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Do you have epilepsy and are pregnant or planning a pregnancy?

Around 2,500 women with epilepsy will have a baby each year in the UK. If you could be one of these women, find out how you can help improve the health of babies born to pregnant women with epilepsy in the future.

UK epilepsy & pregnancy Register

Pregnancy is an exciting time in a woman's life. For pregnant women with epilepsy, a potential concern may be whether their anti-epileptic treatment will cause harm to their unborn child.

There is a major study in the UK investigating which epilepsy treatments show the lowest risk to a baby's health.

The aim is to find out which type of epilepsy treatment women are taking while they are pregnant, and to collect information on the health of their babies after delivery.

By agreeing to register, your valuable contribution will help doctors give the best advice possible to you and to other women who are thinking of becoming pregnant.

If you wish to register, or would like further information about the pregnancy register, please visit **www.epilepsyandpregnancy.co.uk** or call:

Freephone 0800 389 1248

All calls will be answered in confidence by experienced healthcare professionals.

Editorial

Improving cancer statistics – a new cancer centre for Northern Ireland

Fig 1. Belvoir Park Hospital.

Treatment of cancer has improved greatly since the founding of the Belfast Medical Society in 1806. When the society was 100 years old in 1906, the Belfast Fever Hospital opened in the same year at Belvoir Park in Belfast (*fig 1*). Initially some cancer treatment was carried out in the Abercorn unit in the City Hospital from 1924, and in 1952, with the decline in infections diseases following the introduction of antibiotic treatments, space in the Fever Hospital was extended to include a new Northern Ireland radiotherapy centre. Early success rates were poor in comparison to today, although overall survival rates have been one of the worst in Western Europe. French *et al*, in this issue of the journal,[1] show how survival trends have changed for the better with colon and lung cancer survival rates increasing (although death rates for female lung cancer remain worryingly high and will double by 2015). Changes instrumental in this improvement include the Chief Medical Officer's report in 1996 into cancer services[2] which recommended four cancer units throughout Northern Ireland, linked through a managed clinical network to a cancer centre located in Belfast. The Belfast City Hospital cancer centre (*fig 2*) opened appropriately on St Patrick's Day – 17th March 2006 – almost a century after the original fever hospital opened. The Belvoir Park complex officially closed a week later on the 24th March.

THE CANCER CENTRE

The six story structure, with powder coated aluminium panels and warm red areas of terracotta rain screening, is connected via three covered walkways to the City Hospital – the incorporation of 10 linear accelerator vaults and an extensive radiotherapy suite, and availability of haematology, general medical and surgical facilities in the City Hospital and the world class academic cancer research complex at the adjoining Queens University Belfast campus, provides an integrated cancer centre complex rivalling the best in the world. The building itself has already scooped some awards including the top award of the Association of Landscape Contractors of Ireland, for the beautiful gardens (*fig 3*).

Fig 2. The Belfast Cancer Centre.

Fig 3. The award winning gardens.

(Photos courtesy of Belfast City Hospital Trust)

Thanks to the vision of the hospital Chief Executive Quentin Coey, the foresight of Professor Patrick Johnston (Professor of oncology) in obtaining money for buildings and research staff, and Dr Russell Houston, (clinical director of oncology) and Mrs Denise Stockman (project manager), they have allowed the architects to seamlessly produce the most modern integrated cancer centre complex in Europe. When the Ulster Medical Society meets to celebrate the 250-year anniversary in 2056, it will be interesting to see the contents of the programme. Will the decline in infectious disease that we saw in the early part of last century be mirrored by a decline in cancer by the middle of this century? We shall have to wait and see, but progress so far this century has been a good start.

PATRICK J MORRISON, Honorary Editor

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Commentary

General Practitioner Education in Northern Ireland – The use and misuse of power

Philip Reilly

Accepted 30 March 2006

The Ulster Medical Society, through its Journal, is no stranger to historical papers and treatises. While of considerable interest such pieces are usually descriptive and occasionally hagiographical. Significant personalities are described but rarely "warts and all".

To be fair Dr Robin Harland does not venture on to such territory. His is an unusual but very successful approach to recent medical history. He has adopted a rigorous framework from a famous sociologist – not the usual starting point for doctors. The concept of power in its various guises is the focus point of Dr Harland's account of events. It is made even more interesting by the kind of involvement (usually moral or calculative) that the characters and institutions described find themselves in. Just because the author is scrupulous in his focus on power and its uses rather than personality does not stop the reader from "colouring in the background" – especially if they worked during the latter years of the period (1920-1990) described.

It also becomes obvious, as one reads this essay that Dr Harland is both industrious and scholarly in his marshalling of events. He is careful to set what could be a provincial, or even parochial story, in the almost (for a doctor and educationalist) tumultuous events within the medical profession during the period he describes.

All the usual suspects are assembled, but no partisan position is taken. People, institutions and events are examined in an accessible way. A large range of significant sources are well used in pursuit of this thesis on power. The pace and sweep of the work is brisk but the main issues that preoccupied the profession – be they consultants or general practitioners are described in a UK context. In addition, relevant government sources are identified. The interaction of government policy with an evolving awareness of the need for (and not just the ownership of) training, continuing medical education and more recently continuing professional development was as contentious then as it is now.

Dr Harland's hypothetical approach – where the competition for power and the struggle for control are seen as inevitable – is best illustrated as he describes prominent individuals, some of who are still alive. Such figures are no less human for being set in the events of their time. Indeed such events are no less important for us still – given the discernable changes in medical education that continue to grow apace.

General practice may be the particular part of the profession that Dr Harland has studied but there are messages in this excellent piece of work for all of us – whatever type of doctor we happen to be.

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Review

JAK2 V617F: A Single Mutation in the Myeloproliferative Group of Disorders

Donal McLornan, Melanie Percy, Mary Frances McMullin

Accepted 25 February 2006

MYELOPROLIFERATIVE DISORDERS

The myeloproliferative disorders (MPD) are a group of haematological conditions where there is a primary disorder at the level of the multi-potent haematopoietic stem cell leading to increased production in one or more blood cell types. The three main disorders in the group are polycythaemia vera (PV), essential thrombocythaemia (ET) and idiopathic myelofibrosis (IMF). PV is characterised by an increase in red cells, white cells and platelets and clinically a plethoric appearance, itch and splenomegaly. The disease can be complicated by thromboembolic phenomena and haemorrhage and in the end stages can progress to myelofibrosis and acute leukaemia. ET is characterised by an increased platelet count. Clinically it is frequently asymptomatic but the thromboembolic events may lead to disease detection. There is a small propensity to progress to myelofibrosis and acute leukaemia which may be influenced by the treatment modalities used. IMF is defined by a leukoerythroblastic blood picture, splenomegaly and bone marrow fibrosis. The blood picture includes anaemia, thrombocythaemia or thrombocytopenia and variable white cell counts. The disease frequently progresses inexorably to transfusion dependent anaemia, symptomatic splenomegaly and transformation to acute leukaemia.

A number of different biological phenomena have been described in haematopoietic cells from PV patients and other MPDs, the majority of which involve dysregulation of key signalling mediators. The key molecular events in the pathogenesis of these disorders have been poorly defined to date, except in the case of Chronic Myeloid Leukaemia (CML) with the associated characteristic chromosomal translocation 'the Philadelphia chromosome' and associated rearranged gene *BCR – ABL*.

PV progenitor cells have been shown to grow in the absence of added erythropoietin, so called endogenous erythroid colony (EEC) formation[1] and to be hypersensitive to a variety of other cytokines including insulin-like growth factor-1.[2] EEC formation however is not specific to PV and is also identified in other MPDs. Other properties include increased expression of the inhibitor of apoptosis Bcl-x_L in the absence of Epo in PV erythroid cells suggesting that deregulated expression of Bcl-xL may contribute to the erythropoietin dependent survival of erythroid lineage cells in PV.[3] Expression of the thrombopoietin receptor, Mpl, by platelets and megakaryocytes from patients with PV has been shown to be reduced compared to normal controls.[4] This again is not specific to PV however and can occur in other MPDs. RNA synthesis from the polycythaemia rubra vera 1 (PRV-1) gene has been found to be over expressed in PV granulocytes.[5] Erythroid colonies from PV patients have been shown to contain a hyperactive membrane-associated tyrosine phosphatase PTP-MEG2, although the exact role in erythrogenesis requires further investigation.[6]

Under normal conditions binding of the Epo receptor by its ligand induces rapid phosphorylation of Akt and subsequent stimulation of survival pathways for erythroid colonies. Erythroid cells derived from individuals with PV have been shown to demonstrate increased phosphorylation of Akt/PKb and also Glycogen synthase Kinase 3.[7] This contributes to inherent survival properties of the erythroid cells. Microarray analysis has identified candidate genes involved in the pathophysiology of PV including the transcription factor NF-E2 (Nuclear Factor (Erythroid-derived 2)). This has been shown to be over expressed in the bone marrow megakaryocytic, erythroid and myeloid precursors of PV subjects.[8]

Over 50 years ago Dameshek[9] linked together the recognised disorders PV, chronic myeloid leukaemia and IMF and speculated on the common myelostimulatory factors. In the early 1970s chronic myeloid leukaemia was separated as a distinct clonal disorder defined by a single chromosomal and latterly gene rearrangement (*BCR/ABL*).[10] Until very recently the other MPDs continue to be separated and diagnosed on the basis of their clinical and laboratory findings (*Table I*). However, recent molecular findings in the *JAK2* gene are common to all these disorders.

JANUS KINASE 2

The *JAK2* gene was first cloned in 1989[11] and is a member of a family of four Janus kinases 1, 2 and 3 and tyrosine kinase 2.

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TABLE I

Diagnostic criteria for common myeloproliferative disorders

Polycythaemia Vera		*Essential Thrombocythaemia*	*Idiopathic Myelofibrosis*
A1 Raised Red Cell mass (>25% above mean predicted value) or Hct ≥ 0.6 males; ≥ 0.56 females	A2 Absence of cause for secondary erythrocytosis	**1.** Platelet Count > 600 x 10^9/l *	NECESSARY CRITERIA A) Diffuse Bone Marrow Fibrosis B) Absence of Philadelphia Chromosome or BCR-ABL transcript in peripheral blood cells.
A3 Palpable splenomegaly	A4 Clonality marker i.e acquired abnormal marrow karyotype	**2.** No evidence of overt polycythaemia/ polycythaemia masked by co-existing Iron deficiency	OPTIONAL CRITERIA (i) Splenomegaly of any grade (ii) Anisopoikilocytosis with tear drop erythrocytes
B1 Thrombocytosis (platelet count > 400 x 10^9/l)	B2 Neutrophil Leucocytosis (neutrophil count >10 x 10^9 in non smokers; >12.5 x10^9 in smokers)	**3.** Absence of a Philadelphia chromosome **4.** Absence of peripheral blood and/or marrow appearances of myelodysplasia or myelofibrosis	(iii) Presence of circulating immature myeloid cells (iv) Presence of circulating erythroblasts
B3 Splenomegaly (demonstrated on isotope/ultrasound scanning)	B4 Characteristic BFU-E growth or reduced serum erythropoietin	**5.** No known cause of reactive thrombocytosis. Care should be taken to exclude iron deficiency in pre-menopausal women	(v) Presence of clusters of megakaryoblasts and anomalous megakaryocytes in bone marrow sections. (vi) Myeloid metaplasia
Diagnosis A1+A2+A3 or A4 establishes PV A1+A2+any 2 B Criteria establishes PV Adapted from British Committee for Standards in Haematology Guidelines on Polycythaemia[36]		*In asymptomatic patients the platelet count should be observed for a period. Diagnosis is made if all above 5 criteria are met. Adapted from diagnostic criteria in PT-1 trial co-ordinated by UK MPD group[38].	Diagnosis of IMF if: The two necessary criteria (designated A and B) are present <u>with</u> optional criteria as follows (1) any <u>two</u> other features if splenomegaly present (2) any <u>four</u> optional criteria when splenomegaly absent. Adapted from Italian Consensus on Diagnostic Criteria for Myelofibrosis[39].

It was originally named 'just another kinase' but the protein group was renamed Janus kinases after the Roman God of gates and passages. These non receptor kinases have two similar 'active' and 'inactive' domains and this is reminiscent of the God Janus who had the ability to look simultaneously in two directions.

Each JAK has an active tyrosine kinase domain, JAK homology 1(JH1), a catalytically inactive pseudokinase domain, JAK homology 2 (JH2), a SRC homology 2 domain (SH2), and an amino terminal FERM (4-point-1, Erzin, Radixin, Moesin) homology domain where binding to type 1 cytokine receptors takes place. The interactions of the JAK2 FERM domain also comprises a role in trafficking of the EPO receptor (EPOR) cytoplasmic domain to the cell surface.[12] Under normal physiological circumstances when a ligand (for example erythropoietin) binds with a receptor a conformational change occurs (*see fig 1*). The JAK2 protein then makes contact with the cytoplasmic domain of the receptor where it catalyses tyrosine phosphorylation. This primarily leads to the recruitment of STAT (signal transducer and activator of transcription) molecules which are then phosphorylated, homodimerise and translocate to the nucleus where they act as transcription factors. Tyrosine phosphorylation also modifies other key regulatory events involved in cytokine signalling pathways.

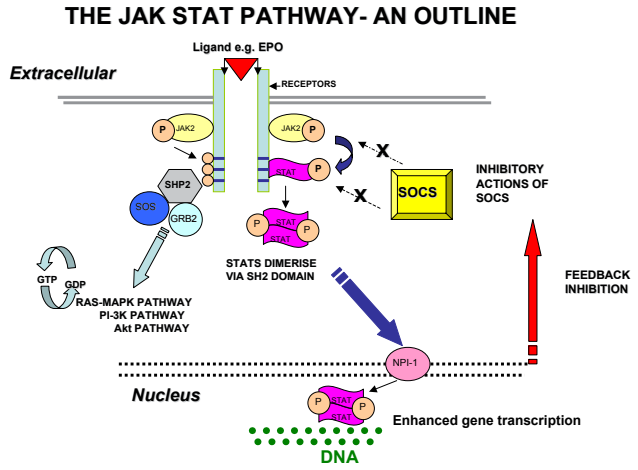


Fig 1. Diagram illustrating Functional JAK STAT Pathway

This "JAK STAT" pathway appears to be ubiquitous amongst vertebrates. Following ligand binding the activated JAK2 protein catalyses tyrosine phosphorylation in the cytoplasmic domain of the receptor and also leads to phospharylation of the Signal Transducers and Activators of Transcription (STATS).

Phosphorylation of STAT leads to dimerisation via conserved Src homology 2 (SH2) domains. Translocation of these dimers to the nucleus then occurs facilitated via Nucleoprotein Interactor 1 (NPI -1). Subsequent regulation of gene expression following interaction with DNA response elements occurs. This leads to a transcriptional response. There is also interaction with the RAS/MAPK, Pl-3 K and Akt downstream pathways.

Under normal conditions the enhanced gene expression is under complex negative feedback mechanisms including amongst others the production of the negative regulator Suppressors of Cytokine Signalling(SOCS).

The JH2 domain is a non catalytic pseudokinase and has several crucial regulatory functions.[13] It appears that in the absence of ligand binding it has autoinhibitory properties, most likely manifest by a JH2/JH1 interaction, and if an alteration in this area occurred dysregulation of this autoinhibition would result. It also appears that maximal JAK2 activity in response to cytokines requires an intact JH2 region.

In a short period in early 2005 four different groups described an identical mutation in *JAK2* V617F in large numbers of patients with MPDs.[14-17] Although all groups arrived at the same result they approached it by different methods. The Vainchenker group, who are acknowledged to have made the discovery first, approached it from the point of view of the underlying biology of the disease.[14] They had previously observed that inhibitors of JAK2 and other kinases interfered with the erythropoietin independent differentiation in PV.[18] Therefore they looked at potential mechanisms leading to the formation of EECs.

Identifying *JAK2* as a potential candidate gene, and aware of its role as an upstream signalling molecule directly linked to the erythropoietin receptor, they focussed attention on this tyrosine kinase. They discovered that down regulating JAK2 expression via the introduction of short interfering RNA led to a marked inhibition of EEC formation in individuals with PV. This obviously alerted the investigators to the key role of JAK2 in the formation of EEC and prompted sequencing of the coding exons and intron – exon junctions of the gene in three patients with PV and in two normal controls. Two of the individuals with PV demonstrated the presence of the *JAK2* V617F mutation. (*fig 2*) In a further, larger group of patients with PV the mutation was present in 88% of cases. In all of the controls, in addition to all 35 samples of patients diagnosed with a secondary erythrocytosis, only wild type *JAK2* was detected.

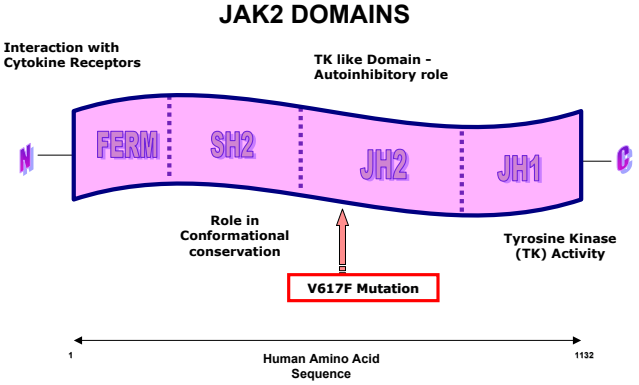


Fig 2. Diagram of JAK2 Domains highlighting main roles and indicating approximate location of V617F Mutation.

The mutation was shown to be acquired, as it was present in the myeloid lineage but absent in T cells. This group also identified the ability of the mutated JAK2 to spontaneously activate downstream STAT mediated transcription in the absence of the ligand erythropoietin. This is in contrast to the inability of wildtype JAK2 to mediate such events. There was also activation of the ERK/MAP kinase and P13K/AKT pathways in the absence of alternative cytokine stimulation. In conclusion, the auto-inhibitory activity of JAK2 was disrupted by the presence of this V617F mutation.

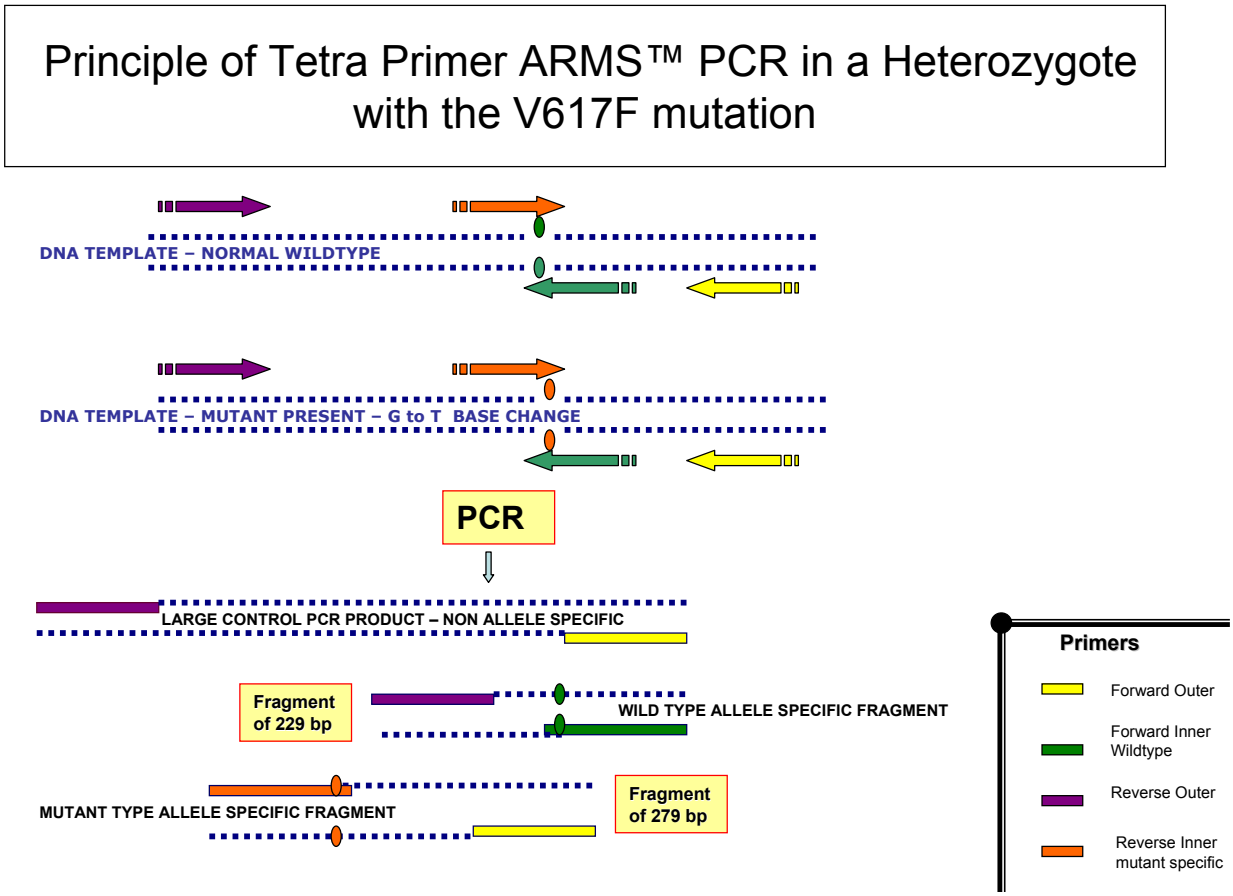


Fig 3. Tetra primer ARMS PCR

- Tetra Primer Amplification Refractory Mutation Screening Polymerase Chain Reaction – ARMS-PCR-is an extremely efficient detection method of single nucleotide polymorphisms (SNPS).
- It consists of two pairs of primers – to amplify wildtype and mutant respectively.
- Two amplification allele-specific reactions occur in opposite directions, simultaneously.
- The mismatch is in the middle of the inner primers in contrast to conventional ARMS PCR.
- There is the outer forward primer, the forward inner wildtype primer, the reverse outer primer and the reverse inner mutant specific primer.
- It requires two temperature programs during the PCR reaction.
- Due to the positioning of the outer primers at varying distance from the site of the mutation there is the generation of three fragments in this example in a heterozygote: two small allele specific fragments and a large control PCR product.
- DNA Fragments can be distinguished via electrophoresis on agarose gel.

Skoda's[15] group followed on from previous work where they had identified loss of heterozygosity (LOH) on the short arm of chromosome 9 in a proportion of MPD patients via genome wide microsatellite screening. This suggested that 9p may harbour a pathogenic mutation. They initally utilised 10 microsatellite markers covering chromosme 9p and found 9p LOH in granulocytes derived from patients with MPDs in 21% (51 /244) of cases and in no control cases, including CML. All 51 patients with 9p LOH possessed the *JAK2* V617F mutation. Further investigation found the mutation in 65% of patients with PV of whom 27% had an acquired homozygous mutation and 38% a heterozygous mutation.

Dysregulation of key tyrosine kinases is paramount to the pathogenesis of many cancers, including CML. This prompted further in depth searches for mutations in tyrosine kinases in the conventional myeloproliferative disorders. Gilliland's group[16] undertook a search for mutations of tyrosine kinases using high-throughput sequence analysis and found the *JAK2 V61F* mutation. As part of a large study looking at protein kinase genes in MPDs, Green's group[17] found the mutation in 57% of individuals with ET, 50% of individuals with IMF and 97% of those with PV. It was detected in both granulocyte-macrophage and erythroid colonies and intriguingly was present in all EECs, demonstrating a link with growth factor hypersensitivity.

The JAK2 V61F mutation accounts for some of the abnormalities described in PV although the molecular events linking the mutation with the biological parameters require further delineation. The JH2 domain is a pseudokinase and possesses autoinhibitory properties which prevent receptor phosphorylation. From modelling studies, the highly conserved valine at position 617 is predicted to lie on the

upper surface of the N-terminal lobe of the JH2 domain. Substituting the valine for a large phenlyalanine destabilises the fold of the domain.[16] Therefore the presence of the mutation would lead to a JAK2 which is constitutively active. Interestingly, in heterozygotes there appears to be competition between the wild-type and mutant genes.

Haematopoietic stem cells from MPD patients are hypersensitive to a range of growth factors and use JAK2 for signalling. Observations suggest a disruption of signal transduction downstream of JAK2 including constitutive activation of STAT3,[20] up-regulation of the anti-apoptotic protein Bcl-x_L[3] and increased AKT activity.[7] Death receptor stimulated apoptotic pathways also appear disrupted in JAK2 V617F PV derived erythroblasts with deregulated expression of the short isoform of c-FLIP[21] which fundamentally plays an essential role in the normal homeostatic apoptotic cascade.

DETECTION METHODS

The *JAK2* V617F mutation in MPDs can be detected by a variety of methods. The simplest method is to isolate DNA from whole blood leukocytes and use PCR-direct sequencing. However, since the mutation is acquired and restricted to the myeloid lineage this method has a sensitivity of between 20 to 30%. By implication the *JAK2* V617F mutant clone would have to constitute a significant proportion of the total leukocyte population to be detectable by this method.

Ficoll gradient centrifugation can be used to isolate mononuclear cells, with subsequent separation into granulocyte/macrophage lineages and lymphocytes. Methods to ensure an absence of gross contamination of the fractions should be utilised, for example magnetic sorting/flow cytometry. Isolation of DNA from the fractions can then occur and direct sequencing methods instituted. This allows detection of an acquired JAK2 V617F mutation in cells of myeloid lineage.

Amplification Refractory Mutation Screening (ARMS) PCR permits a single base change to be detected under ideal PCR conditions. This is ideal for detection of the single base G → T transversion associated with the *JAK2* mutation in question. The ARMS-PCR technique (*fig 3*) uses 4 primers as follows; a forward outer primer, a reverse outer primer, a forward inner wild type specific primer and a reverse inner mutant specific primer. The forward primer from one set and the reverse from the other are able to amplify a positive control band. The other two primers span the site of the *JAK2* V617F mutation. Therefore in the presence of the *JAK2* mutation the reverse inner mutant specific primer and the forward outer primer bind to give a fragment of 279 bp. In the presence of wild-type *JAK2* the reverse outer primer and the forward inner wild-type specific primer produce a fragment of 229bp. Performing a dilution series indicates the level of sensitivity of ARMS-PCR to be 1-2 %.[22] The assay allows discrimination between homozygous and heterozygous individuals with the *JAK2* V617F mutation and has a key role in acting as a reliable screening test for the presence or absence of the mutation in individuals with MPDs.

Although ARMS-PCR can indicate whether an individual is homozygous or heterozygous for the *V617F JAK2* mutation it does not quantify the ratios of the wild type and mutant alleles. This also applies to PCR-direct sequencing. Pyrosequencing which uses a quantitative technique originally designed for the detection of single nucleotide polymorphisms (SNP) has been developed for the detection of the G1849T *JAK2* mutation, providing accurate allele ratios.[23,24] This technique is unique in that it provides a quantitative result for each allele. Pyrosequencing entails amplification by PCR of exon 12 of *JAK2*, with a set of primers where one is labelled with a biotin tag. Single-stranded PCR products are prepared post PCR. Any biotin tagged single stranded DNA molecules are then specifically isolated by capture with streptavidin beads and genotypes are determined using the SNP software, which allows allele frequency quantification and scoring of individuals as homozygous when the mutant allele is greater than 50%.

CLINICAL CORRELATES

Other groups have proceeded to look at their series of patients and identified similar rates of the presence of the mutation in the various disease groups (*Table II*).[14-17, 22-25] Of interest is that the mutation is found extremely rarely in those with no identified cause of erythrocytosis and screening is therefore of benefit for the detection of clonal disease.[26] The presence of the *JAK2* V617F mutation has been correlated with other described biological phenomena such as *PRV1* expression and EEC formation.[27] Patients who are *JAK2* V617F mutation heterozygous or homozygous have been shown to express higher levels of NF-E2 compared to mutation negative individuals.[28]

Those who are homozygous for the mutation may have different or more advanced disease compared to those who are heterozygous. Kravolics[15] showed that those who were homozygous had a longer duration of disease and were more likely to develop secondary myelofibrosis. Tefferi[29] demonstrated that in PV those possessing the homozygous *JAK2* mutation tended to have higher haemoglobin levels, an increased incidence of pruritis and higher rates of fibrotic complications.

