culture and this response, and that of EPO, could be mimiccd by cobaltous ions and iron chelators, suggesting that the sensor might be a ferroprotein.

In view of the previous session on cellular programming and discussion of the Barker hypothesis, the work presented by Dr D Churchill et al (City Hospital NHS Trust, Birmingham), could be regarded as somewhat controversial. Their study involved 24-hour ambulatory blood pressure monitoring of 209 women at three stages in pregnancy. They found that maternal blood pressure was inversely correlated with infant birthweight, and suggested that the work relating low birthweight with adult hypertension could partly be due to an inherited tendency to hypertension.

Dr G J Bellingan (Respiratory Medicine Unit, Edinburgh) described a series of elegant experiments to investigate the fate of inflammatory macrophages during resolution of inflammation, using a mouse model. Few macrophages die at the site of inflammation; most migrate to draining lymph nodes and eventually to the reticuloendothelial system.

Two papers discussed aspects of HIV infection. Dr D Laloo et al (John Radcliffe Hospital, Oxford) investigated mechanisms by which the virus evades the immune response. They showed that a high mutation rate and variation in the region of the viral epitope can cause loss of recognition by cytotoxic T lymphocytes, or produce epitopes which act, instead, as antagonists. A second paper, from Dr I P Everall et al (Institute of Psychiatry, London), noted that HIV infection is associated with neuronal loss in symptomatic patients and in vitro evidence suggests that glutamate is involved in this neurotoxicity.

Conclusions

What were our overall impressions of the conference? Mostly very good, but with a few criticisms. The enthusiasm of the presenters for their work was obvious, and they took the opportunity to give the audience an insight into some exciting areas of biomedical research, and perhaps to encourage students and others to enter this field. In view of this, we were surprised that there were no women among the speakers, although there were many women in the audience who participated in the discussions. An important point for speakers to note at such a wide-ranging conference is that they should avoid using abbreviations, or if that is impossible, they should explain them fully and perhaps more than once during their presentations; otherwise members of the audience not familiar with that field may find it difficult to follow the argument.

Apart from these few reservations, we enjoyed a fascinating two days.

Regional conference in Nottingham

The September 1994 Regional Royal College of Physicians Conference was held in the newly refurbished Postgraduate Medical Education Centre at the Nottingham City Hospital. Over 100 participants enjoyed a broadly based programme where topical issues in many of the specialty areas of general medicine were discussed and posters of local research were displayed. The presentations were given by both local and national experts and were of a uniformly high standard.

Use of radioiodine—efficacy and potential hazards

Dr J A Franklyn (University of Birmingham) identified a number of problems with radioactive iodine treatment of thyrotoxicosis. Assessing the optimum dose for individual patients remains largely empirical. Her policy is to use a single dose of 5 millicuries which cures approximately two-thirds of patients. The prospect of cure is higher and of hypothyroidism lower in those with toxic nodular goitre than in patients with Graves disease. Evidence of severe disease (particularly Graves disease) predicts a poor response to radioactive iodine treatment.

Many non-specialists think that radioactive iodine treatment increases the risk of malignancy and infertility, although several large scale retrospective studies do not support this view and the Administration of Radioactive Substance Advisory Committee has stated that the age restriction for radioactive iodine treatment is unnecessary.

Specialists are concerned over a recent report that Graves ophthalmopathy deteriorated more in patients treated with radioactive iodine than in a matched group treated with methimazole. Although the finding of this study has been disputed by an American retrospective study, many remain concerned about the use of radioactive iodine in patients with Graves ophthalmopathy.

Dr Franklyn recommended radioactive iodine as the treatment of choice in elderly patients and in those with toxic nodular goitre, but that in young subjects with Graves disease a 12 or 18 months course of anti-thyroid drug, which offers a 30% chance of long-term remission, should be tried first.

