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# REPORT FROM A SYMPOSIUM ON MOVING POINTS IN MEDICINE HELD IN NINEWELLS HOSPITAL AND MEDICAL SCHOOL ON 19 NOVEMBER 1997*

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## CHEMOPREVENTION OF CANCER

Cancer chemoprevention is defined as the use of chemoagents to reduce the incidence of cancer. It also extends to the use of diet for the same purpose. This is a relatively new field which has its origins in the confluence of developments in laboratory carcinogenesis, pharmacology and nutritional epidemiology. Knowledge of genetic changes that occur during carcinogenesis is increasing and agents are now identified that can arrest the process at different stages. It is a rapidly expanding field with great potential for reducing cancer morbidity and mortality.

Tamoxifen has been used for 20 years in the management of breast cancer and its use as adjuvant therapy is associated with an approximate 10% improvement in breast cancer cure rates, and a reduction in the likelihood of a second primary breast cancer. Unfortunately tamoxifen has been linked to uncommon side-effects potentially harmful to healthy individuals, in particular an increased risk of developing uterine cancer; associations with other cancers have been proposed but not proven. Fortunately newer second-generation iodinated tamoxifen derivatives appear to be less carcinogenic. Chemoprevention trials with tamoxifen were stopped early; it was noted that the drug brings about a reduction in the incidence of myocardial infarction, possibly due to changes in blood lipids. Further trials in subjects with a high risk of developing breast cancer, such as those with genetic predisposition (for example, p53 disease and ataxia telangectasia) are ongoing and may clarify the value of tamoxifen in prevention.

There is now clear evidence that aspirin and non-steroidal anti-inflammatory medications (NSAIDS) can prevent polyp formation and promote polyp regression in the colon, while a high fibre intake is associated with a reduced risk of colorectal carcinoma.

Of crucial importance in any discussion about chemoprevention is the recognition that the chemopreventative agents may themselves cause more harm than good. This is clearly relevant when considering the long-term administration of NSAIDS to obtain a possible modest reduction in bowel cancer. This aspect was highlighted by a study assessing the chemopreventative effects of beta-carotene for lung carcinoma: active treatment was associated with a higher incidence of the disease.

The potential of other vitamins to prevent cancer has been extensively studied. Unfortunately, at present none can be recommended as the trial results are contradictory and inconclusive.

Thus, while the role of chemoprevention remains to be defined, prospects for the future are good. Research is active and expanding; recent advances in the field of genetic engineering have resulted in the development of transgenic animals which

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have facilitated increasingly sophisticated carcinogenesis experiments. Such research has led to the conclusion that the cause of all cancers is to be found at the genetic level and that in the future the induction of genetic mutations will enable trials of promising chemoprotective agents to be completed more quickly.

### THE CHANGING HEALTH SERVICE

In the last century it began to be understood that social circumstances affect community health, initially with the recognition of a clear association between tuberculosis and poor housing. This association provided the impetus for early public health care including the provision of better housing and improved nutrition. To this day, despite many improvements, the social environment remains a large influence on overall health. Evidence of this is readily apparent both from the observation that with increasing wealth comes increasing health, and also from studies in Scandinavia which show a clear relationship between homelessness and mortality from both cardiovascular disease and cancer. Despite these observations, recent years have seen a shift in health care emphasis away from social and community needs towards the 'high tech' world of the hospital specialist. This is an unwelcome trend which should be redressed.

Public health as a speciality needs to rediscover its roots. Implicit in this is a reappreciation of the importance of epidemiology coupled with increased co-operation between Public Health Services and clinicians. An attempt could be made, possibly through the more widespread introduction of clinical managers, to address the fundamental flaws in the current system whereby acute hospitals, community trusts and primary care physicians operate without clear awareness of each other's activity.

