assistance towards the restoration of external and internal appearances in the College.

Bi-monthly publication by Council of its Newsletter has been welcomed as a more rapid means of communication with the fellowship. The monthly College meeting which would, ordinarily, be the principal means of communication of College affairs, is attended by decreasing numbers of Fellows and Members. This is an unfortunate trend, probably related to demands on time and to clinical commitments, and it could be that National Health Service Trust Hospitals have brought new pressures to bear upon their staff members. Meetings in the city in the late afternoon have become a great problem for individuals. Council has been greatly concerned by the falling attendances, and has searched for better ways of involving more and more of the Fellows and Members in the corporate life.

The College Bulletin's new format, and especially the inclusion of a section of colour photographs, has been well received. The College, at the top of Blythswood Hill in St Vincent Street, is a grey edifice in a grey environment. The Saltire flies, and the College ensign flies occasionally, and they offer flickers of colour against the flat monochrome. The Bulletin tries also to add more colour, equating this, hopefully, with liveliness. As the motto says 'Non vivere sed valere vita', especially vita.

IAN D. MELVILLE

Letters to the Editor

A NEW ERA IN THE DIAGNOSIS OF BLADDER CANCER. THE BELATED CONFIRMATION OF HUBERT HUMPHREY'S DISEASE

Sir, When Hubert Humphrey, the American Vice-President, developed bladder cancer, the consensus of several skilled pathologists favoured a benign lesion although Dr John K. Frost declared the condition was malignant. His physicians settled for a conservative regime during which untreatable malignancy supervened. His history can be summarised as follows. In May 1967 he was admitted to Bethesda Naval Hospital with haematuria, Cystoscopy showed chronic proliferative cystitis and a microscopic focus of dysplastic change. The urinary sediment cells were thought to be benign. In 1969 a biopsy showed *in situ* carcinoma and he remained without symptoms for a further four years when another biopsy revealed *in situ* transitional cell carcinoma with a focus of probable microinvasive carcinoma for which he received both radiation therapy and intravesicular thiotepa. In August 1976 a biopsy showed infiltrative carcinoma and lymph node metastases were present at radical cystectomy. Humphrey died of cancer on January 13 1978. Had he lived the course of history might have changed.

What now is the best way to detect early bladder cancer? In 1987 Mullis discovered the polymerase chain reaction (PCR) by which specific regions of DNA can be copied and amplified, making possible a new approach to the study of genes. In 1991 Sidransky[1] working at the Johns Hopkins, with colleagues from other hospitals, studied invasive bladder cancer for the presence of gene mutations in the p53 suppressor gene! They suspected that the chromosome 17p deletions in bladder cancers reflected underlying mutations in the p53 suppressor gene, p53 gene mutations having been observed in other human tumours with 17p deletions. Eleven of eighteen tumours showed genetic alteration of the p53 gene. Amino acid substitution and base pair deletion were noted, leaving the affected cells with only mutant forms of the p53 gene product. They examined also the urinary sediment from three of their pateints and identified and found in them the same mutation as was in the primary tumour. A small but significant percentage of sediment cells, between 3 and 7 per cent, contained the mutation.

In 1994 Hruban and colleagues,[2] with the permission of Humphrey's widow, obtained formalin fixed paraffin blocks of the invasive bladder cancer resected in 1976. Exons 5–9 of the p53 gene were amplified by PCR and revealed, after cloning and sequencing, a transversion from adenine to thymine. Next they extracted DNA from cells on the filters prepared from Humphrey's urine when he presented in 1967. Their results showed that a number of cells in Humphrey's urine in 1967 harboured the same mutation in p53 that was present in the resected primary carcinoma in 1976. Thus these genetically abnormal cells were present two years before a diagnosis of carcinoma *in situ* and nine years before Humphrey underwent cystectomy.

Hall, Dowell and Lane[3] point out that PCR techniques are costly and are applicable only to a few laboratories.[3] Their approach is based on the over expression of the p53 protein in a wide range of malignant tumours. They recommend the use of immunohistochemistry as an adjunct in the diagnosis of 'borderline' biopsies. Culliton[4] mentions that mutations of another tumour suppressor gene on chromosome 9 are linked with some bladder carcinomas and

goes on to say that more must be learned about the natural history of mutations in bladder cancer before diagnosis can be certain. Difficulties remain, for example mutation of the p53 gene may occur at any number of locations and are not limited to a single codon. However, it is only a matter of time until these problems are solved and meanwhile we should recognise the arrival of a new diagnostic era.