Hypoglycaemia in insulin-dependent diabetes

Dr S Heller (Northern General Hospital, Sheffield) gave a fascinating account of hypoglycaemia, the com-

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mon and feared complication of insulin therapy. He described the paradox of modern therapy of insulin-dependent diabetes where intensive insulin treatment, aimed at achieving near normoglycaemia, halves the risks of microvascular complications but triples the risk of severe hypoglycaemic attacks. Evidence is accumulating that this increased tendency to severe hypoglycaemia is related to a reversible lowering of the blood sugar threshold for activation of the autonomic nervous system, while the blood glucose threshold for cognitive impairment remains more or less unchanged. Thus, in subjects with tightly controlled blood sugar levels, hypoglycaemia might lead to a state in which when autonomic symptoms occur the blood sugar level may already be so low that the subject is unable to recognise them and take action. Unravelling the mechanisms of this important complication of intensive insulin treatment is an important challenge for the future.

The prospects for prevention of insulin-dependent diabetes

Professor E Gale (St Bartholomew’s Hospital, London) reviewed problems in identifying subjects who may be at high risk of developing insulin-dependent diabetes and in whom intervention might be beneficial. Although as yet there is no test that reliably predicts the onset of disease, a family history of diabetes and a high titre of islet cell antibodies gives a five year risk of around 40% for developing insulin-dependent diabetes. How may the onset of insulin-dependent diabetes in those subjects be postponed or prevented? In animal models, several different immune interventions can diminish the risk of progression, suggesting that the disease process is susceptible to treatment. Of the interventions found to be effective in animal models, insulin (either subcutaneous or orally) and nicotinamide prophylaxis offer most promise in man. Nicotinamide is taken up and concentrated in islet cells and appears to protect them against toxic insults. Unlike prophylactic subcutaneous insulin, it is safe and has high patient acceptability, and therefore represents a better prospect for delaying or preventing the onset of insulin-dependent diabetes in those at risk. This hypothesis is currently being tested in an ambitious multinational study of more than 400 patients at high risk of developing diabetes.

Home ventilation

Dr W Kinnear (University Hospital, Nottingham) reviewed the techniques, indications, efficacy and cost of home ventilation in the United Kingdom. Nasal intermittent positive pressure ventilation through a closely fitting nasal mask is now the most widely used technique and is often dramatically effective in individuals with nocturnal hypoventilation or chronic hypercapnic ventilatory failure secondary to chest wall or neuromuscular disorders. There remain serious difficulties in judging the quality of life in those who have progressive disorders or who are completely ventilator-dependent. Dr Kinnear predicted an increasing demand for assisted home ventilation for subjects with ventilatory failure secondary to neuromuscular disorders and to chronic obstructive airways disease, and therefore a need for more specialist centres.

Airways obstruction—are the lungs rusting?

Dr J R Britton (City Hospital, Nottingham) outlined evidence linking a diet poor in antioxidants such as vitamin C, E, selenium and copper to the development of chronic obstructive airways disease and asthma. Several community-based studies, including a large survey in Nottingham, have shown a relationship between estimated dietary intake of vitamin C and forced expiratory volume in one second (FEV₁). In addition, there is preliminary evidence suggesting that vitamin C supplementation protects normal subjects against the adverse effects of inhaled ozone on lung function and reduces bronchial hyperreactivity in asthma, although these effects are small and of uncertain significance.

Cystic fibrosis

Dr A J Knox (City Hospital, Nottingham) gave an overview of recent advances in the management of cystic fibrosis in adults. Projected survival for subjects born with cystic fibrosis in the 1990s is between 35 and 40 years and they will consequently put additional pressure on hospital services and resources.

There has been recent interest in the pathogenicity and the natural history of infection with *Pseudomonas cepacia*, a multi-drug-resistant organism increasingly isolated in adult cystic fibrosis patients. Lung function deteriorates more quickly in patients infected with this organism and there are anecdotal reports of very rapid deterioration after infection with *Pseudomonas cepacia*. Epidemiological studies suggest person to person spread of *Pseudomonas cepacia* via airborne droplets, and many cystic fibrosis units now operate a segregation policy for both inpatients and outpatients.

The use of human recombinant DNase can produce a short-term improvement in FEV₁, and a longer-term reduction, by up to one-third, in the incidence of infective exacerbation. Therapies aimed at correcting the transepithelial ion transport deficit in cystic fibrosis, either pharmacologically or through gene therapy, offer real hope of arresting disease progression.