The significance of considering cases with a very small percentage of *JAK2* mutant positive clones as being "truly" *JAK2* V617F positive remains unclear. Obviously one needs to consider what 'cut off' value we use to distinguish those possessing the mutation from those classified as mutation negative. This is of importance if the presence of the *JAK2 V61F* mutation is to become paramount within the classification system of MPDs. Familial MPDs, including polycythaemia,[30] have been well documented and it appears that even in these rare cases, the *JAK2* mutation appears to be somatic rather than germ-line in nature.

The impact of the mutation in IMF, from a clinical stance, appears somewhat less well defined. In a large study of myelofibrosis, Campbell *et al*[31] showed that patients with the *JAK2* V617F mutation had higher neutrophil and white cell counts compared to patients without the mutation and overall tended to have a poorer prognosis. Tefferi *et al*[32] looked for the mutation in a variety of patients with myelofibrosis and found that the mutation was more likely to be present in patients with a previous history of PV compared to *de novo* MF. The presence of the *JAK2* V617F mutation in this fairly large cohort of 157 patients did not appear to have prognostic significance.

TABLE II

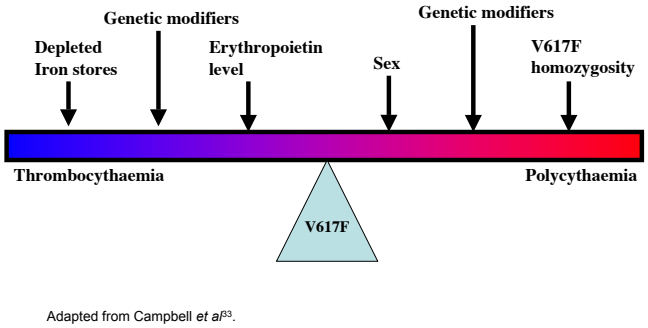
Some reported incidences of JAK2 V61F mutation in myeloproliferative disorders

Investigators / **Disorder**	Green [17]	Vainchenker [14]	Gilliland[16]	Skoda [15]	Tefferi[24]	Cross[22]	Zhao[25]	Jelinek [23]
PV	**97%**	**88%**	**74%**	**65%**		**81%**	**83%**	**86%**
ET	**57%**	**43%**	**32%**	**23%**		**41%**		**30%**
IMF	**50%**	**43%**	**35%**	**57%**		**43%**		**95%**
SM					**25%**	**0%**		
CNL					**17%**	**33%**		
HES					**0%**	**2%**		
UN						**20%**		
MDS					**5%**			**1.5%**
CMML					**3%**			**13%**

KEY TO ABBREVIATIONS

PV: polycythemia vera, ET: essential thrombocythemia, IMF: idiopathic myelofibrosis, SM: systmemic mastocytosis, CNL: chronic neutrophilic leukemia, HES: hypereosinophilic syndrome, UN: unclassified MPD, MDS: myelodysplastic syndrome, CMML: chronic myelomonocytic leukemia.

The MRC-PT-1 prospective study of ET allowed comparison of mutation positive and negative patients.[33] Those with the mutation had features resembling PV, higher haemoglobin, higher neutrophil counts, more venous thrombosis and a higher rate of transformation to PV but they had lower serum erythropoietin levels and ferritin levels. *JAK2* V617F positive patients appeared to more sensitive to treatment with hydroxycarbamide but not anagrelide. Another series of ET patients showed that those with the mutation were more likely to transform to PV.[34] These findings call into question the separation of the diseases PV and ET. There may be a continuum of disease with the effects of the *JAK2* V617F mutation on clinical presentation influenced by other modifiers including iron supply, erythropoietin suppression and other genetic modifiers (*see fig 4*).



Adapted from Campbell *et al*[33].

Fig 4. Continuum model of JAK2 V61F Disease.

OTHER DISEASES

The presence of the mutation has been investigated in atypical MPDs including systemic mastocytosis, hypereosinophilic syndrome, chronic neutrophilic leukaemia, unclassified myeloproliferative disorders .[24] Of interest, McLornan *et al* [35] detected the mutation in one chronic neutrophilic leukaemia patient with an unusual protracted course where the mutation may in some way influence the course of the disease. The mutation has been found in varying proportions of patients as summarised in Table II. It has been detected rarely in patients with myelodysplastic disorders.[22] The prevalence of the mutation is higher in patients with acute myeloid leukaemia (AML) with antecedent PV or IMF than in the overall cohort.[36] It has been reported rarely in other series of patients with AML and no patients with lymphoid leukaemia.[23, 36]

FURTHER QUESTIONS

The fascinating discovery of a single mutation in a wide spectrum of MPDs has lead to rapid progress in the investigation of MPDs but leads to a number of further questions. The hierarchical position of this mutation requires further study. It is still not clear whether the *JAK2 V61F* mutation is the primary initiating event or a secondary event with an as yet unknown primary event. While the presence of the mutation was sufficient to induce erythrocytosis in mice this is a manipulated experimental situation and it may not be sufficient to initiate disease in the human.

Classification of MPD needs revision. The presence of the mutation demonstrates a clonal disorder but splitting of diseases on the basis of clinical characteristics

needs reconsideration. Questions remain about the underlying pathogenesis in those with mutation negative myeloproliferative disorders. In summary, the discovery of a single mutation *JAK2 V61F* in a large number of MPD patients has lead to great progress in the understanding of MPDs but leads to many more exciting biological questions.

The authors have no conflict of interest.

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Paper

Modelling predictions of cancer deaths in Northern Ireland

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ABSTRACT

Background: **An ageing population has service planners concerned about future levels of disease which are age dependent. Predictions of mortality for colorectal, lung and breast cancers, which account for 30% of cancer cases and 40% of cancers deaths, were calculated for 2010 and 2015, based on trends in death rates and the predicted change in the demography of the Northern Ireland population.**

Methods: **The US National Cancer Institute's "Joinpoint" program was used to check for structural breaks in the time series of cancer death rates from 1984 to 2004. The prediction models applied to the data allowed variations in trends across age groups to be taken into account. A linear model was used for increasing or constant trends and a log linear model was used where the trend was decreasing. The models assume the number of deaths in each stratum, defined by age-sex and time-period, is Poisson distributed, with the average value determined by a log or linear function.**

Results: **Recent trends in rates of cancers studied were downwards except for female lung. Predictions include decreased colorectal cancer deaths in females and lung cancer deaths in males. In females, lung cancer deaths are predicted to more than double by the year 2015 (473 deaths), based on the 1984 level. Colorectal death rates in males are predicted to drop, but the number of deaths will increase by more than 10%, due to demographic change. Numbers of breast cancer deaths are likely to rise slightly, despite falling age standardised death rates, due to an ageing population.**

Conclusions: **This work has provided estimates of early future trends, useful to service planners, and highlights the need for tobacco control, to reduce numbers of lung cancer deaths in females. The recently announced control of environmental tobacco legislation is one welcome development which should reduce lung cancer mortality in Northern Ireland.**

INTRODUCTION

In Northern Ireland cancers of the colorectum, lung and breast account for 30% of all cancer cases and about 40% of cancers deaths.[1] The diagnosis, treatment and care of patients with these diseases use significant resources, so any change in numbers is particularly relevant to service planners. Projections can also identify need for health promotion initiatives to reduce risk in a population.

The predicted changes to the population structure, of increases in the proportion of older people,[2] will result in a rise in the incidence of cancer, a disease more common in older people. Disease risk factors are the other major driver for change.

In Northern Ireland, accurate cancer incidence data is available only since 1993; death information is available for a longer period. For lung cancer, the greatest cause of cancer mortality, numbers of deaths are close to incidence levels, due to poor survival rates. Deaths therefore form the basis of this analysis, which aims to identify for planners, future demands on services and highlight areas for disease prevention.

METHODOLOGY

Annual age specific death rates for the period 1984-2004 were calculated using official mortality figures from the General Register Office for Northern Ireland [3] and mid-year population estimates, provided by the Northern Ireland Statistics and Research Agency. The age groups used were 0-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84 and 85+.

Linear and log-linear regression models have been found to be the most practical means by which relatively short-term future patterns of cancer mortality can be estimated.[4] The use of classical age-period-cohort modelling techniques may well improve the "fit" of the model (albeit at the expense of extra degrees of freedom), but the random variation associated with parameter estimates can lead to erratic projections.[5]

In this study, the identification of the most recent trends was assisted through inflexion point regression analysis of the data, using the US National Cancer Institute's (NCI) "Joinpoint" program (Version 3.0),[6] a Windows-based statistical package used to analyse modelled data where several trend-lines are connected together at "joinpoints". The software takes trend

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data (in this case age-standardised cancer mortality rates) and fits the simplest inflexion model that the data allows. The programme starts with the minimum number of joinpoints (e.g. 0 joinpoints, which is a straight line) and tests whether more joinpoints are statistically significant and must be added to the model, thus enabling the user to test whether an apparent change in trend is statistically significant.[7]

Existing incidence-based modelling tools developed by Dyba and Hakulinen from the Finnish Cancer Registry,[8,9] were used to predict cancer mortality, on the principle that the underlying theoretical assumptions apply equally to incidence and mortality data. These assumptions are:

1. Future cancer death trends can be modelled by extrapolating a historic trend.
2. The lengths of the data time-series permit the estimation of models that take account of age-sex group specific trends.
3. The numbers of deaths in each age-sex-timeperiod stratum are Poisson distributed.
4. Where historic trends in standardized deaths are decreasing, a log–linear model is appropriate to estimate the average rate, whereas a linear model is used for increasing or constant trends to avoid explosive growth.

Let $M_{it}=\frac{c_{it}}{n_{it}}$ be the mortality rate for age group i in period t, given n_{it}, the number of persons and c_{it} the number of deaths. Let α_i, $ß_i$ be the model parameters for age group i.

A description of the models applied in various scenarios is given below (*Table I*).

Model 4 is an alternative to model 3 and may be used where model 3 gives large confidence intervals for predictions or unrealistic trends in some age groups. It proves useful for the case, common in practice, where larger baseline death rates give larger trends over time and this functional form explicitly keeps the ratio between baseline rate and trend constant across age groups.

The 95% predicted confidence intervals generated in the output analysis are used to account not only for the uncertainty in the historical data but also for the randomness in the numbers of deaths themselves. Consequently the "95% prediction intervals" reported here may seem quite large.

Estimates of the parameters for each of the models were calculated using the STATA 8.0 Statistical package for Windows.[10]

The Pearson goodness-of-fit test statistic was used to test the adequacy of the model and is given by:

$$\chi^2 = \sum_{i=1}^{N}\sum_{t=1}^{T}\frac{M_{it}-\hat{M}_{it}}{\sqrt{\hat{M}_{it}}}$$

where N is the number of age-groups and T the length of the time series. This statistic indicates the fit of the data to a Poisson distribution.

The 'deviance' is defined to be twice the difference between the maximum achievable log likelihood and the log likelihood at the maximum likelihood estimates of the regression parameters. It forms a useful basis for choosing between models when two models give a reasonable fit. A log-likelihood ratio test of the form $D=D_a - D_b$, where D_a, D_b are the deviances of fit of models a and b respectively, is used to choose between models. D follows a chi-square distribution, with degrees of freedom equal to the difference in degrees of freedom between models a and b, when both models describe the data well.

As the number of parameters increases, the model will inevitably improve. To enable selection of the most parsimonious model, the Akaike Information Criterion (AIC), which penalises the addition of extra parameters was used. Generally, where the log-likelihood test indicated either of two models was acceptable, the more parsimonious model was chosen.

Once the best model was chosen, 2004-based population projections based on assumptions regarding fertility, mortality and net migration, for N. Ireland[2] were applied to predict cancer deaths by gender and site (error range in brackets).

RESULTS

Joinpoint analysis of mortality rates (1984-2004) revealed significant downward trends in: colorectal cancer in males and females; lung cancer in males and breast cancer in females (*Fig 1*). A significant upward trend was demonstrated for female lung cancer. No change in trend was detected over the period (1984-2004) for any site, i.e. a joinpoint model with zero joins (JP_0) was shown to best represent each time series.

TABLE I

Outline of Models

Data Trend	*Decreasing*	*Decreasing*	*Increasing*	*Increasing*	
Significant variation in trend across age groups	No	Yes	Yes	Yes	
Most appropriate model	$\ln(M_{it}) = \alpha_i + \beta t$ Model 1	$\ln(M_{it}) = \alpha_i + \beta_i t$ Model 2	$M_{it} = \alpha_i + \beta_i t$ Model 3	$M_{it} = \alpha_i + \beta_i t$ where $\frac{\alpha_i}{\beta_i} = \frac{\alpha_j}{\beta_j}$	for any two age-groups i, j Model 4

Fig 1A. Trends in Age-Standardised Mortality Rates* (3-year moving averages)
* rates standardised to N. Ireland population projection 2005

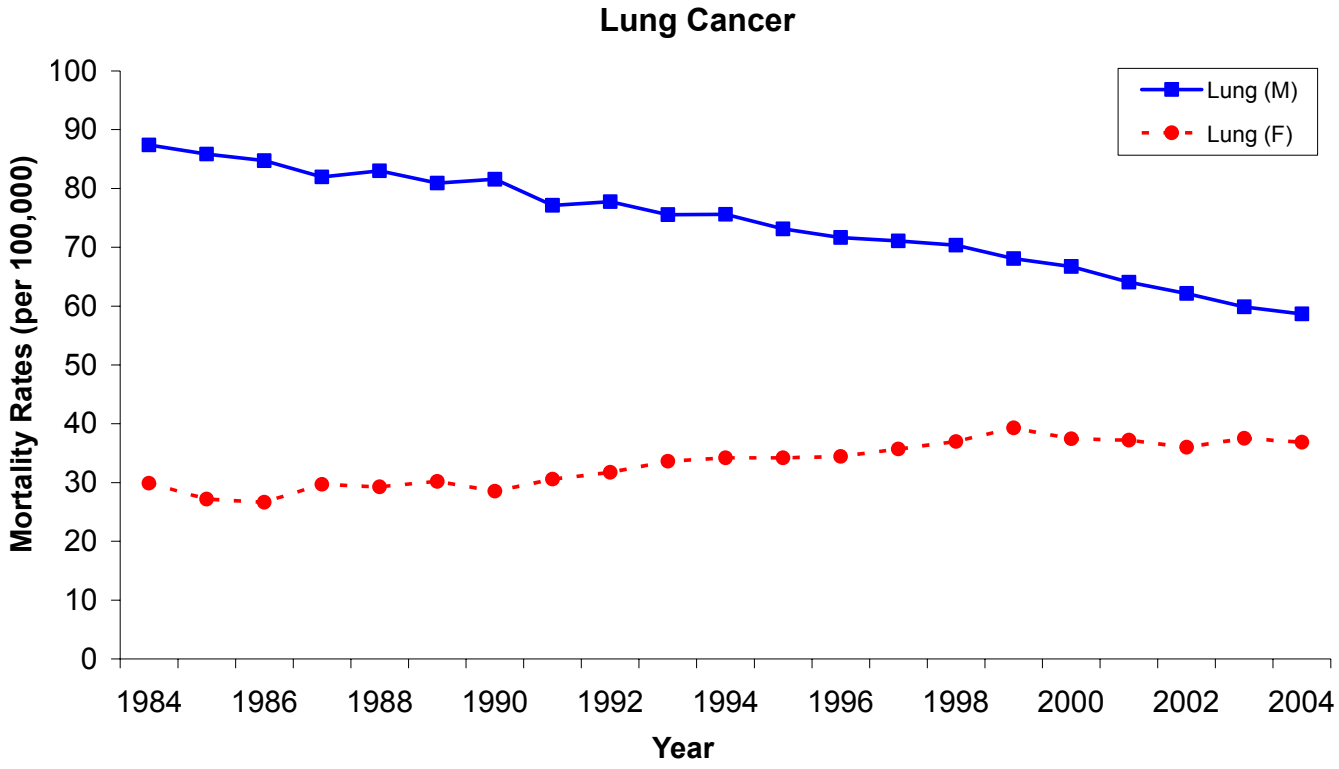


Fig 1B.

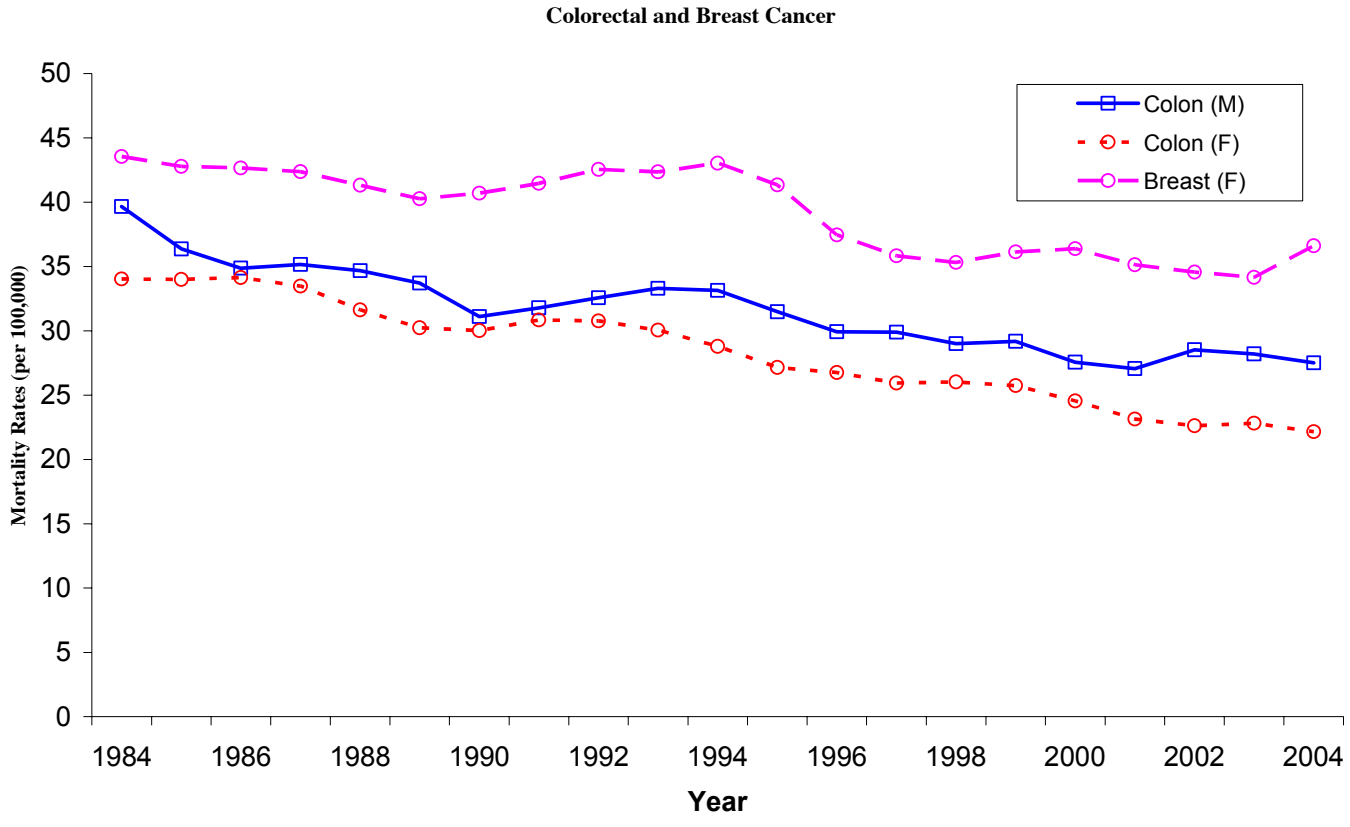


TABLE II

Diagnostic tests by model and cancer site

Site	*Model*	*Pearsons's* χ^2	*d.f.*	*Prob*
Colorectal (male)	Log - single trend (1)	201	199	0.448
Lung (Male)	Log - multiple trend (2)	192	190	0.438
Colorectal (Female)	Log - single trend (1)	193	199	0.602
Lung (Female)	Linear - multiple trend (4)	265	190	0.000
Breast	Log - multiple trend (2)	191	190	0.464

Variations in mortality rate trends across age-groups were also observed for some sites. Since the female lung cancer mortality series (1984-2004) was the only one to demonstrate a significant increasing trend, further scrutiny of age-specific rates for this site was of particular interest, to determine which age-groups were driving this increase (*see Fig 2*).

Joinpoint analysis of age-specific mortality rates for female lung cancer revealed no significant trend among females aged 0-64yrs (combined). Significant upward trends were observed within each of the other age-groups, but most notably among females aged 75-79 years [single continuous increase detected (1987-2004)] and 85+years [increases detected (1984-1988), (1992-2001) & (2001-2004)].

According to the principles outlined in the methods, the appropriate model was selected for each site. Table II details the models selected. All models provide a reasonable fit to the data, except for female lung cancer, where the model selected is very poor.

Colorectal cancer death rates are predicted to fall in males and females, but numbers in males may rise due to demographic pressures (*see Table III*). This reflects the more marked historic decreasing trend in females, counterbalancing the pressure due to an ageing population.

Lung cancer deaths fell in males but increased in females between 1984 and 2004. The prediction follows on the trend for males so that despite demographic change, deaths from lung cancer in males do not rise. In females, however death rates (2015) are predicted to more than double, based on the 1985 level, due to a rising rate of disease and an ageing population.

Breast cancer death rates fell between 1984 and 2004, with a more rapid decline noticed after 1997. The model predicts slightly increasing deaths from breast cancer – despite decreasing age standardized death rates. This is driven by the ageing population.

DISCUSSION

Trends based on incidence are preferable to those based on deaths, as death trends are affected by changes in survival as well as changes in incidence. Also, deaths data are less rigorously checked compared to cancer incidence data. The accuracy of trend predictions however depends on the length of the time series examined and hence deaths are preferred in this instance.

Predictions based on historical data do not take into account future improvements in treatment or changes in the way health services are organised, but only extrapolate mortality patterns from a range of observations. These predictions also assume that current trends will remain unchanged in the future. As the predictions calculated here are only for up to ten years, such effects are likely to be minimal. However, the recent fall in breast cancer mortality, with documented significant survival improvements in the population studied[1] may not have been given enough weight in the model used. Deaths from breast cancer are falling rapidly due to earlier diagnosis and advances in treatment and the predicted increase in deaths may not materialise.

Generally, the models provide a very good fit to the data. However, the model of female lung cancer mortality trend is inadequate. Both male and female lung cancer predictions could be improved upon by the inclusion of information on smoking, as about 90% of lung cancers are directly attributed to tobacco, with very low levels of background disease.[11]

The biggest determinant of the level of cancer in the short and long term is the pressure of an ageing population, as cancer is a disease more common in older people. While age standardised rates may decrease, due to public health initiatives, the absolute number of cases diagnosed and requiring treatment is likely to rise. Service planners must take this into consideration now, to ensure adequate service provision in the future. As tobacco is causally implicated in around a third of all cancers,[11] significant efforts made now, in tobacco control, could counterbalance the pressures due to demographic change and halt the predicted rise in cancers.

Trends in lung cancer mortality can be affected by smoking patterns 20-30 years previously, but the cessation of smoking, even well into middle age, can avoid most of the subsequent risk of lung cancer; stopping before middle age avoids more than 90% of the risk attributable to tobacco.[11] If current smokers can succeed in giving up the habit, mortality from lung cancer in the near future could be substantially reduced.[11] The recently announced environmental tobacco control legislation for N. Ireland is a welcome initiative which should reduce lung cancer mortality.

It is planned to introduce colorectal cancer screening in N. Ireland within the next ten years. This should further reduce deaths from colorectal cancer below that predicted by the model. Service planners should note that disease levels will

TABLE III

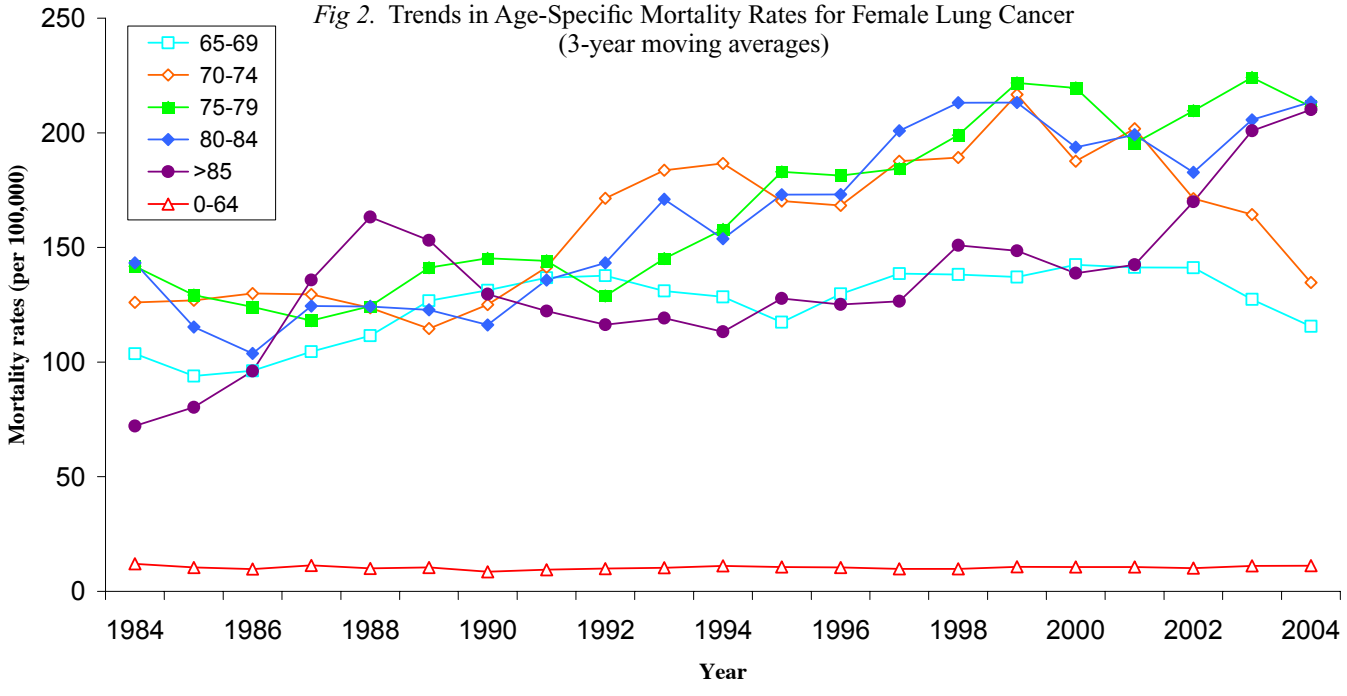
Numbers[1] (n) and rates[2] (r) (per 100,000) of cancer deaths by gender and site (error range in brackets)

	Year	Males				Females					
		Colorectal		*Lung*		*Colorectal*		*Lung*		*Breast*	
		N	r	N	r	n	r	N	r	n	r
ACTUAL	1985	222	36	572	89	237	33	181	24	307	44
	1990	214	32	524	78	228	30	242	31	295	40
	1995	236	33	507	71	219	28	272	34	327	42
	2000	205	27	494	65	221	27	346	42	286	35
PREDICTED	2010	237	25	525	55	187	20	404	43	313	33
		(201, 273)	(21, 29)	(472, 578)	(50, 61)	(156, 218)	(16, 23)	(356, 453)	(38, 48)	(271, 354)	(29, 37)
	2015	251	23	554	51	183	18	473	46	328	32
		(210, 291)	(19, 27)	(493, 615)	(45, 56)	(150, 215)	(14, 21)	(415, 530)	(40, 52)	(281, 376)	(27, 36)

[1] predicted deaths calculated by applying predicted age-specific rates to predicted populations

[2] rates standardised to N. Ireland population projection 2005

Fig 2. Trends in Age-Specific Mortality Rates for Female Lung Cancer (3-year moving averages)



increase due to enhanced detection during the early prevalence round of screening.

Exercise has been shown to reduce colorectal cancer,[12] while obesity in postmenopausal females increases the risk of breast cancer.[13] While changes in these lifestyle factors are unlikely to affect deaths in the short timescale of this study, they will have serious implications in the longer term. Initiatives to increase exercise, increase fruit/vegetable consumption and tackle obesity need to be put in place now.

