

REFERENCES

- ¹ Madely RJ, Hull D, Holland T. Prevention of post-neonatal mortality. *Arch Dis Child* 1986; **61**: 459-63.
- ² Infantile Apnea and home monitoring. Report of US Department of Health and Human Science. NIH (87-2905) Bethesda Md, 1987.
- ³ Beal SM. Sleeping position and SIDS. *Lancet* 1988; **2**: 512.
- ⁴ De Jonge GA, Engelberts AC, Koomen-Liefting AJM, Kostense PJ. Cot death and prone sleeping in the Netherlands. *Br Med J* 1989; **298**: 722.
- ⁵ Gilbert RE, Rudd PT, Berry PJ, Fleming PJ *et al*. Combined effect of infection and heavy wrapping in sudden infant death. *Arch Dis Child* 1992; **67**: 171-7.
- ⁶ Wigfield RE, Fleming PJ, Rudd PT, Golding J. Can the fall in Avon's sudden infant death rate be explained by the observed sleeping position changes. *Br Med J* 1992; **304**: 282-3.
- ⁷ Stewart AJ, Fleming PJ, Berry PJ, Wigfield R *et al*. Reducing the risk of crib (cot) death in the UK locally and nationally. In: Proceedings of the 2nd SIDS International Conference. New York: Perinatology Press, 1992.
- ⁸ Mitchel EA, Engelberts AC. Sleeping position and cot deaths. *Lancet* 1991; **338**: 192.
- ⁹ Annex G. In: Report of the Chief Medical Officer's Expert Group on the Sleeping Position of Infants and Cot Death. London: HMSO, 1993.
- ¹⁰ Golding J, Fleming PJ, Parkes S. Cot deaths and sleeping position campaigns. *Lancet* 1992; **339**: 748-9.
- ¹¹ Scott A, Campbell H, Gorman D. Sudden infant death syndrome in Scotland. *Br Med J* 1993; **306**: 211-2.
- ¹² Wigfield R, Gilbert RE, Fleming PJ. SIDS: Risk reduction measures. *Early Human Development* 1994; **38**: 161-4.

NOTES FROM A SYMPOSIUM ON PREVENTIVE MEDICINE* HELD IN THE COLLEGE ON 9-10 NOVEMBER 1994

DIET AND HEALTH

Dr P. James, Rowett Institute, Aberdeen, spoke on *The scope for prevention and the Scottish diet*. In Scotland the leading cause of premature death between 40-69 years is coronary heart disease (CHD). International comparisons of CHD mortality rates suggest a reduction of 80-90% is possible. Diet has an important role to play as it affects both atherosclerosis and thrombosis. Diets high in fruit and vegetable are protective against DNA damage and micronutrients modulate the immune response. In Scotland only 7% of the population have an adequate fruit and vegetable intake although 69% believe they do.

Are there benefits to health by lowering blood cholesterol? was addressed by *Dr G. Davey-Smith, University of Bristol*. Large epidemiological studies have shown that individuals with raised cholesterol levels have higher cardiovascular disease (CVD) mortality rates. There is no conclusive evidence to suggest a causal relationship between low cholesterol and a higher non-CVD mortality. A meta-analysis has shown that lowering cholesterol levels with drugs is associated with a 21% excess in non-CVD mortality (95% CI 7-37%). A significant excess is not associated with dietary therapy. At an individual level the effect of diet is disappointing and most patients progress to drug therapy. Drugs are only of proven benefit in individuals whose risk of dying from CHD is greater than 3%/year.

Dr A. Robertson, Safeway Stores plc, gave an overview on *Shopping for a healthy diet—a retailer's perspective*. The main role of retailers is to satisfy customers. Increasing the range, quality and accessibility of particular types of food promotes purchasing as do promotional offers. Retailers can assist better nutrition by manufacturing healthier products and providing in-store education. However to change the long term dietary patterns of a population governmental commitment is required so that a co-ordinated approach can be achieved. Lower socio-economic groups must be specifically targeted.

PREVENTION AND THE ENVIRONMENT

The talk by *Dr P. J. Fleming, University of Bristol*, on *Preventing cot death* is published on page 213.

Dr D. P. Strachan, St George's Hospital Medical School, London, spoke on *The impact of traffic pollution on the development of asthma*. Population-based data is only available for school aged children. Studies suggest an increase in prevalence rates for wheeze in children since the 1970s and a rise in hospital admission rates but the severity of wheezing episodes has declined. These changes may be attributable to differences in diagnostic patterns and in changes in health care. There is no

*A full list of speakers and titles of their papers presented at this symposium is recorded in *Proceedings*, Vol. 25, p. 180.

conclusive evidence that nitrogen dioxide and ozone, which are the two most commonly cited traffic air pollutants linked to asthma, have increased over the same period despite a rise in the volume of traffic. Little firm evidence exists for exposure to traffic pollution and the precipitation of asthma episodes from worldwide studies. A causal link between traffic pollution and asthma has not been established. Personal exposure to cigarette smoke and domestic gas merit further attention.