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THROMBOEMBOLIC DISEASE

Sir, The uncertainty regarding the risk/benefit profile of anticoagulation for prophylaxis against embolic complications of non-rheumatic atrial fibrillation (*Proceedings* 1994; 24: 548–53) has largely been cleared by evidence emerging from multicentre trials,[1,2] and from a community based study.[3] Data from the former indicate that the 2·98–4·3 per cent of annual stroke rate in control subjects can be reduced to 0·41–0·9 per cent as a result of anticoagulation with warfarin.[1,2] In the community-based study, using an identical low-intensity anticoagulation regime (INR = 1·4–2·8), the target INR was achieved 50 per cent of the time vs 56–86 per cent of the time in the multicentre trials, with consequent annual stroke rate of 1·3 per cent.[3] This was offset by a 0·6 per cent annual rate of major bleeding,[3] the corresponding rate being 1·3 per cent in the most recent multi-centre trial.[2] Comparable annual rates of minor bleeding (i.e. 14 per cent vs 13·6 per cent) were documented in the trial context and in the community context, respectively.[2,3] Therefore, with low-intensity coagulation the significant risk of minor haemorrhage appears to be largely offset by a decisive reduction in the risk of embolic complications, not only in the artificial context of the multicentre trial, but also in the real life context of the community based anticoagulant clinic.

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CHRONIC FATIGUE SYNDROME

Sir, I was very impressed with the article on the above topic by Dr Leitch which appeared in the October issue of the *Proceedings*. The exhaustive cover of the literature is highly commendable and his honesty in identifying with members of Chronic Fatigue Societies allows the reader to adopt a less partisan assessment of the problem. As he rightly points out many medical conditions are associated with fatigue and his reference to neurasthenia is one example which requires further comment.

In the First World War it was a very common diagnosis used for invaliding and, indeed, in that war there were no psychiatrists but 'neurasthenic experts' of which William McDougall was one for he was a physician before moving to Duke University where he developed his school of Social Psychology. After the Second World War a Labour government decided that there must be many veterans of the First World War who had been invalided, pensioned, recovered, lost their pension but later had a recurrence of their disability and were entitled to have the pension restored. All such pensioners were contacted and a number appealed to have their cases reconsidered. As a consultant to the Ministry I sat on Boards and was able to peruse the files which gave a clear account of the original disability and I was also able to assess the current condition. There was no doubt that the invaliding disability was that of a moderate degree of depression and that the present one was of a similar nature which should respond to effective antidepressant medication. The *virus en cage* as described by Pasteur had not broken out of its cage, if it was ever there. Since coming to Canada I have had a number of patient with 'chronic fatigue syndrome' referred by insurance companies as they were entitled to generous Long-term Disability Insurance. This would account for the age distribution and the preponderance of women for most were school teachers, high category office staff and social and welfare workers while a small but significant number were prison officers. Many were, literally, indefatigable in their pursuit of the insurance benefit and I knew of one lady who, dissatisfied with local medical opinion, took off to Ottawa for 'treatment' which was given by a physician who specialised in the disorder. It struck me as odd that with excellent medical services in Victoria and very highly specialised services in Vancouver one should seek out an 'expert' 3,000 miles away. A moment's reflection provided the answer. If generous insurance schemes were an important part of the answer in Victoria it would be even more important in Ottawa where the concentration of government was much greater and Federal employees' benefits were even more generous. A physician who identified with lay society and had his own 'remedy' which was guaranteed to maintain the patient fully disabled could have a lucrative practice.

Dr. Leitch, rightly, is critical of Cartesian dualism and claims to see the problem as being both organic and functional yet he fails to see the incongruity of criticising those doctors who regard the problem as mainly functional. It is a medical axiom that the patient should be treated for what he has got and not be treated for what he does not have. Even in those who have an illness of undoubted viral origin may still be a severe and persistent depression which steers them towards 'opting out' and collecting their disability pension. As a firm diagnosis of depression even in the presence of enlarged glands carries an excellent prognosis, this treatment should not be denied. I would consider that not less than 85 per cent of those who are genuinely sick will respond. Many will

vigorously deny they are depressed but denial is a common and even sinister sign of depression which can generally be treated successfully by any physician if the patient co-operates.