### TREATING THE COMMON COLD

Despite years of research, a cure for the common cold remains elusive. It remains a considerable burden on the workload of general practitioners and a frequent cause of morbidity. Furthermore it can result in *otitis media*, reactivation of *herpes simplex* infection, and remains a frequent precipitant of exacerbations of asthma or bronchitis. The common cold is caused, in the main, by infection with rhinovirus or coronavirus, with a minority of cases being due to either respiratory syncytial virus, influenza, para-influenza or adenovirus infection. Inoculation occurs through the eye or nose and virus-induced inflammation results in a purulent nasal secretion which predominantly represents the debris of excreted ciliated cells and neutrophils. Once infected, a patient can remain so for up to three weeks. Transmission occurs through direct contact with infected nasal secretion.

Treatment is preventative and involves the obvious precautions of avoiding cold sufferers and maintaining high standards of personal hygiene. Unfortunately vaccination is not feasible in view of the large number of viral antigenic types. Antiviral therapy is impractical as it would involve continuous spraying of the nose all year around. Symptomatic treatment can be achieved with intra-nasal ipratropium which reduces watery rhinorrhoea but it has no effect on the amount of mucopurulent secretion. Antihistamines have a role in reducing both the frequency of sneezes and the volume of secretions. The use of NSAIDs should be reserved for patients with predominant symptoms of pain. Therapies such as the use of menthol or zinc preparations, or vitamin C, remain popular despite lack of proof of efficacy.

### PATIENTS POISONED WITH PSYCHOACTIVE DRUGS

Even at therapeutic doses anti-psychotic medications can have dramatic side-effects. One such is the acute dystonic reaction or oculogyric crisis which may occur especially

in younger people, and is readily treated with pyridostigmine. In overdose, anti-psychotics can variously cause postural hypotension, coma, mydriasis, convulsions and a prolongation of the QT interval which can result in the form of polymorphic ventricular tachycardia known as *torsades de point*. Patients with a history of heart disease, ethanol abuse, severe hepatic or renal impairment are especially susceptible to the consequences of psychotropic drug overdose.

An overdose of tricyclic antidepressant results in tachycardia, arrhythmias and hypotension due to quinidine-like effects. Other features include dilated pupils, hyperreflexia, bilateral up-going plantars and convulsions.

Overdose with psychoactive drugs is reversible. In the first instance the treatment is based on the administration of activated charcoal. Gastric lavage and ipecacuanha are often used, though with little evidence of proven efficacy. Sodium bicarbonate may be helpful for managing the cardiac toxicity but the most important treatment in that complication is to increase the heart rate either pharmacologically or with pacing if necessary.

In tricyclic overdosage, treatment is predominantly supportive and consists of maintaining the arterial circulation, together with anti-arrhythmic and anticonvulsant therapy where appropriate.

Since 1990, safety in overdose has been taken into account when licensing anti-psychotic medication. Encouragingly the death rate per million prescriptions of antidepressant medication has improved from 35 with tricyclic antidepressant to 2 with the newer selective serotonin reuptake inhibitors.

## PHARMACEUTICAL CARE - FACT OR FICTION

Traditionally the pharmacy undergraduate course has been primarily based on natural sciences and therapeutics. More recently, the importance both of clinical and social science and of increasing the rapport between clinicians and pharmacists has become recognised. The Nuffield report (1986) recommended a closer relationship between general practitioners (GPs) and pharmacists. In addition the concept of pharmaceutical care coined by Heder and Strand suggested a shift in the role of the pharmacist from the provision of pharmaceutical products to patient care.

While drugs are tools for health care, it has been estimated that 2.5 tonnes of medication are wasted per year. Sixty-six per cent of GP prescribing is for repeat prescriptions and accounts for 80% of prescribing costs. While this may have benefits in terms of convenience to the patient and practitioner it is at the risk of wastage and poor disease control. Furthermore, adverse events may remain undiscovered.

How can this be improved? One way to reduce wastage would be the collaboration of pharmacists and doctors in reviewing six-monthly scripts. In time this might lead to a shift in traditional roles where pharmacists manage the prescribing of some medications, for example for chronic conditions.

Traditionally pharmacists are remunerated on the basis of dispensed prescriptions and the relationship between pharmacists and the NHS has been driven by this. Other remunerative models would be required to allow role changes. One option would be patient registration and capitation similar to the general medical contract.

These changes could lead to a new age of pharmacy where pharmacists have an increased role in prescribing, especially in managing both common ailments and chronic conditions.