Recent trends in prevention of road traffic accidents (RTAs) were discussed by Mr D. Ney, Willis Corroon London Limited. Over the last 55 years the number of vehicles in the UK has risen sixfold and vehicular use ninefold. Despite this over the last three decades there has been a considerable reduction in the death and injury rates from RTAs. Pedestrian death rates have fallen from around 3000 to 1200 per annum. Contributory factors include the government initiatives of lower speed zones; traffic calming measures; improvements in road technology such as the use of rumble bars; and improvements in vehicular safety. Periods of further training for those holding licences could make a substantial impact, estimated as likely to halve the number of accidents.

PREVENTION AT THE MOLECULAR LEVEL

Dr M. Steele, University of St Andrews, spoke on the *Scope for prevention through molecular epidemiology*. Molecular characterisation may identify individuals at increased risk of a disease such as breast cancer and identify patients with a poor prognosis in whom aggressive therapy at an early stage might be indicated. If a genetically recognisable condition was sufficiently serious termination of pregnancy or selective fertilisation of an ovum may be ethically acceptable. The most immediate application of molecular characterisation is to the development of vaccines against infectious diseases. Dangerous organisms would not have to be cultured and the vaccines could be made cheaply, tested rapidly and standardised. Molecular characterisation is also of use in contact tracing in the control of infectious diseases.

The potential of molecular genetics to reduce colorectal cancer mortality was addressed by Mr M. G. Dunlop, University of Edinburgh. Colorectal cancer (CRC) kills 20,000 per year in the UK and the five year survival rate of 37% has not changed appreciably over the last two decades. Population screening to reduce mortality is impractical but targeted screening of families with particular genes may be a viable alternative. Identification of individuals at risk from familial polyposis is relatively straightforward and an autosomal dominant gene has been identified. The situation is less clear for hereditary non-polyposis colorectal cancer (HNPCC) as mutant CRC susceptibility genes have variable penetrance and are undoubtedly affected by environmental factors. Automated gene sequencing will help with the identification of the 15% of individuals with sporadic cancers who could be HNPCC carriers. A selective approach to screening will result in reduced mortality as well as substantially decreasing the number of colonoscopies required by comparison with a population-based approach. The intensive screening of high risk individuals could also help address many vexed questions about dietary risk factors and possibly provide a more rational approach to anti-cancer therapy and immunotherapy.

Dr. C. S. Muir, Scottish Cancer Registration, discussed *Infective and parasitic agents in cancer: scope for prevention*. Nasopharyngeal, stomach, cervical and liver cancer are common cancers with an infective or parasitic aetiology. The Epstein-Barr virus is associated with nasopharyngeal cancer, and antibody titres are used in screening, as for Burkitt's Lymphoma and Hodgkin's Disease. The association of *Helicobacter pylori* infection and stomach cancer presents a relative risk of six and an attributable risk of 50% suggesting that a vaccine would prevent a substantial number of cases. A relative risk of between 30 and 160 has been found for hepatitis B carriers and hepatocellular liver cancer. The cholangiosarcoma form of liver cancer is associated with fluke infection. Human papilloma virus has been linked to cancer of the cervix uteri. In developed countries bladder cancer is related to smoking and exposures to industrial pollution but, in developing countries, to Schistosomiasis hematobrium infestation. Evaluation of the efficacy of hepatitis B vaccine in protecting against cancer will take three decades. Effective vaccines have not yet been developed for the other infective and parasitic agents mentioned but the potential for the reduction of complicating cancers through vaccines is large.

JOHN MATHESON SHAW LECTURE

The effectiveness of preventive medicine in primary care was the title of the John Matheson Shaw Lecture delivered by Dr G. C. M. Watt, University of Glasgow. See page 204.

DEPRIVATION AND ILL-HEALTH

Dr B. Jarman, St Mary's Hospital Medical School, London, outlined the basis of three indices measuring social deprivation: the Underprivileged area score (UPA), the Townsend index and the Carstairs index. They are computed by calculating the electoral ward value of the particular variables expressed within the index. These variables include unemployment, overcrowding, car ownership, family disruption, ethnic groups, social class and others, each index using a different combination of these factors. The variables of each system are normalised and weighted according to information derived from surveys among general practices in the UK. The method of determining extra payment to general practitioners in deprived areas was described and the problems arising out of this exercise highlighted. Strong correlations between the various deprivation indices and measures of ill-health are found. The information allows identification of those general practices which by the nature of the communities which they serve are likely to have an increased workload and an above average demand on their services. Clearly this permits better resource allocation to purchasers of health care, both general practices and health authorities.