Possible advances in treatment within the next ten years have not been taken into account. Also specialisation of cancer services which has been shown to reduce mortality[14-16] is ongoing in N. Ireland, since the publication of the Campbell Report.[17]

This work has several limitations but it has allowed service planners to explore the issues based on predictions in a developing and costly area of care. It has also highlighted the need to target tobacco control, especially among females.

The authors have no conflict of interest.

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Paper

Laparoscopic adrenalectomy versus open adrenalectomy: results from a retrospective comparative study

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SUMMARY

The relatively new operation of laparoscopic adrenalectomy has now become the procedure of choice for the management of most benign adrenal tumours. We have reviewed the data relating to the first 25 patients on whom we performed laparoscopic adrenalectomy and have made comparison with a group of 25 diagnosis-matched individuals on whom we had previously carried out open adrenalectomy.

The patients who underwent laparoscopic adrenalectomy had a significantly shorter hospital stay and experienced significantly less postoperative morbidity than those who had an open operation, but the operation time was significantly longer for the laparoscopic group of patients. There is now good potential and sound evidence base for extending the indications for laparoscopic adrenalectomy.

INTRODUCTION

The technique of laparoscopic adrenalectomy was first described in 1992.[1] Subsequently, the operation has been performed with increasing frequency in specialist endocrine surgical units and has now become the treatment of choice for most benign adrenal tumours.

Recent studies have demonstrated significant benefits for patients who have undergone laparoscopic adrenalectomy, in terms of reduced operative morbidity, shorter hospital stay and earlier return to normal activity when compared to those submitted to open operation.[2-4]

In the Endocrine Surgery unit in the Royal Victoria Hospital we began to carry out laparoscopic adrenalectomy in 1998. This paper records our early experience of this innovative procedure and makes comparison with historical data relating to open adrenalectomy.

PATIENTS AND METHODS

The first 25 patients who underwent laparoscopic adrenalectomy in our unit, were compared retrospectively with the most recent diagnosis matched group of 25 individuals who had previously undergone open adrenalectomy. All operations in both groups of patients were carried out by one of two consultant endocrine surgeons, working as a team, under general anaesthetic with full muscle relaxation and mechanical ventilation.

The laparoscopic operation was performed in all instances using a transperitoneal approach with the patient placed in an almost full lateral position, and with the operating table "broken" to maximum extension to allow the space between rib cage and pelvis to open fully. Three ports were employed for left adrenalectomy and an additional port utilised on the right side to allow retraction of the liver. Pneumoperitoneum was established using an open technique and a 30-degree laparoscope used in all cases.

On the left side the spleno-colic ligament is freed to allow protection of the splenic flexure of the colon. The lieno-renal ligament is then divided to allow spleen and distal pancreas to fall forward, permitting exposure of the adrenal gland. On the right side, after retracting the liver, the posterior peritoneum is incised widely to allow access to the adrenal gland, right kidney and inferior vena cava. Securing the single, substantial adrenal vein on each side represents a critical part of the operation. On the left side the adrenal vein almost always drains vertically downwards into the left renal vein while, on the right side, the vein invariably passes transversely or obliquely directly into the vena cava. In all patients in both groups the adrenal vein was secured using individual vascular clips. Once the adrenal vein has been secured and divided, the adrenal gland is freed from its various attachments and delivered using a retrieval bag. We have routinely performed total adrenalectomy and have not attempted subtotal resection for any pathology.

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In the open operation, the adrenal gland was approached on either side using a postero-lateral incision through the bed of the 11th rib and with resection of the rib. The retroperitoneum was then opened and the adrenal gland exposed.

The clinical records of all 50 patients were reviewed. Demographic details, body mass index (BMI), American Society of Anaesthesiologists (ASA) classification, length of operation, postoperative complications and length of hospital stay were recorded. Demographic details were analysed using the chi squared test and comparison made between laparoscopic and open groups using an unpaired t test. All statistical analyses were performed using SPSS software (version 10, SPSS Inc., Chicago). Values are reported as mean ± SEM and a probability value of <0.05 considered significant.

Results

Fifty patients were included in the study; twenty-five having undergone laparoscopic adrenalectomy and 25 open adrenalectomy. There were no significant differences between the demographic details of the two patient groups (*Table I*) nor the indications for operation (*Table II*). Four individuals, two from each group, underwent bilateral total adrenalectomy. In one patient undergoing laparoscopic left adrenalectomy for Cushing's syndrome, conversion to open operation was required as the adrenal vein could not be clearly identified. These five patients were excluded from further analysis leaving 22 patients in the laparoscopic group and 23 in the open group.

TABLE I

Demographic details

	Open (n = 25)	*Laparoscopic (n = 25)*	*P value*
Age (years)	47.50 ± 2.17	46.79 ± 2.99	0.96 (ns)
Sex (male : female)	8:17	9:16	0.76 (ns)
BMI	28.07 ± 0.65	29.92 ± 1.17	0.15 (ns)
ASA	2.06 ± 0.13	2.20 ± 0.08	0.38 (ns)

BMI = Body Mass Index
ASA = American Society of Anaesthesiology

TABLE II

Indications for operation

	Open (n = 25)	*Laparoscopic (n = 25)*
Conn's Syndrome	14	13
Cushing's Syndrome	6 (2 bilateral)	5 (1 bilateral)
Androgen producing tumour	0	1
Bilateral congenital Adrenocortical hyperplasia	0	1
Pheochromocytoma	4	4
Non functioning tumour (Cortical adenoma)	1	1

TABLE III

Perioperative data

	Open (n = 23)	*Laparoscopic (n = 22)*	*P value*
Transfusion requirement (units)	0.15	0	0.32 (ns)
Maximum diameter of tumour/gland (cm)	2.41 ± 0.40	3.26 ± 0.56	0.23 (ns)
Weight of tumour/ gland (g)	20.09 ± 3.71	25.80 ± 5.43	0.39 (ns)

There was no significant difference between the two groups of patients studied in terms of perioperative blood transfusion requirement, tumour size or tumour weight (*Table III*). However, the mean operating time for individuals who had the laparoscopic procedure performed was significantly longer than that for those who underwent open adrenalectomy (199.7 ± 14.3 minutes versus 143.7 ± 5.9 minutes; p = 0.001). In contradistinction, the mean duration of postoperative hospital stay for patients undergoing laparoscopic adrenalectomy was significantly shorter (3.95 ± 0.32 days versus 10.16 ± 0.83 days; p < 0.001).

Significantly fewer postoperative complications were encountered in the laparoscopic group than in the open group (3v9; p = 0.04) although no major problems were experienced in either patient group following operation (*Table IV*). There was no operative mortality.

TABLE IV

Postoperative Complications

	Open (n = 23)	*Laparoscopic (n = 22)*
Chest Infection	5	2
Pneumothorax	2	0
Wound Infection	2	0
Atrial Fibrillation	0	1

DISCUSSION

Because of their anatomy, the adrenal glands are, in surgical terms, relatively inaccessible. For that reason a variety of surgical approaches have been employed over the years when open operation on the glands has been practised. These include the anterior, transperitoneal approach using a subcostal incision, the posterior, retroperitoneal approach with the patient fully prone and the postero-lateral approach through the bed of the 11th or 12th rib, again utilising an exclusively extraperitoneal route to the adrenal glands. All of these procedures represent major surgery through large incisions and are associated with significant pain and postoperative morbidity. Against this background, laparoscopic adrenalectomy represents an attractive option for both patient and surgeon with its reduced invasiveness

but without compromise of the ability to visualise and resect the adrenal glands.

This retrospective comparative study has confirmed the findings of others that patients undergoing laparoscopic adrenalectomy require to stay in hospital for very significantly shorter periods of time following operation when compared to individuals who have had open adrenalectomy performed. Patients having the laparoscopic procedure also developed fewer postoperative complications than those submitted to open operation. Although data are not available for our two groups of patients, we have little doubt that postoperative analgesic requirement following laparoscopic adrenalectomy is markedly reduced in comparison to the requirement after open surgery.

The prolonged operation times recorded for our patients who underwent laparoscopic adrenal resection when compared to those who had an open operation are in keeping with the experience of others [5] and undoubtedly reflects, at least to some degree, our learning curve for this technically demanding procedure. Hopefully, the operating times for laparoscopic adrenalectomy will shorten as our experience with the operation continues to grow.

In common with colleagues elsewhere we initially restricted the offer of laparoscopic adrenalectomy to those patients with small tumours, notably individuals suffering from primary hyperaldosteronism (Conn's syndrome) or hypercortisolism (Cushing's syndrome), both of which are typically caused by small, unilateral adrenocortical adenomas. Subsequently however, we have cautiously extended our indications for laparoscopic adrenalectomy to include adrenal medullary tumours (pheochromocytoma) and larger tumours when there has been no preoperative radiological evidence of malignancy. In this regard, careful scrutiny of CT or MRI scans in patients with large tumours in order to ensure that there is no clear evidence of invasion of adjacent structures by the tumour, is critical in terms of patient selection for the laparoscopic operation. Recent evidence confirms that with careful patient assessment and selection, laparoscopic adrenalectomy can be performed safely even when the tumour is large.[6] However, ongoing and longer term review of such patients is essential in order to ensure that the potential for permanent cure has not been compromised.

To date, all of our laparoscopic procedures have been performed via the transperitoneal route. Recently Walz and colleagues have drawn attention to the possibility and the attraction of performing laparoscopic adrenalectomy using a retroperitoneal approach.[7] Currently, we have no experience of this interesting procedure but continue to keep an open mind on its potential benefits.

Finally, it is important to underline the fact that, from time to time, it becomes necessary to convert the anticipated laparoscopic procedure to open operation. It is therefore essential that those surgeons carrying out laparoscopic adrenalectomy are also adequately trained in and comfortable with performing open resection of the adrenal glands.

The authors have no conflict of interest

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Paper

Imported malaria to Northern Ireland: improving surveillance for better intervention

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ABSTRACT

Malaria is a preventable disease, which is under notified in the UK. This study sought to evaluate the current surveillance arrangements in Northern Ireland (NI), describe the epidemiology of malaria and make appropriate recommendations.

A case was defined as a resident or visitor to NI with laboratory confirmed malaria, diagnosed by the NI haematology laboratories and/or the Malaria Reference Laboratory (MRL) from 1998-2003. Laboratory data were compared with notifications and hospital admission data.

One hundred and fourteen laboratory cases were identified compared with 63 notifications received by the regional surveillance centre. Six cases were associated with two episodes of malaria reflecting recurrence and or reinfection. *P. falciparum* was the most common infection with two fatalities reported; this was particularly associated with travel to West Africa. Most cases were associated with short visits to malarious areas. Thirty-three percent of all cases did not take prophylaxis and, of those that did, approximately half were taking a prophylactic regime appropriate to the region visited.

This study highlights the need for improved surveillance of malaria in order to capture risk factors and other relevant information to inform public and professional education. This would facilitate increasing local awareness, enhancing prescription of and compliance with appropriate chemoprophylaxis and enabling early diagnosis and treatment of malaria.

INTRODUCTION

Malaria is a disease that affects 40% of the world's population, mainly in tropical and subtropical countries. The World Health Organisation estimates that malaria accounts for more than 300 million acute illnesses and at least one million deaths annually.[1] Human malaria is caused by *Plasmodium falciparum, P. malariae, P. ovale* and *P. vivax. P. falciparum* has the highest fatality rate compared with the other three types of malaria infection.[2] The number of imported cases of *P. falciparum* in the UK has risen steadily since the 1970s.[3] Challenges to the prevention and control of malaria include raising public awareness and compliance with appropriate chemoprophylaxis. A further challenge is the development of antimicrobial resistance to common anti-malarial drugs such as chloroquine which are used for prophylaxis.

Malaria is a statutory notifiable disease in Northern Ireland requiring the clinician to notify the patient to the Director of Public Health of the Health and Social Services Board. In practice, these notifications are received by the Consultant in Communicable Disease Control (CCDC). Notifications are based on clinical suspicion and laboratory confirmation is not required for the purposes of the legislation. However malaria notifications are frequently under-reported.[4]

The aims of this study were (a) to evaluate the current malaria surveillance arrangements in NI; (b) to describe the epidemiology of imported malaria to NI between 1998-2003; and (c) to suggest appropriate recommendations to improve surveillance for better prevention and control of imported malaria.

METHODS

A case was defined as an individual who was a resident or visitor to Northern Ireland with malaria confirmed by the NI haematology laboratories and/or the London Malaria Reference Laboratory (MRL) from 1998-2003.

The current MRL patient report form was used for data collection. The data was entered on to Epi Info version 6.03 (Centres for Disease Control, Atlanta) and the analysis undertaken at the Communicable Disease Surveillance Centre, Northern Ireland [CDSC (NI)].

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Data sources

Data was sought on age; gender; onset of illness; dates and reason for travel; countries visited; prophylaxis taken; method of diagnosis; species of parasite; and outcome of illness. Information on date of birth and gender was used to identify duplicate reports.

Data was obtained from the haematology laboratories, MRL, Regional Infectious Diseases Unit, CsCDC, Department of Health, Social Services and Public Safety (DHSSPS) Regional Information Branch, Registrar General and CDSC (NI).

RESULTS

Data Source

Requests for malaria tests originated from the Regional Infectious Diseases Unit, acute medical wards and general practitioners (GP). There were 1774 requests (including repeats) for malaria tests (1998-2003) submitted to the main Belfast laboratory of which the majority (approximately 80%) were from hospital sources. Of the 114 positive cases, 99 were from the hospital (i.e. Regional Infectious Diseases Unit and acute medical wards).

Laboratory reports refer to malaria confirmed reports from the haematology laboratories and/or MRL. Fig. 1 illustrates the number of laboratory-confirmed malaria cases per annum and the annual number of falciparum cases from 1998-2003. One hundred and fourteen laboratory confirmed cases were identified which equate to an average incidence rate of 1.1 per 100,000 population using the 2002 mid year estimate. These 114 cases involved 108 individuals as six patients had either a relapse and/or reinfection. Table I describes the proportion of laboratory confirmed malaria cases from each data source. There were 10 cases identified by the MRL with no corresponding haematology laboratory report.

Age, gender, ethnicity

The average age of patients was 33 years (age range 2-80, median 31 years, mode 22 years). The male to female ratio was 2:1 (78 males, 36 females). Ethnicity was available on 104/114 patients of whom 94/104 (90%) were Caucasian. The other ethnic backgrounds 10/104 (9%) included Black African (7) and South-East Asian (3).

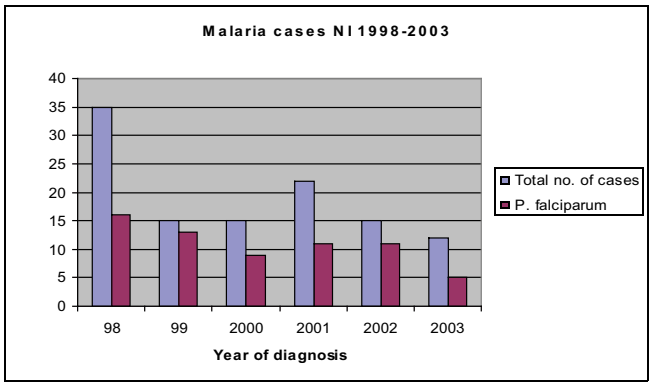

Fig 1. Annual number of laboratory-confirmed malaria cases and those of P. falciparum, 1998-2003, Northern Ireland.

Travel history

Travel history was available on 110/114 (97%) patients. The most frequently visited region was Africa (98/110, 89%), with West Africa being the region with the greatest number of associated cases (39/110, 36%). South-East Asia was visited by 8/110 (7%) of cases followed by India/Pakistan (4/110, 4%).

The reasons for travel were obtained from 52/114 (46%) cases (*Table II*) together with history of prophylaxis. The majority were short term travellers (29/52, 57%) comprising holiday makers or those on short mission trips (18/52, 35%) and business/professional travellers (11/52, 21%). Long term travellers (12/52, 24%) included expatriates living, studying and working abroad (including armed forces) and individuals visiting friends and relatives in their country of origin (4/52, 8%). In 1998 there was a cohort of nine patients infected with *P. ovale* following a church organised trip to Kenya. Seven cases (7/52, 14%) were visitors to NI including three members of an African children's choir.

The length of stay in malarious regions was available on 98/114 (86%) patients. The average duration was 7 months (206 days) but the most common period was two weeks (14 days). The length of stay ranged from five days to eight years with a median of two months (60 days). However there were four patients (UK citizens living abroad) whose length of stay was unknown.

Plasmodium species

The most common species of malaria was *P. falciparum* (65/114, 57%), followed by *P. vivax* (21/114, 18%), *P. ovale* (20/114, 18%) and *P. malariae* (2/114, 2%). The plasmodium species was not identified in three cases. A combination of two plasmodium species (*P. ovale* and *P. falciparum, P. vivax* and *P. falciparum, P. ovale* and *P. malariae*) was noted in three patients. A church group was associated with nine reports of *P. ovale* (see earlier).

Table III describes the number of cases, classified by species, associated with travel history. There were 65 cases with *P. falciparum* infection all of whom had visited Africa. Thirty-three (33/39, 85%) of those acquiring malaria in West Africa had infection with *P. falciparum* compared with 18 (18/37, 49%) visiting East Africa. All those presenting with malaria and travel to the Indian sub-continent and South East Asia had *P. vivax* infection. The time interval for presentation of disease as calculated from date of arrival into the UK to date of laboratory diagnosis is given in Table IV.

Prophylaxis

Prophylaxis history was available on 103/114 (90%) cases of which 65/103 (63%) reporting taking prophylaxis and 38/103 (37%) did not. The number of travellers who sought travel advice was not recorded as part of the data collection. However it is presumed that those who took appropriate prophylaxis probably did seek travel advice. Thirty-four (34/65, 52%) travellers took prophylaxis appropriate to the country they were visiting with 25/34 (74%) taking it regularly while abroad but only 13/34 (38%) continued prophylaxis for four weeks on return from travel as advised under current guidelines.

(Accompanying table)

Year	*Total cases*	*Plasmodium species*					
		falciparum	*vivax*	*ovale*	*malariae*	*unknown*	*combination*
98	16	6	12	0	1	0	35
99	13	1	1	0	0	0	15
2000	9	4	2	0	0	0	15
2001	11	4	4	0	2	1	22
2002	11	2	0	1	0	1	15
2003	5	4	1	1	0	1	12
Total	65	21	20	2	3	3	114

The type of prophylaxis taken and countries visited are shown in Table V. Of the 62/98 (63%) travellers to Africa who took prophylaxis, 26 took mefloquine which is one of the drugs of choice in malarious regions with chloroquine resistance. Chloroquine was used in combination with proguanil by 17 travellers to Africa and as a single agent by six cases. Five took doxycycline of which one took it in combination with chloroquine.

Twelve cases travelled to India/Pakistan, South-East Asia and/or Papua New Guinea of whom three took chemoprophylaxis. Each of the three took chloroquine and proguanil, doxycycline and mefloquine as part of the recommended chemoprophylaxis regime.

Table II shows that twenty four (24/29, 83%) short term travellers (previously defined) took prophylaxis of which 11/24 (46%) was consistent with current guidelines. Fourteen of the former (14/24, 58%) took prophylaxis regularly while abroad but only seven (7/24, 29%) continued the regimen for four weeks on return to NI. Eight (8/12, 67%) of the expatriates took prophylaxis of which 5/8 (63%) took the appropriate anti-malarial drug with four (4/8, 50%) taking it regularly while abroad but only one (1/8, 13%) completed the month's course on return. The foreign visitors to NI did not take any prophylaxis and three of the four visiting friends and relatives in their country of origin did not take prophylaxis (*Table II*).

Table I

Number and percentage of confirmed malaria cases by referring source, 1998 – 2003, Northern Ireland (n=114)

Data Source	No. reported (%)
NI haematology labs	104 (91.2)
MRL	33 (28.9)
CCDC	69 (60.5)
CDSC (NI) (notifications)	63 (55.3)
Regional information branch (RIB)	68 (59.6)
Regional Infectious Diseases Unit	80 (70.2)

Inpatient information

The 114 cases were associated with 99 hospital admissions. The inpatient length of stay was available on 88/99 (89%) cases. The mean length of stay was 4 days (range 1-20 days, mode and median of 3 days). Two patients required renal dialysis and three required ICU support. Among the 114 cases were two malaria related deaths (a case fatality rate of 1.8 %). Both were associated with travel to Nigeria and infection with *P. falciparum*. One had not taken chemoprophylaxis and information on the other was missing.

Recurrence

Incomplete treatment or drug resistance may lead to recurrence of malaria. Co-infection with *P. vivax* or *P. ovale* may result in these species lying dormant in a patient resulting in break-through infection if compliance to chemoprophylaxis is poor or inappropriate. Six (6/108, 6%) patients had two episodes of malaria. In this study each malaria episode was counted as one case. The average time interval between the two episodes was 14 months (range 3-46 months). Two had recurrence of falciparum malaria. The remaining four cases had combinations of falciparum malaria followed by infection with *P. ovale* (2), *P. ovale* followed by *P. vivax* (1) and *P. falciparum* and *P. vivax* followed by *P. ovale* (1).

DISCUSSION

This study demonstrated that statutory notifications of malaria were associated with an under-ascertainment rate of 45%. Possible reasons for under notifying include clinicians being unaware that malaria is a notifiable disease and the mechanism for informing the CCDC. It is not a statutory requirement for laboratories to notify all positive results to the CCDC or send laboratory reports to CDSC (NI). The annual incidence rate of imported malaria to Northern Ireland over this six year period (1.1/100,000) is much lower compared to other parts of the UK. This reflects the travel history and ethnicity of the Northern Ireland population, which is predominantly Caucasian. In a study in southeast London the incidence rate of malaria was 38.8 per 100,000 population, which accounted for 14% of all cases in England and Wales in 20004. In this London study only 6.8% of laboratory confirmed cases were formally notified.

Table II

Reason for travel of malaria patients and prophylaxis history, 1998 – 2003, Northern Ireland (n=52)

Reason for travel	*Frequency*	*Percentage %*	*Prophylaxis Taken*	*Prophylaxis Appropriate to region*	*Regularly abroad*	*4 weeks on return*
Short term traveller	29	56.8	24	11	14	7
Expatriates	12	23.5	8	5	4	1
VFR	4	7.6	1	No history	–	–
Foreign visitors to NI	7	13.7	0	n/a	n/a	n/a

VFR= visiting friends and relatives in country of origin.

Table III

Plasmodium species per patient by region of travel, 1998 – 2003, Northern Ireland

Region	*Plasmodium*						*Total*
	falciparum	*vivax*	*ovale*	*malariae*	*unknown*	*combination*	
Africa							
Central	8	2	3	0	0	0	13
East	18 [1]	3	14 [2]	0	1	1 (fal +vivax)	37*
West	33	0	3	2	0	1 (falc+ovale)	39
South	6	3	0	0	0	0 0	9
South East Asia (SEA)	0	8	0	0	0	0 0	8*
India/Pakistan	0	4	0	0	0	0 0	4
Unknown	0	1	0	0	2	1 (oval+mal)	4
Total	65	21	20	2	3	3	114

* 1 patient in each of these regions also visited South America,[1] One patient also travelled to South Africa,[2] One patient also travelled to SEA.

Table IV

Time of presentation (date of lab diagnosis-date of arrival in UK) to hospital/GP for malaria, 1998 – 2003, Northern Ireland (n = 76)

Plasmodium species	*Time interval between arrival to UK and lab diagnosis (days)*		
	Range	*Median*	*Mean*
P. falciparum	(-2)*- 35	8	10
P. vivax	1-365	90	104
P.ovale	14-244	116	116
P.malariae	36-112	74	74
Combination of 2 species	12-20	16	16

Note: *One patient diagnosed 2 days prior to return to UK

Malaria is a relatively uncommon diagnosis in Northern Ireland. Nevertheless the 114 cases reported between 1998 and 2003 contrast with 18 cases of Legionnaires' disease reported over the same period (CDSC (NI) – personal communication). With the growth in air travel, more independent travel, increased immigration and an increasing tendency to buy "last minute" breaks, there is likely to be more travel between Northern Ireland and malarious regions. A recent example is the increased number of patients returning to the UK from Gambia and developing malaria.[5] Travellers need therefore to be reminded of appropriate precautions and the importance of alerting their general practitioners to their travel history should they develop fever on return from a malarious region. Falciparum malaria usually presents early within two weeks of being bitten but can present up to 90 days later whereas ovale and vivax malaria has been reported to present from 20 days to 10 months on return.[6] Collation of risk factor information on imported malaria enables the development of targeted public and professional awareness programmes for this mainly preventable and curable infection.

Risk factor information on cases was incomplete particularly with respect to reasons for travel (55%) and chemoprophylaxis (12% either missing or unspecified). To ensure that relevant risk factors and epidemiological information are obtained it is suggested the MRL case questionnaire be routinely used by CsCDC when responding to a clinical notification of malaria. To improve ascertainment it is also recommended that haematology laboratories report positive blood films to CsCDC similar to the reporting arrangements developed with bacteriology laboratories for organisms of public health significance. Clinicians also need to be reminded that malaria is a notifiable disease.

Noting the changing epidemiology of malaria and drug resistance, clinicians also require access to updated guidance on chemoprophylaxis and treatment. There are several helpful telephone contact numbers and websites listed in the British National Formulary for healthcare professionals and travellers. These include the Health Protection Agency, the National Travel Health Network and Centre, Health Protection Scotland and the World Health Organisation. Travellers could also contact the London Hospital of Tropical Diseases or MASTA (Minding your Health Abroad) for a travel brief which incurs a charge. These and other sources of travel health advice should be promoted at GP surgeries and high street travel agents in order to raise awareness among intending travellers to malarious areas. Those taking trips abroad at short notice may not have time to consider taking preventative treatment or let appropriate therapeutic drug levels develop before travel. Hence the risk needs to be highlighted at the planning stage by the travel industry. A previous study showed 25% of travel brochures contained no health information at all.[7] Another study showed that spontaneous health warnings

TABLE V

Countries visited and prophylaxis history (n=114)

Drug	*Africa*			*South Asia*					*Total*
	Central	*East*	*West*	*South*	*India*	*Pakistan*	*SEA/ Oceania*	*Un-known*	
NONE TAKEN	5 SEA(1) WA(1)	8 SAM(1)	16	1 WA(1)	1	2	5 SAM(1)	0	38
Mefloquine	3 EA(1)	13	8	2	0	0	1	0	27
Chloroquine +Proguanil	2 SA(1)	10 SA(1)	3	2 EA(1)	0	0	1	0	18
No history available	2 SA(1)	1	3	0	1	0	0	4	11
Chloroquine	0	3 SEA(1)	2	1	0	0	0	0	6
Doxycycline	0	0	3	1	0	0	1	0	5
Medication unspecified	0	1	2 SEA(1)	0	0	0	0	0	3
Proguanil	1 SA (1)	0	0	2 EA(1)	0	0	0	0	3
Proguanil+ mefloquine	0	0	1	0	0	0	0	0	1
Chloroquine +Doxycycline	0	0	1	0	0	0	0	0	1
Fansidar	0	1	0	0	0	0	0	0	1
Total	13	37	39	9	2	2	8	4	114

The letters in superscript indicate the number of travellers that travelled to other places as well. EA= East Africa, WA= West Africa, SA=South Africa, SEA= South east Asia, SAM= South America

Table VI

Comparison of malaria species between studies 1998-2003 Northern Ireland, 1974-1983 Northern Ireland and HPA report 2004

Reports	*Plasmodium species*	
	P. falciparum	*P. vivax*
NI 1974-1983[10]	40% (27/67)	3% (2/67)
NI 1998-2003	56% (65/114)	18% (21/114)
HPA UK report[9] 1987	38% (696/1816)	55% (1005/1816)
HPA UK report[9] 2002	76% (1468/1944)	15% (284/1944)

were not given in 61% (123) of consultations for malarious destinations and, after prompting, only 37% of agents brought up the need for malaria prophylaxis for the journey.[8] This apparent low level of verbal and written advice needs to be addressed by local initiatives and collaboration between public health practitioners and the travel industry.