Myre Sim
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Sir, Thank you for the opportunity to reply to Dr Sim's letter. It is very pleasing that my review of the Chronic Fatigue Syndrome has attracted the attention of so distinguished a psychiatrist and has escaped so lightly. Unfortunately, Dr Sim mistakenly believes that I identify with members of Chronic Fatigue Societies. My intention was to describe for myself, and for others, the historical background to the emergence of ME as a syndrome, a phenomenon which is inextricably linked with the contributions of ME, self-help groups and societies, medical journalists and the media. To describe a phenomenon is not to identify with it.

Dr Sim's observations on the 'neurasthenia' of the First World War are fascinating; I wonder whether he would categorise the 'Gulf War Syndromes' and the recent anniversary recrudescence of illness among veterans of the Second World War as also obviously due to depression. Unfortunately, as reported in my review, most patients with the Chronic Fatigue Syndrome do not improve with anti-depressant medication; indeed, many appear to deteriorate following such an intervention.

Malingering in relation to Long-term Disability Insurance or Social Security Benefits is uncommon in patients with the Chronic Fatigue Syndrome seen in Edinburgh and, by implication, the rest of the UK. I am also unaware of any physicians who are seeking to line their wallets by maintaining their patients fully disabled through the application of ineffective remedies.

Finally, I see nothing incongruous in despairing of the dismissive diagnosis of a disorder as functional whether that diagnosis is made by a physician, a psychiatrist or a practitioner of holistic medicine. 'It's all in the mind' and 'what you need to do is pull your socks up' may discharge the physician's sense of responsibility for the patient but they rarely resolve the disorder and frequently compound it. If the term functional must be used, and I personally deplore it, it should be seen not as a diagnostic end but as the beginning of managing the disorder. I would suggest that success in management of the Chronic Fatigue Syndrome is most likely to be achieved when individual patients' disorders are assessed in the context of the wisdom, experience and knowledge which have accumulated over the years.

That is why I wrote the review.

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College Affairs

An Honorary Fellow: John Anderson Strong

THE TEXT OF AN ADDRESS BY JOHN MATTHEWS AT THE QUARTERLY MEETING, 28TH JULY 1994

President and Fellows: The Honorary Fellowship is the highest honour we can bestow, and over the years there has been a special group of doctors whom we have honoured in this way because of exceptional distinction in Medicine and outstanding service and leadership to the College. The names of Sir Stanley Davidson, Sir Derrick Dunlop, Rae Gilchrist, Christopher Clayson and Sir John Crofton immediately spring to mind. To this distinguished group, not before time, it is proposed to add the name of John Anderson Strong.

He was appointed in 1949 as senior lecturer in the University of Edinburgh and consultant physician in the Western General Hospital. Sir Stanley Davidson, responsible for the appointment, would have been impressed not only by John's ability as a doctor, but also by his enthusiasm as a sportsman, oarsman and air pilot, and by his service as a lieutenant colonel in the RAMC in Burma, for which he was awarded the MBE in 1942 and mentioned in despatches in 1945. Stanley had an intuitive way of assessing good men. He arranged to talk with them at times other than across the interviewing table, and with John Strong I am told the interview continued at the bar of the North British Hotel.

John Strong's main interest was in Endocrinology. He was for many years Secretary to the Clinical Endocrinology Research Unit of the Medical Research Council. He became Honorary Physician to the MRC Cytogenics Unit in 1959. He wrote well-researched papers in general medicine and endocrine journals on subjects ranging from renal diseases, hormonal control of cancer, growth hormone and obesity, and contributed to well known Edinburgh text books of medicine. A personal Chair in Medicine was conferred on him by Edinburgh University in 1966.

He served on many National and Specialist Committees—the British Diabetic Association, the Royal Society of Medicine, the Nutrition Society, the Medicines Commission, the Scottish Health Services Planning Council and the Health Education Committee, and he was for a number of years a member of the Lothian Health Board.

He is well known in London, Dublin, and overseas and his contributions to medicine were recognised by the Queen with the award of the CBE in 1978, which was the year before he became President of our College.

He served on the Council of the College in the 1970s, and was Vice-President from 1976 to 1978. Thus he was well prepared for his Presidency, during which the Tercentenary celebrations took place. Many of you can recall the dignified manner with which he conducted those proceedings in 1981.

We are approaching now the 10th anniversary of the laying of the Foundation Stone of the Conference Centre on 21st September 1994. After ten years we can look back and appreciate the great success of the building. Those who served on the Councils of ten and more years ago will know that it was through the persistent effort of John Strong that the project got off the ground and came to fruition.