, (figure). No other pulmonary or mediastinal abnormality was identified. An urgent outpatient cardiac surgical opinion was sought, but unfortunately the patient died suddenly a few days later.

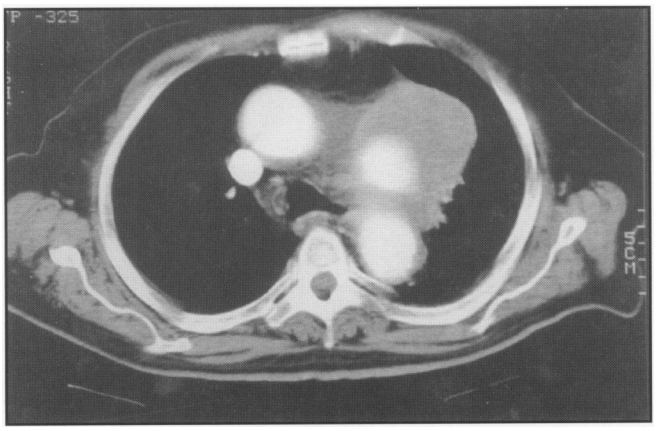

Fig. Contract enhanced axial CT demonstrating large thoracic aneurysm at the level of the aorto-pulmonary window.

DISCUSSION

The left vagus nerve descends into the superior mediastinum between the left common carotid and subclavian arteries before traversing the left side of the aortic arch. At this level it gives rise to the left recurrent laryngeal nerve which hooks around the ligamentum arteriosum before ascending in the groove between the oesophagus and trachea.[6,7] It continues along this groove to supply all the muscles acting on the left vocal cord, with the exception of cricothyroid.[8]

Several studies have identified left-sided vocal cord paralysis to be commoner than right, including those due to extra-laryngeal causes, such as thoracic aortic aneurysm.[8,9] The causes of unilateral vocal cord paralysis are numerous, the commonest being neoplasia.[10,11] Neoplasms account for 32% of cases, closely followed by surgical intervention, 30%, with 16% idiopathic and 11% traumatic.[8] It has been noted that as many as 5% of thoracic aortic aneurysms manifest clinically as hoarseness secondary to recurrent laryngeal nerve palsy.[12] Underlying cardiac disease represents only a fraction, although this is well documented, even in infancy.[2,3,12,13,14]

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This vocal cord paralysis is due to compression or traction on the left recurrent laryngeal nerve between the aortic arch and nearby structures, chiefly the pulmonary artery.[4, 15]

The role of imaging in the diagnostic algorithm of vocal cord paralysis is crucial. Review of existing plain chest radiographs and referral for plain chest radiograph or computed tomography (CT) imaging should be considered in cases of assumed idiopathic vocal cord paralysis, especially with a cardiovascular history. CT has been shown to be of particular value for identifying abnormalities in the aorto-pulmonary window [7] as in this case.

In conclusion therefore, we wish to highlight the importance of imaging in patients with idiopathic vocal cord paralysis. In particular we wish to emphasise the role of contiguous contrast-enhanced CT imaging from the base of the skull to the aortic arch.

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Case Report

Extra-articular migration of the patellar component following total knee arthroplasty

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SUMMARY

Complications related to patellar resurfacing are well recognized. We present an unusual case where the patellar button, after separating from the patella, extruded from the knee joint to lie within the extra-articular soft tissues.

Key words: patella, extra-articular, resurfacing, dislocation.

CASE REPORT An 85-year old male presented with a two week history of a painless swelling on the anterior aspect of his left knee. He had first sought orthopaedic attention for his left knee in 1984 when it was painful. A right total hip replacement had been performed earlier that year. X-ray of the left knee revealed osteoarthritis with patellofemoral degeneratrion and chondro-calcinosis. A synovectomy was performed through medial and lateral parapatellar incisions in the same year. After initial improvement pain returned. In 1995 an Insall-Burstein II (Zimmer, Warsaw, Indiana, USA) total knee replacement with patellar resurfacing was performed. It was

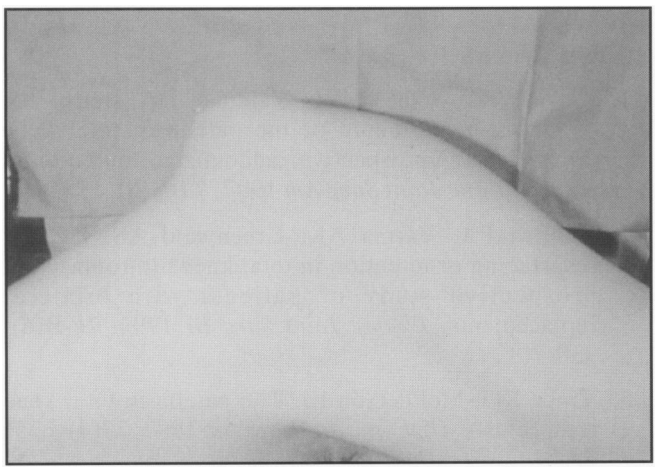

Fig 1. Photograph of left knee in flexion demonstrating the preoperative appearance (note tenting of the overlying skin).

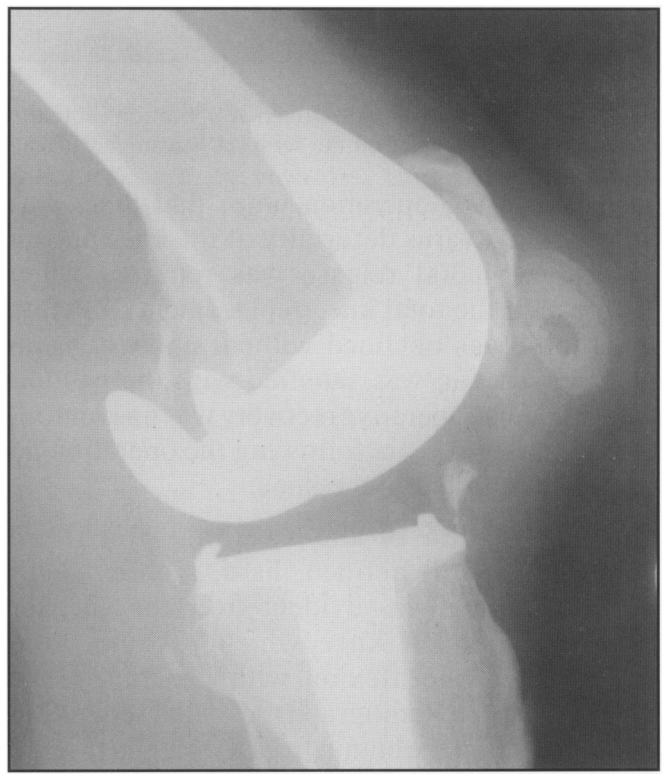

Fig 2. Lateral radiograph of left knee, demonstrating separation of the patellar prosthesis from the patella.

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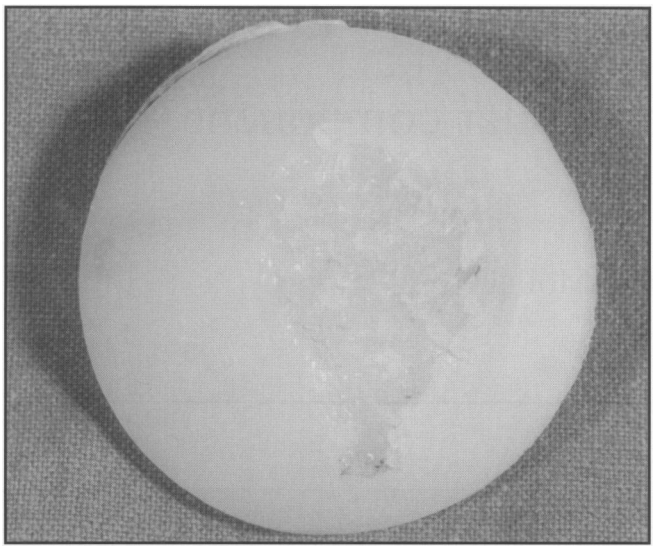

Fig 3. Patellar button as removed at operation (note the degree of wear on the femoral bearing surface).

recorded in the operation notes that there was considerable varus deformity of the knee and an extensive medial release was required when performing the total knee replacement. A stable knee joint was obtained without undue tension and the surgeon was satisfied with the patellar tracking. Post-operative recovery was uneventful. During the five years following the operation no pain was reported in the knee.

On examination of the swelling which had appeared, a well defined, hard, mobile, sharp edged swelling was evident over the anterior aspect of his left knee which became more prominent on knee flexion, with blanching of the skin (Figure 1). Radiographs revealed separation of the polyethylene button from the patella (Figure 2). At operation via a minimal skin incision utilizing the old scar, the patellar button was found extra-articularly within the soft tissues. A local defect was noted in the lateral retinaculum. The button was retrieved (Figure 3) and the defect closed with interrupted vicryl sutures.

Unfortunately there was a significant herniation of synovium through this defect at review four months later.

DISCUSSION

The role of patellar resurfacing in knee arthroplasty remains controversial.[1,2] Reported complications include patellar necrosis and fracture, extensor mechanism rupture, implant loosening, patellar subluxation and dislocation.[3]

In previous reports the patellar component has remained intra-articular.[4] Our case is unusual in that the patellar prosthesis button-holed through the lateral retinacular fibres to lie in the extra-articular soft tissues with evident tension on the scar. The potential for overlying skin necrosis was significant. Simple retrieval was preformed via a minimal incision.

The relationship between the articulating surface of the patellar and femoral components of a knee replacement is of great importance in the development of complications. The articular surface of the patella must conform with the geometry of the femoral component. With an all-polyethylene dome prosthesis, as was used in this case, small contact areas with the femoral component and high contact stresses are common.[5]

Hsu and Walker [6] designed a machine to replicate the forces applied to the patellar component during flexion and extension of the knee. They found that the contact areas of polyethylene patellae increased rapidly due to deformation. Such creep deformation reduces contact stresses. However, the underlying supporting surface also became subject to deformation. They concluded that all-polyethylene patellar domes with low conformity with the femoral condyles are prone to deformation with potential for failure of the underlying bone and loosening.[6] We postulate that patellar dome deformation, as seen in Fig 3. led to deformation of the underlying bone followed by loosening and then separation of the patellar dome. Weakness of the lateral retinacular fibres probably resulted from incision at the previous synovectomy and allowed extrusion of the patellar component into the extra-articular soft tissues.

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Case Report

An unusual case of delayed rupture of the spleen associated with pectus excavatum

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CASE REPORT A 34 year old woman presented as a surgical emergency with left upper quadrant pain of sudden onset which had awoken her from sleep. The pain radiated to her left shoulder tip. No other symptoms were noted. There was no history of trauma nor medical history of note. Interestingly she remarked that she had had a similar, but self-limiting episode of pain some two months previously after sitting bolt upright following a nightmare.

On examination, early signs of circulatory shock were evident with a pulse of 84 bpm and a blood pressure of 90/50mmHg. She displayed marked tenderness with rebound and guarding on abdominal palpation. Bowel sounds were attenuated. A moderate degree of pectus excavatum was also noted. Preliminary tests revealed a mild leucocytosis of 11.8×10^3 cells/ml. Abdominal and chest radiographs were unremarkable. Pregnancy testing was negative. A tentative diagnosis of a ruptured spleen was made and the patient proceeded to laparotomy. This revealed a large haematoma in the superior pole of the spleen with associated splenic rupture. A small splenunculus was also noted. Splenectomy was performed and the patient made an uneventful post-operative recovery. Gross and histological analysis of the spleen revealed areas of fresh recent haemorrhage interspersed with areas of organization, features in keeping with 'old' and 'new' bleeds. No other abnormality was noted.

Further haematological assessment of the patient did not reveal any evidence of haemopoietic or lymphopoietic disorders. Testing for EBV was negative. One year following surgery she remains well.

DISCUSSION

Delayed splenic rupture is a well recognized sequel of blunt left lower chest or abdominal trauma,[1] usually manifested as 'an acute abdomen' with profuse intraperitoneal bleeding. The prevention of this serious and possible life threatening complication is the cause of ongoing debate. No cases of primary spontaneous splenic rupture have been reported in the literature. All have been secondary to trauma, an underlying infective process, or malignancy. Such pathological processes as infectious mononucleosis [2] and lymphoma [3] account for some of these cases. The majority by far are secondary to trauma, usually severe blunt abdominal trauma but rupture following colonoscopic procedures and sporting injuries are well documented.

There have been no reports in the literature of pectus excavatum as an risk factor for visceral injury in abdominal trauma but as the distance between the costal margin and the posterior abdominal wall is reduced in this chest wall deformity it is likely that the upper abdominal viscera could be more easily damaged.

We postulate that the forces produced by the body upon the spleen in sitting up suddenly were

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enough to cause splenic damage and subsequent rupture.

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Case Reports

Rapid Eye Movement (REM) sleep behaviour disorder; an easily missed diagnosis, a readily treatable condition

J J Daly, S A Compton

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Rapid eye movement sleep behaviour disorder (R.B.D.) is a relatively new diagnosis, first described in the mid-1980s.[1] These case reports describe two psychiatric outpatients who presented with typical features of the disorder and who had an effective response to treatment with clonazepam. In one instance the patient had undergone several medical evaluations, including a sleep EEG, but without a definite diagnosis being reached. Both patients were diagnosed on clinical grounds, and showed a positive response to clonazepam. In both cases they experienced recurrence of symptoms of R.B.D. after discontinuation or dose reduction and improved again after rechallenge with clonazepam. This paper highlights the need for clinicians to be alert to R.B.D., a condition which is responsive to clonazepam.

CASE REPORTS

Case 1: A retired manual worker, age 83, married with 2 adult children, who lives with his wife, was assessed by a consultant in old age psychiatry in March, 1999. He had a history of major depression, noted by his general practitioner to have begun in October 1998, which had become more marked, with social withdrawal and anhedonia. Although no formal rating scales were used, the patient reached criteria for a depressive disorder, without psychotic features (DSM-IV). He was also found to be suffering from slight cognitive impairment, marked by constructional dyspraxia, although his scoring was 29/30 on the Mini-mental state [3] and 12/12 on the I/O section of the Clifton Assessment Procedures for the Elderly.[4] Medical history was significant for ischaemic heart disease, left ventricular hypertrophy, diverticular disease and prostatectomy with inguinal hernia repair in 1983. He had been commenced on citalopram 20mg daily by his general practitioner in February 1999. He was continued on citalopram 20mg daily and admitted to a psychiatric day hospital for treatment on 3/3/99. The citalopram dosage was progressively increased to 30mg daily by mid-March 1999, then to 40mg daily by 21/5/99 and finally to 60mg daily by 5/7/99. From about the middle of March 1999, the patient began to complain of disturbing nightmares, which were associated with complaints of his body "jumping" at night while asleep, and occasionally of finding himself on the floor with some associated bruising as a result. He was definite that these were new experiences and stated that the nightmares in particular were both unusual and frightening. These experiences did not appear to be temporally related to the initiation of citalopram. A CT scan of the head, showed mild atrophy, especially of the frontal lobes and a small lacunar infarct of the left basal ganglia. A sleep EEG was carried out in June 1999. This showed that the "awake and early stages of sleep were within normal limits". This sleep study was not an overnight study, but was carried out between 10.00 am and 2.00 pm, the patient having been sleep-deprived from 4.00 am on the morning of the test. By October, 1999

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the patient's mood was beginning to improve on citalopram 60mg daily, however his nocturnal sleep movement disorder continued.