Sleep apnoea and its variants

Dr John Stradling (Churchill Hospital, Oxford) gave a highly entertaining College Lecture on sleep related breathing disorders, liberally illustrated with video
demonstrations. He brought us up to date with the clinical features and modern investigation of suspected obstructive sleep apnoea. The major cause of nocturnal wakening, and hence daytime sleepiness, is a sensation of increased resistive load to inspiration and not necessarily hypoxia and hypercapnia. Therefore, previous definitions of obstructive sleep apnoea, which placed great emphasis on detection of nocturnal hypoxic dips, may no longer be appropriate. A modern sleep laboratory should have a means of detecting nocturnal wakening (eg body movement on a video tape or a speeding-up of the pulse rate on pulse oximetry) and evidence of upper airway narrowing (eg snoring on the video tape recording, or hypoxic dips on pulse oximetry recording). Detecting abnormal inspiratory to expiratory blood pressure variability by ambulatory equipment might become a useful diagnostic tool.

Tonsillectomy or adenoidectomy may occasionally be useful, but dieting to reduce weight, and nasal continuous positive airway pressure (CPAP) remain the mainstays of management of obstructive sleep apnoea. CPAP is effective and is readily accepted and used by patients.

New approaches towards treatment of glomerular disease

In Professor J Savill’s (University Hospital, Nottingham) view the greatest hope for preventing end stage renal failure secondary to glomerular disease lies in the deeper understanding of the mechanisms of glomerular scarring. Studies of this kind may also be relevant to the mechanism of scarring in diseases such as cryptogenic fibrosing alveolitis and rheumatoid arthritis. The key components of glomerular damage and scarring are mesangial cell proliferation and matrix deposition. Platelet-derived growth factor and transforming growth factor beta have an important role in these processes, raising the possibility that antagonists might provide a new approach to treatment.

Imported disease

Professor R Finch (City Hospital, Nottingham) reviewed the causes of early and late imported diseases. He highlighted the importance of malaria, particularly in travellers from East Africa, India and South East Asia. More than 50% of cases are caused by Plasmodium falciparum and are increasingly chloroquine resistant; there are also reports of chloroquine resistance in Plasmodium vivax.

Travellers’ diarrhoea remains an important problem for visitors from industrialised countries to endemic areas such as India, South East Asia and Latin America, with attack rates of between 25 and 50%. At least half have an identifiable microbiological cause, of which Escherichia coli is the most important. Quinolone antibiotics improve recovery rate and travellers with a history of previous attacks or with pre-existing disease should perhaps travel with a stand-by course.

Peptic ulcer—pH or HP?

Professor C J Hawkey (University Hospital, Nottingham) gave an update on the role of Helicobacter pylori in peptic ulcer disease. H pylori infection is thought to be the commonest infectious disease worldwide and begins in early life, probably by faecal–oral transmission. It produces gastric hyperacidity both by increasing gastrin release from antral G cells as a direct consequence of a low grade gastritis and secondary to metabolism of an endogenous H3 receptor agonist, causing loss of negative feedback on gastrin release by somatostatin D cells.

Successful eradication of H pylori reduces the incidence of peptic ulcer relapse. Many still regard triple therapy with colloidal bismuth, metronidazole and either tetracycline or amoxycillin as the gold standard for treating peptic ulcer but this regimen is poorly tolerated and there are concerns about growing resistance of the organism to metronidazole. Simpler regimens with omeprazole and amoxycillin for two weeks result in mean eradication rates of around 60%, and several small studies have recently shown eradication rates of more than 90% after a one week course of omeprazole, clarithromycin and metronidazole.

Bone marrow transplantation

Dr N Russell (City Hospital, Nottingham) highlighted the growing interest in peripheral blood stem cell transplantation as an alternative to autologous bone marrow transplantation. Pluripotent haemopoietic stem cells can be harvested from peripheral blood during the recovery phase of chemotherapy-induced neutropenia. Harvesting can be enhanced by the use of granulocyte colony stimulating factor (GCSF). Peripheral blood stem cell transplantation shortens the duration of neutropenia and thrombocytopenia so that there is less infection, reduced need for blood product support, smaller cost and a lower mortality.

Whether these advantages apply to allogeneic transplantation is yet to be determined although Dr Russell described a favourable outcome after peripheral blood stem cell transplant from a GCSF-treated donor who was medically unfit for bone marrow harvesting.