The epidemiology of imported malaria in Northern Ireland is interesting as it differs from the rest of GB particularly in the ethnicity of cases and reasons for travel. The majority of patients in this study were Caucasians in contrast to GB where the majority were non Caucasian with 50% of all cases visiting friends or relatives.[9] In Northern Ireland the majority were holiday makers and those on business/professional travel, noting that travel history was only available on 45% of cases. Differences were also noted when compared to an earlier study of 67 imported cases of malaria to Northern Ireland between 1974 and 1983 in which the majority of cases were long term residents working overseas (14/67, 21%) whereas short term travellers (29/52, 57%) made up the majority in 1998-2003.[10]

There are over 2000 cases of imported malaria annually in the UK of which the majority are secondary to *P. falciparum*. The predominant species in the UK has changed over the past 15 years from *P. vivax* to *P. falciparum*. In 1987 cases were mainly from the Indian Subcontinent secondary to *P. vivax* infection whereas in 2002 the majority of UK cases were from West Africa with *P. falciparum*.[9] However in NI the predominant species has not changed over the past 15 years.[10] In the UK (1987-2002) P. *falciparum* rates have increased by 38% and *P. vivax* decreased by 40%, whereas in NI the rates of both these species have increased by 15% after 15 years (Table VI).

The average number of malaria deaths from 1977 to 2002 in the UK was 8 per year (a case fatality rate of 0.4% for imported malaria and 1.0% for falciparum cases). In Northern Ireland there were two deaths in six years resulting in an overall case fatality rate (CFR) of 1.8%. The CFR for falciparum was nearly twice as high at 3.1%.

P. vivax and *P. ovale* have persistent liver stages and can give rise to relapses up to a year after the initial infection whereas *P. falciparum* rarely persists for more than two years. *P. malariae* may persist in the bloodstream for many years. The time interval between arrival in the UK from a malarious region and the date of laboratory diagnosis confirms that patients with *P. falciparum* tend to present early whereas those with *P. vivax* and *P. ovale* infection tend to present late. Four patients had two episodes of malaria with two different species. This would suggest breakthrough infection with a species in the dormant phase resulting from co-infection or not complying with the prophylaxis regime and acquiring repeated malarial infections from visiting malarious regions. These cases also illustrate that the physician needs to be aware that a patient treated for one malaria parasite may be infected with another parasite that may be lying dormant.

The current guidelines (2003) recommend four steps to prevent malaria in travellers:[11] (a) awareness of the risk of malaria; (b) preventing and avoiding mosquito bites by using appropriate insecticides, repellents, sleeping in a screened room and using bed nets; (c) compliance with appropriate chemoprophylaxis and (d) diagnosing breakthrough malaria swiftly and obtaining prompt treatment. A useful publication on malaria prophylaxis for long –term travellers was also published in the same year.[12]

Under current guidelines, mefloquine is the drug of choice for travel to Africa and chloroquine plus proguanil for South Asia (Indian subcontinent) and low risk places in South East Asia (Indonesia /Malaysia) or mefloquine, doxycycline or atovaquone/proguanil in Oceania (Papua New Guinea).[11] In this study mefloquine was the most common form of prophylaxis and mainly used for travellers to Africa. Nevertheless a third of cases did not take any form of chemoprophylaxis. Chloroquine and proguanil was the second most common chemoprophylactic drug regime. Over a third of travellers to Africa took chloroquine as prophylaxis despite chloroquine resistance being a major problem with *P. falciparum*. Travellers to the Indian subcontinent, South-East Asia and Oceania who took prophylaxis took the appropriate drug combination.

RECOMMENDATIONS

The following are recommended:

- increase awareness among clinicians that malaria is a notifiable disease through multidisciplinary educational meetings.
- haematology laboratories to report positive results to CsCDC for public health purposes as part of good laboratory practice
- enhanced surveillance (using a standard proforma such as the MRL case report form) to be used by CsCDC

to collect appropriate epidemiological and risk factor information which is essential for targeted public and professional education.

– CDSC (NI) should produce regular epidemiological reports to inform public and professional education including the travel industry.

– GPs and travel agents require information on accessing appropriate travel health advice.

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Correction:

In the article by Lappin *et al* (Hox genes: seductive science, Mysterious mechanisms. *Ulster Med J* 2006; **75(1):** 23-31) there are two small corrections:

Page 23; Abstract: line 3– '... at 7p15, 17p21,' should read '... at 7p15, 17q21'

Page 26; Hox GENES IN VERTEBRATES, Line 5 '... at 7p15, 17p21, 12q13' should read '... at 7p15, 17q21, 12q 13'

This was amended on the website PDF online on 7th February 2006 and the correct PDF may be downloaded free from the website.

Patrick Morrison, Honorary Editor.

Ulster Med J 2006; **75 (2)** *136-140*

Paper

Progressively increasing operative risk among patients referred for Coronary Artery Bypass Surgery

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SUMMARY

Objective: **Advances in surgical, anaesthetic and percutaneous interventional techniques may have led to higher risk patients being referred for coronary artery bypass graft surgery (CABG). The purpose of this study was to compare the predicted mortality risk (EuroSCORE) of a contemporary cohort of patients referred for isolated elective CABG (2002) with that of a cohort referred five years previously (1997) and to examine temporal trends in patient demographics.**

Methods: **Records (n=2873) of weekly cardiac surgical referral meetings were examined and the age, sex, type of operation and surgical decision for every patient referred from 1997 to 2002 inclusive were recorded. Furthermore samples of patients referred in 1997 (n=111) and in 2002 (n=110) were chosen, and a complete EuroSCORE was calculated for each patient and compared between groups.**

Results: **In both 1997 and 2002 the median EuroSCORE among patients not accepted for surgery was significantly higher than those accepted (1997; 3 vs 2, p<0.001. 2002; 5 vs.2, p<0.001). The median EuroSCORE of patients referred in 2002 was significantly higher than those referred in 1997 (3 vs. 2; p< 0.001). There was a progressive increase in median patient age throughout the study period and this accounted for the observed temporal increase in EuroSCORE.**

Conclusions: **Predicted mortality risk among patients referred for coronary artery bypass surgery is increasing, mainly due to patient age at referral.**

INTRODUCTION

Recent advances in surgical and anaesthetic techniques have been associated with reduced mortality rates from cardiac surgery.[1] Improved surgical outcomes, along with major advances in percutaneous coronary intervention[2] and changes in the demographics of patients undergoing cardiac catheterisation[3] are likely to have resulted in higher risk patients being referred for cardiac surgery compared with previously.[4]

There are several risk-predicting methods for patients undergoing cardiac surgery.[5,6] The EuroSCORE index[7,8] gives a practical and numerical prediction of early mortality risk following coronary artery bypass graft surgery (CABG). Its reliability has been demonstrated in clinical practice[9,10] and it is used commonly in the pre-operative assessment process.

The aims of this study were to audit the clinical and demographic profile of patients referred for isolated CABG at our institution, to detect any changes in calculated operative risk (EuroSCORE) over time and to identify factors contributing to any change observed.

METHODS

All patients referred for isolated CABG at Belfast City Hospital were identified from the records of a weekly combined cardiology-cardiac surgery meeting at which all referrals for non-emergency cardiac surgery are made. In all, 2873 patients referred between the beginning of 1997 and the end of 2002 were identified and their age, sex, type of surgery and decision regarding acceptance were collected. Patients referred for valvular surgery were excluded, as were those for whom no decision regarding acceptance was made at the time of discussion.

To study changes in risk profile in detail, a sample of patients was chosen from each of 1997 (n=111) and 2002 (n=110). These were the first patients referred in a calendar year for which complete medical records were available and the EuroSCORE was calculated based on identification of relevant patient and cardiac-related factors.[5,6] There were no operation-related factors as all patients were scheduled to undergo elective isolated CABG.

Statistical analysis

Variables are presented as median and interquartile range. Between-group analysis used the Mann-Whitney rank sum test. A P value of <0.05 was considered statistically significant.

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RESULTS

Activity figures showed a progressive increase in the number of diagnostic coronary angiograms performed annually and a gradual decrease in the percentage referred for elective CABG (*Fig 1*).

Changes in patient demographics over time

The median age of patients referred for CABG rose progressively between 1997 and 2002 (*Table I*). Although not reaching statistical significance, the following trends were observed: patients turned down for CABG tended to be older than those accepted in each individual year and patients referred between 2000 and 2002 were more likely to be turned down for CABG.

Changes in EuroSCORE over time

The calculated EuroSCORE of the patients sampled from 2002 was significantly higher than those sampled from 1997 (*Table II*). In both 1997 and 2002 the EuroSCORE among patients turned down for surgery was significantly higher than in patients accepted. In 2002 the median EuroSCORE of all patients referred was similar to that of patients being turned down for surgery in 1997.

Further analysis of the observed rise in EuroSCORE between 1997 and 2002 revealed that patient age was the dominant component with almost 100 extra EuroSCORE points being awarded for age in 2002 (*Table III*). In both 1997 and 2002, the largest age group of patients referred for elective CABG was in the 60-69 year bracket (*Fig 2*). The second largest group in 1997 was 50-59 years while it was 70-79 years in 2002. In 1997 no patient in the age group 80-89 was referred compared with 4% in 2002. The percentage of females referred for CABG remained similar over time (*Table I*).

DISCUSSION

Results from this audit indicate a progressive, temporal increase in the risk status of patients referred for CABG as assessed by the EuroSCORE. This increased risk is predominantly a reflection of older patient age. The observations may reflect changes in the population undergoing diagnostic cardiac catheterisation, changes in cardiology practice or advances in cardiac surgical and anaesthetic practice.

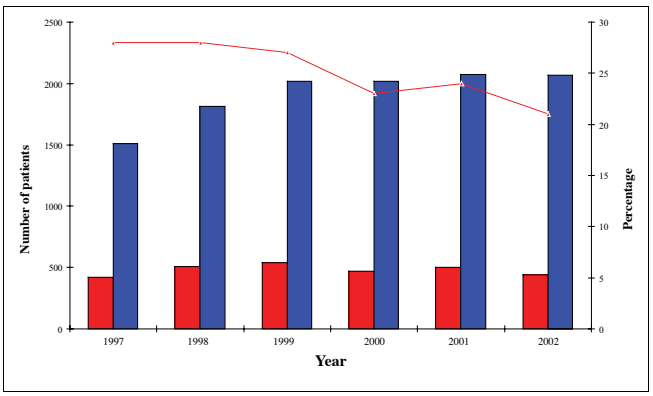

Fig 1. Yearly trends in the number of diagnostic angiograms performed at Belfast City Hospital (blue bars) and the number of patients referred for isolated coronary artery bypass graft surgery (red bars). The solid red line, referring to the right-hand Y axis, represents the percentage of patients undergoing angiography who were referred for isolated CABG

The EuroSCORE as a risk predictor for CABG mortality

The EuroSCORE was derived from analysis of 19,030 patients undergoing CABG across Europe.[7] It is calculated by additive point scoring based on preoperative patient, cardiac and operation-related factors. Subsequently it has been validated as an accurate predictor of mortality in Europe[9] and North America.[10] Based on the EuroSCORE, patients are designated as low risk (EuroSCORE 0-2, average predicted mortality 0.8%), medium risk (EuroSCORE 3-5, predicted mortality 3%) and high risk (EuroSCORE >6, predicted mortality 11.2%).[7]

When applied to the population in the present study, the average patient referred for elective CABG in 2002 was of medium risk status (median EuroSCORE 3, Table II) compared with low risk status in 1997 (median EuroSCORE 2). The median EuroSCORE of patients accepted for CABG did not change between 1997 and 2002 although the distributions of EuroSCORE values point to a higher risk cohort in 2002. Patients turned down for CABG had substantially higher risk scores compared with those accepted and this disparity increased markedly with time. The data suggest that high-risk patients were more likely to undergo diagnostic cardiac catheterisation and to be referred for elective CABG in 2002 compared with 1997.

Reasons underlying the increase in EuroSCORE over time

The progressive increase in EuroSCORE in the present study is largely due to rising patient age. While populations in the industrialised world are aging, this has not occurred rapidly enough to account for the rise in EuroSCORE we observed. Changes in the epidemiology and treatment of cardiovascular disease may have resulted in patients presenting for the first time later in life.[11,12] This may be due to advances in primary prevention, secondary prevention or both. Advances in medical therapy[13,14] and in percutaneous coronary intervention[15] may delay or prevent patients' referral for surgery. Patients' and clinicians' expectations of standard care may also have changed from a conservative to a more invasive view, resulting in increased angiography rates in elderly patients.[16]

As a result, increasingly only those patients who have a survival benefit from surgery[17] or those for whom PCI is technically not feasible are being referred for elective CABG. Furthermore the wider availability of PCI compared with CABG may have resulted in some patients undergoing percutaneous treatment who might otherwise have been referred for CABG.

While elderly patients (>70 years) have a higher mortality rate after cardiac surgery than their younger counterparts,[16] in selected elderly populations, CABG can achieve excellent improvements in quality of life without excessive mortality, even in those over 80 years.[16,18-20] Therefore it is recommended that CABG not be denied on the basis of age alone, especially if elective procedures prevent the subsequent need for emergency surgery with higher associated mortality.

TABLE I

Demographic profile of patients referred for coronary artery bypass surgery between 1997 and 2002

Year	*All patients referred*	*Accepted*	*Rejected*	*No decision made*
1997				
Number (%)	420	298 (70.9)	39 (9.3)	83 (19.8)
Median age (IQR)	62 (55-67)	61 (55-67)	63 (57-69)	62 (55-67)
Number (%)female	74 (17.6)	49 (16.4)	11 (28.2)	14 (16.9)
1998				
Number (%)	507	368 (72.6)	46 (9.1)	93 (18.3)
Median age (IQR)	62 (55-68)	62 (55-68)	63 (57-70)	61 (55-67)
Number (%)female	97 (19.1)	62 (16.8)	8 (17.4)	27 (29.0)
1999				
Number (%)	541	374 (69.1)	59 (10.9)	108 (20.0)
Median age (IQR)	62 (55-69)	61 (55-68)	63 (55-69)	63.5 (54-69)
Number (%)female	112 (20.7)	76 (20.3)	10 (16.9)	26 (24.1)
2000				
Number (%)	468	313 (66.9)	106 (22.6)	49 (10.5)
Median age (IQR)	63 (56-69)*	62 (55-68)	65 (59-72)	63 (54-69)
Number (%)female	93 (19.9)	50 (15.9)	31 (29.2)	12 (24.5)
2001				
Number (%)	500	323 (64.6)	101 (20.2)	76 (15.2)
Median age (IQR)	63 (57-70) †	63 (57-69)†	65 (57-71)	63 (57-69)
Number (%)female	108 (21.6)	55 (17.0)	31 (30.7)	22 (28.9)
2002				
Number (%)	437	286 (65.5)	82 (18.7)	69 (17.8)
Median age (IQR)	65 (58-71) †	64 (58-71)†	66 (59-73)*	68 (59-73) †
Number (%)female	89 (20.4)	55 (19.2)	21 (25.6)	13 (18.8)

*p<0.05 versus 1997, †p<0.001 versus 1997. IQR = interquartile range

Table II

EuroSCORE values in 1997 and 2002 cohorts. P value column compares accepted with rejected groups

	All referred Median	*Accepted*	*Rejected*	*P*
1997				
Number (%)	111	80 (72.1)	31 (27.9)	
EuroSCORE	2 (1-3)	2 (0-3)	3 (2.25-4)	<0.001
2002				
Number (%)	110	81 (73.6)	29 (26.4)	
EuroSCORE	3 (2-5)*	2 (1-4) †	5 (4-8)*	<0.001

Median (interquartile range). *p<0.001 vs. 1997, †p<0.05 vs. 1997.

TABLE III

Components of the EuroSCORE calculation (reference 5) and analysis of the total number of EuroSCORE points awarded for each of these components in samples of patients referred for isolated CABG in 1997 (n=111 patients) and 2002 (n=110 patients)

	Definition	*Score*	*1997 cohort*	*2002 cohort*
Patient-related factors				
Age	Per 5 years or part thereof over 60 years	1	118 (44.5%)	214 (57.2%)
Gender	Female	1	23 (8.7%)	14 (3.7%)
Chronic pulmonary disease	Long term use of bronchodilators or steroids	1	9 (3.4%)	9 (2.4%)
Extra cardiac arteriopathy	See below[a]	2	14 (3.4%)	9 (2.4%)
Neurological dysfunction	Disease severely affecting ambulation or day-to-day functioning	2		
Previous cardiac surgery	Previous surgery requiring opening of the pericardium	3	9 (3.4%)	3 (1%)
Serum creatinine	≥200μmol/L pre-operatively	2	2 (1%)	0
Active endocarditis	Under antibiotic treatment for endocarditis at time of surgery	3		
Critical pre-operative state	See below[b]	3		
Cardiac-related factors				
Unstable angina	Requiring iv nitrates until arrival in the operating room	2		
LV dysfunction	Moderate (EF 30-50%) Poor <30%	1 or 3	58 (21.9%)	56 (15%)
Recent myocardial infarct	<90 days	2	32 (12.1%)	42 (11.2%)
Pulmonary hypertension	Systolic PA pressure >60mmHg	2		
Operation-related factors				
Emergency	Carried out on referral before the beginning of the next working day	2		
Other than isolated CABG	Major cardiac operation other than or in addition to CABG	2		
Surgery on the thoracic aorta	Ascending, arch or descending aorta	3		
Post infarct septal rupture		4		

[a] Any of: claudication, carotid occlusion or >50% stenosis, previous or planned surgery on the abdominal aorta, limb arteries or carotids

[b] Ventilation before arrival in the operating room, pre-operative inotropic support, intra-aortic balloon counterpulsation (IABP) or preoperative acute renal failure (anuria or oliguria <10ml/hr). Several patient- and operation-related factors did not apply to this study of elective CABG

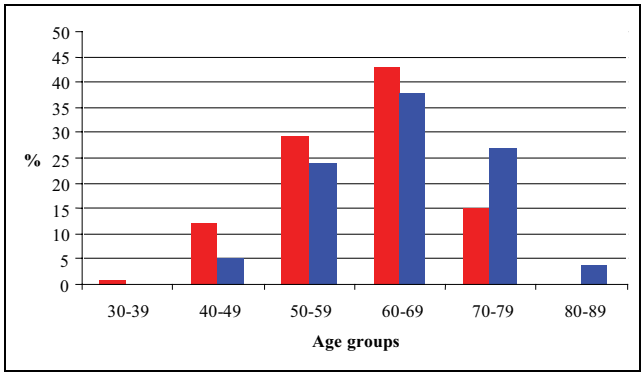

Fig 2. Age profiles of patients referred for elective coronary artery bypass surgery in 1997 (red bars) and 2002 (blue bars).

Among the patients we sampled in 1997 and 2002, no risk-predicting factor other than patient age changed over time (*Table III*). Specifically there was no increase in the numbers of patients being referred with severe LV dysfunction, renal impairment, chronic lung disease or other co-morbidity. The present study focused on patients referred for isolated CABG (approximately 80% of all referrals), and therefore excluded those being referred for valve surgery and emergency surgery, among whom different patterns of co-morbidity may have been observed.

Implications for health care funding

The increase in EuroSCORE we observed has implications for those involved in health care funding. Although the EuroSCORE is designed to predict mortality rather than morbidity, our observations anticipate an increase in the number of patients who might expect a complicated post-operative course and a prolonged intensive care stay.

CONCLUSION

The risk status of patients referred for CABG in 2002 was substantially higher than in 1997, due entirely to differences in patient age. Reasons for this trend are likely to be multifactorial, including changes in preventive medicine and invasive cardiology practice. It is likely that such trends will continue, with implications for cardiologists, cardiac surgeons, intensive care providers and health care purchasers.

The authors have no conflict of interest.

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Essay

GP Education in Northern Ireland 1920 – 1990. A Study of the Use and Misuse of Power

The 2005 Rose Prize Essay*

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** This article is adapted from the 2005 Rose Prize, commemorating the lives of William Rose, a 17th century apothecary whose court case in 1701-04 established a legal foundation of General Practice in England and Wales, and later, Fraser Rose, cofounder of the Royal College of General Practitioners. The prize, established in 2005, is awarded biennially jointly by The Worshipful Society of Apothecaries of London and The Royal College of General Practitioners.*

POWER RELATIONSHIPS

PREFACE

Modern medical historians are not mere chroniclers of events. In addition to recording otherwise neglected detail, they are invited to explain the causes of these incidences. In this way their work is differentiated from ordinary journalism, or any of the purely observational pursuits such as writing. The development and testing of a theory is the distinctive function of this type of academic exercise. The creation of a hypothesis becomes crucial.

This paper seeks to explore the hypothesis that there is a conflict perspective in General Practitioner (GP) education; "where the competition for power and the struggle for control are seen as inevitable".[1] The methodology adopted is to break down and clarify the evidence of how and why power was used and misused during the development of the GPs' educational system in Northern Ireland in the time frame 1920 –1990. A linear year-by-year modus operandi is avoided.

The key quest is to understand the power relationships between the different groups involved in that process: hospital consultants, medical academics, local and national government, and GPs; and also different individuals such as the Dean of the Faculty of Medicine at the Queen's University of Belfast (QUB) and the Professor of General Practice QUB. An analysis of the outcomes of this competition for power ensues.

POWER

Consideration of a wide range of theoretical backgrounds becomes imperative. Diversified sources can be found in the storehouses (The word 'apothecary' comes from the Greek, meaning 'storehouse') of different academic areas such as the Social Sciences, History, Education and even Philosophy. In particular, some of the works of the scholars Etzioni, Foucault and Kuhn are highlighted (*Table 1*).

TABLE I

Amitai Etzioni – Born: Cologne, Germany, 4 January 1929. After receiving his PhD in Sociology from the University of California, Berkeley in 1958 he served as a Professor of Sociology at Columbia University for 20 years. He is the author of twenty-four books. In 1991, the press began referring to Etzioni as the 'guru' of the communitarian movement. In 2001 Etzioni was named among the top 100 American intellectuals.

Michel Foucault (15 October 1926 - 26 June 1984) – was a French philosopher and "historian of systems of thought". He had an enormous impact on many fields including literary criticism and theory, philosophy (especially philosophy of science in the French-speaking world), history, psychoanalysis, history of science. Part of Foucault's work investigates the relationship between power and knowledge – the sociology of knowledge. He was a prolific author, and gathered detailed historical evidence to support his belief in the historical organization of power.

Thomas Samuel Kuhn (18 July 1922 - 17 June 1996) – obtained his PhD in physics from Harvard University in 1949, and taught a course in the history of science at Harvard from 1948 to 1956. After leaving Harvard, Kuhn taught at the University of California, Berkeley until 1964, at Princeton University until 1979 and at the Massachusetts Institute of Technology (MIT) until 1991. The enormous impact of Kuhn's work can be measured in the revolution it brought about even in the vocabulary of the history of science e.g. "paradigm" and "paradigm shifts".

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Etzioni[2] explained that Power may be classified in three different forms – Coercive (forced to conform); Remunerative (get material rewards like money or goods); and Normative (offering characteristics of persuasiveness, manipulation or suggestion). With these three types of Power come three kinds of Involvement – 'Alienative', 'Calculative' and 'Moral'. Each combination offers a different kind of Compliance. Etzioni's classification shows that three kinds of Compliance are of major importance, but only two of these have real significance in this study. These are Compliance between 'Remunerative Power' and 'Calculative Involvement'; and between 'Normative Power' and 'Moral Involvement'. (Coercive Power with Alienative Involvement is rarely used in medicine except in the area of compulsory psychiatric management). "Power relationships are multiple; they have different forms, they can be in play in family relations, or within an institution, or an administration. … It is a field of analysis and not at all a reference to any unique instance".[3]

PLACE

Royal assent was given to the Government of Ireland Act on 23 December 1920. This single act of parliament at Westminster created two new states, the Irish Free State (later the Republic of Ireland) and Northern Ireland. It follows that 1920 is the natural starting point for this study. The new state of Northern Ireland meets most of the necessary criteria to form an epidemiological unit;[4,5] and these factors justified its choice as a basis for local research. But there are both overt and hidden dangers, as well as some advantages, in limiting any study to these small-scale dimensions. For example, Imhof's warning[6] states that "the narrower the limitation, the greater the danger of myopic vision". Jean-Pierre Goubert's lifetime of study[7] of the history of health of the French province of Brittany confirms the value of studying a relatively small geographical area. This was a positive finding. However, his analysis also revealed that there are many dangers created by the historian's prejudices, the analysis of sources, and methodological difficulties. Every effort is taken to avoid the effects of such provincialism or parochialism. The explanation for the choice of the end-point of 1990 will come below.

THE POWER OF THE CONSULTANTS

PARTITION

The partition of Ireland is known all over the world as a source of enduring conflict: but the partition of the medical profession had (and has) its own shortcomings and hostilities too. The division of the medical profession into specialties had started before the beginning of the 20th century and gradually became irreversible. Up until 1948 the schism was incomplete because most consultants did generalist work in their private consulting rooms; while many GPs, especially in rural UK, acted as both GPs and consultants. These doctors worked in the local hospitals as well as in their own surgeries, and took referrals from their GP colleagues.[8] Examples of this type of service were common in Northern Ireland,[9,10] but any future development of that hybrid type withered in the UK with the creation of the rigid structure of the NHS in the 1946 Act.

When looking back from the 21st century to pre-NHS days it is important to remember that there was a strong moral and ethical background to the consultant staff of the voluntary hospitals then, because those doctors all worked in such hospitals in a voluntary unpaid capacity.[11] But, although unpaid, these hospital consultants were the most powerful group within the profession. They appear to have had the best of intentions; however, it is worth recalling Foucault's pessimistic dictum that good intentions do not guarantee good outcomes.[3] With the following interesting equation WJM Mackenzie[12] underlined this concept that gives another line of thought on consultant power:

"Beds = Status: Status = Power. Power being understood in various senses: as disposable income, as decision-making in respect of patients, as scope for intellectual exercise, and as scope for moulding successors in the profession".

A power struggle between the hospital-based specialists and the community-based generalists became inevitable. Fifty years ago, when Frazer Rose was a lad, the great majority of consultants knew with certainty that their GP colleagues were of a lower social, intellectual and professional order than themselves; just as the physicians of William Rose's time had despised and rejected the apothecaries. The metaphor of 'Lord Moran's Ladder' is pivotal. The opening of Curwen's paper[13] describes the juxtaposition very eloquently:

"On the 17 January 1958, Lord Moran of Manton, who was at that time Chairman of the Awards Committee administering merit awards for consultants in the National Health Service, was giving evidence before the Royal Commission on Doctors' and Dentists' Remuneration. He was defending the principle of merit awards against a certain amount of criticism by the members of the Commission and he made the point that those selected for those awards were chosen from a group of doctors, the consultants, who had already distinguished themselves from the rest of the profession by achieving that status. He described the process by which they did so, and mentioned 'a ladder which people are constantly falling off'. The Chairman asked him the following question: 'It has been put to us by a good many people that the two branches of the profession, general practice and consultancy, are not senior or junior to each other but they are level. Do you agree with that?' To which he replied as follows 'I say emphatically "No" – Could anything be more absurd? I was Dean of St. Mary's Hospital Medical School for 25 years ... and all the people of outstanding merit, with few exceptions, aimed to get on the Staff. There was no other aim, and it was a ladder off which some of them fell. How can you say that the people who get to the top of the ladder are the same as people who fall off it? It seems to me so ludicrous'. In reply to further questions the noble lord made evident his distaste at having to discuss such contentious matters in public, but he stuck to his guns, and maintained that his 'ladder' was real enough, although that this did not imply that general practitioners did not include among their number men of ability doing splendid work in their own field".

Clearly the hospital consultants perceived Lord Moran's archetypal GPs, 'the fellows who fell off the ladder', as of a much lower caste than theirs. This common heresy persisted into the 21st century; despite the fact that today's GPs receive extensive compulsory specialist postgraduate training, not unlike their consultant colleagues.[14] A ready explanation for the continued support for such a misconception may be found in the conflict perspective with its inevitable competition for power and struggle for control.

The medical profession assumed that the consultants could or should be its only educators. They were the only providers of undergraduate teaching for the medical students in the Medical Faculty of QUB until that described below. The

Royal Victoria Hospital (RVH) honorary staff (or its national health service (NHS) equivalent) had a very long history of educational provision. Since the 1880's they had shared undergraduate teaching with the consultants in the other Belfast teaching hospitals (notably the Ulster Hospital for Children and Women, the Mater Infirmorum Hospital, the Belfast Hospital for Sick Children (Queen Street), and, after 1923, the Belfast City Hospital). Later consultants from hospitals throughout Northern Ireland were enrolled.