He was clinically diagnosed in January, 2000 with R.B.D. and commenced on clonazepam 500 micrograms nocte. Within one week of increasing the dose to 1mg nocte his "dreams, sleep activity", as described in his clinical record, had significantly improved. During the following several months it was noted that decreases in the clonazepam from 1mg to a lower dosage resulted in recurrence of R.B.D. symptoms, typified by recurring injuries e.g. to his head and left shoulder. He also commented himself that he would feel "sore all over on awakening" and that the nightmares involved a frightening image of "chasing or fighting with a female" figure. By May, 2000 the patient's mood had begun to show signs of relapse, despite claiming compliance with the citalopram, with recurrence of agitation and initial insomnia along with anhedonia. Accordingly the citalopram was replaced with mirtazapine 30mg nocte. In September, 2000 his depression had improved to a sufficient extent to allow discharge from the day hospital. To date, the patient has been followed at a psychiatry outpatient clinic and continues to maintain improved sleep pattern from clonazepam 1mg nocte, which he generally complies with despite ongoing complaints of a slightly sedated "hungover" feeling in the mornings; this he attributes to the medication. It is worthwhile noting that the change from citalopram to mirtazapine was not, in itself, associated with any changes in the frequency or intensity of the nocturnal sleep movement disorder symptoms. He was not treated at any point with beta adrenoceptor antagonists, which have known abilities to alter sleep patterns.

Case 2: A retired manual worker, age 74, living with his wife, also in her 70s; he was well, from a psychiatric standpoint, up until February 1999. At that time he suffered a myocardial infarction and had a cardiac arrest, from which he was successfully resuscitated. During the subsequent hospitalization he suffered from a delirium but recovered well from the cardiac standpoint. He was assessed by a consultant psychiatrist for "possible visual hallucinations or vivid dreams" at the request of his general practitioner in February, 2001. The patient gave a history, confirmed by his wife, of having experienced sleep disturbance since June 1999. He would typically have vivid nightmares, which would be accompanied by "thrashing around" in bed and frequently falling out of bed. It had got to the point where his wife had to sleep elsewhere because she was afraid of suffering bodily injury. The patient would typically have nightmares of being attacked and would awaken, as a result, usually about two hours after falling asleep, according to his wife. In his mental state examination the patient had signs of mild cognitive impairment with scores of 24/30 in his Folstein MMSE and 10/12 on the CAPE I/O. His previous medical history was significant for angina, myocardial infarction, arthritis, distant history of traumatic blindness in left eye, distant history of road traffic accident with head trauma but no loss of consciousness, 35 years previously.

A clinical diagnosis of R.B.D. was made and the patient was prescribed clonazepam at a dosage of 1mg nocte. He was subsequently seen for follow-up at the outpatient department, where it emerged that he had had a good clinical response to clonazepam but had found himself feeling somewhat "groggy" and sedated on the following morning. Because of this he discontinued the clonazepam and quickly noted a recurrence of the R.B.D. within a week of doing so. The patient was recommenced on clonazepam 1mg nocte and has noticed a dramatic improvement in his sleep quality. The resolution of the nightmares and the potentially dangerous thrashing movements, which was confirmed by his wife, has greatly improved the quality of his life and that of his wife also. Of note in this patient's case was the use of metoprolol 12.5mg bd, in addition to elantan LA 25mg daily. The use of these medications was not temporally related to the onset of the R.B.D. symptoms and it would appear unlikely that these symptoms were related to the use of the beta adrenoceptor antagonist.

DISCUSSION

Schenck *et al* [1, 2, 5] identified and described a form of acute behavioural disturbance occurring during the REM phases of sleep, which was associated with a lack of the usual voluntary muscle atonia, leading to vigorous and unexpected motor behaviours. This is in contrast to somnambulism, and night terrors, which occur during the non-REM phases of sleep. In R.B.D. the patient typically develops a progressive sleep disorder with the abnormal motor behaviours appearing during the middle or final third of the night, and

almost never within the first 60-90 minutes after sleep onset. The motor behaviours are typically accompanied by the patient experiencing nightmares involving his or her being attacked or pursued by frightening dream characters. The patient talks loudly, shouts or jumps out of bed during sleep, occasionally injuring himself or others in the process. Once awake the patient may take several minutes to reorient himself and may have visual hallucinations before regaining full consciousness. These perceptual distortions on awakening often arise during delta sleep, not REM sleep.

Schenck and Mahowald [6] reported 70 consecutive cases, which showed a marked predominance among older males with mean age at onset of 53. These findings were mirrored by Olson *et al* [7] who examined 93 consecutive cases, finding a mean age at onset of 60.9 years with an 87% male preponderance. Both case series found a high incidence (33%-57%) of neurological disorders, including Parkinson's disease, dementia without parkinsonism and multiple system atrophy. Recent research has led to the realization that R.B.D. is often an early sign of impending neurodegenerative disease, particularly conditions involving alpha-synuclein deposition e.g. Parkinson's disease and Lewy body dementia.[8,9] This has given rise to the theory that R.B.D. results from a decrease in the normal inhibitory outflow from pontine centres to the spinal motor neurones during REM sleep, allowing motor behaviours to emerge. Also impressive, in these case series, was the high incidence of injuries to self or to bed partners which had been sustained (32%-75%) because of the sleep disorder, which included occasionally fractures, dislocations and even subdural haematomas. Chiu *et al* [10] examined the occurrence of R.B.D. in a community sample of 1034 Hong Kong residents, aged 70 years and above, finding an estimated prevalence of 0.38%. Of interest, two of these patients had been hospitalized for R.B.D. related injury before they were correctly diagnosed. In the Schenck and Mahowald series many of the patients had been suspected initially of having conditions such as nocturnal epilepsy, obstructive sleep apnoea, and various psychiatric conditions. (In Case 1 in this paper, the patient was initially suspected to have been suffering from side-effects to antidepressants or alternatively from epilepsy.) Polysomnographic studies show preservation of the usual distribution and cycling of sleep stages. During non-REM sleep periodic and aperiodic limb twitching is common. The defining characteristic, on sleep E.E.G., is intermittent loss of the normal electromyographic atonia during REM phases. It is important to note here that polysomnographic abnormalities can exist without any clinical behavioural effects,[12] and that there is also some evidence of the existence of long-standing REM sleep prodromes before the R.B.D. becomes manifest.[2] These findings are not surprising given the increasing evidence [8,9] that R.B.D. may well represent a common symptom array resulting from a variety of diffuse, progressive, neurodegenerative disorders.

The treatment of choice for R.B.D. is clonazepam, which has been shown to be partially or completely successful in treatment in up to 87% of patients who used the drug.[7] In some patients with contraindications to this drug e.g. respiratory depression or obstructive sleep apnoea, alternative interventions such as safety the bed environment [7] my be sufficient. Alternative pharmacological treatments include desipramine, carbidopa and clonidine. There are also some cases reported [10,11] of positive response to the acetylcholinesterase inhibitor, donepezil.

Both cases illustrate the clinical features of the disorder; episodic loss of skeletal muscle atonia during REM sleep with consequent complex, often injurious, behaviour as patient acts out their dreams. These cases also demonstrate the degree of disturbance of the patient's and/or spouse's quality of life which can result, the diagnostic difficulties involved and the ready response to clonazepam of R.B.D. Both these patients were typical clinical presentations of R.B.D.; elderly males with evidence of neurological damage who present with new-onset sleep disturbance marked by the presence of violent nightmares (of being attacked, threatened etc) and vigorous gross motor movements, leading to injury or potential injury to self or to bed partners. In the first case described the patient was referred for a sleep EEG, but this did not aid in making a diagnosis. The authors believe that this is because the study did not cover the full overnight period. Developments in EEG technology now allow patients to wear a portable monitor at home overnight, in a way analogous to a cardiac Holter monitor. This, in conjunction with the usual EMG monitoring which accompanies any EEG, should facilitate to an improved extent the correct diagnosis of R.B.D,

as it will allow full overnight monitoring of the patient. This should also be available at most district general hospitals, rather than requiring referral to specialist tertiary care hospitals. These cases also illustrate the ready response of this disorder to low dose clonazepam, ranging between 0.25mg and 1mg here, with marked improvement in the quality of life for the patients and their spouses. The authors believe that a reasonable practice would be, in the first instance and on clinical grounds to make a diagnosis of R.B.D. and to initiate a trial of clonazepam, with evaluation of clinical response. Further tests such as sleep EEG could be reserved for cases which do not show a response to the usually effective doses of clonazepam, or which are atypical in other ways. This report also describes a potential difficulty with clonazepam in this age group, namely an adverse side-effect of sedation which may have implications for compliance and require psychoeducation on the part of the physician treating these patients. A final point is that R.B.D. should always be considered as part of the differential diagnosis in elderly patients with nocturnal wandering and falls.

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Case Report

Pyoderma Gangrensum – a complication of breast biopsy

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CASE REPORT A sixty-three year old woman underwent a frank needle biopsy to explore a previously diagnosed mammographic abnormality. Subsequent histology of the specimen proved to be benign. Initially healing occurred without incident.

Three months later the site of the biopsy, and the surrounding skin, became erythematous and dehised. Wound swabs at this stage showed no bacterial growth. The wound subsequently showed little tendency towards healing, and eight months following the biopsy, a breast sinus was apparent. This was laid open, and a "pus-like" fluid expressed. Delayed primary suturing of the wound was carried out two weeks later. The wound failed to heal and sinus formation deep to the nipple was apparent.

Sixteen months after the initial biopsy, a wedge resection of the right breast (including the nipple) was undertaken, after referral to the Regional Plastic Surgery unit. Histology revealed acute-on- chronic inflammation, with the presence of scattered foreign-body giant cells. Again the wounds failed to heal, and a persistent flat granulating ulcer developed, which showed no inclination towards healing. (Fig 1 & 2).

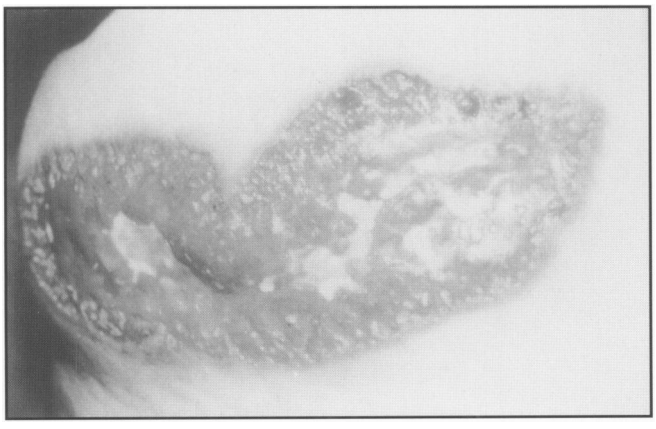

Fig 1. Initial appearance of flat granulating persistant ulcer with areas of slough.

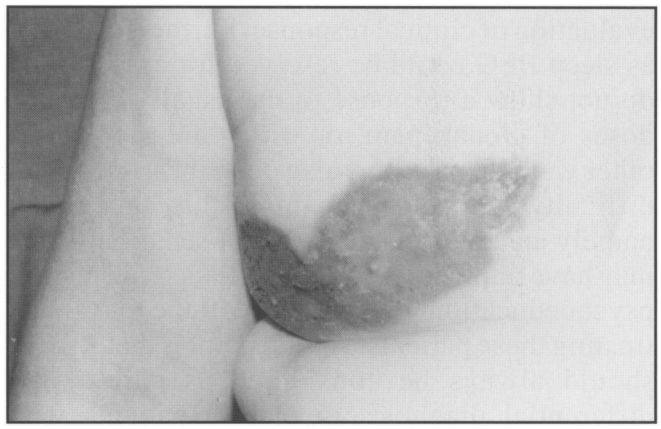

Fig 2. The lesion at commencement of treatment.

A Bacteriological consultation suggested the diagnosis of a Meleneys post operative synergistic gangrene, though this failed to be confirmed by either blood cultures or bacteriological swabs. Prior to further surgery, a dermatological consultation based on the clinical appearance, suggested the diagnosis of Pyoderma Gangrenosum. Investigations were undertaken to exclude secondary causes. Thorough clinical examination, inflammatory markers and colonoscopy proved negative for inflammatory bowel disease. A full blood profile, rheumatoid factor, inimunoglobulins and liver function tests also failed to demonstrate a secondary cause.

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Further bacteriological swabs similarly failed to show any growth. Treatment with systemic corticosteroids and topical medication were commenced and within days the wound began to show signs of healing, both from the wound edge, and surprisingly from its base (Fig 3).

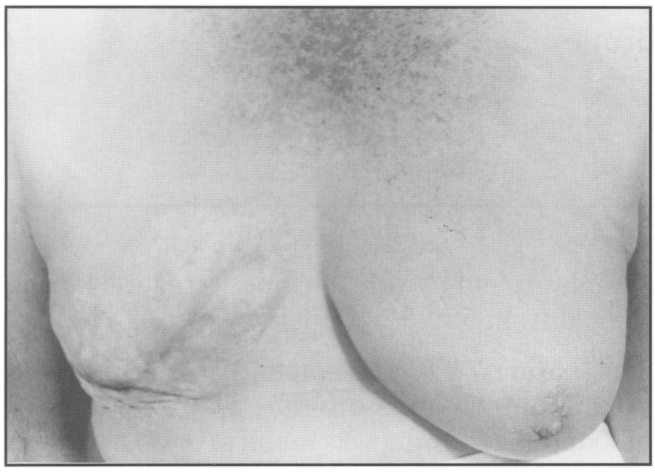

Fig 3. Healing of the lesion fourteen days following corticosteroid treatment.

DISCUSSION

Pyoderma Gangrenosum is a rare, destructive non-infective ulceration of the skin. The condition was first described by Brunsting in 1930.[1] It usually presents as innocuous, erythematous, tender lesions, which break down to form an ulcerated area with a necrotic base and undermined violaceous border. The lesions may be single or multiple and remain quiescent or rapidly progress with marked tissue destruction.