Management of coronary thrombosis

Professor J R Hampton (University Hospital, Nottingham) explained how large scale clinical trials have altered the management of myocardial infarction over the last 25 years, both in the acute and late post-infarction period. Treatment with streptokinase and aspirin is now standard, with the greatest benefit in patients treated within a few hours of infarction. There
is little evidence that therapy is effective if given more than 12 hours after the onset of chest pain. The ISIS-4 study shows very little benefit in the acute treatment of unselected myocardial infarct patients with captopril, nitrates or magnesium.

Late intervention with the β-blockers timolol, propranolol and a cebutolol significantly reduced late, post-infarct mortality. The SAVE (survival and ventricular enlargement) and AIR (acute infarction ramipril efficacy) studies showed a reduction in cumulative mortality in patients with left ventricular failure treated with angiotensin-converting enzyme inhibitors.

The message from these studies is clear: in the acute stage of infarction all suitable patients should be treated with thrombolysis and aspirin. Before hospital discharge, patients without impaired left ventricular function should be given a β-blocker, while those with signs of heart failure should be given an angiotensin converting enzyme inhibitor.

Parkinson's disease

Dr G Lennox (University Hospital, Nottingham) said that even in the best hands Parkinson’s disease is commonly misdiagnosed. The best clues to the diagnosis are an asymmetrical onset rest tremor which responds well to treatment. The differential diagnosis includes vascular- or drug-induced pseudoParkinson’s or degenerative conditions such as the Steele–Richardson syndrome, multi-system atrophy or corticobasilar degeneration. The rigid akinetic presentation of Wilson’s disease can be confused with Parkinson’s disease.

In the management of Parkinson’s disease, the monoamine oxidase inhibitor selegiline is now thought not to be neuroprotective but remains a useful addition in patients with severe symptoms or with the ‘on-off’ phenomenon. Dopamine agonists such as bromocriptine, pergolide and lysuride are of some benefit but nausea may be troublesome. Dispersible Madopar (levodopa and benseradine) and subcutaneous apomorphine are useful in the ‘on-off’ phenomenon.

The stereotactic placement of fetal tissue cells is still at an experimental stage and is thought unlikely to become a widespread treatment because of difficulty in getting fetal tissue of appropriate age, but it may become possible to use a patient’s own genetically engineered fibroblasts to switch on dopamine production.

Functional magnetic resonance

Professor P G Morris (University of Nottingham) gave a stimulating account of the potential use of this technique in the further understanding of cerebral function. Echo-planar imaging, a high speed, high resolution technique, allows brain activity to be studied directly. For example, occipital stimulation can be recorded following appropriate visual stimulation and changes in the left motor cortex can be recorded after tapping the right finger.

Magnetic resonance spectroscopy (MRS) can be used to study metabolic activity of tissues. MRS has been used to follow the depletions of glycogen in muscle with exercise and its restoration after food ingestion. The potential role of magnetic resonance neurospectroscopy in measuring rates of aerobic and anaerobic brain metabolism after acute stroke was discussed. By giving a 13C-labelled glucose solution, the rate of anaerobic and aerobic metabolism could be measured by following the incorporation of label into lactate and glutamate, respectively. The use of 13C-labelled acetate in distinguishing between glial and neuronal components of cerebral metabolism was also discussed.

Genes and morphogenesis

Dr I D Young (City Hospital, Nottingham) informed us that there are now 6–7,000 recognised single-gene disorders or traits, and that in about 500 the causative gene has been mapped or identified. Mutations in both structural and regulatory genes play important roles in human development.

Dr Young illustrated the spectrum of abnormalities caused by structural gene mutilations with examples of disorders of collagen. Mutations in different collagen genes result in disorders as diverse as osteogenesis imperfecta, the Ehlers–Danlos syndrome and Alport’s syndrome. Dysmorphic syndromes and congenital abnormalities have also been shown to be due to mutations in transcription control genes, which are highly conserved across the animal kingdom. Mutations in genes with oncogenic potential can also cause congenital malformations. Therefore, knowledge gained from the study of morphogenesis could also have important implications for oncology in particular and medicine in general.