In addition to their undergraduate teaching they also provided a postgraduate education service. The minutes of the RVH Medical Staff tell how the honorary visiting medical staff provided extensive postgraduate courses from 1931 onwards to 'panel doctors' on the national health insurance (NHI) list.[5] The independent tradition for teaching in voluntary hospitals in the north of Ireland had started in Belfast in 1817, and was continued by the medical staff of the Royal Victoria Hospital Belfast from 1903. They were particularly diligent and faithful in their provision of postgraduate education for GPs. The earliest record goes back to 1905 - 1906. This provision greatly expanded after 1965 when several postgraduate centres were opened throughout Northern Ireland. This development went far beyond the Belfast teaching hospitals for it extended to many of the outlying provincial hospitals, notably the Altnagelvin Hospital, County Londonderry;[15,16] the Waveney Hospital, County Antrim; and the Craigavon Hospital in County Armagh.

The 'refresher courses' offered throughout Great Britain (GB) and Northern Ireland had many weaknesses: e.g. Gray wrote:

"the content was predominantly to do with the management of disease, with little or no discussion on psychological aspects … The lecture was the dominant teaching method. Small-group discussions hardly ever occurred".[16-18]

New problems within the teaching hospitals emerged as the 20th Century advanced. These included an ever-increasing turnaround rate of patients and the fact that it was the 'teaching' hospitals that came to house the new super-specialist units, e.g. cardiac and thoracic surgery, endocrinology, oncology, and genetics. The allocation of regular teaching time became increasingly problematic because of clinical demands.[19] In addition, some consultants in these units were so specialized that they had increasing difficulty in teaching the basic medical courses for undergraduates or postgraduates, in a generalist or holistic way.

Some kind of assessment of the costs and benefits is required. Although hospitals' consultant staffs consistently provided all (or nearly all) the undergraduate and postgraduate teaching for GPs, they commonly failed to meet the generalists' real educational needs.

THE POWER OF THE UNIVERSITIES

The Belfast Medical School was founded in 1835 and transferred to the Queen's College Belfast in 1847, (QUB from 1908). The senior academic staff of this school wielded enormous power, and not just in their own domain; e.g. the five men from the north of Ireland who were elected President of the BMA at national level between 1884 and 1999 had all been senior medical academics at Queen's.[5]

Power relationships are a field of analysis and not a description of particular instances. They have many different forms, from battles between full medical corporations or governments down to single combat. With this in mind this Section uses pen-portraits of three of the doctors who wielded power in university medical education in Northern Ireland during the time frame in use. It might be helpful to remember that the use of power is demonstrated by "an actor's ability to induce or influence another actor to carry out his directives or any other norms he supports". It is essential to focus in on their actions rather than on their personalities, if worries concerning parochialism are to be avoided.[2]

Professor Sir John Henry Biggart (1905 – 1979)

Within the field of medical education in Northern Ireland such a single protagonist was Professor John Henry Biggart, CBE, (later KB), DSc, MD, FRCP. (*Fig 1*) He was a pathologist and an outstanding administrator. Between 1944 and 1971 this very influential and charismatic character was the Dean of the Faculty of Medicine at QUB. Everyone knew him affectionately as 'John Henry'. Professor Biggart's story has been well told elsewhere.[20,21]

A plan for the improvement of all postgraduate specialist training in the UK emerged from an extraordinary private conference organized by the Nuffield Hospitals Provincial Trust in Christ Church Oxford in December 1961. Almost as an afterthought GP education was added to the agenda.[22] In Northern Ireland the work of this conference stirred both the civil servants in the Ministry of Health at Stormont (on the outskirts of Belfast) and Professor Biggart. However, local government was concerned almost entirely with general

Fig 1. Professor Sir John Henry Biggart. A photographic copy of a portrait by Leslie Stuart, Belfast, hung in the NICPGMDE.

practitioner postgraduate teaching for which it had funding, while Biggart followed the Conference protocol, which aimed to develop the postgraduate education of all specialist groups. From 1962 on, this created a huge power struggle. By 1964, Professor Biggart's drive and guile had created a new local system to meet the needs of all postgraduate medical education – The Postgraduate Board of Medical Education. It was a university exercise, but funded by local government.

Biggart foresaw great dangers in having single funding for undergraduate and postgraduate medical education, offered from two competing rival sources, the Ministry of Education and the Ministry of Health at Stormont. So he decreed that they should have separate accounting. This decision soon compounded the power struggles between university and government, and the Board only functioned from 1965 until 1970. Some of its achievements are described below.

On 4 December 1970 the Northern Ireland Council for Postgraduate Medical Education (NICPGME) came into being, matching similar, although quite distinct, developments in that year in England, Wales and Scotland. Unlike the structures chosen in GB, the new Northern Ireland Council was a single tiered structure with much the same operational staff as the Board that preceded it. But it came with a very different ethos. Professor Biggart, who had just retired from QUB, was appointed Chairman, and Dr John McKnight, previously Director of the QUB Board, Secretary.

With the focus still on deeds, not personalities, it is clear that the power of the university became greatly diminished at this point. The NICPGME was a Quasi-Autonomous National (or Non-) Governmental Organization (QUANGO). It became the main body responsible for all postgraduate medical teaching (including GP) and continued with this function up to 1990 and beyond.

Professor John Pemberton (1912 -)

Lectures concerning general practice had started in University College Dublin from 8 May 1953.[23] A postal survey of medical schools in the UK and the Republic of Ireland in February 1953,[24] showed that most of the London medical schools were already committed to GP contact for nearly all of their students. This same report showed that QUB was only offering six placements with GPs, for obstetrics. It is clear that QUB had little interest in this type of undergraduate teaching in the 1950s. Things changed when John Pemberton became the head of the new Department of Social and Preventive Medicine at QUB in 1958 (*fig 2*).

At that time the incomes per capita in Northern Ireland were 25% lower and the unemployment rate five times higher than those in Great Britain.[25] Pemberton came from Sheffield, where, as a third-year medical student, he had offered succour to the Jarrow marchers in 1933. He was very well aware of how poverty, poor housing, over-crowding and such social conditions altered patterns of illness. He knew that the hospital doctor might be protected from such socio-economic observations because of the uniformly levelling effect of the ward environment. But GPs knew these things, for they met them on a daily basis. The new professor was convinced that medical students should be taught about these important influences by GPs themselves.

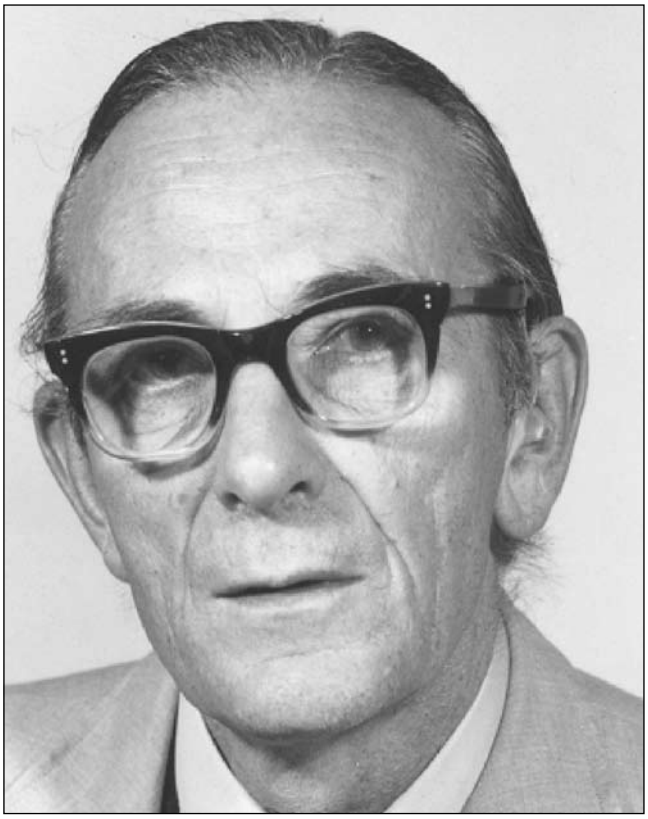

Fig 2. Professor John Pemberton. A copy of a photograph held in the Department of Social and Preventive Medicine QUB.

Pemberton himself had had the finest instructor on a one to one basis: for he had acted as locum tenens for Dr Will Pickles of Aysgarth, Yorkshire for ten summers. He went on to write and publish the biography *Will Pickles of Wensleydale; The Life of a Country Doctor.*[18,26] Dr William Pickles was a very important figure in the College of General Practitioners (CGP) – a founder member and its first President 1953-1956. Pemberton was needed in Belfast. He brought new insights to QUB's medical curriculum. He launched a voluntary GP visiting scheme for fourth-year medical students in 1963. He had to seek out GPs who were willing to face the challenges posed by unknown teaching requirements that could be very disquieting. Initially the GP volunteers did not receive any financial reward; even so the experiment worked and continued annually.

Pemberton also invited GPs to give lectures in his own curricular area from 1964. Amongst these were two GPs who later became very prominent in GP education circles; Dr Noel Wright, in the NICPGME; and Dr George Irwin in undergraduate education.

From 1964 onwards Pemberton started promoting the novel idea of a GP health centre, built specifically for undergraduate teaching as well as for the care of 24,000 patients. Few members of the Faculty supported this concept. However it was energized in 1968 when the General Health Services Board (Northern Ireland), strongly supported by the British Medical Association (BMA) in Northern Ireland, presented £59,653 to the University to create a professorial chair in

general practice. The money came from a fund that had accrued because of an under-spend on general practitioners' 'refresher' courses. Here was a fine example of group remunerative power coupled with the normative power of one leading activist.

Professor William George Irwin (1924 -)

Although already in possession of some £60,000 of government money since 1968, it was not until 23 February 1971 that the Senate of QUB assigned a chair of General Practice. There was only one applicant for this new professorship, and the Senate duly appointed Dr WG Irwin to it.[5] So, on 1 October 1971 Professor Irwin (*fig 3*) became the head of the fifth department of general practice in the UK, the fourth Professor of General Practice in the UK, and the first in Ireland. He found himself very much on his own, with minimal backup. Edinburgh, Aberdeen, Dundee and Manchester preceded QUB. Dr Pat Byrne was in charge at Manchester; but was not awarded the professorship until 1972. Dr Philip M Reilly was appointed Senior Register-Tutor in 1972, and in 1973 Dr Agnes McKnight was appointed to a similar position. Dr Jack Henneman was appointed senior lecturer in January 1974.

To be the creator of something worthwhile is always arduous, and Professor Irwin's courage and determination were fully stretched. Up until 1971 all the previous Departments of General Practice in GB had used a "practice based department" structure.[27] This title is used to describe a unit that has the sole responsibility for running its own NHS Practice. In this model, the principals, with their own NHS lists, are all clinical lecturers. This option had very many attractions, not least that of allowing for a much easier collection of data for research. Although on the face of it the 'Practice Based Department' should have had a theoretical advantage, in due course some serious disadvantages began to show. The full-time university lecturers were swamped by the ever-increasing demands of patient care. For example, they had nobody else available to provide '24 hour cover' while they were involved in academic work. So academic productivity, in both teaching and research, was often disappointing. Irwin saw this as a flawed solution. So he became the first in the UK to select a "practice linked department", "where the academic clinical staff undertook part-time clinical work (of about 21 hours per week) in partnerships, which were otherwise staffed by full-time general practitioner principals".[27] Many other centres in the UK adopted similar systems later, e.g. Leicester, Nottingham, Liverpool, and Glasgow.

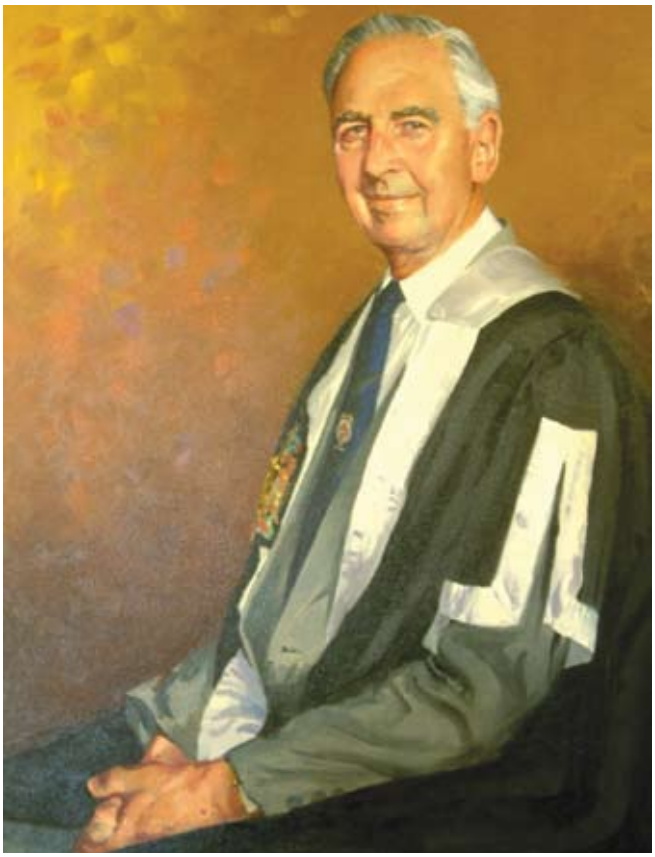

Fig 3. Professor William George Irwin. A photographed copy by Dr Kieran McGlade of a portrait by L Nesbitt hung in the Department of General Practice QUB.

Irwin was involved from the outset in the planning and building of the completely new teaching health centre. He had identified the chosen site for the Dunluce Teaching Health Centre in 1971; but it did not open until 1 January 1980 because of a plethora of managerial problems. It was adjacent to the Medical Biology Building and the Whitla Medical Building of QUB, which housed the pre-clinical and some clinical departments. Positioned close to both the main university campus and to Belfast City Hospital (BCH) it was ideally positioned for medical students, as well as for patients. Irwin had turned Pemberton's vision into reality.

Some wonderful co-operative work was developed. At the outset the greatest burden fell on partners of the Irwin Group Practice in the Finaghy Health Centre; for it was there in the 1970s, with the willing co-operation of his partners, that Professor Irwin was able to create an early teaching outlet in the community for medical students. Later on the four partnerships that shared in the Dunluce Health Centre agreed to take on a heavier load of medical students than the average teaching practices further afield.

Irwin developed small group teaching in the seminar rooms in his department and in the specially developed consulting suites with their one-way mirror systems. The new Teaching Health Centre was provided with very modern teaching aids including CCTV in each consulting room. But bricks and mortar were not enough. Irwin had a huge task in building up a team of well over 100 GPs who taught students in small groups, mainly in their own surgeries. These doctors had to be taught how to teach undergraduates and how to ensure the co-operation of their patients. GP teaching took place in every year of the curriculum. Irwin provided overall learning aims and specific course learning objectives relevant to each year of clinical teaching.

The university and government authorities were slow in dealing with the complex financial problems involved in this exercise – perhaps another example of the misuse of Remunerative Power. As the Department grew in stature, the new professor realized that he would have to create a new and attractive career structure for his academic staff. To achieve this goal Irwin had to win over the Department of Health

and Social Services Northern Ireland (DHSS (NI)) and the Faculty of Medicine. The power struggle was intense, and even included a threat of resignation at one point. But from then on younger members of his academic staff were no longer at any serious financial disadvantage when compared with their peers in the NHS.[28] The QUB Senate accepted this new career structure in March 1979. The staff responded magnificently. Eight of them graduated with MD by thesis between 1983 and 1992.

Normative Power, with Moral Involvement, was in evidence when Irwin fought to raise the status of his department's work within the curriculum. Curricular time is guarded very jealously in the academic world and Irwin struggled hard to find allies. Through research and publications he developed overall teaching objectives and specific learning aims to be taken on board by academic tutors and by medical students in the consulting room. He developed new methods of teaching, particularly in the field of communication skills. Again with the focus on deeds and not the personality, very real advances have been illustrated by the time Irwin retired on age limit in 1990. The Medical Faculty QUB had come to acknowledge both the quantity and quality of the teaching, and had accepted General Practice as a core curricular subject.

OVERVIEW OF UNIVERSITY POWER

The actions taken by the medical faculty of QUB to improve medical education throughout the time frame in question have been reported. Foucault taught that all change has its reasons, and all modes of rationality involve structures of power. From the late 19th century onwards universities planned to graduate 'the complete doctor', and they were very slow to change this concept. It was not until 1950 that a compulsory postgraduate 'provisional year' was accepted; even after its introduction in 1953 the universities only took part in its administration with considerable reluctance. The universities left most specific postgraduate qualifications in the care of an ever-growing number of Royal Colleges, while CME was entrusted to learned societies. Local examples were the Ulster Medical Society (founded 1862) and its antecedent the Belfast Medical Society (founded 1806).[29-31]

During the 1970s the Medical Faculty at QUB investigated its methods of assessment, and a new Finals Examination structure was developed. 10% of final year students came to know that they would be examined in 'their major case' in the Department of General Practice. In addition, the Faculty adopted the Modified Essay Question (MEQ) as one of two main written tests in the Final MB Part 2 examination – The other being the Multiple Choice Question (MCQ). This test had been developed by the Royal College of General Practitioners (RCGP) for its own entrance examination, and it was of proven value.[32] At QUB it became the combined written assessment for both medicine and surgery. The MEQ was set and marked by the staff of the Department of General Practice. Academic General Practice had been empowered.[33]

QUB started to use an almost unique selection procedure for medical students in 1974, and continued with the same system up until 1990 and beyond. To avoid any suggestion of sectarianism local students were admitted on A-level results only. No interview was required. Certainly this achieved the desired effect with students from Roman Catholic schools claiming over 50% of the places. But because many more women than men achieved higher grades in A-level examinations, the gender ratio gradually changed until some 70% of the students were women. Planners had never suggested that the UK should follow a model unknown outside Soviet Russia, but this is what this selection strategy achieved. Very many women graduates prefer part-time work; so this one life-style factor will have a big impact on the future educational provision by and for the profession.

The management team at QUB was adept in the use of delaying tactics, of 'putting off until the morrow'. This was, and is, a well known management style in many universities. In 1964/5 QUB had the opportunity to control all undergraduate and postgraduate medical education in Northern Ireland. Why it relinquished this position in 1970 is unclear; but consider these facts. Universities in the UK did not have any history of such provision: Professor Biggart had reached the end of his long reign as Dean: fears over competitive funding were ever-present: the remunerative power of government was applied in full force: and the QUB Department of General Practice did not yet exist as a counterweight.

POWER OF CENTRAL AND LOCAL GOVERNMENT

Power relationships are multiple. In this section the power struggles within medical education involve the big battalions. Foucault stated that the struggle against disease must begin with a war against bad government. It is clear that bad government was in evidence in Northern Ireland 1920 - 1950 and beyond. A startling picture of economic disarray was on show, with the local government at Stormont perpetually teetering on the edge of financial insolvency. The economic situation in Northern Ireland, even in the immediate post-war period, was also much worse than anywhere else in the UK.

Titmuss[34] had shown that infant mortality rates were highly dependent on social class.[35] Everything that happened in Northern Ireland confirmed this observation. Poverty and unemployment were always higher in this part of the UK while maternal death rates were the worst too. There is a very large choice of references on this topic.[16,26,36-43] Patterson[43] explained that as economic failure loomed in 1952, 'Brookeborough descended on Churchill and his ministers demanding a range of special measures'. By 1954 'the Treasury representatives on the Joint Exchequer Board accepted not simple parity of social services and standards, but the necessity to incur special expenditure'. By 1955, the Northern Ireland Development Council chaired by Lord Chandos was conceded. In 1960 capital expenditure on hospitals in Northern Ireland was 12% of the UK total at a time when the Northern Ireland's share of the population was 2.5%. The opening of the Altnagelvin Hospital in Londonderry in 1960, the first completely new hospital in the whole of the UK (and indeed Europe) since the end of the Second World War was a direct result of this initiative.[16] Drastic action was needed in the 1920s, 1930s and 1940s. But nothing happened. Buckland[37] explained the power struggle in this way:

"Parochialism and amateurism are features of the government of many small states and most local authorities even in highly developed societies, while the tensions between a regional authority and other tiers of government are an inescapable consequence of any devolved or federal system of government".

Extraordinary revolutionary forces were unleashed by the upheaval of the Second World War, which allowed the creation of the Welfare State and the National Health Service throughout the UK. In 1945 the Stormont government invited the University Grants Committee to visit QUB and to report 'on its position and needs'. This led to immediate additional funding for the university. One belated example of this new money allowed the creation of Pemberton's chair in 1958. By the early 1960s both central and local government had taken a much more positive role. The Ministries of Health at both Westminster and Stormont developed a profound interest and involvement in the provision of postgraduate education for GPs. It is the historian's task to demystify such a linkage.

Belfast's tradition of rope manufacture suggests another image. This three-stranded metaphoric rope binds together government's tight control on medical education. The first section is that administered by the General Medical Council (GMC). The second strand of this houseline is continuing medical education (CME) for GPs: while the third twist is the so-called vocational training for the 'trainees' (later 'registrars') in general practice. Some unravelling of these interwoven strands is required.

THE GENERAL MEDICAL COUNCIL

The Medical Act of 1858 created the General Council for the Education and Registration of Doctors. It was renamed, in the later legislation of 1886, the General Medical Council.[44] Whatever the name this Council had, and continues to have, an important involvement in medical education, as well as in its better-known registration and disciplinary work. The GMC is rated as the most powerful medical body in the land. The Council and its Education Committee developed much of the curricular planning for medical schools. It is not possible to cover details concerning the GMC in this paper, but its many inherent weaknesses have produced several recent, widely reported, changes in its structure and function.

CONTINUING MEDICAL EDUCATION

It is self-evident that life-long learning is an essential target for any working professional. One strategy is a self-directed learning style, known as 'Continuing Professional Development' (CPD). This might be ideal for a few, but most postgraduates appear to prefer tutor-led group learning (CME).

The consultants took on a task as difficult as that imposed on Sisyphus with his stone when they tackled the creation of a 'teacher-led' curriculum for CME. Its planning and production proved to be very problematic – and evaluation caused even more difficulties.[5]

Since the 1920s some funding had been available for 'refresher courses' for NHI 'panel doctors'. From the start of the NHS in 1948 payments were available to GPs. These regulations came under Section 48 of the 1946 National Health Act. In Northern Ireland, Dr JM Hunter, Medical Adviser at the General Health Services Board, had taken personal responsibility for the provision of most of the annual 'refresher courses', although he always invited members of the Medical Faculty at QUB to provide the expertise. There is an interesting note in the RVH Staff minutes of 9 October 1961 that reads. 'Dr Hunter of the General Health Services Board commented on how successful the recent refresher course for GPs had been'. He also arranged evening meetings in places like Armagh and Enniskillen, when he personally transported the consultants, usually the professors, to give the lectures. (This benign service was affectionately known as Hunter's Circus).

From 1965 there was a rising graph of recorded attendance at CME courses. This increase coincided with the appointment of Dr John McKnight as full-time Director of the Board of Postgraduate Medical Education QUB. Nevertheless, his contribution can only be given part of the credit, because the first postgraduate hospital tutors were appointed concurrently with McKnight on 1 October 1965. These appointments had been one of the many recommendations of the Christ Church Oxford Conference of 1961.[22,45] Unlike the rest of the UK,[45] local government found funding to pay these tutors, while making each of the individual hospital management committees meet the costs of the provision, equipment, staff and services required in these Postgraduate Centres. This expansive funding grew generously after 1970 when the NICPGME was financed – another good example of the application of government's remunerative power.

One of the big changes wrought by government on medical education provision in the 1960s was the Health Services and Public Health Act (1968) – and in particular Section 63 of that Act which stated 'The provision of a service under the law in force in Northern Ireland corresponding to service mentioned in paragraph (b) above, and an activity involved in or connected with the provision of such a service'.

Throughout the UK, GPs were given financial incentives, of both 'carrot and stick' varieties to attend CME sessions. An unhappy link joined the Seniority Payments offered to experienced GPs and income from Section 63 activities. This caused some anger, and the relationship was eventually broken in 1977. There was a dip in attendance that year following its severance. At first sight this might have underlined both its necessity and its effectiveness. But by 1979/80 attendances took an upward turn again.[18] A generation of GPs devoted part of their lives to 'Section 63'. But big changes took place in 1990 – the most significant development was the replacement of Section 63 by the Postgraduate Education Allowance (PGEA). These new developments, coupled with Professor Irwin's retirement, explain why this year became the chosen cutoff point for this study.

VOCATIONAL TRAINING

The ultimate goal of this type of postgraduate training was to produce doctors who could provide personal, primary and continuing care to individuals in their homes and in the community. The complete system had to include preventive medicine and health education. Proper management and audit skills had to be learned, and a desire for continuing education imbued. While in training these doctors had to receive adequate remuneration, commensurate with their postgraduate student status.[17] However, it took many years to conceive and deliver this fully-fledged offspring; and this issue may be contrasted with that of the old 'assistantship with a view to partnership' where generations of isolated doctors received desultory training and claimed justifiably that they had been 'exploited as a cheap pair of hands'.

Prior to 1970 very few doctors entering general practice had any specific training. To quote McCormick,[46] "Those who became practitioners from choice or necessity entered practice in total ignorance of the real nature of the work that they were expected to do. Their training had been confined to the laboratory and the hospital, especially the teaching hospital. In the novel situation in which they found themselves, their past experience was of very limited value".

As early as 1946 a government report from the Interdepartmental Committee on the Remuneration of General Practitioners had produced simple proposals for assistantships in general practice. These had led to the Spens Report that same year, which spawned the Trainee General Practitioner Scheme in 1948. But it was only in Inverness, from 1952, that a permanent vocational training scheme had operated.[47] Following Inverness, St Bartholomew's Hospital, London, started a one-year course from 1956. In 1962 combined hospital and GP schemes were opened in Canterbury and Durham (the author was the first trainer in the Durham scheme). By 1964 there were further similar developments in Lancaster and Birmingham. The early pioneer 'trainers' only dimly understood the educational requirements of their posts.

Development was somewhat slower in Northern Ireland. But, the Ministry had started pressing QUB for the introduction of a sophisticated vocational scheme in its own domain from 1963. It was well aware that methods of selection for both teachers and postgraduate students had to be developed.

TRAINERS IN NORTHERN IRELAND

Dr John McKnight, the Director of the new Postgraduate Medical Education Board at QUB, took up his appointment on 1 October 1965 (*fig 4*). One of his very first tasks was to form a university committee to select the first GP trainers in Northern Ireland. Twelve stalwarts were chosen from 80 applicants in January 1966.[5] In June 1969 a second dozen was selected. The Board first minuted a special General Practice Sub-Committee, called the Trainers' Selection Committee on 4 February 1969. That task was handed over to the NICPGME in 1970, which then entrusted the work to Dr Noel Wright, the Postgraduate (later Regional) Adviser in General Practice, from 13 December 1971. Subsequently he was given the help of two Associate Advisers in General Practice – Dr H Baird, on 10 December 1973 and Dr AG McKnight, 3 January 1974. Five Course Organisers were added later. Patrick McEvoy, an Ulsterman and his remarkable book, 'The Course Organiser's Guide' deserves special mention and study.[48]

Fig 4. Dr John McKnight. A photographic copy of a portrait by Francis Neill Studios hung in the NICPGMDE.

After 1980, selection became much more sophisticated. Even experienced trainers were re-interviewed before each re-election to the office. The trainer had to have had a minimum of five years experience as a principal in general practice, and could not be appointed over the age of 50 for the first time. The experienced trainers had to retire shortly after their sixtieth birthday. They were expected to have thought through their teaching objectives and methods. All trainers had to work in well-equipped surgeries or health centres, with an emphasis on good organisation, including an age/sex register for the practice, an up-to-date library, and good ancillary staff.[5,18]

TRAINEES (LATER GP REGISTRARS) IN NORTHERN IRELAND

At the start of the scheme in Northern Ireland in 1966 there was a dearth of applicants. There was only one trainee in 1966 and none in 1967. Manpower shortages were the main cause, and the same was true throughout the UK. Dr Myles Shortall was the first representative of a trickle of volunteer trainees in Northern Ireland that gradually grew to a flood of some 50 GP registrars per annum. By 1981 a full three-year training programme became mandatory.