As a result of its benign initial appearance and infrequent involvement of surgical sites, Pyoderma Gangrenosum is often mistaken for resistant infection and inappropriately managed. Many patients undergo either prolonged courses of antibiotics or surgical debridement, leading to even further extension of the disease.[2,3] The lack of pathognomonic histological features makes the diagnosis very difficult for the pathologist if it is not suggested as a differential diagnosis.

The true aetiology of Pyoderma Gangrenosum remains unclear but it is felt that an altered immune system may play a part.[4] Approximately 50% of the cases are idiopathic but the remainder are associated with systemic illness, the most common being inflammatory bowel disease. Other associations include regional enteritis, Crohns disease, arthritis – both rheumatoid and seronegative and haernopoietic neoplasms.[4] Less common associations are osteoarthritis, psoriatic arthritis, chronic active hepatitis, primary biliary cirrhosis, myeloma, systemic lupus erythematosis, hypogammaglobulinaemia and paraproteinaemia (especially IgA).

The recognised treatment of Pyoderma Gangrenosum is immunosuppression with corticosteroids and topical medication. Hyperbaric oxygen is also claimed to be effective in a small number of patients.[9] Other drugs which show benefit, include cyclosporin, dapsone, cyclophosphamide and azathioprine. Though it is important to stress the difficulty in obtaining healing with this condition.

Evidence of this condition occurring in surgical sites has previously been reported,[6,7,8] with reduction mammoplasty, not infrequently cited, though rarely has it been documented following a needle biopsy. This case illustrates that Pyoderma Gangrenosum should always be considered in the differential diagnosis of idiopathic skin ulceration which fails to respond to conventional treatment.

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Case Report

Anti Jo-1 Myositis. 'Mechanic's hands' and interstitial lung disease

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The presence of myositis specific antibodies allows classification of polymyositis into clinically important subsets. Anti Jo-1 autoantibodies are associated with 'mechanic's hands' and interstitial lung disease.

We report three patients who presented with painful weak muscles, a violaccous rash on the extensor aspect of their hands, elevated muscle enzymes, electromyographic and muscle biopsy findings typical of polymyositis. All three patients had anti Jo-1 autoantibodies, 'mechanic's hands' and evidence of interstitial lung disease on CT scan. An incomplete response to corticosteroids was observed in all three patients and additional immunosuppression was required.

CASE REPORT 1

A 41-year -old unemployed man was referred by his general practitioner to a general physician. He presented with shoulder muscle stiffness and weakness. On questioning he was found to have breathlessness on walking two hundred yards. He also described symptoms of Raynaud's phenomenon. On clinical examination he had a heliotrope skin rash over the extensor aspect of his metacarpal-phalangeal and interphalangeal joints. Fissuring and cracks were noted on the distal digital skin pads on his thumbs and fingers. A proximal muscle weakness of grade 4/5, was noted in his upper limbs. Respiratory examination was reported as unremarkable and without signs of cardiac insufficiency.

Serum creatine kinase was elevated at 1467 IU/L (normal range 0-180 IU/L). Subsequent electromyography and histological findings on muscle biopsy showed typical features of inflammatory myopathy. The patient was commenced on 40mg of prednisolone. An incomplete response was noted in terms of symptoms and muscle enzymes (creatine kinase ranged from 539-928 IU/L).

The patient was subsequently referred to a consultant rheumatologist where anti Jo-1 autoantibody testing was found to be positive and CT scan of chest revealed predominantly mid and lower zone interstitial pattern markings with some 'ground glass' appearances. On pulmonary function testing, transfer factor per litre of alveolar volume (KI.CO) was found to be 1.58 m mol min^{-1} kpa^{-1} (94% predicted). Azathioprine was commenced in addition to corticosteroids.

CASE REPORT 2

A 40-year-old housewife was referred by her general practitioner with a gradual onset of neck, shoulder and thigh pains. She noticed while playing badminton that her serve 'wasn't as strong'. Over this period of time she also described breathlessness. On examination, she had a heliotrope rash over the extensor aspect of her metacarpal-phalangeal/inter-phalangeal joints and 'mechanic's hands' (Figure 1). She had mild proximal muscle weakness, graded 4+/5 in her shoulder and pelvic girdles. Fine bibasal early

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inspiratory crepitations were heard on auscultation.

Serum creatine kinase was 1518 IU/L (normal range 0-180 IU/L). Anti Jo-1 autoantibody testing was positive. Subsequently an electromyogram revealed mild myopathic changes and muscle biopsy revealed features in keeping with inflammatory myopathy. Early interstitial fibrosis was seen on CT scan of chest. K1.CO was measured at 2.01 m mol min^{-1} kpa^{-1} (113% of predicted).

This patient was commenced on 40mg of prednisolone daily. A moderate symptomatic improvement was observed but her serum muscle enzymes remained elevated. The addition of azathioprine coincided with a symptomatic improvement and normalisation of muscle strength and enzymes. Her corticosteroid therapy was slowly reduced to 7.5mg of prednisolone daily, without relapse.

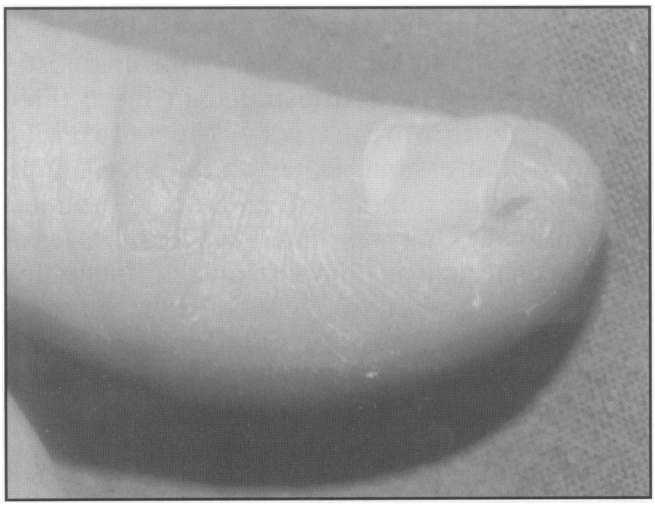

Fig 1. 'Mechanic's hands' – characterized by scaling and hyperkeratosis of the distal skin pad and lateral aspect of the fingers.

CASE REPORT 3

A 30-year-old school teacher was referred by his general practitioner. He reported an acute history of painful shoulders and 'roughening' of the skin at his fingertips. During this period he noted himself to be 'breathless' on exertion. On examination fissuring and cracking of the skin pads in his distal fingers, typical of 'mechanic's hands' was observed. A typical dermatomyositis rash was present on the extensor aspect of his hands. Muscle weakness was not observed. Fine bibasal early inspiratory crepitations were heard on auscultation of his chest.

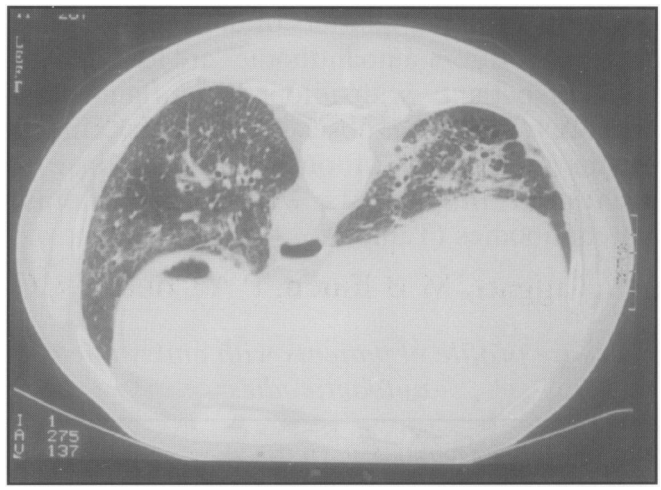

Fig 2. CT scan of chest revealing bibasal interstitial changes in a patient with anti Jo-1 autoantibodies.

Initial serum creatine kinase was mildly elevated at 296 IU/L. Other muscle enzymes were mildly elevated AST 51 IU/L (normal range 10-42 IU/L) and Aldolase 8.2 U/L (Normal range 0.5-3.12 U/L). Anti Jo-1 antibody testing was positive, confirming the clinical suspicion of antisynthetase syndrome. Mild myopathic changes were noted on his electromyogram. CT scan of his chest revealed bibasal interstitial changes (figure 2). K1.CO was 1.3 m mol min^{-1} kpa^{-1} (76% of predicted). An incomplete response to 40-60mg of prednisolone was observed. A clinical improvement was noted in terms of breathlessness and muscle enzymes with the addition of azathioprone. His corticosteroid therapy was reduced to 5mg of prednisolone daily, without relapse.

DISCUSSION

These cases illustrate that the presence of 'mechanic's hands' and serum antibodies to anti Jo-1, should alert physicians to the possible presence of interstitial lung disease.

The annual incidence of polymyositis/dermatomyositis has been estimated at 6 cases per million per year, with peak age of onset at 45-55 years.[1] Bohan and Peter's classification[2] of patients with idiopathic inflammatory myopathies, defined subgroups with specific clinical and pathological criteria, More recently, the detection of myositis specific autoantibodies, has been found to aid classification of defined subgroups with regard to clinical features, response to treatment and prognosis.[3]

Antisynthetase autoantibodies are the most common myositis-specific autoantibody. Anti Jo-1

accounts for three-quarters of the antisynthetase family. Anti Jo-1 autoantibodies are found in 20-30% of patients with idiopathic inflammatory myositis. Love *et al* observed particular clinical features, rapidity of onset and response to treatment in patients with antisynthetase autoantibodies (Table).[3]

TABLE

Disease profile of patients with antisynthetase autoantibodies

Sex ratio – Female/Male	1.7
Age at diagnosis	4th decade
Onset	Acute
Major clinical features	Interstitial lung disease Fever Raynauds phenomenon 'mechanic's hands'
Steroid response	Moderate
Mortality (%)	20

Anti Jo-1 myositis usually has an acute onset in the spring. Patients with antisynthetase autoantibodies, compared to patients without these autoantibodies, have significantly more frequent distinctive clinical features – 'Mechanic's hands', non-erosive arthritis, fever, Raynaud's and interstitial lung disease. As illustrated in *fig. 1*, 'Mechanics hands' is characterised by scaling, fissuring and hyperkeratosis of the distal skin pad and lateral aspect of the fingers. 'Mechanic's hands' are present in approx. 70% of patients with antisynthetase autoantibodies.

Interstitial lung disease has been reported in approximately 90% of patients with antisynthetasc autoantibodies [3] and is an important cause of mortality. Asymptomatic patients may have radiographic manifestation of interstitial lung disease and breathlessness may be due to non-pulmonary problems. Respiratory muscle weakness, cardiac disease and aspiration pneumonia may also cause breathlessness in patients with inflammatory muscle disease.[9, 10, 11] However, the presence of 'mechanic's hands' and anti Jo-1 autoantibodies suggests that interstitial lung disease is the likely cause of breathlessness on exertion. Sauty *et al* reported four cases of patients who presented with interstitial lung disease without muscle involvement and whose serum was positive for anti Jo-1 autoantibodies.[4]

Patients with antisynthetase syndrome tend to have a moderate response to corticosterolds. Sixty percent of patients will experience a flare-up of their myositis during tapering of corticosteroid therapy.[3] Late relapses after initial remission appear to be more frequent in patients with antisynthetase syndrome.[5] Therefore corticosteroid therapy should be tapered slowly, and close surveillance is necessary to monitor for disease exacerbation. Because of the poor response to corticosterolds, immunosuppressive agents should be considered early in patients with antisynthetase syndrome. This may have benefits in terms of reducing steroid side-effects and possibly improved response.[6] A report by Joffe *et al* suggests that patients with antisynthetase autoantibodies may respond more favourably to methotrexate than to azathioprine.[7] Although there is no evidence that methotrexate pulmonary toxicity is more common in patients with interstitial lung disease, the development of this complication in a myositis patient with interstitial lung disease, may increase the risk of respiratory failure and present with diagnostic difficulties. Thus, as illustrated in these three cases, azathioprine was the preferred immunosuppressant. Deteriorating K1.CO in patients with interstitial and antisynthetase autoantibodies may respond to moderate doses of cyclosporine and azathioprine in addition to low dose corticosteroid.[4] In other reports cyclophosphamide in association with corticosteroids has shown a clinical and functional response.[8]

Patients with antisynthetase syndrome have a higher mortality rate (21%) than myositis overall (7%),[3] which is probably related to interstitial lung disease.

The physical sign of 'mechanics hand' is a useful sign for identifying patients with anti Jo-1 myositis. The presence of anti Jo-1 autoantibodies is particularly important because it alerts the clinician to interstitial lung disease and the fact that additional immunosuppression may be required.

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Case Report

Acute B Cell Lymphoblastic Leukaemia and Human Immunodeficiency Virus Infection (HIV)

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Accepted 24 April 2002

Highly active anti-retroviral therapy (HAART) and prophylactic therapy for opportunistic infection have significantly improved the survival and quality of life for patients infected with the Human Immunodeficiency Virus (HIV).[1,2]

Lymphoproliferative disease complicates the clinical course of HIV infection in approximately 10% of patients and the incidence of Non Hodgkins Lymphoma is 60-200 times more common than the general population.[3,4] Diffuse large B cell lymphoma, Burkitt's Lymphoma, Burkitt like Lymphoma and Primary Cerebral Lymphoma are the most common subtypes with Hodgkins Disease, Plasmacytoma and Body Cavity Based Lymphomas also increased in incidence.[4] Acute B cell lymphoblastic leukaemia (B ALL) is uncommon representing 5% of all adult patients with ALL.[5] An association with HIV infection is rare and limited to case reports. We report the case of a 40 year old man and discuss his treatment and clinical course. We suggest that B cell ALL should be included in the criteria for a diagnosis of the Acquired Immunodeficiency Syndrome (AIDS) and that patients presenting with this type of leukaemia should be fully assessed regarding risk factors for HIV infection and when necessary tested following appropriate counselling. We support present recommendations that patients with HIV associated lymphoproliferative disease receiving chemotherapy should receive concurrent HAART and when possible are entered into clinical trials where the maximal therapy can be addressed.

CASE REPORT A 40 year old homosexual male presented to a District General Hospital in March 1999 with a short history of a chest infection, shortness of breath, night sweats, weight loss and left facial weakness. Physical examination revealed a complete left lower motor neurone facial nerve palsy, dullness and crepitations at the right base and smooth hepatosplenomegaly. There was no peripheral lymphadenopathy sternal tenderness or testicular enlargement. He had been previously well and working as a fitness instructor. Six years previously he attended a genitourinary clinic where he tested positive for HIV. He declined treatment at this time and was lost to review.