The isolated metastasis

Professor J Carmichael (City Hospital, Nottingham) explained that the progression of cancer involves the loss of normal growth control, the loss of the regulation of proteolysis and motility and the induction of angiogenesis. The potential of tumours to metastasise depends on the histological subtype and grade, with epithelial tumours tending to disseminate at an early stage.

The management of metastatic disease depends on the sensitivity of the tumour and the site of the metastasis. The therapeutic modalities available include systemic or regional chemotherapy (eg for germ cell tumours), surgical resection, and cryotherapy (eg hepatic metastases from colorectal carcinoma). Surgical removal of isolated brain metastases followed by postoperative radiotherapy can be beneficial in selected patients.
Professor Carmichael predicted that the greater understanding of the molecular mechanisms involved in carcinogenesis and tumour spread will allow us to identify patients who are at high risk of developing metastases and select them for more aggressive therapy. There is currently much interest in metallo-proteinase inhibitors which, in animal models, have been shown to inhibit tumour spread.

Malnutrition in hospital

Dr S P Allison (University Hospital, Nottingham) reviewed evidence that malnutrition in hospital is an important cause of morbidity and mortality and that recovery from illness can be improved by appropriate nutritional supplementation; options include total parenteral nutrition in those with gastrointestinal failure, fine bore naso-gastric tubes or, if patients are unlikely to be able to swallow for some time, a percutaneous endoscopic gastrostomy. Supervision of nutritional supplements in a hospital setting is best done by a specialist nutritional team, though such services in the United Kingdom are as yet relatively underdeveloped.

The scope of work in Africa

Professor E H O Parry (London School of Hygiene and Tropical Medicine) gave general advice to trainees wishing to spend time overseas. He stressed the importance of support and enthusiasm from trainers at home. Possibilities include short visits to overseas research centres funded by the Medical Research Council and Wellcome Trust or a secondment to such units as a trainee or, for more senior staff, a sabbatical with assured return. These overseas visits bring much needed research skill and fresh ideas to overseas centres as well as establishing long-term links with British institutions. Trainees benefit from exposure to a fascinating range of clinical material and gain experience in health care organisations quite different from those at home.

General comments

The whole conference was efficiently organised by Professor Anne Tattersfield and College staff. They succeeded in their goals of providing a timely and useful update on a number of contentious issues in general medicine. The speakers largely achieved the difficult task of making their presentations understandable to trainees and non-specialists whilst remaining interesting to experts.

The scientific programme was followed by a free ranging discussion of many topical medico-political problems; participants also welcomed the move to bring the College closer to its Members by organising conferences in the regions.

Physicians—practicalities, problems and perspectives

On Wednesday 6 July 1994 the College held a successful conference on the principal issues currently before physicians. Despite industrial action on the railways, attendance was excellent. Indeed it might have been difficult to accommodate all delegates if the trains had been running! The conference formed part of a College Day which included the first annual Comitia for Fellows, a discussion led by members of the Standing Committee of Members and a major lecture of general interest.

The training and certification of specialists

The plans

Dr Kenneth Calman (Chief Medical Officer) gave the opening address and discussed a range of issues relating to the report on UK specialist training. A properly planned and carefully conducted scheme of medical education has long been held to be the foundation of a successful health service. The report Hospital doctors—training for the future appeared in April 1993 and dealt with postgraduate training, the amalgamation of registrar and senior registrar posts into one combined training grade and the need for competitive entry into that training grade and envisaged assessment of competence at the end of training. His brief had been to consider the relationship between present UK arrangements and European Union (EU) law, to look for a harmonisation between the two and to prepare a report within six months. Three subgroups were set up to look at specialist training, the UK contribution to developing EU legislation on medical training, and to ensure that the appointment of consultants was compatible with EU legislation.

Dr Calman sought to correct various misconceptions about the scheme. He emphasised that the length of training was a minimum, not a maximum and that it could be varied by the Colleges in the light of their advice.

The essentials of the plan are that specialist training should form part of continuing medical education (CME), that standards have to be met in order to improve training and the clinical service, and that any assessment of doctors' training will be based on their clinical competence. A certificate of completion of specialist training (CCST) will be issued by the General Medical Council on the advice of the Medical

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