DECISION TO CONTROL NUMBERS IN TRAINING IN NORTHERN IRELAND

Unlike other parts of the UK, Stormont decided to control the number of doctors who could enter training for general practice. In the Report on Manpower Requirements in General Practice 1984-89, (created for the General Medical Care Sub-Committee of the Central Medical Advisory Council of Northern Ireland) it was stated that, by August 1983, 220 men and 110 women had completed vocational training within its jurisdiction. This Report went on to say that Northern Ireland would need 39 new GPs annually between 1984 and 1989. They recommended that the intake should be around 50 doctors per annum, thus allowing for some flexibility. These bureaucratic rules caused many problems. The enforced introduction of the 'fallow year' principle proved very unpopular. The original selection procedures were set out in Circular HSS (TM) 3/80, and planned intakes each February and August. The selection panel was organised by the NICPGME, and, from January 1982, was serviced by the Central Services Agency (CSA).

OVERVIEW OF GOVERNMENT'S POWER

After serious inadequacies in its early years, the Ministry of Health at Stormont became much more efficient. Many of its

senior civil servants showed remarkable insight. As early as November 1963 the ministry put forward proposals 'that there should be a compulsory period of training prior to entry to general practice and the Board's lists'. This was two full years before the QUB Board was functioning, and 17 years before such rules were finally introduced.[5]

It may be accepted as an axiom that it is the duty of all of the noble professions to pass on their own particular skills of 'art, wisdom, and intuition' to their apprentices. However, Downie[49] raised doubts concerning the involvement of the medical profession: "The attitude to the whole subject of medical education among doctors is usually negative. Those who are interested in it are often regarded as second-rate and boring".[49] Such negative attitudes could partly explain why the medical profession sacrificed its independence and allowed control of its education to pass from itself to politicians and civil servants.

THE POWER OF GENERAL PRACTITIONERS

In 1844 a Bill was introduced in The Westminster Parliament to set up a College of General Practitioners. But the lawmakers were unable to satisfy the critics who demanded a system that would separate the qualified from the unqualified practitioners. Thomas Wakley was a firebrand MP and also Editor of The Lancet. In one of his journals of that year he labelled the proposed law "The Quacks' Bill". It failed to reach the Statute Book, and it was another 108 years before a similar Act became law.[18]

This time lag alone confirms the total lack of GP power in that period. The 19th century provision by government of poor law, workhouses, and the dispensary system had shaped health care provision for that period of over 100 years (most particularly in Ireland). Details are described by Digby,[50] and many by other authors. By 1875 there were 201 dispensary districts in the six counties that later constituted Northern Ireland and they recorded treatment for over 170,000 patients in that year. These were later reduced to 178 districts; each served by a medical officer, and usually a district nurse or midwife. The dispensary doctors in Northern Ireland had been appointed right up until the start of the NHS in 1948.[8] They were certainly not highly paid: for example in 1927 their average salary was £248 p.a. (according to the Ulster Year Book, in 1929) The 'remunerative power' of local government saw to that. This average sum remained remarkably constant throughout the 1930s and 1940s reaching only £264 p.a. by 1947. The doctors supplemented these sums by additional work in 'private practice'. However, state-financed medicine had become an important facet of the GPs' professional life.

At the time of the launch of the NHS on 5 July 1948 the service provided by many GPs in the UK was of a very poor standard.[51] An Australian, Dr JS Collings, published his scathing report in 1950; a bleak, but accurate, contemporary record. In particular Collings criticized the two room surgery premises, 'so often ill-furnished and under-equipped' that he found all over GB. 'There did not seem to be any place for adequate record keeping, nor for any ancillary staff'. He made it clear that this unsatisfactory state existed in spite of, and not because of, the NHS. His criticisms had a profound effect on a whole generation of doctors.[52]

Something had to be done. The writings of Kuhn – he of the somewhat controversial conceptualization of 'the paradigm shift' – can be applied to this problem. Kuhn pointed out how to recognize such a group in these words:

"A scientific community consists of the practitioners of a scientific specialty. Bound together by common elements in their education and apprenticeship, they see themselves and are seen by others as the men responsible for the pursuit of a set of shared goals, including the training of their successors. Such communities are characterized by the relative fullness of communication within the group and by the relative unanimity of the group's judgment in professional matters. To a remarkable extent the members of a given community will have absorbed the same literature and drawn similar lessons".[53]

In earlier writing Kuhn[54] argued that:

"Scientific revolutions are inaugurated by a growing sense, again often restricted to a narrow sub-division of the scientific community, that the existing paradigm has ceased to function adequately in the exploration of an aspect of nature to which the paradigm itself had previously led the way … The sense of malfunction which can lead to crisis is a prerequisite to revolution … The choice between competing paradigms proves to be a choice between incompatible modes of community life".

A Kuhn-model paradigm shift occurred in 1952 when 'a narrow sub-division' of GPs used normative power to produce great changes in the education and training of their peers. The College of General Practitioners was founded by a Steering Committee on 19 November 1952 (Report of CGP, 1953). Dr Fraser Rose, Dr John Hunt and a 'remarkably few activists' led these momentous events.[18] Within six months the College had a membership of over 2,000.[17] Originally entry to membership was by application and vetting; but an entrance examination (MRCGP) was set up by 1965, and became a prerequisite after 1968. The debate concerning admission to the specialty of general practice via summative assessment rather than by the MRCGP examination will have to be pursued elsewhere. The vast majority of doctors entering the specialty in Northern Ireland have passed the MRCGP examination.

One of the strengths of the new College was the early decentralization of the organisation with many regional faculties throughout Great Britain and Ireland. Faculties were founded in the east, west, and south of Ireland between 1 May 1954 and 28 January 1956.[23] But the first Irish faculty was in Northern Ireland for it was founded on 30 April 1953, in the Whitla Institute, Belfast, under the chairmanship of Dr J Campbell Young. The Fellows of the Northern Ireland Faculty continue to award an annual internal prize for published GP research. It honours the name of this first Provost.

Progress was rapid and Her Majesty the Queen conferred the Royal Charter in 1967, so allowing the name to be changed to the Royal College of General Practitioners. Just like its 1844 precursor this organization met with a great deal of initial opposition. But on this occasion the planners overcame dissension, external resistance and the natural opposition of the multitude of independent minds of its many potential members. The work of the RCGP is very well documented elsewhere. The 'conflict perspective' explains why the policies of the RCGP could never be universally popular.

The new College needed a structure that could be clearly recognized as a discipline. The four essential features of

such a discipline are a unique field of action; a defined body of knowledge; an active research programme and a rigorous training programme.[55] The College undertook to define and illustrate all of these factors, right from its inception, and to publish the results in a Journal. 'In the development of any discipline, the literature is the key'.[56] After a number of title changes the British Journal of General Practice (BJGP) continues this proud tradition.

From its earliest days the CGP linked CME with entitlement to membership.[18] It experimented with medical meetings in most faculties as well as annual events such as faculty symposia. An excellent example of this educational approach was the Medical Recording Service established by John and Valerie Graves. From 1957 they developed a completely new educational tool in the provision of tape recordings and slides that were available to general practitioners all over the country.[18]

Professor George Irwin (*fig 3*) and Dr John McKnight (*fig 4*) were two local examples of the busy enterprising membership of the RCGP. They and their like-minded colleagues were the "actors who had the ability to induce or influence other actors to carry out directives".[2] Together these activists changed the course of medical education in both undergraduate and postgraduate settings: e.g. in turning General Practice into a core curricular subject of the Medical Faculty QUB: in contributions to the Education Committee of the RCGP: in the provision of the trainers required for vocational schemes: in teaching the registrars up to specialist level: and in the provision of a constant supply of examiners for the RCGP membership entrance tests. This paradigm shift had advanced GP power.

POWER REALIGNED?

Some final assessment of the costs and/or benefits of the conflicts between the different sections of the medical profession and government is required. This appraisal should be capable of generalization, allowing application far beyond the geographical confines of this paper.

The internecine dissensions of the medical profession described above were certainly not restricted to the period 1920 - 1990. They were just as well known to the apothecaries of the seventeenth century like Nicholas Culpeper (1616–1654) – the author of "The English Physician"; ("Culpeper's Complete Herbal") or William Rose, as to Frazer Rose and his colleagues in the twentieth century. The use and misuse of power has been a continuum. Should attempts be made to modify or readjust these effects on the provision of medical education?

ANSWERABLITY

Today's Westminster parliamentarians like to divide and rule and so the schisms within medicine suit their purposes. These politicians, when in government, give every appearance of wanting to take complete control of all educational matters, from pre-school to adult learning, and even medical education. They have adopted the mantles of the professional planners, administrators and educators simply because they have the remunerative power to hand. This is a frank misuse of power, and demands readjustment.

The professions could and should be much more directly responsible for these educational duties. In Northern Ireland in 1989 a firm proposal was made – that control of postgraduate medical education should be transferred back to the medical academics at QUB. But, the medical academics lost the argument, and the council moved for even more governmental control.

The hospital consultants of yesteryear had a strong moral and ethical background that provided a sure foundation for the provision of medical education. However, in today's world, it has become clear that the teaching must be shared with the GPs – at all levels. The whole profession benefits when this input of knowledge, skills and attitudes is maximized in this way. But the partitioned groups within the medical profession have chosen to fight amongst themselves, rather than tackle the essential reformation in unity.

The QUB department of general practice could enlarge to include much more postgraduate teaching. This has already been accomplished in Scotland. Allen[57] and Rathid[58] have argued forcefully for this integrated approach. They envisage an increase in the efficiency of both teaching and research that would naturally enhance the quality of the service of general practitioners. The first formally integrated undergraduate and postgraduate unit in the UK, at Dundee, has been reported.[59] QUB and the government at Stormont have a very real opportunity here. This is but one local example of how the universities and government could be more effective in the provision of GP education throughout the UK.

ACCOUNTABILITY

The government at both national and local level misapplied its remunerative power at times; nevertheless its civil servants did many good things, and they found themselves repeatedly frustrated by the laggard nature of systems within the universities. These conflicting facts leave a conundrum. However, any attempt to amend the costing involved would soon uncover the inevitable competition for power and struggle for control.

The financing of vocational training and CME has always been seen as generally unsatisfactory. Government held most of the purse strings, but costing difficulties were compounded by the largesse of the pharmaceutical industry. Because of the overt financial advantages, many of the recipients of this benefaction were and are reluctant to accept its real motivation. These tensions persist. The quite extraordinary power of the advertising industry must be recognized, and feared. In 2003 the British Medical Journal (BMJ) devoted a whole week's issue to addressing this problem.[60]

SUMMARY

The use and misuse of power has been demonstrated. It has been shown that GP education has changed very significantly between 1920 and 1990. Many excellent improvements have been achieved. Nevertheless, despite these gains, it is quite impossible to accept the hypothesis that there has been a constant steady improvement through history to the present perfect state (so-called Whiggism). Rather, it is clear that each and every one of the participants who provided GP medical education in Northern Ireland have made mistakes, of varying magnitude.

TABLE II

Developments coming after the end of this historical study in 1990 include some or more of the following:

1. The Postgraduate Education Allowance (PGEA), which replaced Section 63 in 1990.
2. The introduction of entrance into the Fellowship of the RCGP by examination in addition to the original 'chosen' route.
3. The repeated re-modelling of the management structure of the NICPGME. This is well illustrated by its changes of name. The first change is a good indication of another power struggle, when it became the Northern Ireland Council for Postgraduate Medical and Dental Education (NICPGMDE). In 2004 it changed again and became the Northern Ireland Medical and Dental Training Agency (NIMDTA), emphasizing an ever-increasing use of governmental power.
4. The introduction by the NICPGMDE of a rolling four-year curriculum for CME in Northern Ireland in 2002. ("The Master Classes")
5. The proposed introduction of far-reaching plans for regular repeated re-assessment for all GPs.
6. A decline in the number applying for training in general practice.
7. Proposed lengthening of vocational training for GPs.[14]
8. The significance of the new GP contract and the increasing number of part-time GPs, mostly women, will have to be assessed. The recent gender debate in medicine [61] should avoid some of the basic accusations of low pay; but it generates arguments far beyond the scope of this paper. Part-time doctors can only be appointed as trainers of part-time registrars – a very small number annually. This must be yet another example of the increased burden placed on the dwindling percentage in full-time employment.
9. The development of some postgraduate medicine at The University of Ulster.
10. The managers of some modern Hospital Trusts who have started to complain about the use of limited funds for educational purposes.
11. The quite proper demands of patients' groups for an input into medical education.
12. 'The International Campaign to revitalise Academic Medicine'.[62]

However, the hypothesis of the conflict perspective is proven – the inevitable competition for power and the struggle for control were ever-present, and have been illustrated.[5] This paper acknowledges that it is axiomatic that the medical profession should teach both its 'apprentices' and CME. For the medical profession to achieve a more independent position in this provision, the powers of state and the pharmaceutical industry would have to be curbed or controlled – in short, realigned.

To reach this goal the medical profession's future planners would need to change. The various cliques would have to become a unified force. Only then would they have sufficient power to orchestrate and achieve the profession's proposals for GP education. An armistice could be agreed by the warrior bands (hospital consultants, the multiplicity of royal colleges including RCGP, and medico-political bodies such as the BMA) to allow this to happen. At this point, successful renegotiation of the conditions for GP education could become a real possibility.

As a postscript, it must be acknowledged that there have been a great many significant developments in GP education since 1990; some are listed in Table II. These will require research elsewhere. Nevertheless, even after a further 15 years, the hypothesis remains sound; the competition for power and struggle for control are constants, and the schisms within medical education continue unabated.

Conflict of interest

The author was a GP for most of his life

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Medical History

A replica of Alexander Fleming's Nobel Medal

HW Gallagher

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INTRODUCTION

Recently some Swedish friends expressed great interest in my replica of the gold medal presented to Alexander Fleming when he received the Nobel Prize for his discovery of penicillin (*fig 1*). They were equally interested in the silver border, which relates how I received the replica. It states:

A present from Lady Fleming to Lady Thomson 1956 given to Herbert Gallagher 1971

I explained that Fleming and Thomson had served in the same Royal Army Medical Corps Research Unit in France in the 1914-18 war. They had become friends and their friendship continued after the war. WWD Thomson became Professor of Medicine in Queen's University, Belfast.[1] He became very ill and was treated in a Nursing Home in London. The Flemings befriended Mrs Thomson who, having gone to London to be with her husband, was alone in a strange city. Also because of the friendship Fleming gave his first lecture on Penicillin outside London to the Ulster Medical Society when he was the Robert Campbell Orator in 1944.[2] He also addressed the Belfast Medical Students Association in the Great Hall

Fig 1A. Obverse of medal.

1B. Reverse of medal.

of Queen's University on the same visit. The war was still on and although travel restrictions were extremely tight Lady Fleming came with him. When on the platform of the railway station for the boat train to Larne they discovered that Fleming's slides had been left behind in the Thomson home in University Square[3] (*fig 2*). The train departure was delayed until the slides had been retrieved by Thomson's chauffeur!

In 1946 Queen's University conferred on Fleming the honorary degree of Doctor of Science.

LADY THOMSON AND LADY FLEMING

When Lady Thomson was widowed she lived in Donaghadee, Co. Down, and became my patient. The relationship of my

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Fig 2. Sir Alexander and Lady Fleming on the steps of 25 University Square.

wife and myself to her became very much like that of a surrogate son and daughter-in-law. Her own son, and only child, had been killed in the Far East while serving as a Regimental Medical Officer in The Royal Army Medical Corps. Lady Thomson's gift to me included a signed photograph of Fleming (*fig 3*). The original is now in the office of the Head of the School of Medicine and Dentistry, Queen's University, Belfast.

The Lady Fleming who gave the replica to Lady Thomson was Fleming's second wife. She had had a colourful career both before her marriage and in her widowhood. During the 1939-45 war the Germans had imprisoned her for assisting allied prisoners to escape from her native Greece. In 1947 she, Mrs Amalia Voureka, came to work, as a postgraduate student, under Fleming in St Mary's. They immediately struck up a very close rapport.

She returned to Greece to head a bacteriological department in a hospital and became a voluble critic of the various dictatorial regimes. She gave evidence in favour of thirty-four people accused of plotting to overthrow the regime of the Colonels and was convicted and imprisoned for assisting at the attempted escape from prison of the assassin of a Prime Minister. Later she was prominent in the campaign for the return the Elgin Marbles to Greece.

Fleming and she met again in 1951 and 1952 after he had been widowed and her marriage had been dissolved. They married in 1953 and unfortunately he died suddenly in 1955 aged 75.

I do not know if the second Lady Fleming and Lady Thomson ever met and if the gift was in memory of the friendship of the two families. As far as I know three copies of the medal were made. Lady Fleming brought one to Greece and the third

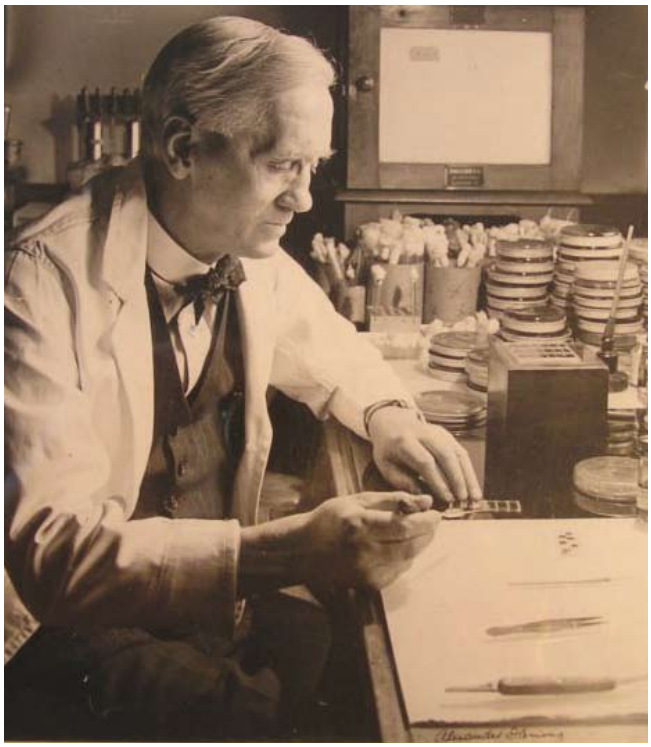

Fig 3. Signed photo of Fleming.

may be in the Pasteur Institute in Paris. The original is in the Fleming Museum in St Mary's Hospital, London.

I told my guests that I thought that the Nobel Committee had made a mistake in awarding the Prize to Fleming, Florey and Chain excluding the third member of the Oxford Team – Dr Heatley. (At that time I did not know that the Nobel Prize was never given to more than three persons). I really knew very little about Heatley and resolved to do what I should have done, probably in 1970, when Mrs Ida Edgar told me that his work had been absolutely essential in penicillin's development. Had I then carried out even a cursory investigation of his work, and written a letter about it to the British Medical Journal, Heatley may well have had his due recognition during his working life.

The book review of *The Mould in Dr Florey's Coat* in this issue of this journal[4] is the fruit of my long delayed investigation.

ACKNOWLEDGEMENTS

I thank Harry Martin for help with photography.

Conflict of Interest – none

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Ulster Med J 2006; **75 (2)** *155-157*

Case Report

Successful Stenting in Endobronchial Wegener's Granulomatosis

J Tiernan, C Shah, J McGuigan, JS Elborn

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INTRODUCTION

Wegener's Granulomatosis (WG) is a multisystem disorder characterized by granulomatous necrotizing vasculitis. Classic Wegener's granulomatosis is a triad of necrotizing angiitis of the upper and lower respiratory tract and focal glomerulonephritis of the kidney.[1] The classic respiratory feature is multiple pulmonary nodules on chest radiograph.[2] In many cases extensive medical evaluation and laboratory test have proven non-diagnostic. In 1966, Carrington and Liebow introduced the concept of "limited Wegener's" granulomatosis to identify otherwise classic vasculitis lacking renal involvement.[3] Limited Wegener's granulomatosis has a better prognosis than classic disease but it may be extremely challenging to recognize and diagnose.[3,4]

We report an unusual case of limited Wegener's granulomatosis presenting with focal endobronchial WG with lobar collapse requiring stenting.

CASE REPORT A 19 year old female student presented to Otorhinolaryngology in June 1997 with a 3-week history of nasal obstruction, anosmia, headache, post-nasal drip and cough, unresponsive to recurrent antibiotic courses. X-Ray of paranasal sinuses revealed both maxillary sinus opacity. She was admitted in January 1998 for bilateral antral washouts and nasal endoscopy. Postoperatively, she developed fever, malaise, anorexia and unexplained weight loss. CT scan of paranasal sinuses revealed pansinusitis. She had bilateral functional endoscopic sinus surgery without much benefit. A CT Scan of brain excluded intracranial abscess. Revision endoscopic sinus surgery, performed 9 days later, revealed pus with necrotic material in the maxillary sinuses. Despite repeated sinus drainage procedures and intravenous broad-spectrum antibiotics during her hospitalisation, she continued to be febrile with weight loss. She had persistently elevated C – reactive protein [130 – 393 mg/l]. Her Westergren erythrocyte sedimentation rate was 110mm/hour. All cultures were negative. No granuloma or fungus was observed on biopsies. Initial autoimmune and vasculitic tests demonstrated no elevation in autoantibodies. She developed a normocytic anaemia, transient polyarthralgia and destructive inflammation of her nasal bridge.

Despite the initial absence of granuloma on histology or Anti Neutrophil Cytoplasmic Antibody (ANCA) in serum, a provisional clinical diagnosis of Wegener's granulomatosis was made. The patient was commenced on high dose oral steroids and co-trimoxazole. Steroid therapy resulted in prompt response and rapid clinical improvement, evident within 24 hours.

Indirect serum immunofluoresence in early February 1998 showed an atypical positive pattern for cANCA and Antiproteinase 3 level 6.2U/L [Normal <2]. Cyclophosphamide was added to her management regime. Rapid symptomatic improvement followed and she was discharged home.

In June 1998 she presented acutely unwell with shortness of breath and fever. A chest radiograph revealed complete collapse of the left lower lobe (*fig.1*). Bronchoscopy confirmed

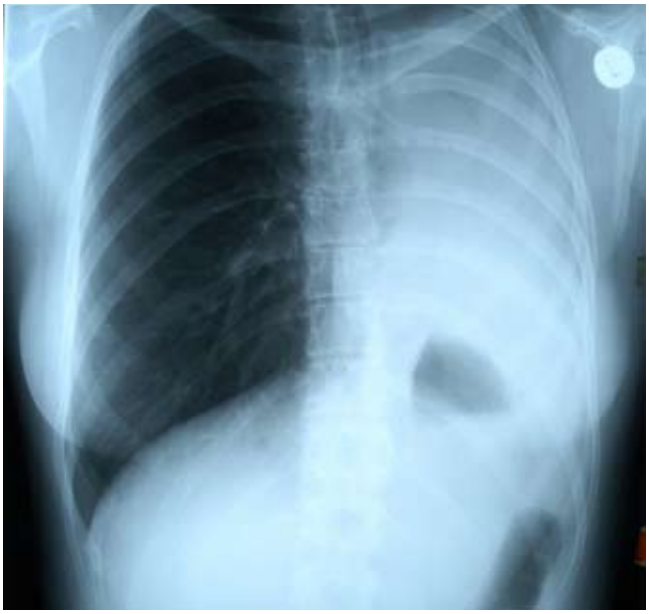

Fig 1. Chest X-ray pre-stent.

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complete occlusion of the left main bronchus. Treatment was commenced with intravenous methylprednisolone, cyclophosphamide and antibiotics. Repeat bronchoscopy and biopsy of firm tissue at the stenosed left main bronchus showed superficial fragments of oedematous and reactive mucosa with extensive squamous metaplasia. There was no dysplasia, malignancy, granulation, vasculitis or fungus. Rigid bronchoscopy with laser ablation of the stenotic segment followed by dilatation was performed. Rapid improvement ensued.

Her health deteriorated within three weeks, with restenosis of the left main bronchus. Repeat bronchoscopy and laser ablation of stenotic segment followed by dilatation gave immediate relief. Restenosis occurred and the cycle continued. In a 2-month period, a total of 9 dilatations were carried out, several with laser resection. Each gave transient symptomatic relief.

The patient proceeded to stenting in October 1998. Rigid bronchoscopy provided accurate measurement of the extent of the stenotic segment of left main bronchus. An endobronchial stent was deployed after laser ablation and balloon dilatation (*fig. 2*).

Fig 2. Chest X-ray post stent

She improved dramatically following stenting. Follow up at the respiratory outpatient clinic enabled slow tapering of her steroid therapy to zero by July 2000. All bloods were normal and azathioprine therapy was discontinued in October 2000. She underwent nasal reconstructive surgery in 2001. She was able to complete her studies and was married early in 2003. Her only complaints during this 5-year period were occasional upper respiratory tract infections, which responded well to short courses of oral antibiotics.

A deterioration in FEV_1 late in 2003 raised suspicion of restenosis (FEV_1 3.4L May 2002 - FEV_1 1.75L November 2003). Bronchoscopy in November 2003 demonstrated a well epithelialised, stented left main bronchus with mobile, occluding but not actively inflamed, tissue at the distal end of stent. In the coming weeks she was monitored closely. At surgical review in February 2004 she was 8 weeks pregnant and subjectively well. Intervention was postponed.

A further acute presentation with a left lower lobe pneumonia occurred in April 2004. Subsequent bronchoscopy revealed a circumferential stenosis of greater than 50% at the origin of the left main bronchus. Histology confirmed recurrence of acutely inflamed granulation tissue and laser ablation was undertaken in May 2004.

She had a baby girl by caesarean section in September 2004. In 2005 laser debulking of the endobronchial lesion has been performed twice. A repeat biopsy in January 2005 revealed further stent hyperplasia with granulation tissue. Both treatments have provided symptomatic relief.

DISCUSSION

In this patient the upper airway disease due to Wegener's Granulomatosis responded to corticosteroids, cyclophosphamide and co-trimoxazole. Endobronchial WG is an uncommon manifestation of the disease. Koyama *et al* (2003) reported the incidence of endobronchial involvement to be as low as 16%.[5] Hirsch *et al* (1992) further stressed the rarity of endobronchial WG. They described a patient in whom the only manifestation of WG is severe proximal bronchial stenosis, which developed despite management with oral steroid and cyclophosphamide. That case responded well to IV cyclophosphamide and oral co-trimoxazole whereas our case required further intervention.[6] A further case report by Breton *et al* (1986), illustrated the difficulty in diagnosing WG from such a presentation and emphasise the need for tissue biopsy.[7] These highlight the importance of awareness of this infrequent but potentially life-threatening feature of the condition.

Subsequent to presentation with left main bronchus occlusion, our patient underwent repeated dilatation and laser ablation therapy. Each of these afforded her only temporary relief of airway obstruction. Several authors suggest that balloon dilatation is safe, efficacious and cost-effective.[8,9] It is easily performed and has few complications. Eagleton *et al* found repeated endoscopic dilatation effective for 18 months in a patient with endobronchial WG.[10] Until now, no long-term follow up has been published. When combined with laser therapy, endoscopic dilatation may be acceptable as a first line measure to restructure the occluded airway but to further enlarge the airway and maintain patency, stenting is required.

Endobronchial stenting is not without complication. Problems include displacement of the stent and obstruction with secretions or granulation tissue (as in our patient). Less commonly the stent may perforate the airway wall, sometimes into the accompanying blood vessel.[11] Most studies of endobronchial stenting demonstrate that they are an effective treatment modality for airway stenosis. The long term efficacy of endobronchial stents is superior to laser ablation, debulking or dilatation therapy though the long term patency of stents is uncertain.[12-14]

Stents have been effective in achieving immediate resolution of respiratory symptoms from various tracheobronchial obstructions.[15] In the majority of cases, however, the success

of such a management option cannot be judged on such short term outcomes. Currently, the ideal course of action is unclear, as none are free from complications, nor able to consistently provide life-long patency.[15]

This patient's endobronchial stenosis was successfully managed with endobronchial stenting which maintained airway patency for 5 years. No other reports were found with such encouraging longterm outcomes.

