Ampullary cancer in chemical workers

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Although a relatively uncommon neoplasm, cancer of the ampulla of Vater does account for over 300 deaths a year in the United States.¹ Among biliary tract tumours, ampullary cancer is regarded as having a favourable prognosis because the early onset of symptoms, low grade histopathology, and late and infrequent metastases allow the possibility of surgical cure; nevertheless, high operative mortality and overall five year survival figures of between 4% and 40%, depending on type of tumour and disease spread at diagnosis, show that these cancers cannot be considered as having a good prognosis.¹ These figures also serve to underline the importance of the identification of underlying aetiological factors for these tumours. In previous research we had identified the possible importance of chemical exposures in the development of these tumours; however, statistical significance was limited by the small numbers involved.^{1,2} Expansion of these studies has now confirmed our previous predictions.

Materials and methods

Information data files on causes of mortality among chemical workers were described previously and have now been expanded as described elsewhere.^{2,3} Cases of biliary cancer were segregated out by site specific categories—for example, gall bladder, extrahepatic bile ducts, intrahepatic bile ducts, and ampulla of Vater. Fifty cases of biliary cancer (11 of which were ampullary) were identified in this expanded mortality data base. An adjusted proportional mortality ratio (PMR) analysis was performed on the combined cases by dividing the number of deaths observed in each category by the number expected based on the proportion of deaths in this category in the United States general population and multiplying by 100.⁴ The statistical significance was tested using Fisher's exact test and statistical significance was assumed for *p* values of less than 0.05.

Results and comments

We have previously reported raised PMR for ampul-

lary cancer among chemical workers (280) which was not statistically significant due to the small numbers involved.² The 11 cases of ampullary cancer now identified among a population in which fewer than five deaths from carcinoma of the ampulla of Vater would be expected yields a PMR of 228, in reasonable agreement with the earlier figure. In this case, however, statistical significance was confirmed (*p* = 0.011). The PMRs for cancers at other sites in the biliary tract were not significantly raised.

This finding is consistent with our previously reported study of necropsy records which showed the frequent incidence of employment in the chemical industry with exposure to polycyclic aromatic hydrocarbons and aromatic amino compounds among cases of ampullary cancer.^{1,3} Furthermore, these cases with exposure tended to be younger and to be more likely to have second primary malignancies than other cases of ampullary cancer or other types of cancer.^{1,3} In addition, animal studies support this association since various organic chemicals such as toluene diamine and aminoazotoluene have been shown to induce pre-malignant and malignant lesions of the biliary tract.¹ Earlier epidemiological studies of cancer in the chemical industry may have failed to find such an association since cancers of the ampulla have tended to be grouped with other hepatobiliary cancers. For example, in a recent Swedish study tumours of the ampulla were grouped with all other extrahepatic biliary malignancies exclusive of the gall bladder, and although the standardised incidence ratio for this group of tumours was 1.5 times that expected among male chemical workers, the finding was not statistically significant⁵; in this instance, ampullary tumours accounted for only 30% of the cancers in the group, and thus a statistically significant increase may have been diluted by the inclusion of tumours from other sites in the biliary tree.⁵

From the current data, it would seem likely that employment in the chemical industry may predispose to the development of cancer of the ampulla of Vater. This study, however, did not show any apparent clustering of cancer by job description or by likely exposure. Thus further research will be necessary to confirm these findings. In particular, it will be important to pursue the identification of specific

chemicals that might be involved in the hope of preventing future cases.

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- ¹ International Steering Committee of Medical Editors. Uniform requirements for manuscripts submitted to biomedical journals. *Br Med J* 1979;1:532-5.
- ² Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosino-phil chemotactic factor of anaphylaxis during cold challenge. *N Engl J Med* 1976;294:687-90.
- ³ Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: W B Saunders, 1974:457-72.