PANCREATIC ISLET CELL AND OTHER TUMOURS INDUCED IN RATS BY HELIOTRINE- A MONO-ESTER PYRROLIZIDINE ALKALOID; THE EFFECTS OF ADDITIONAL TREATMENT WITH NICOTINAMIDE. R. SCHOENTAL, The Royal Veterinary College, London.

The carcinogenic action of diester pyrrolizidine alkaloids (Schoental, *Cancer Res.*, 1968, **28**, 2237) has been confirmed in several laboratories (Harris and Chen, *Cancer Res.*, 1970, **30**, 2881; Svoboda and Reddy, *ibid.*, 1972, **32**, 908; Newberne and Rogers, *Plant Foods for Man*, 1973, **1**, 23).

The mono-ester alkaloid, heliotrine, has been claimed not to be carcinogenic (Bull, Culvenor and Dick, *The Pyrrolizidine Alkaloids*, 1968, North Holland Publishing Co.).

In experiments to be described, heliotrine induced in white rats various chronic lesions and tumours, including adenomata of the pancreatic islet cells. Pancreatic islet cell tumours have already been described among rats treated with pyrrolizidine alkaloids, including the mono-esters from *Amsinckia intermedia* (Schoental, Fowler and Coady, *Cancer Res.*, 1970, **30**, 2127).

TREATMENT OF A METASTASIZING MURINE TUMOUR WITH *CORYNEBACTERIUM PARVUM*. T. E. SADLER and J. E. CASTRO, Urology and Transplant Unit, Royal Postgraduate Medical School, London.

Effects of *Corynebacterium parvum* (*C. parvum*) on the metastasizing Lewis lung carcinoma were studied in C57/Bl mice. Intravenous or intraperitoneal *C. parvum* given at the same time as subcutaneous inoculation of tumour significantly reduced the primary tumour mass, and the number of pulmonary metastases observed at 21 days. Subcutaneous *C. parvum* had no effect on either primary tumour or metastases. Macroscopic pulmonary metastases were not observed 10 days after tumour inoculation. When the primary tumour was excised at that time pulmonary metastases were found at 21 days.

Combined effects of surgical excision and *C. parvum* on pulmonary metastases were studied. There was minimal protection when *C. parvum* and surgery were on the same day but protection occurred when *C. parvum* was given before tumour excision.

In defined conditions surgery and *C. parvum* prevent pulmonary metastases from the Lewis tumour. (This work is supported by the Cancer Research Campaign.)

MECHANISM OF ACTION OF TUMOUR INHIBITORY NITROSOUREAS. T. A. CONNORS and J. R. HARE, Chester Beatty Research Institute, London.

1,3 - Bis(2 - chloroethyl) - 1 - nitrosourea (BCNU) and related nitrosoureas are highly selective anti-tumour agents. Because of their chemical structure, it has been suggested that they act similarly to the bifunctional alkylating agents. They have been compared with two alkylating agents and shown to be quite distinct in a number of properties: (1) They have a much wider spectrum of action and can cure animals with tumours insensitive to alkylating agents; (2) tumours resistant to BCNU are cross-resistant to other nitrosoureas but are collaterally sensitive to alkylating agents; (3) nitrosoureas rapidly inhibit the incorporation of precursors into both nucleic acids and proteins, unlike the alkylating agents which have a specific effect on thymidine incorporation into DNA; (4) labelled nitrosoureas react predominantly with nuclear protein and only to a small extent with nucleic acids; (5) BCNU interferes specifically with the incorporation of thymidine triphosphate into DNA, and its cytotoxicity can be prevented by low doses of thymidine.

Although the toxicity of the nitrosoureas may be due partly to their alkylating properties, they are quite distinct from the bifunctional alkylating agents and probably act by a different mechanism.

DISTRIBUTION STUDIES WITH AN AMINOPHOSPHONIC ACID ANALOGUE OF DOPA IN MICE BEARING THE HARDING-PASSEY MELANOMA. M. J. STRINGER, J. A. STOCK and L. M. COBB, Chester Beatty Research Institute, London.

A compound which is incorporated selectively into melanin during biosynthesis *in vivo*, and which carries an isotope of adequate radiotoxicity and short half-life, has a potential application in the treatment of malignant melanoma. Such therapy would