are at least 3 essential elements in any such prevention programme: (1) A system for routine toxicity and carcinogenicity checking of all industrial chemicals currently in use or likely to be introduced in the future; (2) provision for routine environmental monitoring of factory atmospheres for the presence of known or suspected pollutants and (3) careful and continuing epidemiological control of workers who may be at risk. Above all else, these elements will require an urgent revision and improvement of present systems of record keeping, maintenance and linkage, not only in the factory but also in the community.

NICKEL AND CADMIUM CARCINOGENESIS. G. KAZANTZIS, Department of Community Medicine, Middlesex Hospital, London.

Workers at a nickel refinery in Wales were first noted to have an unusually high mortality from cancer of the respiratory tract some 30 years after the plant had become operational. A proportional mortality study by Doll (*Br. J. indust. Med.*, 1958, **15**, 217) showed a five-fold increase in deaths from lung cancer and a 150-fold increase from nasal cancer in these men. While at first the Mond nickel process involving exposure to nickel carbonyl gas was thought to have been responsible, a similarly high mortality experience was found among refinery workers in Ontario where the Mond process had not been used (Mastromatteo, *J. occup. Med.* 1967, **9**, 127). In both plants mortality experience fell to that expected from national mortality data in men first employed after changes had been made which involved drastic reduction in exposure to nickel.

Experimental work supports the epidemiological evidence for the carcinogenic activity of nickel. Malignant tumours have been produced in several animal species by nickel as the powdered metal and by a variety of nickel compounds introduced by different routes. These, with possible mechanisms of nickel carcinogenesis, have been reviewed by Sunderman (*Fd Cosmet. Toxicol.*, 1971, **9**, 105) who provided evidence for inhibition by nickel carbonyl of DNA dependent RNA synthesis.

Cadmium is a biologically active metal responsible for emphysema and renal tubular dysfunction following long-term exposure. A survey of men who had been occupationally exposed to cadmium oxide dust for a minimum period of one year revealed an increased mortality from prostatic carcinoma (Kipling and Waterhouse, *Lancet*, 1967, i, 730). No further epidemiological evidence incriminating cadmium in human carcinogenesis has been produced. Traces of cadmium are present in cigarette smoke and smokers accumulate more cadmium in kidney, liver and lung than non-smokers. However, a causal role for cadmium in bronchogenic carcinoma has not been postulated.

A carcinogenic potential for cadmium has been demonstrated in several experimental animal studies. Finely divided cadmium metal injected into the thigh muscle of the rat gave rise to rhabdomyosarcoma (Heath and Daniel, *Br. J. Cancer*, 1964, **18**, 124). Cadmium sulphide and cadmium oxide injected subcutaneously and intramuscularly led to fibrosarcoma at the injection site with metastases in a high proportion of the dosed rats (Kazantzis and Hanbury, *Br. J. Cancer*, 1966, **20**, 190) and repeated injections of cadmium sulphate were followed by testicular atrophy and interstitial cell tumours of the testis (Haddow *et al.*, *Br. J. Cancer*, 1964, **18**, 667). No prostatic changes were observed following the repeated subcutaneous injection of cadmium sulphate or following its long-term administration in drinking water in concentrations below those required to demonstrate a toxic effect in the rat (Levy *et al.*, *Ann. occup. Hyg.*, 1973, **16**, 111).

Further epidemiological surveillance is required before the question of the carcinogenic potential of cadmium in man can be decided.

ASBESTOS CARCINOGENESIS. J. C. WAGNER, Medical Research Council, Penarth.

Carcinoma of the lung and diffuse mesotheliomata of the pleura and peritoneum have occurred in people exposed to asbestos dust. Various types of asbestos are used in industry and studies have been undertaken to establish whether these tumours are associated with exposure to specific types of fibre.

Carcinoma of the lung was first reported in cases of asbestosis in 1935. The incidence of these tumours has increased rapidly and by 1964, 60% of those workers in the United Kingdom diagnosed as having asbestosis to a

degree warranting compensation developed carcinomata. Recently, the fact that cigarette smoking and asbestosis have a multiplicative carcinogenic effect has been recognized. The accepted evidence is that the carcinomata occur in cases of definite asbestosis and that excessive exposure to all major types of asbestos used commercially are implicated, the incidence of carcinoma being higher in those exposed in industry compared with the mining areas.

In contrast to the carcinomata, the mesotheliomata have been associated with exposure to asbestos dust and can occur without evidence of scarring in the lungs. The first series was reported from South Africa in 1960. International investigations have confirmed that these tumours are more clearly associated with exposure to crocidolite (blue asbestos) dust from the Cape Province in South Africa and to a lesser extent to the fibre in Western Australia, than the other types of asbestos. The physical parameters of these fibres may permit more penetration into the lung parenchyma and pleura than other types of commercially used asbestos. The tumours occur after a considerable lapse period from the initial time of exposure, and can develop in people who have had a relatively brief exposure, as little as 6 weeks in some cases. Recent studies have shown a definite dust dosage relationship. There is no evidence that there is an association between the mesotheliomata and cigarette smoking. Several epidemiological surveys have shown a slight but significant increased incidence of gastrointestinal tumours in asbestos workers. A study of women asbestos workers has not shown an increased incidence of ovarian tumours.

In animal experiments it has been possible to produce mesotheliomata by the intrapleural inoculation of all types of asbestos fibre, the highest percentage of tumours being produced by very fine chrysotile which, when implanted into the pleural cavity, is more carcinogenic than the crocidolite. Further experimental studies with other types of mineral fibres, both natural and synthetic, can produce tumours. The finer the ultimate fibre, the greater the incidence of tumour. In inhalation studies squamous and adenocarcinomata have been produced in rats, the majority of the tumours occurring in animals with a moderate degree of asbestosis. A few mesotheliomata were seen.

URBAN, OCCUPATION AND "PERSONAL" AIR POLLUTANTS IN RELATION TO LUNG CANCER. R. E. WALLER, MRC Air Pollution Unit, St Bartholomew's Hospital Medical College, London.

The overwhelming effect of cigarette smoking on the occurrence of lung cancer and the resulting "tidal-wave" that has swept through the mortality statistics during the past 50 years have made it very difficult to search for other factors by the traditional means of relating death rates to occupation or to area of residence, as recorded on death certificates. It is necessary to ensure not only that populations being compared are similar in respect of their current smoking habits but also that these smoking habits are in phase: the low lung cancer death rate among coal-miners may, for example, be partly a reflection of a more gradual swing from pipes to cigarettes than in the general population. Similarly, any "phase-lag" in the development of cigarette smoking habits in rural areas would tend to enhance the ratio of urban to rural death rates, making it difficult to isolate any urban factor that might be related to air pollution.

Although these problems could only be overcome by conducting prospective surveys on a very large scale, they can at least be seen most clearly if the relevant mortality data are presented on a cohort basis. This has been done for lung cancer deaths classified by area of residence, and the results indicate substantial phase differences between London, other urban areas and rural areas. The present situation is that the peak in male lung cancer mortality in London seems to have been passed already, with the more recent cohorts (those born since about 1911) having lower rates than their predecessors. The trends in rural areas are lagging behind those in conurbations and ultimately there may be only a small urban/rural gradient in lung cancer mortality.

It is still not clear whether remaining urban/rural differences should be attributed to air pollution, and in particular to the inhalation of smoke particles containing benzo(a)pyrene. The Clean Air Act has certainly led to a substantial reduction in smoke concentrations in the larger towns, particularly in London, and recent measurements indicate that benzo(a)pyrene concentrations in central London are now only about