INVESTIGATIONS

Haemoglobin was 10 g/dl with a platelet count of 135 x 10^9/l and a white cell count of 9.6 x 10^9/l. The differential white cell count revealed lymphocytes at 4.0 x 10^9/l, neutrophils at 4.5 x 10^9/l, monocytes at 0.8 x 10^9/l and blasts cells of L3 morphology at 0.2 x 10^9/l. Lactate dehydrogenase (LDH) was 10 828 iu/l with a urate level of 0.58 mmol/l.

Chest radiograph showed a right hilar mass with an associated pleural effusion. Subsequent pleural aspiration revealed the presence of blast cells.

Computerized axial scanning (C.T.) confirmed the chest findings and hepatosplenomegaly. C.T. scan of the brain was normal however Cerebrospinal fluid (CSF) examination revealed L3 blast cells. Bone marrow aspirate and trephine

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biopsy revealed a packed marrow with blast cells exhibiting characteristic L3 morphology with basophilic cytoplasm and vacuolation. (Figure). Immunophenotype of these blast cells revealed strong positivity for the B cell markers CD19 and CD22 with weaker expression of CD10. Terminal deoxynucleotidyl transferase (TDT) was negative. This immunophenptype in combination with the morphological findings was in keeping with a diagnosis of Acute B cell Lymphoblastic Leukaemia. Virology confirmed HIV positivity with a viral load of 1.3 x 10^6 copies per/ml.

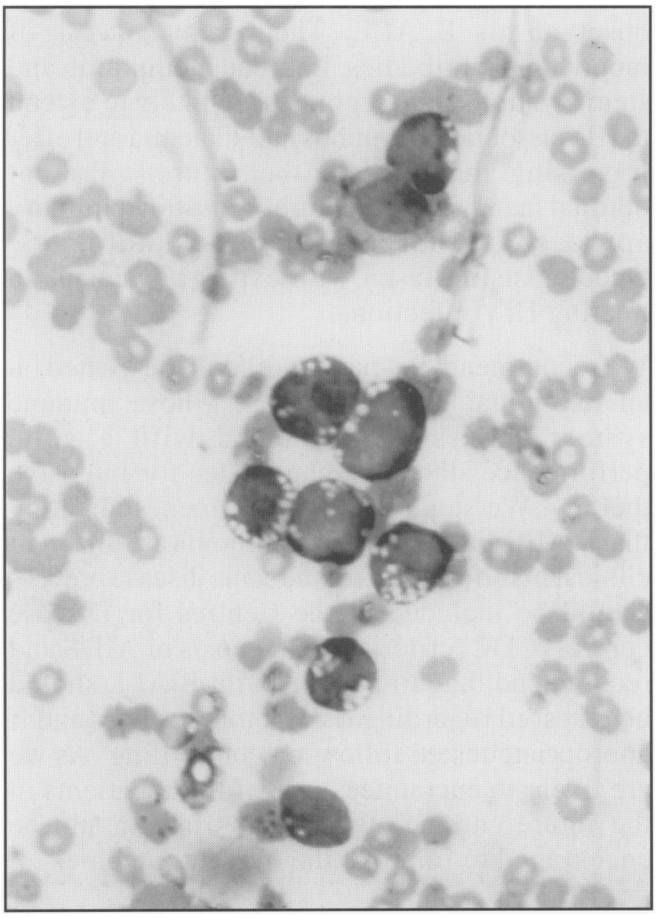

Fig. Bone marrow aspirate showing blast cells of L3 morphology exhibiting basophilic and vacuolated cytoplasm. (Wrights Stain)

Hepatitis A B C, Epstein Barr Virus and Cytomegalovirus all tested negative and the CD4+ve lymphocyte count was 475 µ/l. Due to biohazard regulations within the Cytogenetics Laboratory we were unable to obtain a cytogenetic result.

TREATMENT

He received combination chemotherapy with the COP/COPADM/mini CYVE regimen. This containing combinations of the drugs cyclophosphamide, vincristine, prednisolone, doxorubicin, ARA-C, etoposide and methotrexate. High dose methotrexate was administered at a dose of 8 gm/m.[2] Intrathecal chemotherapy was given and followed by cranial irradiation.

He declined anti-retroviral therapy initially however following discussion this was commenced in August 1999 with zidovudine, lamivudine and efavirenz. Repeat viral load was <150 copies/ml in December 1999. Chemotherapy was well tolerated with no opportunistic infections and interestingly a period of prolonged thrombocytopenia responded to commencement of the anti-retroviral therapy. Co-trimoxazole and fluconazole prophylaxis were administered.

Haematological remission was achieved in his blood and bone marrow with resolution of the chest x ray appearances. Despite the absence of blasts in his CSF there was no resolution of his facial nerve palsy. He had 2 HLA matched siblings and was considered for allogeneic transplantation however his remission was short lived and he relapsed 2 months later within his chest, CSF and bone marrow with an LDH measuring 40 000 µ/l. Despite further attempts at re-induction he was unable to achieve a complete second remission and died in February 2000.

DISCUSSION

Highly active anti-retroviral therapy (HAART) and prophylactic therapy against opportunistic infection have significantly decreased the morbidity and mortality associated with the Human Immunodeficiency Virus (HIV).[1,2] Lymphoproliferative disease complicates the clinical course in approximately 10% of patients. This incidence may be decreasing since the introduction of HAART as suggested in a recent meta-analysis and appears most marked for Primary Cerebral Lymphoma.[3] The pathogenesis is not completely understood however continued B cell proliferation in the absence of normal T cell immunosurveillance is a likely factor with the Epstein Barr Virus implicated in many cases.[3,4] Rarely HIV may be directly oncogenic in T cell lymphomas and Human Herpes Simplex Virus 8 (HHV 8) has been implicated in Body Cavity Based Lymphoma.[4] Treatment is difficult as the disease is often advanced at diagnosis with extranodal and bone marrow involvement present. The risk of opportunistic infection is increased with

intensive chemotherapy and viral induced myelodysplasia may delay recovery of bone marrow function.[3] There is also a concern that chemotherapy may exacerbate HIV infection. Adverse prognostic features are a poor performance status, a prior diagnosis of AIDS (Acquired Immune Deficiency Syndrome), CD 4 lymphocyte count <100 μ/l and extranodal disease, particularly central nervous system involvement. The overall survival is usually less than 1 year.[6] Several chemotherapy regimens have been investigated and an initial randomised trial comparing a low dose and standard dose chemotherapy regime (mBACOD) with granulocyte – macrophage colony stimulating factor (GIVI-CSF) support showed no difference in response or survival in the two groups however there was an increase in the incidence of neutropenic sepsis in the full dose arm.[7] Recently developed protocols have resulted in improved response and survival rates, particularly in good risk patients. There is also the suggestion of improved survival since the introduction of HAART in 1996 with further studies required for confirmation.[8, 9]

Acute B cell lymphoblastic leukaemia (B ALL) is characteristically associated with central nervous system involvement and a poor prognosis. The cytogenetic abnormality t(8:14) is present in the majority of cases this resulting in dysregulation of the c-myc proto-oncogene which is implicated in pathogenesis. Morphology is characteristic with blast cells exhibiting strongly basophilic cytoplasm and vacuolation (Figure). Recent intensive protocols incorporating high dose methotrexate and ARA-C have shown improved survival rates in both children and adults.[10]

B ALL in association with HIV is rare and limited to case reports. Approximately 22 cases have been reported to date.[11] In most previously reported cases there was no history of AIDS and the CD 4 count was reasonably well preserved at diagnosis.[11] This pattern of presentation was similar in our patient. Treatment with intensive combination chemotherapy was well tolerated and no atypical opportunistic infections were encountered. An episode of prolonged thrombocytopenia of less than 20 x 10^9/l for 5 months responded to the initiation of anti-retroviral therapy with counts improving to 70 x 10^9/l and was suggestive of viral induced thrombocytopenia. Prior to relapse this patient had been considered for an allogeneic bone marrow transplant, syngeneic transplantation having previously been described in an HIV positive haemophiliac patient with ALL.[12] The poor survival of our patient was similar to the majority of cases reported.

The impact of HAART on survival remains to be seen and although overlapping toxicities and interactions may occur it is recommended all patients receive this therapy in combination with chemotherapy. Although more evidence is awaited it is possible that had our patient received anti-retroviral therapy earlier in the course of his infection this may have delayed or prevented the onset of his B ALL. The recent success of monoclonal antibodies, immune modulation and stem cell transplant regimens are likely to extend to HIV associated lymphoma/leukaemia and offer promising therapies in the future.[13] Present optimal management requires a multidisciplinary approach with specialist Haematologists/ Oncologists in liason with expert physicians in treating HIV infection.

We recommend that patients should be treated on an individual basis and those whose immune system is less compromised with a good performance status are candidates for intensive therapy. We suggest that a statement indicating that B ALL and Burkitt's Lymphoma are different clinical manifestations of the same disease process should be included in the Centres for Disease control (CDC) criteria for diagnosis of AIDS and recommend that all patients with B ALL should be assessed regarding risk factors for HIV and if appropriate tested following counselling. As we are likely to encounter more of these patients in the future entrance to clinical trials should be encouraged to improve the overall outcome.

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Case Report

Primary torsion of the omentum

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Accepted 12 March

Primary torsion of the omentum often presents as an acute surgical emergency, with typical signs and symptoms of acute appendicitis.

CASE HISTORY A 26-year-old man presented with a one day history of right iliac fossa pain which was aggravated by movement and coughing. He had a similar episode which lasted a few hours, two weeks previously. There was no history of trauma. On examination he was pyrexic, with marked tenderness in the right iliac fossa and right flank. His white cell count was 17.1 X 10^3/ul. A diagnosis of appendicitis was made.

At operation, through a Lanz incision, a normal appendix was found. The terminal ileum appeared normal and a Meckel's diverticulum was not found. However, there was some serosanguineous fluid in the right paracolic gutter and an ischaemic segment of omentum. A small midline laparotomy above the umbilicus was made. A segment of omentum had twisted and become ischaemic and necrotic (Figure). This was excised and an appendicectomy was performed. Histopathology revealed a normal appendix and 56g of infarcted omentum. He made an uneventful post-operative recovery.

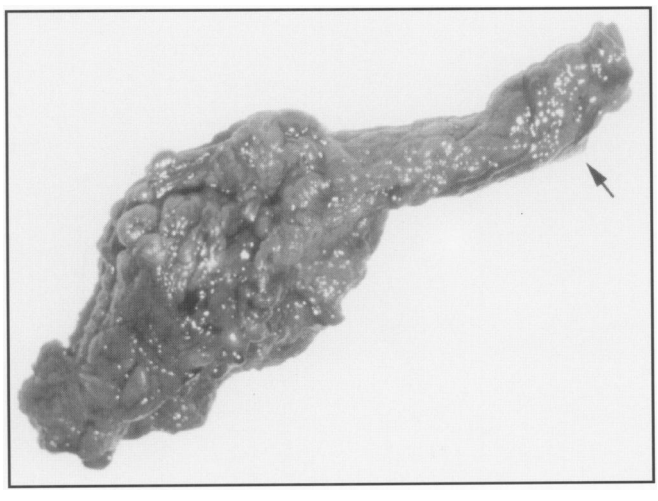

Fig. Infarcted omentum – arrow showing point of torsion.

DISCUSSION

Torsion of the omentum can be either primary (idiopathic) or secondary. Secondary torsion is usually associated with adhesions to the omentum, for example, to a cyst, tumour, hernias or foci of intra-abdominal inflammation. Primary or idiopathic omental torsion is rare and was first described by Eitel in 1899.[1] The cause is obscure. Leither *et al* described predisposing and precipitating factors.[2] Predisposing factors were anatomical variations including tongue like projections from the free edge of the omentum, bifid omentum, accessory omentum and obesity associated with irregular distribution of fat within the omentum.[2] Payr suggested that venous redundancy relative to the omental arterial blood supply was also a predisposing factor.[3] Its longer and tortous veins allow kinking, thus offering a point of fixation around which twisting may occur.[3] Precipitating factors were those that cause displacement of the omentum, such as heavy exertion, sudden change in body position, coughing, straining and hyperperistalsis with over-eating.[2]

Primary torsion of the omentum is always unipolar as there is only one locus of fixation, whereas secondary torsion, which is more common, is usually bipolar – that is, torsion of a central portion between two fixed points.[2] The omentum in both primary and secondary torsion twists a variable number of times. An interesting aspect is the predominance of torsion involving the right side of the omentum. This may reflect its larger size and hence its greater tendency to tort.[4] The

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important differential diagnosis of appendicitis makes it imperative to operate on patients who are clinically unwell. In contrast, left sided primary omental torsion could possibly be diagnosed as acute diverticulitis and managed non-operatively.[7] Hence, left sided torsions may be seldom seen because they are less often operated on and less frequently diagnosed.[7]

When torsion occurs, venous return becomes restricted and the distal omentum becomes congested and oedematous. Haemorrhagic extravasation results in a characteristic serosanguineous fluid in the peritoneal cavity. If the process continues for sufficient duration, haemorrhagic infarction and eventual necrosis occurs. If not excised, the mass becomes atrophied and fibrotic, and on rare occasions is autoamputated.

Clinically, primary and secondary torsion of the omentum are similar and occur in the fourth and fifth decades, males being affected twice as commonly as females. The most frequent presentation is pain in the right iliac fossa which is usually of sudden onset, and is constant with a gradual increase in severity. There may be a past history of similar but less severe pain,[5] as occurred in our case. Nausea and vomiting occur in less than 50% of cases.[2] Moderate leucocytosis and fever are usually present. Tenderness with peritonism is invariably present. A mass may be felt if a large segment of omentum is involved.[2]

Computerised tomography has been used in diagnosing torsion of the omentum. It is very sensitive for showing an omental mass but not specific for making a diagnosis of torsion.[6] During surgery, the presence of serosanguineous fluid in the peritoneal cavity in the absence of pathological conditions in the appendix, gall bladder and pelvic organs should alert the surgeon to the possibility of torsion of the omentum.[2] Treatment consists of resecting the infarcted omentum and treating the underlying aetiological condition in patients with secondary omental torsion.

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Selected abstracts for Junior Members Forum: 22 February 2001

Last year junior doctors were invited to present research abstracts for poster or oral presentation at the Junior Members Forum. More than 60 abstracts were received and were reviewed, assessed and scored by the Honorary Secretary of the Society.