Dr J. Greenwood, Royal Edinburgh Hospital, addressed the question *Teenage drug use: how should we respond?* Character, past learning and experience, and current social circumstances influence whether a teenager will take drugs. Children from all backgrounds pass through a phase of experimenting with recreational drugs but it is children from the more deprived areas with social problems who are at greater risk of progressing on to hard drugs and becoming regular users. To influence drug taking a multidisciplinary approach is required. Parents need to encourage children to care for themselves and provide them with sensible infor-

mation in which they should be assisted by health professionals. The government needs to engage the media to educate the public and to address the underlying social problems. Decriminalisation of drugs should also be considered. Concentration on reducing the demand for drugs rather than on their supply may be a more effective way of addressing illicit drug use.

Post traumatic stress disorder: the lessons of Lockerbie was considered by Dr D. N. Brooks, St Andrew's Hospital, Northampton. Sixty-six residents of Lockerbie had their mental state assessed a year after the airplane tragedy. The most common mental disorder identified by questionnaire was post-traumatic stress disorder (PTSD), followed by depression and panic disorders. No baseline variables were found to be predictive of a particular diagnosis. Follow-up of 24 of the individuals three years after the accident showed a small group of persistent PTSD sufferers and two new cases of both depression and panic disorder which occurred in the same individuals. If a person had one or more significant intervening life event they were more likely to have PTSD or new psychopathology. People with an avoidance strategy for coping had higher levels of psychiatric morbidity.

Pointers to the prevention of psychiatric disease were discussed by Dr E. C. Johnstone, University of Edinburgh. Partial knowledge of the causes of the common disorders limits prevention. This is true of schizophrenia the genetic component of which is unidentified thus limiting the possibility of primary prevention. Early treatment may improve the ultimate prognosis and maintenance therapy reduces relapse rates. Substantial benefit may be accrued from detection of depression and its tertiary prevention. Maintenance therapy for bipolar affective disorders reduces relapses. Prevention has little to offer in dementia due to Alzheimer's disease but in multi-infarct dementia reduction of the established risk factors for stroke is of use. Primary and secondary prevention is relevant to mental handicap as specific causes can be identified and genetic counselling offered. Primary prevention of the disorders relevant to forensic psychiatry is limited because of inadequate understanding. Harm reduction within the prison system provides the best chance of prevention at present.

COMMUNICABLE DISEASE

Dr L. P. Omerod, Blackburn Royal Infirmary, spoke on *The resurgence of tuberculosis*. WHO has declared tuberculosis (TB) in the 1990s to represent a medical emergency. The driving force behind the increase on a world-wide scale is infection with the human immunodeficiency virus (HIV). In Africa approximately 70% of people with TB have HIV whilst in Britain it is 5%. The rise in TB in Britain is multi-factorial and is linked to deprivation, HIV infection, immigration, refugees, and individuals returning from working overseas. There is also an artefactual rise due to more complete reporting of cases. There are three key elements in the response to recrudescence of TB namely prevention, case-finding and effective therapy of which the last two are the more important in Britain. Drug resistance is now emerging as a major problem in some areas but not in Britain. TB control requires an integrated policy covering prevention, contact tracing, screening of new immigrants, treatment, compliance monitoring and outbreak plans and adequate resources at local, national and international levels.

Immunisation: Where do we go from here? was addressed by Dr N. D. Noah, King's College School of Medicine and Dentistry, London. Conjugate and subunit vaccines, time-release antigens and live vectors are areas of vaccine research. The use of combination vaccines is generating much interest and these may comprise different serotypes of the same agent or antigens from different agents. Potential advantages include a reduced number of immunisation visits, decreased administration costs, and better acceptance. The disadvantage is the high development cost. Post-marketing surveillance is important to provide information on the safety profile, effectiveness, duration and the nature of the protection conferred. Data will accumulate on the changes in the epidemiology of the disease that occurs following the use of vaccination, covering the age distribution of attacks, herd immunity and the emergence of rare strains.

CONTROVERSIES IN PREVENTIVE MEDICINE

Dr N. McIntosh, University of Edinburgh, asked *Can the consequences of low birth-weight be prevented?* Dramatic improvements in perinatal mortality have been made over the last 20 years especially for smaller babies. Recent evidence suggests that improvements in morbidity are now outpacing those in mortality. Current management includes stabilising babies on ventilators with good vascular support, which has reduced the neurodevelopmental disability caused by periventricular haemorrhage, leukomalacia and from poisons such as bilirubin. Monitoring oxygen therapy forms a key part of management against retrolental fibroplasia. Rickets of prematurity due to an inadequate mineral supply is now no longer a major problem as special mineralised milks are now used. The aetiology of bronchopulmonary dysplasia is still unclear but oxygen is implicated. Data from multicentre trials in the USA suggest that good respiratory support in the early days of life decreases its incidence.