The authors have no conflict of interest

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Letters

Solitary caecal diverticulitis

Editor,

I have had recent experience of three cases of solitary caecal diverticulitis which presented over an 18 month period to Causeway Hospital[1] and wished to add to the case by Abogunrin *et al*.[2] There have been over 1000 cases of caecal diverticulitis reported in the literature. A review of 881 cases showed that the average age was 43.6 years (range 7 to 87 years) with a 3:2 male to female ratio.[3] 85% present with symptoms similar to appendicitis.[3] Cutajar[4] suggested clinical features which could help differentiate caecal diverticulitis from appendicitis. There is a relatively long history of abdominal pain with lack of toxicity. Tenderness is not as marked and only elicited on deep palpation, and vomiting is less frequent. Abogunrin *et al*[2] suggested that CT scanning was the most useful pre-operative investigation as ultrasound was not sensitive. However, Chou[5] proved the accuracy of ultrasound in diagnosing caecal diverticulitis. In a prospective study of 934 men with indeterminate right lower abdominal pain, ultrasound had a sensitivity of 91.3% and a specificity of 99.5% in differentiating right sided diverticulitis from appendicitis. Ultrasound also has the advantage of avoiding radiation exposure and being generally more accessible. Given the low incidence and difficulties with diagnosis, there have been no randomised trials comparing conservative with aggressive treatment. Most studies are retrospective note reviews comparing outcomes in those treated with antibiotics alone to diverticulectomy or hemicolectomy, and also tend to be from mainly Asian populations, which may not be truly representative of the UK.

Lane *et al*[6] in a study of 49 patients with 78% of non-Asian descent, found that 40% of those treated with diverticulectomy or antibiotics alone required subsequent hemicolectomy due to an ongoing inflammatory process. In a US population, they recommended diverticulectomy in cases of a solitary inflamed diverticulum. Our cases, treated with diverticulectomy or inversion of the diverticulum had no postoperative complications or recurrence of symptoms. We agree with Abogunrin *et al*[2] that surgery should be conservative when carcinoma is excluded and there is not extensive inflammation.

The author has no conflict of interest

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Benign Headache in the Elderly – A Case Report of Hypnic Headache

Editor,

New headaches in the elderly raise the suspicion of serious pathology such as space occupying lesions, temporal arteritis, or cerebrovascular disease. Alternatively such headaches may simply represent the re-emergence of a previous headache such as migraine. However, benign headache syndromes are increasingly being recognised in this population.

The Hypnic Headache Syndrome (HHS) is a rarely reported disorder of the elderly characterised by recurrent nocturnal headaches of moderate severity that waken patients in a predictable pattern.

Case Report A 79 year old man had a four week history of headaches occurring predictably 2-3 hours after falling asleep and lasting for about one hour, during which time he sat up believing that this relieved the headache. This recurred every night, once or twice per night, with no daytime headache. He described it as a 'choking, full' headache, distributed 'like a cap'. It was associated with mild nausea but no vomiting or other autonomic features. There was no previous history of headaches.

Past history included ischaemic heart disease, a previous basal ganglia lacunar infarct, controlled epilepsy, hypertension, osteoarthritis, diverticulosis, prostatic hypertrophy, peripheral vascular disease and chronic renal impairment. Examination was normal.

Initial investigations revealed creatinine 134, sodium 129. Hyponatraemia was felt secondary to carbamazepine; a synacthen test and thyroid function were normal. Sodium subsequently normalised. Chest X-ray was normal and a CT scan of Brain showed mild cerebral atrophy and the previous infarct. Other investigations included a normal US abdomen/pelvis, normal CT chest/neck, normal FBP, Liver function tests, C reactive protein, CEA, CA19.9, PSA and urinary catecholamines.

Based on the above we diagnosed Hypnic Headache Syndrome and commenced the patient on 200mg lithium carbonate. Within 48 hours there was sustained complete resolution of the headache. After discharge the general practitioner discontinued the lithium because of concerns about drug interactions, and the headaches returned. Simple analgesia was substituted but headaches continued.

DISCUSSION

Hypnic Headache is a benign nocturnal headache which predominantly affects elderly people. This case illustrates some classic features of the syndrome. Evers and Goadsby[1] reviewed the 71 reported cases giving us the clearest picture of the syndrome to date. 37% were male and 63% female. Mean age of onset was 63 +/- 11 years (range 36-83). Headache was described as: Moderate - 67%, Severe - 31%; Dull - 57%, Throbbing/Pulsating - 38% and Sharp/Stabbing - 5%; Diffuse - 57%, Frontotemporal - 42%, Posterior - 1.6%. Average duration was 67 +/- 44 minutes (range 15-180). Onset was 60 - 120 minutes after falling asleep in 77%. Nausea was reported in 19%. The pathophysiology of HHS is currently theoretical, but associations with the sleep/wake cycle and circadian rhythms form the basis for theories of its nature. Polysomnography has revealed the onset of hypnic headaches may be associated with REM sleep.[2] It may be that inactivation of antinociceptive structures, e.g. dorsal raphe, during REM mediates the headache.[3]

Commonly patients experience the headache at a predictable time each night, suggesting a link with the circadian rhythm, which is orchestrated by the suprachiasmatic nuclei in the hypothalamus (also involved in antinociception). These nuclei produce, among others, melatonin, an important mediator of circadian rhythm. With advancing age the function of the hypothalamus, and thus melatonin secretion, is impaired.[4] This could also be involved in the pathogenesis of hypnic headache. Lithium is believed to increase melatonin levels[5] and may explain its mode of action. However, undoubtedly it is more complex than any one of these associations as many different drugs have been tried with variable success. Lithium remains the most effective but is often limited by side effects and interactions, and requires monitoring of plasma concentrations to avoid toxicity. Other reported treatments include indomethacin, caffeine, verapamil, prednisolone, gabapentin, melatonin, and acetazolamide.

Awareness of benign headaches is important to avoid unnecessary investigation but it must be stated that brain imaging and routine biochemical/haematological investigations are usually indicated when presented with new onset headaches in the elderly.

The Authors would like to thank Dr J Craig (Consultant Neurologist, Royal Victoria Hospital).

The authors have no conflict of interest

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Myopathy, hypokalaemia and pica (geophagia) in pregnancy

Editor,

Pica describes the persistant ingestion of nonnutritive substances.[1] Geophagia describes pica of clay.[2] We present a case of geophagia resulting in hypokalaemic myopathy.

Case History: A 29 year Gravida 3 Para 2 presented to a tertiary referral centre in Cape Town, South Africa, at 30^{+4} weeks gestation. She gave a two week history of photophobia, vomiting and weakness of the left side of her body. No other symptoms were reported. Fetal movement was reported to be normal. Her two previous pregnancies, in 1997 and 2001, were uneventful and resulted in normal vaginal deliveries at term. She had no significant medical or family history, was not on medication and did not report any allergies. She was a non-smoker and non-drinker. She was from the coloured community in Cape Town. She was a single mother, lived in an informal dwelling settlement, and had no monthly income.

She booked at 22 weeks gestation and an anomaly scan reported no fetal abnormality. Her booking Body Mass Index was 33, BP 110/85 mmHg, Hb 9.3g/dl, blood group A+ve, no abnormal antibodies, VDRL negative and HIV negative. Her pregnancy was uneventful up until presentation at hospital.

Examination of the cardio-vascular, respiratory and gastro-intestinal systems was normal. Neurological assessment of the central nervous system was normal. Proximal muscle strength was reduced bilaterally with muscle groups demonstrating 4/5 strength. Biceps and patellar reflexes were reduced and plantar reflexes were normal. Sensation was normal. The provisional diagnosis was a myopathic process of unknown aetiology.

Haematological investigations showed a Hb of 9.9g/dl, WCC 11.2×109/L, Platelets 391×109/L and an ESR of 73mm in 1 hour. Biochemistry showed a sodium of 145mmol/L, potassium 1.5mmol/L, urea 2.2mmol/l, and creatinine 116µmol/L. Liver function tests were also abnormal. Her creatine kinase was 9920U/L. Further investigations as an in-patient included and EMG, MRI scan of brain and muscle biopsy. The EMG reported features in keeping with a myopathy. The MRI scan and muscle biopsy were normal. Biophysical assessment of the fetus was reassuring.

Further questioning of the mother revealed that throughout the pregnancy she had regularly been eating clay from outside

her house. It was impossible to accurately quantify the amount eaten. The patient's symptoms slowly responded to intravenous and oral potassium supplementation over 14 days. Her liver function and renal function returned to normal. She was discharged 18 days after admission to hospital. Her care, for the remainder of her pregnancy, was in the community. Further follow-up information is not available. The patient did not have a telephone land line nor a cellphone. A request was made to the community services to follow-up the patient. On receiving the address, we were told that they only went into the patient's district with a police escort and our request was not justified.

DISCUSSION

The aetiology of pica is not known. Theories on pica range from nutritional deficiencies and psychological problems to obsessive-compulsive behaviour and specific brain lesions.[3,4] Pica can cause a number of serious conditions including iron-deficiency anaemia, bowel obstructions and perforations, lead poisoning, and helminthnic infestations.[5] This is only the second report in the literature of geophagia causing hypokalaemic myopathy in pregnancy.[6] The pathophysiology, it is suggested, is that clay binds to potassium in the gut. This leads to increased intestinal excretion of potassium, resulting in hypokalaemia.[7] It appears that the effect is dose dependent on the amount of clay ingested.

Unfortunately, our patient was lost to follow-up. This also occured in the other reported case.[6] The long-term maternal, fetal and neonatal outcomes in the severely hypokalaemic mother, would be of interest.

The author has no conflict of interest.

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Atypical presentation of HIV in a pregnant patient

Editor,

We report a case of Kaposi's sarcoma (KS) of the epiglottis in a pregnant lady who presented with stridor. It is very rare for stridor caused by laryngeal KS to be the initial presentation of HIV infection in a pregnant patient that has not been previously reported.

Case Report: A 33-year-old, 13 weeks pregnant lady presented with shortness of breath and noisy breathing. She also had odynophagia, bilateral neck swelling, sore throat and night sweats for the past 3 days. She had a discharging ear and a chronic non-productive cough for 3-6 weeks. Distaclor, commenced initially, was discontinued when she was confirmed to be pregnant. She was on nystatin mouthwashes for her oral thrush. She was a non-smoker and took alcohol occasionally. There was no history of intravenous drug abuse or other risk factors for HIV infection.

On examination she was pyrexic, had inspiratory stridor, tachycardia and tachypnoea. Oral cavity and oropharynx examination revealed extensive candidiasis.

Flexible nasoendoscopy revealed a very large, oedematous and inflamed epiglottis with extensive white patches. The epiglottic swelling was so large that the vocal cords could not be visualized and only the posterior portion of the arytenoids was seen. Neck examination revealed bilateral cervical lymphadenopathy. Lateral soft tissue X-ray of the neck revealed an enlarged epiglottis and a normal trachea. Chest X-ray was clear. Full blood count showed WCC - 6.1×10^9/L, Hb - 13.2 g/dl and platelets – 215×10^9/L. Routine blood tests and viral serology was normal. Her CD4 count was 40/mm^3.

A provisional diagnosis of severe fungal / bacterial epiglottitis was made. The treatment regime included high dose of intravenous fluconazole, cefuroxime, metronidazole and nystatin mouthwashes. An HIV test was positive which was again confirmed on retesting.

An ultrasound scan revealed an anembryonic and nonviable pregnancy. After discussion with the patient she had a medical evacuation of the pregnancy with mifepristone.

Anti-retroviral therapy and prophylaxis with co-trimoxazole, azithromycin and dapsone was commenced. Two weeks later on review with flexible nasoendoscopy, the epiglottis still appeared inflamed and grossly swollen. A CT scan of the neck and upper thorax showed a 4 cm swelling of the epiglottis extending down into the aryepigolttic folds and into the vestibule. Bilateral cervical lymphadenopathy was also noted on the CT (*Fig 1*).

In view of her slow recovery, a microlaryngoscopy and biopsies of the epiglottis were performed to reach a firm diagnosis. The histopathology revealed necrotic inflammatory tissue with ulceration and dense proliferation of anastomosing vascular channels. A tentative diagnosis of KS was made. The specimen was sent to a tertiary referral centre for human herpes virus 8 (HHV8) staining which proved positive. The diagnosis was finally confirmed when the samples were sent to the national center of KS pathology.

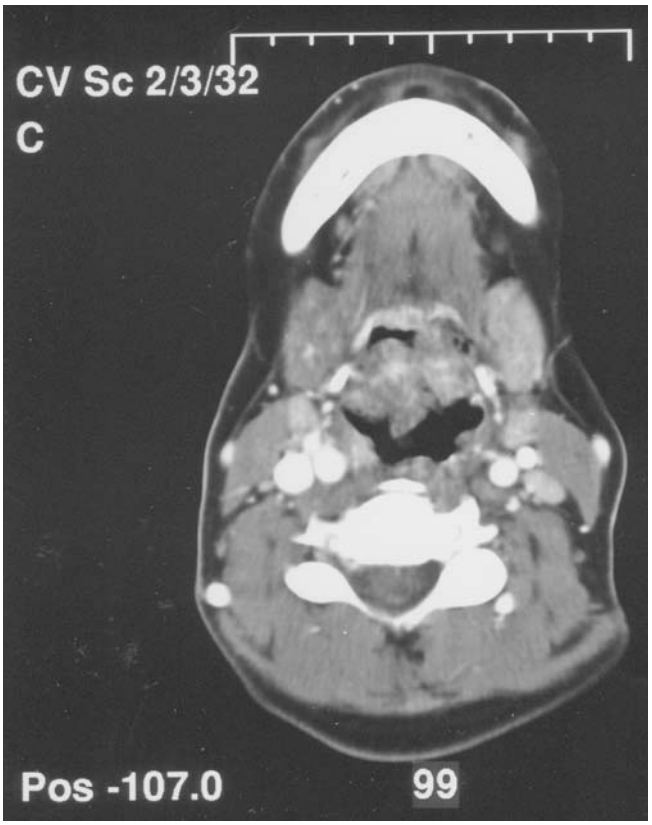

Fig 1. Axial CT scan of the neck showing the grossly enlarged and irregular epiglottis with bilateral cervical lymphadenopathy.

Antiretroviral medical therapy, consisting of efavirenz and zidovudine, was commenced and the patient's symptoms regressed. Eight weeks after her initial presentation the larynx appeared normal, her viral load was undetectable and her CD4 count was raising.

DISCUSSION

The diagnosis was difficult as the patient had no risk factors for HIV infection. Extensive oropharyngeal candidiasis and the fungal appearance of the epiglottitis should alert the clinician to the likelihood of immunosuppression. In such cases a HIV test and an examination and biopsy under general anaesthetic is necessary for histological diagnosis.

This case is noteworthy in three aspects: first – KS of the epiglottis is itself very rare, second – the patient was pregnant, and third – KS with stridor is an atypical initial presentation of HIV infection. Clinicians should be aware of this rare condition as a cause of airway obstruction in the immunocompromised.

The authors have no conflict of interest.

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Abstracts

Ulster Society of Internal Medicine

Autumn Meeting, Friday 21st October 2005

The Board Room, King Edward Building, Royal Victoria Hospital

PROGRAMME

2.00 pm Welcome

2.15pm Presented Abstracts

3.15pm Invited Abstract: Is there a place for liver transplantation from living donors? Dr John O'Grady, Consultant Hepatologist, Liver Unit, Kings College Hospital, London.

3.40pm Tea/Coffee

4.00pm Presented Abstracts

4.35pm Guest Lecture: Prospects for stem cell therapy in cardiac regeneration. Prof Tim O'Brien, Director, Regenerative Medicine Institute, National University of Ireland, Galway.

5.30pm Close

PRESENTED ABSTRACTS

Use of Estimated Glomerular Filtration Rate (eGFR) To Guide Nephrological Referral for Patients with Stage 4 Chronic Kidney Disease (CKD): Service Implications.

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Current guidelines recommend nephrology referral when eGFR <30mls/min. To determine the implications of this guideline on our nephrology unit which serves the Southern Health and Social Services Board (SHSSB) area of Northern Ireland (population 320, 000) we identified: (i) the number of patients in this area with an eGFR of 15-29 mls/min (stage 4 CKD) (ii) the factors influencing outcomes (dialysis or death) in this group.

Laboratory tests of renal function performed in 2001 were screened to identify all patients with an eGFR of 15-29 mls/min. An electronic database identified all patients referred to our unit between June 1998 and December 2000 with stage 4 CKD. Baseline and follow–up data including eGFR, 24hr proteinuria, blood pressure and death or need for dialysis was obtained.

In 2001, 1,730 patients with stage 4 CKD were identified, of whom 176 (10.2%) were known to the nephrology service. Between June 1998 and December 2000, 95 patients were referred with CKD stage 4, of whom 25% required dialysis within 5 years. This group had a lower baseline mean eGFR (21.0 vs.24.9mls/min, p=0.0001) and a higher mean proteinuria (2.42 vs. 0.81g/dL, p=0.01) than those who remained dialysis-independent. 50%, 33% and 9% of patients with baseline eGFR of 15-19, 20-24 and 25-29 mls/min respectively required dialysis. Currently guidelines require nephrological referral for a large number of persons, of whom only 25% require dialysis within 5 years. Future guidelines should focus on a demonstrated decline in eGFR and level of proteinuria rather than a threshold level of eGFR.

The MEF2A gene and ischaemic heart disease in Ireland.

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Ischaemic heart disease (IHD) is a complex disease due to the combination of environmental and genetic factors. The MEF2A gene codes for an important protein in myocardial muscle development. In a large US family a 21bp deletion (Δ7aa) was reported to be associated with IHD with an autosomal dominant pattern of inheritance (Wang *et al*. Science, 2003). We investigated this region of the MEF2A gene using an Irish family-based study, where affected individuals had early-onset IHD.

A total of 1494 individuals from 580 families were included (800 discordant sib-pairs and 64 parent-child trios). The Δ7aa region of the MEF2A gene was investigated based on amplicon size.

The Δ7aa mutation was not detected in any individual. Coincidentally, considerable variation in the number of CAG (glutamate) and CCG (proline) residues was detected in a nearby region. However, this was not found to be associated with IHD.

The Δ7aa mutation was not detected in any individual within the study population and is unlikely to play a significant role in the development of IHD in Ireland. Using family-based tests of association the number of tri-nucleotide repeats in a nearby region of the MEF2A gene was not associated with IHD in our study group.

Comparison of cardiovascular risk factors in rheumatoid arthritis and osteoporosis

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[1] Department of Rheumatology, Royal Victoria Hospital, Belfast.

[2] Department of Rheumatology, Musgrave Park Hospital, Belfast.

There is increasing awareness of the importance of cardiovascular risk control in rheumatoid disease, and more recently speculation that osteoporosis may also carry an increased risk of atherosclerotic disease.

We performed a comprehensive risk analysis on 100 rheumatoid arthritis (RA) patients (20 male, 80 female, median age 60.0 years 95%CI 57.0-62.0) and 30 primary osteoporosis patients (3 male, 27 female, median age 67.5 years, 95%CI 62.8-70.0) in the outpatient setting. 8% of RA patients had a personal history of MI or stroke, compared with none of the osteoporosis cohort, although only 62% of RA had a BP check in the last year, and 28% a fasting cholesterol check, compared with 83% and 47% in osteoporosis patients.

17% of both RA and osteoporosis patients had systolic BP >160mmHg, and 17% and 18% respectively diastolic BP >90mmHg. There was an interesting correlation between diastolic BP and low trauma fracture in the osteoporotic patients ($r=0.56$, $p<0.01$), and between diastolic BP and BMI in RA patients ($r=0.37$, $p<0.01$). HDL:cholesterol ratio correlated with BMD at spine in the osteoporosis group ($r=0.51$, $p=0.01$). 57% of osteoporosis patients, and 54% of RA patients had fasting cholesterol levels >5.2. 4 RA patients and none of the osteoporosis patients were taking lipid-lowering drugs.

Conclusion: Levels of cardiovascular risk were similar in both RA, a disease with known accelerated atherosclerosis, and osteoporosis, although monitoring appeared better in the osteoporosis group. Despite this, a substantial unmet need remains. A possible correlation between cardiovascular risk factors and bone health requires further investigation.

Diet and insulin resistance: comparison of high and low sucrose diets, a randomised controlled trial.

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[2] Department of Medicine, Queen's University Belfast, BT12 6BJ.

The long-term impact of dietary carbohydrate, in particular sucrose, on insulin resistance and the development of diabetes and atherosclerosis is not established. Current guidelines advise restriction of sucrose intake to 10% of total energy intake.

We investigated the effect of a high versus low sucrose diet (25% versus 10% of total energy intake). Thirteen healthy male volunteers, aged 34 ± 3 years (mean ± SEM), BMI 26.7 ± 0.9kg/m2 were included in a randomised crossover design with sequential 6-week dietary interventions separated by 4-week wash-out.

Weight maintenance diets with constant macronutrient profiles and fibre content were designed. Subjects were monitored and all food was weighed and distributed 3-5 times weekly. Insulin action was assessed using a 2-step euglycaemic clamp and the isotope dilution method (3-3H glucose) was used to determine glucose utilisation and endogenous glucose production rates.

There was no change in weight or physical activity during the study period. Suppression of endogenous glucose production was similar after each diet. At an insulin infusion rate of 2mU/kg/min, the peripheral glucose utilisation after 25% sucrose diet was 57.0 ± 4.9 mmol/kg/min compared to 47.6 ± 3.6 mmol/kg/min after a 10% sucrose diet, p=NS.

In this study, a high-sucrose intake as part of a eucaloric, weight-maintaining diet had no detrimental effect on insulin sensitivity in healthy non-diabetic subjects. These results suggest that than carbohydrate quality may be a less important determinant of insulin action than caloric excess, physical activity or weight gain.

Takotsubo cardiomyopathy: an uncommon cause of acute ST-segment elevation on the 12 lead electrocardiogram

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[2] Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast.

[3] Regional Intensive Care Unit, Royal Victoria Hospital, Belfast.

A 63 year old female was admitted with a three month history of increasing lethargy, anorexia, diarrhoea, weight loss, depression and confusion. Past medical history included hypertension, cerebrovascular disease, heavy smoking and alcohol abuse. On clinical examination she was dehydrated, malnourished and disorientated. Initial laboratory investigations demonstrated anemia and thrombocytopenia. A profound hypokalemic hypochloremic metabolic alkalosis was present. Proteinuria was noted. Chest radiograph was normal. Electrocardiography demonstrated a prolonged corrected QT interval. Treatment with empirical intravenous antibiotics, electrolyte replacement, red cell and platelet transfusion was instituted. Computed tomography of brain, cardiac and abdominal ultrasonography were initially normal. On the sixth day following admission the patient developed fluid overload with type I respiratory failure and radiographical evidence of pulmonary oedema. She was transferred for intensive care

and required intravenous antibiotics, diuretics, non-invasive ventilation and inotropic support.

On the tenth day the patient deteriorated acutely. Repeat electrocardiography revealed ST-elevation consistent with acute inferoposterolateral myocardial infarction. Echocardiography demonstrated corresponding wall motion abnormalities. Emergency coronary angiography revealed no causative atherosclerotic, thrombotic, embolic or vasospastic lesion. Left ventriculography showed inferoposterolateral akinesia in keeping with Takotsubo cardiomyopathy.

Takotsubo cardiomyopathy is a recently recognised cause of acute reversible left ventricular systolic dysfunction. The condition typically affects elderly females and presents with clinical and electrocardiographic features mimicking acute myocardial infarction. A characteristic ventricular wall motion abnormality (apical ballooning) is observed. The condition is often associated with acute physical or psychological stress and may result from catecholamine excess. Patients surviving the acute phase tend to recover spontaneously.

Type 1 diabetes and road traffic incidents: a case control study.

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[2] Regional Centre for Diabetes and Endocrinology, the Royal Hospitals, Belfast.

[3] Department of Epidemiology and Public Health, Queens University, Belfast.

Type 1 diabetes in drivers of motor vehicles is assumed to be a hazard for road safety. Identification of particular risk factors may enable preventive strategies. We performed a case referent study to identify factors linked to road traffic incidents in drivers with type 1 diabetes.

An initial postal questionnaire was sent to a population of 942 patients with type 1 diabetes mellitus attending the Diabetes clinic at the Royal Victoria Hospital, Belfast. Four hundred and eighty two responders included 311 eligible participants and 171 who were ineligible. Structured telephone interviews were undertaken with the 311, identifying 92 cases (who had a road traffic incident in the past 2 years) and 219 referents.

Following multivariate analysis, risk factors for road traffic incidents were the absence of awareness of hypoglycaemic symptoms (OR 44.2, $p<0.001$), the presence of only neuroglycopaenic symptoms of hypoglycaemia (OR 7.4, $p<0.01$), higher insulin dose (OR 5.3, $p<0.01$), a frequency of driving 5+ times per day (OR 5.6, $p<0.001$), a history of having a previous hypoglycaemic episode while driving without taking sugar (OR 22.6, $p<0.01$) and being on a Beta Blocker (OR 6.1, $p<0.01$). Higher HbA1C level was protective (OR 0.3, $p<0.001$), as was testing blood sugar before driving (OR 0.2, $p<0.001$).

In conclusion the results demonstrate that intensive blood glucose management, hypoglycaemia unawareness and frequent driving are risk factors for road traffic incidents. Patients, clinicians and occupational physicians should be aware of these risk factors and of the protective value of self blood glucose monitoring before driving.

Use of N-Terminal-pro-Brain Natriuretic Peptide in the Diagnosis of Ischaemic Heart Disease in Patients Presenting to a Rapid Access Chest Pain Clinic.

AR Muir, J Neill, J Dougan, AAJ Adgey, Department of Cardiology, Royal Victoria Hospital, Belfast.

N-terminal-pro-BNP (NT-pro-BNP) is a proven diagnostic marker of congestive heart failure and predictor of recurrent ischaemic events and mortality in both stable and unstable ischaemic heart disease (IHD).[1,2]

We hypothesized that NT-pro-BNP may be a useful diagnostic marker for IHD in patients presenting with previously undiagnosed chest pain to a rapid access chest pain clinic. NT-pro-BNP was compared as a diagnostic marker to standard risk stratification methods combined with exercise stress testing. Positive diagnosis ranged from acute coronary syndrome to possible IHD requiring further investigation.

447 consecutive patients were studied. NT-pro-BNP was significantly higher among those diagnosed with IHD versus non-IHD (95ng/L [interquartile range 44 to 199] vs 43ng/L [interquartile range 22 to 72] $p=0.029$). Patients in the highest NT-pro-BNP quartile were older, had lower creatinine clearance and more cardiovascular risk factors than those in the lowest quartile. Those in the highest quartile were statistically significantly more likely to have a positive exercise stress test (EST) ($p<0.001$).

Following logistic regression analysis, NT-pro-BNP in the highest quartile was predictive of a diagnosis of IHD, independent of standard risk factor profile and biochemical markers including creatinine clearance and troponin I ($p=0.001$). After inclusion of EST result in the regression model, no NT-pro-BNP quartile was a significant predictor of IHD ($p=0.988$).

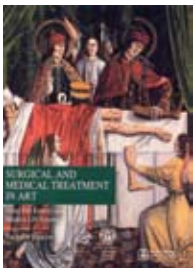
In the setting of a rapid access chest pain clinic, NT-pro-BNP quartile does not improve IHD diagnosis more than an EST. It may be a useful prognostic indicator of morbidity and mortality in this group, and follow up data will be useful.

1. Kragelund C, Gronning B, Kober L, Hildebrant P, Steffensen R. N-Terminal Pro-B-type natriuretic peptide and long-term mortality in stable coronary heart disease. *N Engl J Med* 2005; **352:** 666-75.

2. Omland T, Persson A, Ng L, O'Brien R, Karlsson T, Herlitz J, Hartford M, Caidahl K. N-Terminal Pro-B-type natriuretic peptide and long-term mortality in acute coronary syndromes. *Circulation* 2002; **106:** 2913-18.

Book Reviews

Surgical And Medical Treatment In Art: Alan EH Emery, Marcia LH Emery. Royal Society Of Medicine Press, October 2005. 138pp. £45.00. ISBN 1-853-15695-7



This is a fascinating compilation of sixty-six paintings chosen by the authors to demonstrate the relationship between medicine and art from 1275 BC to 2002. Paintings are taken from all over the world and deal with all branches of medicine (including some which are no longer mainline practice!).