Three abstracts were accepted for oral presentation and eight abstracts were accepted for poster presentation at the Junior Members Forum. This innovative endeavour, pioneered by the President of the Society Dr Robin Harland, proved a great success in providing the opportunity for junior doctors from different medical and surgical disciplines throughout the province to present their research work to fellows and members of the Ulster Medical Society.

G McVeigh, Hon Secretary.

COMPLICATIONS OF PAEDIATRIC CARDIAC CATHETERISATIONS: A FOUR YEAR SURVEY

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Aims: To determine the frequency and nature of complications arising from both diagnostic and interventional paediatric cardiac catheterisation performed in a Regional centre, and to assess the risk of various procedures in relation to age.

Methods: A retrospective study of 421 consecutive paediatric cardiac catheterisations performed on 374 infants and children under 14 years in the cardiac catheterisation laboratory, over a 4-year period (1 January 1994 – 31 December 1997). Information was collected from clinical casenotes and from the central catheterisation database.

Results: Data was analysed from 421 procedures. A total of 243 (58%) diagnostic and 178 (42%) interventional procedures were performed. Forty were neonates and 127 (34%) were under 1 year. General anaesthetic was given in 24 (5.7%) cases.

There were 51 documented complications in 40 catheterisation procedures (9.5%), of which 28 were major and 23 were minor. The highest complication rate was in neonates (22.5%). Serious complications during the procedure included respiratory arrest (5, 1.2%), dysrhythmias (11, 2.2%), heart failure (1, 0.2%), and occluder embolisation (5170, 7.1%). Post-catheterisation complications included dysrhythmias (2, 0.5%), heart failure (3, 0.7%), respiratory arrest (3, 0.7%) and limb ischaemia (12, 2.9%). Six of the 8 respiratory arrests (75%) occurred in infants under 10 weeks of age. There was no significant difference in the complication rate of interventional (9.6%) over diagnostic (9.5%) procedures. There were no deaths in this study group as a direct complication of the catheterisation.

Conclusions: Major complications are an infrequent association with paediatric cardiac catheterisation but occur most commonly in younger patients. Overall the complication rate in this series is comparable to nation-wide figures from Regional Paediatric Cardiac Catheterisation Centres.

THE EFFECT OF ANTAGONISTS TO PLATELET ACTIVATING FACTOR AND TUMOUR NECROSIS FACTOR IN AN ANIMAL MODEL OF GUT MUCOSAL INJURY

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Introduction: Necrotising Enterocolitis (NEC) is a disease of premature neonates, which is thought to originate with a gut mucosal injury. Using an animal model, we investigated the effect of antagonists to Platelet Activating Factor (PAF) and Tumour Necrosis Factor a (TNFα) on mortality and cytokine production at 24 hours.

Materials and Methods: Adult Wistar rats (weight: 250-300g) were divided into 6 groups of 12 and antagonists given as outlined in table 1. Each rat was anaethetised (Ketamine 0.3ml/

Xylazine 0.15ml IM) and a midline laparotomy performed. A microvascular clamp was applied to the superior mesenteric artery for 45 minutes, and after clamp removal the bowel was reperfused for 24 hours.

At the end of this time period, blood samples were taken for assay of plasma IL-6 and TNFα. The animals were sacrificed, and the bowel removed for assessment of mucosal damage using a pre-defined injury score. During the experimental period, any animals showing signs of undue distress were sacrificed immediately.

TABLE

Group 1	*Group 2*	*Group 3*	*Group 4*	*Group 5*	*Group 6*
Sham loparotomy (no antagonist)	Ischaemia Only (no antagonist)	Pentpoxifylline given prior to clamp release	Pentoxifylline given post clamp release	Lexipafant given prior to clamp release	Lexipafant given post clamp release

Pentoxifylline (PTX) is a TNF α antagonist Lexlipafant (LPT) is a PAF antagonist

Results: All antagonists under test tended to attenuate rise in plasma IL-6 and TNFα seen at 24 hours, but differences were not significantly different from controls.

The antagonists did not alter the degree of mucosal injury seen in any of the groups.

Survival at 24 hours was increased in all antagonist groups (group 2 v group 6: survival 58.3% v 91.7%) but differences did not reach statistical significance.

Conclusions: The use of LPT and PTX in this animal model of ischaemic gut injury tends to attenuate the expected cytokine rise and increases survival rates at 24 hours. Unfortunately differences aid not reach statistical significance.

"NIGHT PAIN, KNEE DEFORMITY AND THE OXFORD KNEE SCORE IN GENERALISED AND ISOLATED PATELLO-FEMORAL OSTEOARTHRITIS - AN ANALYSIS OF 560 PATIENTS."

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Pain is a common symptom of arthritic disease. When it is not satisfactorily controlled it may lead to changes in personality, lifestyle and functional ability, as well as, depression and sleep disturbance. Night pain in particular, is a very distressing symptom for patients, which produces varying degrees of insomnia. This often leads to an increased use of potent analgesics and night sedatives.

Degenerative disease affecting the patello-femoral joint most often occurs as part of a generalised knee arthritis, but can also occur in isolation with sparing of the tibio-femoral compartments. This occurs in approximately 5% of patients with arthritis of the knee.

Following a review of a series of patients with isolated patello-femoral arthritis, we noted that these patients reported a high frequency of nocturnal knee pain. As a result we set out to determine if patients with isolated patello-femoral arthritis have significantly more night pain, than those patients with generalised knee osteoarthritis. Furthermore we also evaluated the influence of knee deformity, body mass index and gender on the night pain and Oxford Knee Scores.

We reviewed the preoperative knee scores of 560 consecutive patients undergoing primary total knee arthroplasty. Thirty knees had isolated patello-femoral disease (5.7%). It was found that females suffer significantly more night pain than males ($p=0.001$). The site of disease and preoperative knee deformity did not appear to significantly influence the degree of night pain suffered by patients with degenerative knee arthritis. No simple relationship between increasing knee deformity and night pain score was evident. The Oxford Knee Score displayed a similar pattern. Patients with generalised osteoarthritis and those with a preoperative valgus knee deformity were however found to have significantly more preoperative fixed flexion deformity ($p<0.05$) than those with isolated patello-femoral osteoarthritis or a preoperative varus knee deformity.

EPIDEMIOLOGY OF ILLICIT DRUG USE IN PATIENTS PRESENTING WITH DELIBERATE SELF-POISONING IN A BELFAST HOSPITAL

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Objective: Illicit drug use is common in our society. Recent surveys suggest a lifetime

prevalence of drug trying for 16-59 year olds in the UK at 24-30%. Deliberate self-poisoning is also a major public health problem. Socio-economic depravation is associated with both behaviours. This study aims to determine the prevalence of substance abuse in patients presenting with deliberate self-poisoning in the Belfast area.

Methods: The study consisted of an anonymous questionnaire. A sample of patients in the age range 15-45 years presenting with deliberate self-poisoning was identified and informed consent was obtained. Details recorded included age, sex, drugs taken in overdose and recreational drug use. If illicit drugs were used the type of drugs were recorded as was whether use had been in the past week, month, year or longer ago. In addition, a 20ml urine specimen was taken as soon as possible after admission to screen for drugs of abuse (amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine metabolites, opiates, LSD and methadone).

Results: Forty-nine patients admitted to hospital following deliberate self-poisoning were interviewed. The pattern of drugs taken in overdose was similar to other recent studies with paracetamol being the most commonly ingested drug (40.8%). Alcohol was involved in 30.6% of overdoses. Twenty-five out of the forty-nine patients (55.1%) had used drugs at some time in their lives. 14.3% of individuals had used drugs within the week prior to admission and a further 6.1% within the preceding month. Cannabis was the most commonly used drug having been tried by 51% of subjects. Ecstasy had been used by 26.5% of subjects, 10.2% having used the drug within the week or month or month preceding admission. Only 34 urine samples were received by the laboratory. Positive results for benzodiazepines, alcohol and codeine were in keeping with drugs taken in overdose.

Conclusions: Illicit drug use is more common in patients presenting with deliberate self-poisoning than in the general population. Patients were happy to volunteer their drug history and urine screening did not yield any useful additional information.

CHARACTERISATION OF AN *IN VITRO* MODEL OF ENTEROCYTE BARRIER FUNCTION

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Background: The barrier function of the gastrointestinal epithelium is important in preventing translocation of enteric bacteria and their products to the systemic circulation. Loss of intestinal barrier function contributes to the morbidity and mortality associated with critical illness in surgical patients, but the factors which determine intestinal barrier function are poorly understood. Enterocytes are the

main physical component of the gut barrier and are the 'first line' of cellular defence against luminal factors. This study examined the properties of a polarised enterocyte monolayer grown *in vitro* as a simple model of the gut barrier.

Methods: Caco-2 enterocytes were seeded into the apical side of a two-chamber Transwell system containing Dulbecco's modified Eagle's medium which was replenished every 2 days. The system was studied for 25 days, and the following features were assessed:

1. cell morphology
2. lactate dehydrogenase release
3. electrical resistance
4. clearance of a probe molecule, fluorescein sulphonic acid (FSA)
5. trans-monolayer transport of live enteric bacteria (*E coli* C25) and synthetic fluorescent-labelled microbeads (1.5 micron diameter, similar to bacterial size)

Results: Light microscopy confirmed the formation of a confluent cell monolayer 4 days after cell seeding. Lactate dehydrogenase release was low at all time points, indicating maintained cell viability. Electrical resistance of the monolayer was shown to rise steadily for 15 days and then stabilise. Clearance of FSA across the monolayer fell steadily over 15 days and remained at low levels thereafter. The cell monolayer formed a significant barrier to the passage of bacteria and microbeads by 7 days after seeding, although there was still appreciable transcytosis in the mature, 21-day-old monolayer. Transport of *E coli* C25 was almost 30 times more efficient than that of fluorescent microbeads.

TABLE

Days	*Electrical resistance (ohms/cm²)*	*FSA Clearance (nl/cm²/gr)*	*C25 transcytosis (bacteria/hr, 1000s)*	*Microbead transcytosis (beads/hr, 1000s)*
0-3	3(1)	12622(1063)	23000(0)	33300(6140)
4-6	273(21)	7999(702)	16800(3170)	14800(4660)
7-13	660(69)	3672(1248)	3830(0)	29(9)
14-20	1111(63)	283(30)	1010(66	53(11)
21-25	1122(28)	395(29)	1670(668)	58(21)

All figures are mean (s.e.m.)

Conclusions: Caco-2 enterocytes form a viable, confluent cell monolayer which has high electrical resistance and low permeability by 15 days after seeding. Bacterial transcytosis across the monolayer is much more efficient than microbead transcytosis, suggesting that the passage of enteric bacteria through enterocytes is not simply a passive process but may involve active mechanisms of uptake and translocation. This model allows a number of features of enterocyte barrier function to be assessed simultaneously and we hope it will prove useful in the elucidation of the factors which determine intestinal barrier function.

EXAGGERATED HIND LIMB ISCHAEMIA-REPERFUSION INJURY IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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Background: It has been suggested that diabetes mellitus may accentuate ischaemia-reperfusion injury following lower limb revascularisation and that may lead to more local and remote organ dysfunction.

Aim: This study investigates whether diabetes mellitus accentuates hind limb ischaemia-reperfusion injury in Wistar rats.

Method: Male Wistar rats rendered diabetic (n=40) following injection of streptozotocin were compared to non-diabetic control rats (n=30). Each group was divided into sham, 4h of hind limb ischaemia, 4h of ischaemia followed by 10 min, 30 min or 60 min of reperfusion. Plasma concentrations of the end product of lipid peroxidation (Malondialdehyde (MDA)) and the antioxidants (vitamin A & E) were measured. The resting membrane potential (RMP) of the ischaemic gastrocnemius muscle was recorded at the same time points.

Results: Median (interquartile range), *p<0.05 versus Ischaemia, +p<0.05 versus Non diabetic group.

TABLE

	Sham	*Ischaemia*	*Rep 10min*	*Rep 30min*	*Rep 60min*
			Non diabetic group		
MDA(pmol/ml)	1.3(0.6)	1.1(0.3)	1.5(0.4)*	2.2(l)*	1.4(0.3)
Vit A(μmol/l)	1.5(0.2)	1.5(0.3)	1.5(0.1)	1.4(0.2)	1.3(0.2)*
Vit E(μmol/l)	27.9(3.9)	28.9(4.6)	26.9(3.8)	24.4(4)	24.7(4.6)*
RMP(mV)	78(8)	64(11.8)	57(6.8)	53(14.8)	62(10.8)
			Diabetic group		
MD.A(pmol/ml)	4.5(1.8)+	2(1.9)+	3(1.6)+	4.2(1.2)*+	2.3(0.3)*+
Vit A(μmol/l)	1(0.2)+	0.9(0.1)+	0.8(0.1)*+	0.8(0.2)*+	0.7(0.2)*+
Vit E(μmol/l)	26.3(4.6)	28(4.2)	27.2(7.7)	24.4(6.6)*	22.5(4.5)*
RMP(mV)	75(21.5)	55(5.8)	51(3)+	47(7.3)+	57.5(15)

Following reperfusion, the diabetic group showed greater and more persistent elevation of MDA, greater reduction of antioxidants Vit A & E. This was associated with reduction in the RMP only in the diabetic group. There was significant correlation between MDA level and the RMP in both groups ($_r$=0.63 (non-diabetic group), $_r$=0.57 (diabetic group)).

Conclusions: These results indicate that oxidative stress following reperfusion injury is greater in the presence of diabetes mellitus. This may lead to decrease in the resting membrane potential and increase in the vascular permeability leading to more local and remote complications.

A NEW GENETIC LINK IN THE AETIOLOGY OF SCHIZOPHRENIA?

TWO NORTHERN IRELAND CASES OF 22q11 DELETION

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Background: Chromosome 22q11 deletion (*Velo-Cardio-Facial Syndrome, Catch 22, Shptintzen Syndrome, Di George Syndrome)* is a syndrome of congenital abnormalities first

reported by Strong in 1968 and further delineated by Shprintzen in 1978. It is autosomal dominant with an estimated prevalence of 1 in 4000 live births. The phenotype includes cardiac anomalies, facial dysmorphology including cleft palate, hypernasal speech, hypocalcaemia, delayed development (68%) and a high incidence of schizophrenia-like psychosis (10-29%). A characteristic behavioural phenotype includes bland affect, monotonous voice, impaired attention and poor social interaction with disinhibited or shy behaviour.

Aims: We describe two men who presented with mild learning disability (LD) and schizophrenia-like symptoms, and were found to have 22q11 deletion. We also describe the structural (CT) & functional (SPECT) neuroimaging findings in these patients.