Eliminating dental caries in Scotland was the subject of Dr A. J. Rugg-Gunn's talk. In the UK in 1993 58% of children aged five had dental caries. Preventive measures include decreasing snack and soft drink consumption, water fluoridation, tooth-brushing, and regular visits to the dentist. Water fluoridation cuts dental caries by half but less than 10% of households in Britain receive it due to public resistance. Social class is the best indicator of risk but prevention requires a change in behaviour which is more difficult to achieve in deprived families. This is one of the reasons why fluoridation of water is so desirable. Prospects for eliminating dental caries in Scotland are not good as the diet remains rich in non-extrinsic milk sugars besides the lack of fluoridation. The problem is compounded by the reduction in state support for the cost of dental care.

Dr C. J. Bulpitt, Royal Postgraduate Medical School, London, addressed the question *Is treating hypertension in the elderly worthwhile?* The Medical Research Council trials show that 840 middle aged hypertensive patients must be treated to save one stroke death compared to 370 older patients. A reduction of 25 to 46% in stroke mortality has been observed in the elderly. Treating hypertension also reduces the non-fatal cardiac events in the elderly ranging from 9 to 40% and decreases fatal events by 20 to 75%. Side effects of anti-hypertensive therapy need to be borne in mind as they impact on the quality of life. For example in the European Working Party Study of Hypertension in the Elderly 7% of the

patients developed diarrhoea. The value of treating hypertension in people over the age of 80 years is currently being addressed in the SYST-EUR and HYVET studies.

Dr S. M. Cobbe, University of Glasgow, spoke on *The impact of treating cardiac arrest in the community*. Half of all cardiac deaths are sudden, unexpected and occur outside hospital. An integrated system of care is required to optimise survival and the components of this are early access to cardiopulmonary resuscitation, defibrillation and advanced care. Heartstart Scotland, a non-randomised controlled study, showed an improvement in survival from 2–3% to 8% with an out-of-hospital defibrillation service. Only 2% of the survivors had neurological sequelae requiring institutionalisation whilst 9% had moderate impairment. Sixteen per cent of initial survivors died from a further cardiac arrest during a four year follow-up. Overall the service reduced community mortality from CHD by 1%. In terms of the lives saved and of useful survival in relation to the number of patients treated it compares favourably with other forms of treatment available for cardiovascular disease.

J. W. BALLANTYNE PRIZE LECTURE

Dr W. W. Holland, United Medical and Dental Schools of Guy's and St Thomas's Hospitals, delivered the J. W. Ballantyne Prize lecture and spoke on *Policies on prevention: the hazards of politics*. See page 189.

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MOLECULAR BIOLOGY OF HYPERTENSION*

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INTRODUCTION

Hypertension is a common condition. If defined on the basis of diastolic blood pressure >90 mmHg, >95 mmHg or >100 mmHg the prevalence figures are 25.4%, 14.6% and 8.4% respectively;¹ it is a major risk factor for the development of coronary heart disease and stroke and a reduction in blood pressure is associated with a reduction in risk.

Adoption studies and studies on twins with hypertension indicate that 30–60% of the variability in blood pressure in the population is genetically determined.² Identifying the genes that contribute to the pathogenesis of hypertension has been the subject of several recent studies. There was an extensive and now infamous debate in the 1960s between Sir George Pickering and Sir Robert Platt. Pickering argued that because of the unimodal distribution of blood pressure throughout the population, hypertension was probably a polygenic disease, i.e. involving the complex interaction of many different genes. If a single genetic defect was the cause of a significant number of patients with hypertension then a bimodal distribution of blood pressure would have been expected with a more easily recognised Mendelian form of inheritance. Platt on the other hand argued that hypertension could be monogenic, i.e. resulting from a single gene mutation.

The aim of this review is to highlight how molecular biology has advanced our knowledge regarding the pathogenesis of hypertension. As we shall see the theories of Pickering and Platt are not mutually exclusive, and indeed both have turned out to be correct.

IDENTIFYING GENES THAT CAUSE HYPERTENSION

Studies have been carried out both in man and in animal models of hypertension. It has been argued that studies of animal models of hypertension (principally hypertensive rat strains) provide more clear genetic evidence than human studies. This may be the case, but studies that suggested linkage of hypertension with a particular gene in a particular hypertensive rat strain (for example the renin gene in the spontaneously hypertensive rat) have not been substantiated in alternative hypertensive rat strains nor in human hypertension.³ Thus the use of such models to identify genes which may be of relevance to hypertension in man may be misleading.

The methodological principles for the identification of genes in human hypertension can broadly be categorised as follows:

A. Population to be studied

Mutations in genes that cause hypertension can be sought either by association or linkage studies. The former seek to identify a difference in genomic structure between hypertensive populations and controls. However there are several draw-

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