Each painting is accompanied with a potted biography of the artist and a commentary which places the painting in its context: sociological, medical and artistic.

Whilst I was aware of some of the paintings, many are new to me. I particularly liked the portrait of Sir Alexander Morrison by Richard Dadd – the father of Psychiatry in the United Kingdom. This is a stunning portrait by an inmate and is absolutely timeless in its style.

The mediaeval representations of consultations between doctor and patient show just how much medicine has changed. Although on the previous page, the mediaeval surgery on haemorrhoids is a little distressing! In a wider sense, it is fascinating to see how our work has progressed over the years particularly since the Renaissance. It is also fascinating to see just how atmospheric so many of the paintings are – for example, that of Theodore Billroth operating by Sligenn. Here, we have a Master at work with seven scrubbed attendants and at least forty observers. Given the increasing numbers of medical students expected in our own medical school in Belfast, could this be the way of the future?

I would commend this beautiful book to all with an interest in medical and surgical art: it is a fascinating read.

NEIL McCLURE

Natural Standard Herb & Supplement Handbook – The Clinical Bottom Line: Ethan M Basch, Catherine E Ulbricht. Mosby. December 2004, 1008pp. £26.99. ISBN 0-323-02993-0

Those of us who has been in clinical practice for many years will have undoubtedly encountered the patient who despite our best intentions is never cured or relieved of their symptoms by conventional medicines. Then one day they come into your consulting room and announce that they have been to an alternative practitioner, who has prescribed homeopathic medicine and this has miraculously cured them.

Due to several experiences like this, I looked into the possibility of prescribing homeopathic medicine and I consulted the available textbooks. None really attempted to look at the various homeopathic medicines on a scientific basis. One was expected to believe that they all worked because the author stated that they did.

However, at that time I wish I had had a book like this, which does attempt to try and bring a scientific basis to homeopathy and makes judgements on the basis of proper scientific trials. The qualifications of the chief editors are beyond dispute; one having received his medical degree from Harvard Medical School and the other a senior attending pharmacist at the Massachusetts General Hospital. Likewise, the qualifications of the senior editorial board and contributors to this book again are excellent. Some are qualified doctors, some are pharmacists and some have engaged in research into homeopathic medicines.

The format of the book makes it excellent as a reference to look up those medicines that your patient has been taking. The various potions are arranged in alphabetical order. Each condition is listed for which the substance could be used and given one of the grades below to show how effective the substance is in treating the condition.

A. There is strong scientific evidence that the medicine is of benefit.

B. There is good scientific evidence that the medicine is of benefit

C. There is unclear or conflicting scientific evidence that the medicine is of benefit

D. There is fair negative scientific evidence that the medicine has no benefit

E. There is strong negative evidence that the medicine has no benefit

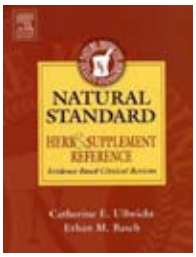
Fish oil is one of the substances evaluated. It is rated grade A for treatment of high blood pressure and for prevention of cardiovascular disease, a fact few cardiologists would dispute. It is given a C for treatment of depression and dysmenorrhea and D for diabetes.

Tea tree oil, which is used, for treatment of children's skin infections is given a C grade for treatment of several specific skin infections and a D grade for mouth plaque.

Melatonin is given grades A and B for several sleep disorders including jet lag. I know from my practice that it is beneficial for children with learning difficulties who have sleep problems. It is graded C for several other disorders from seizures to thrombocytopaenia.

I would recommend this book as a useful addition to the reference library for any clinician in order to keep up with what the patients (or their parents) are telling us.

CHARLES SHEPHERD



Natural standard herb and supplement reference: evidence based clinical reviews. Catherine E Ulbricht, Ethan M Basch. Mosby. January 2005, 1040pp. £75.99. ISBN 0-323-02994-9.

This is a very well referenced source providing detailed evidence-based systematic reviews for almost 100 herbs and supplements. It is particularly valuable for those clinicians who are using or who wish to use herbal medicine in their everyday practice and for doctors and patients who wish to know more about the efficacy and tolerability of herbal medicines. The volume confirms that although a few complementary treatments have been assessed in well-designed clinical trials, high quality information relating to effectiveness, dosage, mechanism of action and safety is limited or controversial for most therapies tested. As a result for almost all the products listed it is not possible to guarantee strength, purity or safety of products even though some have been shown to have clinical benefit.

More than 100 health professionals have contributed to the volume, mostly physicians and pharmacists but also nurses, microbiologists, educationalists, herbalists and other alternative practitioners and over 40 contributors make up the Editorial Board. The text is arranged alphabetically starting with Acidophilus and finishing with Yohimbe Bark. The layout is highly structured and easy to use as a reference source. The main headings are synonyms for the substance, clinical 'bottom line', grades of scientific evidence, summary table, dose and standardization of formulation, adverse effects, interactions and use in pregnancy. The grades of scientific evidence range from A to F with levels below B representing no evidence or evidence against the clinical effectiveness of the product. Grade A implies that there are more than 2 studies of reasonable design supporting the use of the substance and Grade B that there are one or two clinical trials. Overall Grade A evidence is rarely very good and the studies do not compare with the outcome trials undertaken within conventional medicine in terms of design, statistical power and analysis. Based on A and B grades there are a few surprises. I am sure that those physicians managing dementia and heart disease would be surprised that Ginkgo biloba and Ginseng are useful for enhancing memory and that Hawthorne gets an A Grade for the treatment of congestive heart failure. The latter benefit appears to be for Grades 1 and 2 New York Heart Association Classification, which is notoriously difficult to define accurately. Hepatologists might also like to know that Milk Thistle improves liver function tests in patients with chronic liver disease and urologists might be interested that Pygeum Africanum and Saw Palmetto might improve symptoms and reduce the size of the gland in patients with benign prostatic hypertrophy.

Otherwise most of the findings are as expected. Ephedra remains a very toxic substance with no clinical benefit and adverse effects and addiction potential similar to amphetamines and cocaine. Several dietary agents appear to lower the serum cholesterol – barley, soya, almonds, yeasts, garlic and fish oils and some evidence exists for feverfew in migraine prophylaxis and for St. John's Wort in depression. A number of agents are confirmed as having some analgesic or anti-inflammatory activity – Boswellia Serrata, Devil's Claw, Glucosamine, hypoglycaemic effects – Bitter Melon, Gymnema Sylvestre, and others appear useful for sleep disturbance – Valerian Officinalis, Melatonin. Cranberry juice and echinacea may be useful for urinary and upper respiratory infections.

The two final appendices, A and B, relate to drug interactions and conditions tables. In Appendix A a list of possible pharmacodynamic and pharmacokinetic interactions are listed. Unfortunately, reporting is generally low or goes undetected and the interactions are mostly based on additive effects of similar acting drugs, expert opinion and anecdote rather than clinical studies. The best evidence available relates to St. John's Wort, its interactions with antidepressant drugs and its effect as an enzyme inducer/inhibitor. Appendix B deals with the different medical conditions for which herbs and supplements have been used. These are also arranged alphabetically and identify treatments for which Grades A-D evidence is available. This section is likely to be consulted even more than the main alphabetical section as a rapid treatment reference.

In conclusion, this volume represents a most reliable source of up-to-date and balanced information on herbal medicine and the use of supplements. It provides an extremely useful systematic and easy to read resource for all drug prescribers with evidence-based reviews to identify the small amount of wheat from the large quantity of chaff in this area of alternative medicine.

DENIS JOHNSTON

Medical Word Su Doku: Bk. 1: Ayan Panja, The Royal Society Of Medicine Press Ltd, December 2005. 80pp. £4.99. ISBN 1-853-15613-2

I'll be honest here – I don't really know why Sudoku has taken off to the extent it has. You can't walk into a bookshop on the high street (and certainly not the airport) without tripping over stands of the latest compendia of Sudoku and its multifarious variants. The ubiquitous Carol Vorderman has become the Sudoku poster-girl, although quite why that should be escapes me also, unless the intellectual reputation of the TV show "Countdown" is more extensive than I had thought. Whatever the underlying explanation, this puzzle fad certainly seems to have grown into quite a phenomenon.

The first sighting of this puzzle appears to have been in the pages of the magazine Scientific American many years ago. The "Number in Place" puzzle, as it was then, was re-used in several subsequent publications, before becoming a serious craze in Japan in the 1980s. It entered the British press in the early 2000s, with the Daily Mail and Times running it under its exotic Japanese name (which, I am led to believe, is an abbreviation for Japanese for "Number in place").

And now, in 2006, the place is coming down with it.

Perhaps it is superfluous to describe the principles of Sudoku, but for the benefit of the uninitiated (non-anaesthetists, in

the main), a short explanation is probably in order. Sudoku is a logic puzzle centred around a square grid of 9 cells by 9, which is subdivided into 9 blocks of 3 cells by 3. Each cell contains one of the digits 1-9 (but any letter or symbol can be used, as there is no arithmetical relationship between the numbers). The fundamental rule is this: each row, each column, and each 3x3 block must contain only one instance of each digit (or letter or symbol). Each individual puzzle is seeded with some digits already in place, and your role, as the Sudokeur (I made that up) is to put all the other digits back in place, and complete the grid. That's all there is to it – a puzzle of pure unadulterated logic.

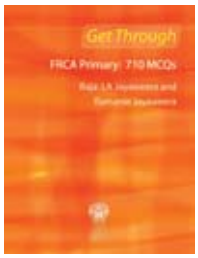
The best strategy is usually to start with the digit/letter/symbol which is most frequent in the grid, and systematically work out where its remaining instances should be placed. At one level, it seems very straightforward (as indeed it is), but in the more advanced puzzles, the logical analysis required can be quite intensive. Apparently the first World Sudoku Championships are to be held later in 2006, which suggests to me that there are some people who have far far too much time on their hands.

So how would one go about constructing a Sudoku puzzle to appeal to medics? In "Medical Word Sudoku", Ayan Panja has woven a classic anagram puzzle into a Sudoku, the tag being that each anagram is a medical word. Of course, for a Sudoku to work, each word must have exactly nine letters, and each of the nine letters must occur only once. An extra clue is that the word itself will occur somewhere (forwards, backwards, up, down) within the Sudoku grid, so once you've solved a few of the cells, and solved the anagram, you can figure out where to place the word, and this will provide extra clues to help you complete the full thing.

I have to say, I was initially rather sceptical. Weaving medical words into such a puzzle struck me as potentially a bit elitist; if nothing else, unless granny was a doctor, she wasn't going to be as much help with solving one of these as she would be with cryptic crosswords. But, despite these preliminary misgivings, Medical Word Sudoku is surprisingly enjoyable and engaging, if you have a moment or two to spare. The puzzles are arranged in four categories, based on difficulty: "Medical Student", "Junior Doctor", "Consultant/GP" and "Professor". I'm sure there is more than a hint of irony behind these classifications, but suffice it to say that the Medical Student ones are pretty easy, and the Professor ones can be fiendishly tricky – especially if you have difficulty solving the anagrams.

Ayan Panja has done a good job in crafting some slippery Sudoku problems, which will keep both afficionados and novices amused. There are some psychologists who recommend Sudoku as a mental exercise to keep the grey cells in trim; maybe we should be recommending this book to our juniors, with the firm instruction that they must progress to "Professor" level before they can complete their specialist training. On the other hand, maybe life is too short for all this, but if you're into puzzles, I think you'll find that this book hits the spot pretty well – and not a Carol Vorderman in sight.

SHANE McKEE



Get Through FRCA Primary – 710 MCQ's: Raja LA Jayaweera, Ramanie Jayaweera. The Royal Society of Medicine Press Ltd, London, UK. October 2005. 347pp. £19.95. ISBN 1-85315-666-3

There are a number of books on Multiple Choice Questions (with answers) for candidates taking the FRCA examination. These include books published by the Royal College of Anaesthetists itself for both the Primary and the Final FRCA examinations.

This book follows the usual pattern of questions followed by answers in a separate section. The book itself is divided into two sections. There is an initial section of 260 questions followed by section 2 which has 5 practice papers of 90 questions each. Although the initial section contains only 260 questions, the questions in the practice papers add further volume to the overall bank of questions.

The 260 questions in the first section are divided into 10 questions on anatomy, 128 on physiology, 66 on pharmacology, 44 on physics and 12 on other subjects. The physiology section is split into different sub-sections dealing with the cardiovascular, the respiratory, the liver, the central nervous systems and a sub-section on general physiology. I could not find any questions on renal physiology. The pharmacology part is relatively small with a total of 66 questions all grouped together in a somewhat uneven pattern.

Although the questions conform to the usual FRCA examination style there is some imbalance in the content. I found very few questions on opioids which is a big area in the examination and some of the questions related to drugs such as nalbuphine and propoxyphene are probably not relevant now. There are also fewer questions on the pharmacology on the basic aspects of drug action such as pharmacokinetics, receptor classification and drug-receptor interactions. There are also not many questions on newer local anaesthetics.

I would regard this as an average book which has questions which many of which do not examine the knowledge in depth. It will however be useful for candidates for practice so that they can perfect their timing etc. It should also be remembered that the candidates still need a good textbook knowledge to be able to do the MCQs. The content and the depth of the questions might reflect the relative lack of experience of the authors in the examination process and the technique, but overall, the book is good value for £19.95.

RAJINDER K MIRAKHUR

First Steps In Vesico-Vaginal Fistula Repair: Brian Hancock, The Royal Society of Medicine Press Ltd, London, UK. August 2005. 63pp. £19.95. ISBN 1-85315-611-6

Vesico-vaginal fistula is a rare occurrence in the UK and is usually associated with malignant disease or trauma (including surgical trauma). However in Africa it is

relatively more common and indicative of the poor standards of obstetric care that prevail in many parts of the continent.

This slim and easy to read volume deals with the aetiology of obstetric causes of Vesico-vaginal fistula (VVF) and the variety of fistulae encountered.

The main purpose of the book is to demonstrate to potential fistula surgeons that this is an important problem, which can and should be addressed by more surgeons than at present. By careful patient selections, a surgeon can build up experience based on simple cases which yield good results before embarking on more challenging operations. There are step by step descriptions of procedures illustrated with excellent photographs and adequate text devoted to postoperative care and complications. Whilst this book is aimed at surgeons who are considering performing fistula surgery it is of interest to all gynaecologist's and urologist's who may never encounter this type of problem. It is particularly easy to read and should be considered essential reading for anyone who is considering working on the African continent.

If there is any criticism it is the lack of information about the personal disaster that VVF represents to the individual. Not only have they lost their baby they are left in pain, discomfort and misery compounded by abandonment from their partner, family and society.

Millions of women are consigned to this fate in Africa and their only hope is to meet a caring surgeon such as Mr Hancock who can restore normal function for the vast majority of patients.

JOHN H PRICE

Teleneurology: Richard Wootton, Victor Patterson (Eds). Royal Society Of Medicine Press, London. April 2005. 208pp. £24.95. ISBN 1-85315-671-X.

My first introduction to telemedicine was rather off-putting for reasons not directly related to the process itself so unfortunately I became a bit of a "telesceptic" for a while until I had further exposure. Happily, subsequent experiences have been much more positive culminating in this book which has been a pleasure to read.

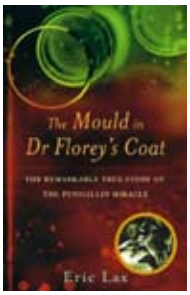
The editors have assembled a series of excellent reviews of aspects of teleneurology – that is the delivery of neurological care at a distance. All of these are clearly written, and include a review of relevant literature, description of how the authors' personal services are provided plus some analysis of benefits and mention of problems and pitfalls. I would point out that in places the references to the literature are somewhat wanting, for example there are many publications on the use of telemedicine for remote consultation in paediatric cardiology. In addition many of us had not considered telephone advice as a type of telemedicine so that most of us practise it already.

The chapters are divided in three sections: techniques; applications and practical issues. Within these sections teleneurology by telephone, email and videoconferencing are described in a range of neurological disciplines and specialisms – epilepsy, stroke, rehabilitation, radiology, clinical neurophysiology, paediatric neurology and the developing world. Practical issues are covered in some detail and there are excellent chapters on websites and educational applications. High points for me were the involvement of nurses, application to rehabilitation; "physiotherapy at a distance" and the use of email consultation to assist colleagues in the developing world.

While there is, of necessity, some technical information, this is mercifully kept to a minimum. The review of equipment choice is straightforward. However since the technical competence of any system used for delivery of telemedicine is fundamental to success, the advice to ensure adequate technical advice and backup at all stages is appropriately emphasised. The details of different modes of connection should be reasonably comprehensible to the average clinician (whoever that is) and presumably will be second nature to our increasingly ICT-competent trainees.

I strongly recommend this book to everyone engaged in the practice of clinical neurology and equally importantly to those with responsibility for the commissioning and management of services for people with neurological disorders.

ELAINE M HICKS



The Mould in Dr Florey's Coat: Eric Lax. Abacus, 2005. 389pp. £9.99. ISBN 0-3491-1768-3.

The sub-title of the book is "The Remarkable True Story of the Penicillin Miracle". The author had the full cooperation of Florey's family and the widow of the third member of the Oxford team, Dr Norman Heatley. It gives a very readable account of the discovery of penicillin by Fleming and its development in Oxford by Florey, Chain and Heatley. Also for the first time, in an easily accessible manner, it records the work done by the biochemist Heatley, for many years the unsung hero of the miracle.

The first chapter has the heading "The Quiet Scot" and records Fleming's discovery of lysozyme the "antibiotic" that occurs widely throughout nature. The bacteria that it does not destroy are, of course, the pathogens. Dr VD Allison was a research student with Fleming when lysozyme was discovered and while working with Fleming, he made lysozyme the subject of his MD thesis. He came to Belfast as a Bacteriologist and ended his career as Director of Laboratory Services for the Northern Ireland Hospitals Authority.

Lax deals briefly with Fleming's war work in a makeshift laboratory near Boulogne where he worked with Thomson, later Sir William, Professor of Medicine, Queen's University, Belfast. However most of the chapter describes the discovery of penicillin and Fleming's attempt to isolate it and how his papers and lectures were completely ignored.

The book is particularly good at describing the very different personalities of the main collaborators: Florey, the bluff, taciturn, irascible Australian who was always "The

Professor" who, frequently was unable to praise a junior to his face but was fulsome in his praise to other people. Lax calls him "The Rough Colonial Genius". He was the clinical physiologist who had the brain wave to look for a biological drug better than the recently introduced sulphonamides. Chain, "The Temperamental Continental" – a refugee, some of whose family were eventually murdered in the holocaust. He anticipated criticism where none was intended and reacted over sensitively to any disagreement. He thought the laboratory should be run on the same lines as in Germany – a strict hierarchy with everyone doing what the chief wanted without discussion or demur. Before starting any research he explored the literature and found the long-forgotten paper on penicillin by Fleming.

The third member of the triumvirate was Heatley the diffident English gentleman easy to work with and respected and beloved by the technical staff. The contrast with Chain could not be more marked – "…. he and Chain were opposites in temperament, in personality, in scientific approach … Heatley was reticent and shy, Chain was voluble and demonstrative; Heatley was reluctant to seek credit, Chain was quick to claim his due."

Chain was a very difficult colleague. Sometimes when he and Florey were arguing the very walls of the room seemed to vibrate. Although Heatley worked with Chain he collaborated with Florey.

Heatley, a biochemist was also an expert in the recently introduced technique of micro-assay and developed a technique of measuring the potency of any sample of penicillin in what became internationally known as Oxford units. His first task was to culture sufficient penicillium from which Chain was to extract the active principle – penicillin and determine its formula. However penicillin proved to be highly unstable and Chain was making very little headway in isolating it. That problem was not solved until after Heatley joined the team.

Vast quantities of culture medium were required for the isolation of a minute quantity of the active principle. All sorts of containers were used – bedpans were the best but took up too much room in a steriliser. Heatley devised and had made rectangular "bedpans" that proved eminently suitable. He also invented and built an apparatus from bits and pieces and glassware that he made himself for the continuous extraction of what at first was thought to be pure penicillin. The first isolated powder was yellow and later shown to be only 1 percent pure. When Heatley suggested that the yellow colour was not the active principle he was shouted down by Chain but went on to prove that he was right.

"Without Heatley, No Penicillin" is the heading of one chapter. The phrase was coined by Professor Sir Henry Harris, a successor to Florey as head of the Sir William Dunn School of Pathology where the "miracle" happened.

Three very different men, each a genius in his own field, fortuitously came together and isolated penicillin, a task that Fleming had been unable to accomplish. Its wonderful power in killing staphylococci in vitro and in vivo in mice was soon proven. And it was not long before an expanded team demonstrated its life-saving power in humans.

All the pharmaceutical firms in Britain were too fully committed to war work to undertake the commercial production of penicillin. Florey and Heatley went to the United States of America to get that started. Fortunately, using apparatus unavailable in England, a method of deep culture of the penicillium was discovered. Also a different strain of the fungus was isolated that gave a much increased yield of penicillin.

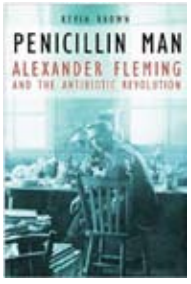
Lords Beaverbrook and Moran ensured that Fleming's discovery was well publicised, thereby getting funds for St Mary's Hospital. Fleming was by no means averse to basking in the spotlight but he did occasionally refer to the work done in Oxford. He shared the Nobel Prize with Florey and Chain, was knighted, elected to the Royal Society and received a multitude of other awards. In 1941 Florey was elected to the Royal Society mainly for work before his quest for penicillin commenced. He also received many awards, was knighted and later received a Life Peerage. Chain also was elected to the Royal Society, received many awards and was knighted. Heatley whose work had been essential received no recognition during his working life. However his widow says that he was never embittered by this oversight. He was appointed to the Order of the British Empire in 1978 and 12 years later Oxford University repented of its neglect and awarded him the first Penicillin Fellowship at Lincoln College, named the lab in which he worked for 42 years The Heatley Laboratory and instituted an annual lecture and a lectureship in his honour. Thirty years after the penicillin work was completed Oxford made him its first non-medical Honorary Doctor of Medicine.

Heatley married Mercy Bing, a medical graduate of Oxford and the daughter of the founder and first Headmaster of Rockport School Holywood, Co. Down which has honoured Heatley by naming their Science Laboratory "The Heatley Laboratory". Rockport School is celebrating its centenary this year.

There is another connection to Northern Ireland. The War Office sent Florey and Lieutenant Colonel Ian Fraser, RAMC (later Sir Ian) of the Royal Group of Hospitals, Belfast to North Africa to test penicillin in the treatment of war casualties. The taciturn Florey did not enjoy the company of the ebullient Fraser!

The Mould in Dr Florey's Coat was no accident. The three collaborators and the pathologist Sanders had penicillium spores rubbed into clothing so that, if in the war the laboratory were destroyed or three of them killed, or if the country were invaded, the research could start again elsewhere.

The Penicillin Man: Kevin Brown. Sutton Publishing, London, 2004. 320pp. £20.00. ISBN 0-7509-3152-3.



This book was published in 2004 to commemorate the 75th anniversary of Fleming's discovery of penicillin. It is subtitled "Alexander Fleming and the Antibiotic Revolution". Kevin Brown, the Trust Archivist and Alexander Fleming Laboratory Museum Curator at St Mary's NHS Trust, Paddington, is the author. Naturally Fleming takes centre

stage. Most of the book is given over to Fleming's career before and after the discovery of the bactericidal powers of the penicillium mould. Seven and five pages respectively are required to list all his publications and honours.

The work in Oxford is not neglected but is condensed to occupy about 20 pages. However the author gives a good account of the difficulties Florey and Heatley encountered in the USA when trying to interest pharmaceutical companies in the manufacture of penicillin. He also deals very well with the different attitudes in the UK and the USA to patenting.

The penultimate chapter summarises the development of subsequent antibiotics and how they have become less and less useful. "The hope is that alternative approaches to the fight against infection, such as the development of vaccines and gene therapy, will prove useful".

This book is essentially a book of reference and should be in every Medical Library as should "The Mould in Dr Florey's Coat" which is a "good read" and would be a useful addition to the library of any one interested in Medical History.

ACKNOWLEDGEMENTS

I wish to thank Dr Mercy Heatley for her cooperation and help in producing this review, Professor Richard Clarke for details of the Belfast career of Dr VD Allison and Mrs Margaret Copeland for her constructive criticism and editorial skill.

H W GALLAGHER
(Former President, Ulster Medical Society)

DVD Reviews

Birmingham PLAB Course Teaching DVD for PLAB 2 (OSCE) Series 1. Surgical Examination: Hemanth Kaukuntla, Nikhil Shah Royal Society of Medicine Press Ltd. September 2005. £24.95. 1-85315-637-X.

This DVD has been produced by the well-known Birmingham PLAB course. It is aimed at overseas doctors preparing for the PLAB Part 2 (OSCE) examination conducted by the General Medical Council.

Series 1 demonstrates the patient examination for the surgical OSCE, and the orthopaedic part of the examination. There are two other series demonstrating medical examinations and resuscitation. The demonstrations on this DVD are by a General Surgeon, and the orthopaedic demonstration is demonstrated by a Specialist Registrar.

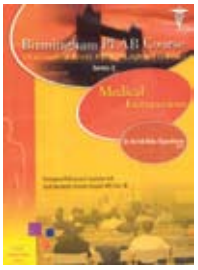
Of interest, two common areas of examination are omitted, namely, examination of herniae and examination of the breast. Apart from this, the body systems for both General Surgery and Orthopaedics are clearly outlined and a running commentary is provided by each examiner. Each station takes five minutes.

Overall, the idea is good and the DVD is helpful. However, there are some critiques which should be highlighted. In general terms, there is only one camera angle for each examination. At times, it is impossible to see precisely how certain parts of the examination are being conducted. For example, in the palpation of the distal arteries, and palpation of the liver. This critique aside, overall, the examinations are clear, although some minor points can be made about each section.

1. In the abdominal section, a lot of time is spent examining the patient's hand, tongue, eyes and neck. The ballotting of the kidney is exceedingly forceful.
2. In an examination of the thyroid gland, all our trainees are taught to use a glass of water, to ask the patient to swallow. This was omitted.
3. As mentioned, it was difficult to see the examiner examining the distal arteries in the legs. It was curious that he could not palpate the distal pulses in a patient so young. The examiner palpated the femoral artery through the clothing, and tried to listen to the femoral artery for a bruit, again through the patient's clothing!
4. The orthopaedic section was better, with a good clear introduction. However, the old-fashioned lead from the microphone attached to the examiner was a distraction. The examiner could have used his commentary better to explain in detail the words varus and valgus. The multiple tests which he did, particularly for the shoulder joint, could have been done more slowly. He could have stated more clearly which muscle group he was testing on each occasion.
5. Similarly, when he tested the muscle groups in the hand, it would have been helpful to state which muscle groups he was testing, for example, the interossei.

This DVD would be worthy of a second edition and a re-make, taking into account these comments, and with better and more professional camera work. All in all, the concept of a DVD for this purpose is to be applauded.

ROY AJ SPENCE



Birmingham PLAB Course Teaching DVD for PLAB (OSCE) Series 2. Medical Examination: Arvind Babu Rajesekaran. Royal Society of Medicine Press Ltd. September 2005. £24.95. ISBN 1-85315-642-6

The PLAB is a daunting examination for candidates, and any assistance is undoubtedly welcome. This DVD is a series of videos to take a candidate through clinical examination as required of the Objective Structured Clinical Exam (OSCE). The video quality is clear and Dr Rajesekaran's delivery is deliberate, if not rather laborious.

As a neurologist it is tempting to say that the neurology videos perpetuate myths of little benefit in a real clinical setting. Overall, a safe, traditional method of assessment is portrayed, which is far removed from working practice. To be generous, the examination technique is accurate, but does not suggest smart short cuts to make a budding candidate shine above the rest.

For PLAB candidates, this DVD is worth viewing, but it is not a substitute for that increasingly rare experience – clinical demonstration at the bedside with an expert.

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Legend for cover :

The award winning gardens of the new cancer centre for Northern Ireland

(Photo courtesy of Belfast City Hospital Trust)

See Editorial on page 110