Method: Two case reports describe history, psychopathology and clinical progress. 22q11 deletion was diagnosed using fluorescence *in situ* hybridisation [FISH] analysis. Brain structure was investigated by CT scan. Brain function was investigated by Single Photon Emission Computed Tomography (SPECT). SPECT is a functional neuroimaging technique which demonstrates cerebral blood flow (and, by implication, metabolism) *in vivo*.

Results: In both cases, SPECT scans demonstrated widespread marked reduction of cortical blood flow, including frontal areas. In one patient, reduction in frontal blood flow was dramatic, particularly on the left. CT scans confirmed ventricular enlargement. Enlargement of the lateral ventricles, reduced brain size and impairment of cognitive functions associated with the frontal lobes are consistent findings in severe chronic schizophrenia. However, in these two patients with 22q11 deletion, effects of medication, epilepsy, head injury, psychosis and genetic abnormality cannot be differentiated.

Conclusions: Any of the characteristic physical features in the presence of LD and/or psychosis should raise the suspicion of a chromosome 22q11 deletion, and screening become part of standard practice. Close liaison between psychiatry and medical genetics is recommended, providing expert genetic counselling where appropriate. Advances in genetics and neuroimaging will help to delineate the structural and functional brain abnormalities in chromosome 22q11 deletion. This may contribute to the search for the aetiology of schizophrenia as it is possible that the neuroimaging findings in 22q11 deletion may represent exaggerations, or advanced forms, of findings associated with schizophrenia.

The following work presented at the Forum has been published elsewhere.

1. "Primary Nitric Tolerance in Diabetes Mellitus" given by Dr D R Morgan.
2. "Can Rheumatologists Agree on a Diagnosis of Inflammatory Arthritis in an Early Arthritis Clinic"? given by Dr G Gormley.
3. "Factors Predicting Stoma Complications" given by Dr H Jazair.
4. "Epilepsy in a Hospital Population of Adults with Learning Disability: Demography, Diagnosis and Response to Treatment" by Dr D M Hughes.

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Abstracts of the Autumn (2001) Meeting of the Association of Clinical Pathologists – Irish Branch

MOLECULAR CHARACTERISATION OF MONOCYTE ESTERASE DEFICIENCY

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Monocyte specific esterase activity is a useful marker for identification of cells of the monocytemacrophage lineage. At present little is known about the *in vivo* role of MSE. Epidemiological evidence suggest a link between monocyte esterase deficiency (MED) and malignant neoplasia. Familial studies indicate that the trait may have an autosomal dominant pattern of inheritance, which is uncommon for an inherited enzyme deficiency. Monocyte esterase deficient cells have a reduced ability to lyse tumour cells *in vitro*. We are currently undertaking an investigation into the molecular defect responsible for MED. Sequence analysis of genomic DNA from affected individuals is being used to identify novel single nucleotide polymorphisms (SNPs) in the MSE gene, *Ces 1*, which may be linked to MED. We have identified two novel SNPs in intron nine of *Ces 1* in two patients who originally presented with cancer of the gastrointestinal tract (GI) tract. Since growing evidence suggests that the MSE status of patients with GI cancer may be significant in determining an appropriate treatment strategy we aim to determine whether these SNPs will be clinically important.

PRIMARY CUTANEOUS LYMPHOMAS, THE UNFORGOTTEN LESSONS

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Skin is the second most frequent site for extranodal lymphomas following the gastrointestinal tract. Before immunohistochemistry was introduced in the late 1970's, most cases were considered malignant proliferations of T-cells with mycosis fungoides/Sezary syndrome being the classical example. However, by using immunohistochemical stains, it has been found that at least 25% of all cases of primary cutaneous lymphomas are of B-cell origin. Even more recently, a small subgroup of primary cutaneous lymphomas was found to express the CD56 marker, and so was classified as primary cutaneous lymphoma of natural killer cells.

We are presenting three cases of primary cutaneous lymphomas, two of which are primary cutaneous B-cell lymphomas and a case of CD56 positive (natural killer) cutaneous lymphoma, with special emphasis on the clinical presentation and the histopathological and immunophenotypical patterns.

LYMPHOPLASMACYTOID LYMPHOMA AND HAEMOLYTIC ANAEMIA

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Lymphoplasmacytoid lymphoma is a low grade lymphoproliferative disorder that may be associated with cold haemagglutinin disease (CHAD). We described a case of CHAD in a patient with CD20 positive lymphoplasmacytoid lymphoma, resistant to standard therapies, treated successfully with Rituximab (anti-CD20 antibody).

A 75 year old man present to our Haematology outpatient department in March 1998 with weight loss, night sweats and increasing shortness of breath. Full blood count revealed anaemia (haemoglobin 6.2g/dL) with an elevated mean cell volume (100 fL). A cold agglutinin and serum lgMk paraprotein (13g/L) were present and the direct Coombs test was positive. Serum lactate dehydrogenase was markedly elevated. Bone marrow trephine biopsy showed an infiltrate of lymphoplasmacytoid cells which was paratrabecular and at times diffuse. Immunohistochemical studies showed these cells

to be CD20 positive. Computerised tomography showed a few enlarged lymph nodes in the para-aortic and pelvic regions. Based on these results a diagnosis of lymphoplasmacytoid lymphoma with secondary cold haemagglutinin disease was made.

The patient was treated with several courses of chlorambucil and prednisolone. His lymphadenopathy resolved but he continued to haemolyze. Despite further courses of chlorambucil and prednisolone, maintenance prednisolone and warmed blood transfusions he remained anaemic.

Following several recent reports on the use of Rituximab in cold haemagglutinin disease we commenced this patient on Rituximab at a standard dose of 375mg/m^2 once weekly for four weeks (days 1, 8, 15 and 22). Rituximab therapy was well tolerated and has resulted in control of haemolysis with a normal haemoglobin, normal lactate dehydrogenase and decrease in paraprotein level (to 2 g/L) despite cessation of steroid therapy.

This case emphasises that cold haemagglutinin disease associated with an underlying lymphoproliferative disorder remains a difficult therapeutic problem and consideration should be given to therapy with Rituximab in patients whose disease is resistant to standard therapies.

FOLLICULAR DENDRITIC CELL SARCOMA OF THE MEDIASTINUM

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Follicular dendritic cell sarcomas are extremely rare, the majority occurring within lymph nodes. They have, however, been described at extra-nodal sites. We describe a recurrent follicular dendritic cell (FDC) sarcoma occurring within the soft tissues of the mediastinum in order to raise awareness amongst pathologists of this uncommon neoplasm.

An 84 year old lady presented with a posterior mediastinal mass. Nineteen years earlier a mass had been removed from the same location and had been diagnosed as a "neurogenic tumour". The recurrent tumour was well circumscribed, and histologically was composed of bland spindle shaped cells with interspersed inflammatory cells, predominantly lymphocytes. Immunohisto-chemically the spindle cells were positive for S100 protein, LCA, CD68 and vimentin, but negative for CD21 and CD35 (markers of follicular dendritic cells). Ultrastructural examination demonstrated elongated cell processes joined by desmosome-like junctions. The ultrastructural features were diagnostic of follicular dendritic cells.

FDC sarcoma is a rare neoplasm and a high index of suspicion is required in order to reach a correct diagnosis. Immunohistochemistry and, or, electron microscopy is required for a definitive diagnosis. This case demonstrates that not all cases are immunoreactive with CD21 and CD35 and illustrates the role of electron microscopy in establishing a diagnosis.

AN UNUSUAL CASE OF ANAEMIA

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A fifty year old female presented with Coombs positive haemolytic anaemia. This was refractory to first line treatment. Search for a primary cause uncovered a solid area within the liver. Biopsy of this revealed a diffuse large cell B-cell Non Hodgkin's Lymphoma. She received six courses of CHOP resulting in rapid remission of her haemolytic anaemia and lymphoma. Sixteen months later she developed a right-sided buccal swelling with simultaneous relapse of her haemolytic anaemia. Repeat biopsy proved this to be relapse of her large cell Non Hodgkin's Lymphoma. Imaging showed no evidence of relapse elsewhere. She proceeded to salvage chemotherapy using the ESHAP regime and after one course her buccal swelling had reduced completely and her haemolytic anaemia entered a second remission. She proceeded to two further courses of ESHAP and an autologous peripheral blood stem cell transplantation.

There are less than 100 cases of primary extra nodal lymphoma arising in the liver reported and although the association between lymphoproliferative disorders and haemolytic anaemia is well recognised there are no recorded cases of primary B- cell Non Hodgkin's Lymphoma of liver with associated haemolytic anaemia in the literature.

AN UNUSUAL PAROTID SWELLING

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Unilateral parotid gland swelling when associated with facial nerve palsy is strongly suggestive of malignancy. We report a case in which the pathology indicated a very unusual presentation of Wegener's granulomatosis in which the involvement was subsequently shown to be multisystem, in spite of the apparently localised clinical presentation.

The patient, a previously healthy 65 year old man, presented with a six week history of a clinically malignant swelling of his right parotid gland with right facial nerve palsy. The gland was surgically explored and histology revealed necrosis, active inflammation and granuloma formation, with a vasculitic process suggestive of Wegener's granulomatosis. Subsequent serological investigation indicated a cANCA of 320 (normal 0-19) and PR3 ANCA 13.4U/ml (normal 0-2). The patient was diagnosed as Wegener's granulomatosis with limited right parotid involvement. He was treated with corticosteroids, cyclophosphamide and voltarol. Two weeks later he collapsed and subsequently died following severe haematemesis.

Autopsy revealed massive gastrointestinal haemorrhage from a 5cm diameter, deep pyloroduodenal peptic ulcer with a bleeding artery at its base.

The artery did not show any histological evidence of vasculitis but there were lesions of Wegener's granulomatosis in both lungs and in many other organs including the left parotid gland.

This case highlights the fact that parotid enlargement may be the presenting feature of Wegener's granulomatosis and can mimic a malignant tumour. Pathologists should keep this in mind when faced with an unusual inflammatory process in the head and neck and recommend the appropriate serological investigations to help confirm the diagnosis.

SNOOKERED BY THE BLUES BROTHERS!

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Almost 60 years ago two brothers who were deeply cyanosed came to the attention of a local practitioner. He administered vitamin C to one brother and this alleviated the cyanosis. Initially this was thought to be due to congestive heart failure but cardiologists later ruled out that diagnosis. Analysis of the spectral properties of the brothers' haemoglobin resulted in the detection of methaemoglobin. A local biochemist Dr Gibson, who was interested in the biochemical pathway controlling the reduction of methaemoglobin, intensively studied the erythrocytes from these patients. Gibson was able to elucidate the enzyme, now known as NADH-cytochrome b5 reductase, responsible for methaemoglobin reduction and was the first person to attribute a hereditary trait to a specific enzyme deficiency.

Since the characterisation of the NADH-cytochrome b5 reductase gene in the 1980s numerous mutations have been detected in with patients methaemoglobinaemia. To complete the study initiated by Gibson the genetic lesion was sought in the original blue brothers. Sequencing of genomic DNA detected a heterozygous mutation in exon 9 of the gene from one brother, which causes an amino acid substitution thereby making the enzyme less stable and hence non-functional. This mutation was also detected in an asymptomatic sibling. To complicate things the level of functional enzyme is 1% in the original brother therefore this mutation cannot account for complete loss of activity. Another mutation or loss of expression of the normal b5 reductase gene is being sought but remains elusive.

BASOPHIL-ACTIVATION MARKER ANALYSIS-A NEW APPROACH TO DIAGNOSE DRUG HYPERSENSITIVITY REACTIONS

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Type 1 hypersensitivity reactions to drugs are reported to occur in 0.1% and 0.01% cases in medical and surgical wards, respectively.[1] Detection of specific lgE antibodies (RAST) and skin prick testing (SPT) is not helpful in all cases,

and diagnosis is usually made on clinical grounds. Flow cytometric assessment of drug induced basophil activation may offer an additional approach for diagnosis of these hypersensitivity reactions. We report the use of this methodology in the investigation of 2 cases of suspected drug-induced allergy.

Case 1: A 44-year old woman was referred to Immunology after she experienced a Grade IV reaction during exposure to general anaesthesia with Suxamethonium as a muscle relaxant. Elevated mast cell tryptase and urinary methylhistamine were demonstrated post-reaction. Suxamethonium-specific IgE antibodies were detected and SPT with Suxamethonium was positive. In vitro induction, by Suxamethonium, of CD63 expression on basophils was demonstrated by flow cytometry.

Case 2: A 30-year old woman with history of migraine was referred with recurrent episodes of urticarial rashes and swelling of eyelids after taking Paracetamol and Aspirin. RAST and SPT to Paracetamol and Acetyl Salicylic acid were negative. Drug challenge to both Paracetamol and Aspirin in controlled environment proved positive in two separate occasions. In vitro, induction by Paracetamol, of CD63 expression by basophils was demonstrated. Recently, drug challenge with Vioxx (COX-2 inhibitor NSAID) was negative.

Analysis of basophil activation may prove useful in the investigation of drug induced hyper sensitivity reactions, particularly when SPT and RAST are negative or SPT cannot be performed or in cases where clinical and laboratory evidence is equivocal.

1. Vervloet D and Durham, S. Adverse Reactions to Drugs. BMJ 1998: 316 (7143) 1511.

VASCULITIS PRESENTING AS PULMONARY THROMBOEMBOLIC DISEASE

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Vasculitis and thrombosis are two conditions that can occur in the pulmonary circulation. However, an association of these two conditions is rare. Here we reported two cases of different types of vasculitis presenting as thromboembolic disease. The first case is a 34 year old female with a known history of Wegener's granulomatosis who presented with shortness of breath. Investigations revealed thrombosis and stenosis in the main pulmonary arteries. Histological examination of these large elastic arteries showed features of Wegener's granulomatosis. Presentation as thromboembolic disease and large elastic artery involvement by Wegener's granulomatosis is unusual and has never been described before. The second case involves a 46 year old female who also presented with shortness of breath, and was clinically diagnosed and treated as chronic thromboembolic disease with a subsequent development of anti-coagulant and anti-cardiolipin antibodies. Her condition deteriorated and she died. Histological examination of autopsy specimens showed features of giant cell arteritis involving distal muscular pulmonary arteries. An association of giant cell arteritis with anti-phospholipid antibody syndrome has never been reported. These cases highlight the importance of consideration of vasculitis in pulmonary thromboembolic disease even when there is no prior suspicion of a vasculitic process.

HER-2/NEU OVEREXPRESSION AND AMPLIFICATION IN BREAST CANCER: A DIRECT COMPARISON OF IMMUNOHISTOCHEMISTRY AND FLUORESCENCE IN-SITU HYBRIDISATION (FISH)

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Background: her-2/neu status is an important prognostic and predictive factor in breast carcinoma, and is central to selection of patients for treatment with the humanised anti-her-2 monoclonal antibody (Herceptin). Accurate assessment of her-2 status is, therefore, important in the pathological evaluation of breast carcinoma. There is no consensus on the preferred methodology for assessment of her-2 status in

breast cancer. This study was undertaken to compare evaluation of her-2 status by immunohistochemistry and by fluorescence in-situ hybridisation (FISH).

Methods: her-2/neu status was evaluated in 83 consecutive unselected cases of invasive breast carcinoma. All biopsies were fixed in formalin, routinely processed and embedded in paraffin. her-2/neu status was assessed by immunohistochemistry (IHC) using the FDA approved Herceptest (DAKO) and by fluorescence in-situ hybridisation (FISH) using the PatVysion her-2 DNA kit (Vysis). IHC staining was evaluated by the manufacturer's recommended scoring system (score 0 to 3+). Cases scoring 0 or 1+ were considered negative for her-2 overexpression, cases scoring 2+ or 3+ were considered positive. FISH was evaluated by the ratio of her-2 signals to chromosome 17 signals: a ratio of ≥2 was considered amplified.

Results: 31/83 (38%) cases were positive by IHC (11: 2+, 20: 3+), 52 were negative (32: 0+, 20: 1+). 17 (20%) cases exhibited her-2 amplification by FISH, 66 (80%) cases were not amplified. The results of IHC and FISH were discordant in 1/52 IHC negative cases (IHC score 0) and in 15/31 IHC positive cases. 10/11 (91%) of IHC score 2+ cases were negative for amplification, 5/20 (25%) of IHC 3+ cases were negative for amplification.

Conclusions: The results of IHC for her-2 using the DAKO Herceptest method correlate well with amplification status in negative (score 0/1+) cases. The majority of cases scored 2+ are not amplified and these are considered to represent IHC false positives. Cases scored 2+ on IHC should be further evaluated by FISH if therapeutic decisions are to be based on her-2 status.

HER-2 ANALYSIS IN TISSUE MICROARRAYS OF ARCHIVAL HUMAN BREAST CANCER: COMPARISON OF IMMUNOHISTOCHEMISTRY AND FLUORESCENCE IN SITU HYBRIDISATION

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HER-2 gene alterations have been shown to have prognostic and predictive value for the treatment of breast cancer patients with therapeutic agents, in particular, the monoclonal antibody, Herceptin. Because of this, the accurate and consistent evaluation of HER-2 status is crucial. HER-2 status is assessed at the protein level (overexpression) by immunohistochemistry (IHC) and at the DNA level (gene amplification) by fluorescence *in situ* hybridisation (FISH). IHC is a reliable and economical test to assess HER-2 status while FISH is regarded as the gold standard method for detecting HER-2 amplification. Although the best approach is to combine both IHC and FISH assays this approach is not very practical or cost- effective for routine histopathological laboratories. The recent development of tissue microarray technology has allowed large-scale studies using formalin-fixed, paraffin-embedded material. We employed this technique to assess HER-2 status in a cohort of 54 invasive breast cancer cases by both IHC and FISH assays to determine if the results obtained were representative of the protein/gene expression patterns of the original whole tissue section. Concordance for HER-2 IHC between the tissue microarray and full sections was 93%.

Concordance for HER-2 FISH between the tissue microarray and full sections was 91%. Concordance between HER-2 FISH and HER-2 IHC on the tissue microarray was 98%. The use of three cores per tumour adequately represents the antigen expression on a whole tissue section. To the best of our knowledge this is the first study to validate the use of tissue microarray for FISH assessment of HER-2. We conclude that tissue microarrays provide highly comparable results in the assessment of HER-2 protein levels and allow large-scale analysis of the HER-2 gene by FISH. The methodology described in this study for HER-2 analysis is both time saving and cost-effective and with minimal technical training is suitable for use in a diagnostic setting.

FIRST REPORT OF CANDIDA DUBLINIENSIS BLOODSTREAM INFECTION IN NORTHERN IRELAND

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A 35 year-old lady with metastatic carcinoma of the uterine cervix had an episode of *Candida dubliniensis* bloodstream infection (BSI) following a laparotomy performed to repair a broken down ileocolic anastomosis. She had received broad spectrum antibacterial therapy for two weeks prior to this for the treatment of a polymicrobial septicaemia. In addition, a central venous catheter had been placed and she had been receiving total parenteral nutrition. Unfortunately, the patient deteriorated and died three days postoperatively; on the same day blood cultures became positive with yeasts.

There were several interesting issues arising from this episode. Firstly, the described patient had several typical risk factors for common candidal BSI, but did not conform to any of the classical profiles (neutropenic, peri-transplant or HIV-seropositive) of patients with C. *dubliniensis* BSI described in the literature.

Secondly, the case outlined might serve as a reminder of the role for pre-emptive prescription of an antifungal agent in the regimen of any patient at risk of deep candidal infection failing to improve despite apparently appropriate antibacterial therapy.

Finally, the isolate was misidentified by routine phenotypic methods as C. *albicans*. The identification as C. *dubliniensis* was made, producing 100% homology, by molecular analysis. This raises the question whether more discriminating methods should be routinely used for the phenotypic speciation of germ tube positive yeasts. Alternatively one might suggest that the epidemiology of candidal BSI is important enough, and phenotypic identification difficult enough, to justify the routine use of molecular methods to identify such isolates from blood.

PHENOTYPIC MISIDENTIFICATION OF *CANDIDA* SPECIES

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The aim of the study was to estimate the degree of error associated with phenotypic methods of identifying *Candida* spp.

Retrospective identification of 39 isolates from *Candida* stock was undertaken by sequencing of the large internal transcribed spacer (ITS) region (ie the ITS1- 5.8SrRNA-ITS2 region) which had been initially recovered from blood between 1994-2000 and were initially identified by phenotypic methods. The molecular identity was taken to represent the true identity when >98% homology was achieved.

Of the 39 isolates tested, 5 were found to have been phenotypically misidentified. Critically, no recurring pattern of error, such as any particular species being repeatedly misidentified, was seen. An isolate which had been initially thought to be *C. krusei* was found to be *C. tropicalis*; an unspeciated isolate which was initially misidentified as *C. norvegensis* were found to be *C. krusei*. One isolate phenotypically identified as *C. glabrata* was found to be *C. parapsilosis*. Two isolates had been initially misidentified as *C. albicans*; one was genotypically identified as *C. glabrata* and the other, *C. dubliniensis*.

Our study estimated an error rate of one in eight phenotypic identifications; we consider this to be unexpectedly substantial. If the epidemiology of *Candida* bloodstream infections is of importance then we should further examine our phenotypic methods of identification and perhaps consider giving a role to molecular identification methods in routine practice.

MYXOPAPILLARY EPENDYMOMA, AN UNUSUAL OUTCOME. CASE REPORT AND REVIEW OF LITERATURE

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Ependymomas are primary tumours of the nervous system which can occur in many locations. However, there is an entity called myxopapillary ependymoma which occurs almost exclusively at the cauda equina. They may cause surgical difficulties of excision due to entrapment of the spinal nerve roots and recurrence is occasionally a problem. However, metastases are rarely described. We wish to report the case of a myxopapillary ependymoma showing widespread

metastatic dissemination throughout the subarachnoid space in a 65 year old gentleman fifteen years after initial diagnosis. One of the metastatic foci caused a tumour mass completely filling the 4th ventricle and blocking the outflow foramina causing hydrocephalus.

ANGIOLYMPHOID HYPERPLASIA WITH EOSINOPHILIA, CASE REPORT AND REVIEW OF LITERATURE

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Angiolymphoid hyperplasia with eosinophilia is a rare disorder of uncertain histogenesis. It presents clinically as single or multiple nodules mostly around the head and neck region of adult patients. Because of the vascular component, it is usually misdiagnosed clinically as angiosarcoma. However, angiolymphoid hyperplasia with eosinophilia has characteristic microscopy with prominent nodular pattern. This is caused by florid proliferation of blood vessels lined by endothelial cells with a distinct epithelioid appearance. These blood vessels are surrounded by a mixture of inflammatory cells with prominence of eosinophils, thus the name.

We are reporting a case of an elderly lady who presented with several nodules on the back of several years duration. Histology showed the typical vascular pattern and the associated inflammatory component. Follow-up confirmed the benign nature of the lesions.

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Northern Ireland Surgical Registrars Prize Day: 7 December 2001

The winners of the prizes were as follows:

1st Prize: The Ethicon Endosurgery Surgical Registrars Prize – Mr. Mark Jones, SpR Cardiothoracic Unit, RVH.

Runner-up Prize: The Ethicon Product Division Surgical Registrars Prize – Mr. Mark Taylor, SpR Department of Surgery, RVH.

Runner-up Prize: The Jansen-Cilag Surgical Registrars Prize – Mr. Gary Spence, SpR Antrim Area Hospital.

Mr T Diamond, Regional Adviser in General Surgery for Northern Ireland.

ß$_2$ ADRENERGIC RECEPTOR GENE TRANSFER DURING CARDIOPULMONARY BYPASS IN PIGS IMPROVES CARDIAC FUNCTION FOLLOWING SURGERY: POTENTIAL FOR MOLECULAR VENTRICULAR ASSISTANCE

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Objective: We assessed if cardiac-selective adenoviral based transfer of the human ß$_2$-adrenoceptor (ß$_2$AR) transgene to the arrested heart during cardiopulmonary bypass (CPB) was possible and if it would enhance postoperative cardiac function.

Methods: A first-generation adenoviral vector (1 X 10^{12} total viral particles) containing the human ß$_2$AR transgene (Adeno-ß$_2$AR; n=6), or phosphate buffered saline (PBS; n=6) was delivered to neonatal piglets through the proximal aorta, following aortic cross-clamp and cold crystalloid cardioplegia. Animals were recovered and 2 days later had a left ventricular micromanometer inserted under sedation to assess basal and isoprenaline (0.01 to 0.1µg.kg^{-1}.min^{-1}) stimulated cardiac function prior to euthanasia. ßAR density was measured in left ventricle, liver and lung by radioligand binding. Statistical analysis was performed using Student's t-test, Mann-Whitney test and two way analysis of variance with repeated measures on one factor (ANOVA).

Results: Left ventricular receptor density (fmol.mg^{-1} membrane protein) was greater following Adeno-ß$_2$AR compared to PBS (520±250.9 v 104±5.7; p<0.01). ß adrenergic receptor density in liver (79±6.0 v 67±5.3; p=ns) and lung (250±16.3 v 260±22.2; p=ns) was similar between groups. Basal cardiac function was similar between groups. However, following isoprenaline infusion enhanced dP/dt_{max} (p=0.02), enhanced heart rate (p=0.0002), and reduced end-diastolic pressure (p<0.002) were observed in Adeno-ß$_2$AR treated animals, indicating increased cardiac function.

Conclusions: Cardiac-selective adenoviral based gene transfer is possible during cold cardioplegic arrest and CPB. This is associated with enhanced postoperative cardiac function following ß$_2$-AR gene transfer. This may have clinical applications for patients with impaired ventricular function undergoing cardiac surgery.

SEPSIS IN OBSTRUCTIVE JAUNDICE: IS IMMUNE ANERGY TO BLAME?

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Background: An imbalance in hepatic pro and anti-inflammatory cytokine responses to portal endotoxaemia may contribute to the observed organ dysfunction associated with intervention in obstructive jaundice. The aims of this study were to: (1) Measure individual hepatic proinflammatory (TNFα, IL6) and anti-inflammatory (11-10) cytokines in response to endotoxaemia in obstructive jaundice and (2) Assess the overall effect of these mediators on neutrophil respiratory burst activation.

Methods: Male Wistar rats were randomised to either bile duct ligation (BDL, n=8) or sham operation (n=8). Isolated *in-situ* hepatic perfusion was performed in each group one week after surgery. Animals were perfused with buffer containing Ecsherichia coli serotype 0111:B4

(T=10-20) for 10 minutes and subsequently endotoxin-free buffer for a further 100 minutes (T=20-120). Aliquots of effluent perfusate were collected for cytokine analysis (T=100 and 120). Neutrophil respiratory burst activity in response to perfusate (T=80 and 100) was assayed using a BioOrbit 1251 Luminometer.

Results: Results are expressed as median (interquartile range). There were significantly higher levels of TNFα and IL6 in the BDL group compared to the sham operated group at T100 and T120 [TNFα: 3594 pg/ml (1243.2-6696.4) v 421.4 (240-708.8) and 3566.3 (1212.4-8398.5) v 1168 (667.6-2382) respectively. IL6:

246.8 (158-691.5) v 0 (0-4.7) and 1168 (667.6-2382) v 0 (0-42) respectively, $p<0.05$]. The BDL group had significantly higher levels of IL10 at T120 [11.25 (7-25.6) v 7.5 (5-8.3), $p<0.05$]. Effluent perfusate from the BDL group resulted in a significant attenuation of neutrophil activation [13.60 (12.04-18.75) v 19.48 (17.13-28.45) at T80 and 11.44 (8.45-25.56) v 23.63 (16.34-43.99) at T100, $p<0.05$].

Conclusions: Both pro and anti-inflammatory cytokines are elevated in our model of obstructive jaundice. The net effect of this increased inflammatory response is a down-regulation of neutrophil respiratory burst activity. The immune depression and anergy resulting from this anti-inflammatory response may be responsible for increased septic complications in jaundice. The use of the neutrophil chemiluminescence assay may be a more reliable assessment of the effects of the inflammatory balance in obstructive jaundice rather than measurement of individual cytokines.

ANGIOGENESIS AND SYSTEMIC TUMOUR CELL DISSEMINATION IN GASTROESOPHAGEAL CARCINOMA

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Aims: There is mounting evidence that tumour metastasis is anglogenes is -dependent. Detection of bone marrow micrometastases (BMMs) indicates systemic tumour cell dissemination and poor prognosis. We aim to establish if detection of BMMs correlates with putative markers of anglogenesis in patients with gastroesophageal carcinoma.

Methods: At time of surgery 49 patients with invasive oesophago-gastnic cancer had single bone marrow aspirates taken from the left illac crest. The presence of micrometastatic tumour deposits was assessed by immunocytochemical analysis using cytokeratin markers, CAM 5.2 and AE 1 /AE3. Using ELISA, circulating and tumour levels of the angiogenic cytokine, vascular endothelial growth factor (VEGF) were determined in plasma and tumour homogenate respectively (P-VEGF, T-VEGF). Tumour microvessel count (MVC) was evaluated by counting anti-CD34 positive neovessels using the Kontron Interactive Image Analysis System.

Results: Seven patients (14.3%) were found to be inoperable, 22 (44.9%) were BMMs+.

	MVC (n=42)	*P-VEG17 (pg/rnL) (n = 49)*	*T-VEG17 (pgVEGF/mg total protein) (n = 40)*
BMMs +	166 (125-207)	19.61 [13.33-47.44]*	277.78 [154.11-394.97]
BMMs -	137 (112-162)	10.27 [0-21.70]	213.09 [128.39-511.07]

MVC is represented by mean (95% C.I. for mean). P-VEGF and T-VEGF are represented by median [IQR]. *p=0. 018, Mann Whitney U.

Conclusions: No difference was found in MVC or T-VEGF between BMMs + and BMMs patients. MVC and T-VEGF reflect the angiognic status of the primary tumour. The angiogenic status of the primary tumour does not appear to be a determining factor for tumour dissemination in this study. P-VEGF however, was significantly higher in patients with BMMs. VEGF detectable in the circulation, may be derived not only from the primary tumour but also from alternative angiogenic sources such as micrometastatic deposits. P-VEGF may thus reflect a measure of the total tumour 'angiogenic burden' in patients with gastroesophageal cancer.

METHYLPREDNISOLONE SIGNIFICANTLY REDUCES PULMONARY FUNCTION IN A PORCINE MODEL OF INFRARENAL AORTIC ISCHAEMIA-REPERFUSION

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Background: Methylprednisolone (MP) has been shown to reduce perioperative pro-inflammatory cytokine responses and increase interleukin-10 anti-inflammatory responses. Methylprednisolone reduces neutrophil adhesion molecule expression perioperatively. Despite these anti-inflammatory effects, MP administration has, paradoxically, been associated with impaired pulmonary function. We investigated the hypothesis that methylprednisolone significantly reduces pulmonary function in a porcine model of infrarenal aortic ischaemia-reperfusion.

Methods: Thirty-four male 10-12 week old pigs underwent pentobarbitone anaesthesia followed by tracheostomy and mechanical ventilation. The inspired oxygen concentration was maintained at 70% during the procedure and all animals had invasive monitoring of their systemic and pulmonary pressures. At laparotomy the infrarenal aorta was cross clamped for 150 mins and then released to allow 180 mins of reperfusion. The animals were randomly allocated to treatment (n=17) or control groups (n=17). After a baseline arterial blood sample was taken the treatment group received 30 mg/kg of MP and the control group a saline placebo. Arterial blood samples were obtained after 30, 60, 90, 120 and 150 min of ischaemia. Further samples were collected at 30, 60, 90, 120. 150 and 180 min into reperfusion. Within group statistical analysis was with Wilcoxon signed rank and between groups with Mann-Whitney U test.

Results: During the ischaemia-reperfusion period all animals showed a significant time dependent deterioration in arterial oxygen tension. The PaO_2 was significantly lower ($p<0,05$, Mann-Whitney U test) in the treatment group compared to the control group during ischaemia at time points 60, 90 and 120 mins and during the reperfusion period at 60, 90, 120, 150 and 180 mins.

Conclusions: We have demonstrated that MP significantly increases pulmonary dysfunction in a porcine model of ischaemia-reperfusion. Although MP reduces neutrophil adhesion, leading to potential organ protective effects, a reduction in endothelial intercellular adhesion may lead to increased capillary leak reflected in decreased pulmonary function.

PROSPECTIVE, RANDOMISED TRIAL COMPARING ENDOSCOPIC VEIN HARVEST VS OPEN VEIN HARVEST

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Background: Open vein harvesting (OVH) is a long under appreciated component of CABG and is associated with higher prevalence of wound complications and pain compared to median sternotomy. Endoscopic vein harvest (EVH) is a new technique proposed to alleviate wound pain, reduce leg wound infection and lead to greater patient satisfaction. This study aims to compare the two techniques on this basis and determine whether EVH is a viable technique within normal operative time.

Methods: During September and March 2001, 80 saphenous vein harvests were prospectively randomised to EVH (n=40) and OVH (n=40); all performed by one surgeon with the Clearglide® endoscopic vein harvest system (Cardiovations Inc). End points were impaired wound healing (ASEPSIS score). Secondary endpoints included operative time, harvest time, vein quality, postoperative outcome and postoperative pain (Visual analogue scale). Statistical analysis done using Fisher's exact test and Mann-Whitney U test as appropriate.

Results: The groups were well matched demographically. The vein was harvested at 0.96cm/min (0.43-1.5±0.33) in the OVH group compared to 0.81cm/min (0.41-1.13±0.19) in the EVH group ($p=0.09$). The new procedure did not prolong the overall operative time ($p=0.53$). Patients in the EVH group had significantly lower ASEPSIS scores ($p<0.001$) and postoperative pain ($p<0.001$). There was no difference found in the vein quality by histological analysis.

Conclusions: Endoscopic vein harvest results in less impaired wound healing, reduced post-operative pain allowing earlier ambulation and does not prolong the operative time significantly with no compromise in vein quality.

THE EFFECTS OF DIFFERENT INFUSATES IN THE MEASUREMENT OF PERIPHERAL RESISTANCE : IN-VITRO AND IN-VIVO STUDY

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Background: Increased Peripheral Resistance (PR) has been shown to predict poor graft patency. Studies have used either saline or blood as the infusate to measure PR and it is not clear whether the results obtained by using different mediums are comparable.

Methods: In-vitro study – PR was measured by infusing different fluids (saline, gelofusine, and blood), at different rates (50 and 75 ml/min) through a segment of tubing whose lumen was gradually reduced. *In-vivo study* – PR was measured in six patients undergoing bypass grafting, using saline, gelofusine and blood at 50 and 75 ml/min.

Results:

In-Vitro

Infusion Rate – ml/min

Diam	*Blood*		*Gelofusine*			
mm	50	75	50	75	50	75
2	80	93	601	67	20	13
1.95	80	107	80	80	60	67
1.9	200	200	160	187	80	80
1.85	300	333	260	307	180	200
1.8	600	680	480	573	200	253
1.75	1200	1280	920	1080	580	707
1.7	2380	2653	2180	2533	1100	1360
1.68	3160	3573	3620	4080	2240	27071

milli-Peripheral Resistance Unit

In-Vivo

Infusion Rate – ml/min

Pts	*Blood*		*Gelofusine*		*Saline*	
	50	75	50	75	50	75
1	144	119	123	103	79	53
2	313	296	404	331	240	206
3	187	249	208	180	148	126
4	197	177	222	216	141	80
5	875	1278	1250	1153	734	719
6	139	94	96	74	60	34

milli-Peripheral Resistance Unit

Correlation of Blood with:

	In Vitro				*In-Vivo*			
	50 ml/min		75ml/min		50ml/min		75ml/min	
Medium	R	P	R	P	R	P	R	P
Gelofusine	0.99	<0.0001	0.99	<0.0001	1	<0001	0.90	<0.0001
Saline	0.97	<0.0001	0.98	<0.0001	1	<0.0001	1	<0.0001

Conclusions: Even though the values of PR obtained using different infusates are dissimilar, there is correlation between these values. Hence a correction factor can be employed to compare studies in which PR was obtained by using different infusates, and pooled analysis of data can be carried out.

LIPOSOME-MEDIATED ADENOMATOUS POLYPOSIS COLI (APC) GENE TRANSFER IN FAMILIAL ADENOMATOUS POLYPOSIS (FAP): A NOVEL APPROACH TO ANTI-ADENOMA THERAPY

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Familial Adenomatous Polyposis (FAP) is a highly penetrant, autosomal dominant disease resulting from germline mutation of the adenomatous polyposis coli *(APC)* gene. The association of FAP with colorectal polyps is well established and development of colorectal cancer is almost inevitable in the fourth decade of life if untreated. More than 90% of FAP patients also develop duodenal polyposis with a 5% lifetime risk of malignant transformation. As there is evidence to suggest a "gatekeeper role" of APC in the adenoma to carcinoma sequence, targeting the earlier molecular events by replacing APC function may prevent polyp progression. This study aims to study the functional outcome of per-oral, liposome-mediated *APC* gene replacement therapy in a multiple intestinal neoplasia (Min/+) mouse model.

Twenty mice, heterozygous for the human homologue *Apc* gene, were randomly assigned to three groups:

1. Min/+ (n=8) received no treatment.

2. Min/+ (n=6) treated with control plasmid containing green fluorescence protein (GFP) reporter gene.
3. Min/+ (n=6) treated with plasmid containing the full-length *APC* gene downstream to the constitutive cytomegalovirus promoter (pCMV-Neo-Bam-APC).

For the *APC* and *GFP* treated groups, each mouse received an average 49μg of plasmid mixed with 294μl of LipofectAMINE ™, administered by twice/week oral gavage route. Treatment commenced when the animals were 5-weeks old and lasted over four weeks. All the animals were sacrificed at the end of treatment period with harvesting of intestinal tissue for polyp number estimation.

Examination of the intestinal mucosa under a 10x magnifying lens demonstrated a significant reduction in polyp multiplicity in Min/+ treated with *APC* gene replacement therapy. There was a significant reduction in the total number of polyps in the *APC*-treated (73.1±1.4) group compared to untreated control (97.8±5.3, $p<0.01$) and Min/+ treated with control *GFP* gene (103.3±1.7, $p<0.01$).

APC dysfunction underlies tumorigenesis in FAP patients and murine model of polyposis. This *in vivo* study provided evidence to support a novel anti-adenoma strategy using enteral *APC* gene replacement therapy.

ROUTINE HAEMATOLOGICAL INDICES CAN PREDICT OPERABILITY IN OESOPHAGEAL CARCINOMA: A MODEL BASED ON LOGISTIC REGRESSION ANALYSIS

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Introduction: Current methods for the pre-operative staging of oesophageal carcinoma are sub optimal in assessing tumour operability. As a result patients with locally advanced disease may be subjected to unnecessary surgery. The aim therefore was to develop a model based on routine haematological indices to predict the likelihood of an inoperable tumour in patients with oesophageal cancer.

Methods: Patients with pre-operative investigations, which suggested that their tumour was resectable and who were fit for oesophagectomy, were enrolled in this study. A full blood count and coagulation screen were obtained pre-operatively from each patient. Haematological indices, age and sex were recorded for each patient. Forwards-stepwise logistic regression analysis was utilised to determine which of the above factors were important in identifying operability.

Results: Eighty-three patients (59 male: 24 female) were enrolled prospectively in the study between August 1999 and August 2001; the mean age was 67.8 years. Sixty-one (73.5%) had a resectable tumour, 22 (26.5%) had inoperable disease. Platelet count (PLT) ($p=0.0195$), Pro-thrombin Time (PT) ($p=0.0047$) and Activated Partial Thromboplastin Time (APTT) ($p=0.0075$) were identified by logistic regression analysis as being significant variables in the determination of operability. A logistic regression model was produced to predict inoperability based on pre-operative PLT, PT and APTT results. The model predicted the likelihood of tumour inoperability: positive predictive value (73.3%), negative predictive value (83.3%), sensitivity (50%), specificity (93.4%) and overall accuracy (82%).

Conclusions: Based on 3 haematological indices this model can predict operability with an accuracy of 82%. Patients predicted by the model to be inoperable could be considered for neo-adjuvant chemotherapy. This model may aid the clinician in the selection of patients for curative surgery.

PROSPECTIVE RANDOMISED STUDY OF SCAN-DIRECTED UNILATERAL EXPLORATION VERSUS BILATERAL CERVICAL EXPLORATION FOR PARATHYROID ADENOMA

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Background: Focused unilateral cervical exploration for primary hyperparathyroidism (PHPT) due to presumed solitary adenoma is now practised with increasing frequency. However, there remains the concern that this approach may result in additional, enlarged parathyroid glands

being left in situ on the contralateral, unexplored side of the neck.

Methods: All patients diagnosed with PHPT and who had positive preoperative sestamibi-technetium scintigram (one residual focus of activity following subtraction) were randomised to unilateral or bilateral cervical exploration.

Results: Between 20 March 1998 and 20 March 2001, 57 patients were studied. Of these, 30 were randomised to unilateral exploration and 27 to bilateral operation. During the same period 45 individuals underwent elective bilateral exploration for PHPT. Following operation none of the 57 study patients demonstrated persistent hypercalcaemia. However, two patients randomised to bilateral exploration were each found to have a second enlarged parathyroid on the contralateral side of the neck.

Conclusion: Preliminary results suggest that scan-directed unilateral cervical exploration represents a satisfactory surgical strategy for most patients with presumed solitary parathyroid adenoma. The study is ongoing.

ENTERAL ADMINISTRATION OF FRUCTOOLIGOSACCHARIDES DOES NOT AMELIORATE GUT MUCOSAL BARRIER DYSFUNCTION IN THE IL 10 KNOCKOUT (IL10 KO) MOUSE MODEL OF COLITIS

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Background: Prebiotics are non-digestible oligosaccharides that selectively stimulate the growth of problotic-like bacteria normally present in the gut. Fructooligosaccharides fulfil these criteria.

The aim of this study was to investigate fructooligosaccharides as a modulator of gut mucosal barrier function in the IL10 KO mouse model of Colitis.

Methods: 4 week old IL 10 KO mice were randomised to receive 5mg of fructooligosaccharide (FOS) [Optima, USA] for six weeks or 25mg FOS for eight weeks or 0.25mls water administered once daily by gavage. Gut mucosal barrier function was assessed by:

1. Intestinal permeabilty (IP) – Percentage urinary excretion of orally administered ^{14}Carbon labelled Polyethyleneglycol 4000.
2. Systemic Endotoxin concentration – Limulus Amoebocyte Lysate assay.
3. Systemic IgG Endotoxin Core Antibody ELISA (EndoCAb) – Results expressed as a percentage of pooled normal mouse serum (NMS)[Sigma].

Results: All results expressed as Median, IQR.

	5mg FOS (n=15)	*6 wks water (n=15)*	*25mg FOS (n=15)*	*8 wks Water (n=15)*
IP (%)	0.89 (0.64,1.82)	0.85 (0.55,2.49)	1.1 (0.71,1.73)	0.88 (0.71,1.52)
Endotoxin pg/ml	95.46 (44.95,107.20)	17.17 (5.25,109.0)	67.75 (30.51,114.73)	28.52 (0,117.0)
IgG EndoCAb (% NMS)	12.57 (5.61,20.16)	14.16 (7.84,24.44)	10.48 (3.91,35.52)	12.82 (8.23,46.17)

Conclusion: Fructoligosaccharides did not enhance the gut mucosal barrier dysfunction in the IL 10 KO mouse model of colitis.

ERRATUM

Owing to a printer's error Dr I Mainie's name was omitted from the paper in Ulster Medical Journal 2001; 70: 108-110. **The correct reference is Electrocardiogram and rhythm strip interpretation by final year medical students.**

B Little, I Mainie, K J Ho, L Scott.