B.C.G. TREATMENT OF PLEURAL AND PERITONEAL TUMOUR GROWTH IN RATS. M. V. Pimm. Cancer Research Campaign Laboratories, University of Nottingham.

Growth of intrapleurally injected cells of immunogenic 3-methylcholanthrene induced rat sarcomata was suppressed by intrapleural injection of viable or radiation sterilized B.C.G. organisms. As little as 10 μg of B.C.G. was effective and treatment was successful even if given several days after tumour challenge. B.C.G. administered intravenously or subcutaneously was without influence on pleural tumour growth. Similarly, peritoneal growth of these sarcomata was suppressed only by the intraperitoneal injections of B.C.G. organisms.

In contrast, pleural or peritoneal growths from cells of other rat tumours, which lacked significant immunogenicity, were not controlled by this type of B.C.G. treatment. Nevertheless, these studies indicate the potential of B.C.G. (contact) immunotherapy for treatment of thoracic and peritoneal tumour deposits, which might perhaps have a clinical application, for example in the treatment of malignant mesothelioma of the pleura and peritoneum.

DETECTION OF TUMOUR ASSOCIATED EMBRYONIC ANTIGENS. M. R. Price and R. C. Rees. Cancer Research Campaign Laboratories, University of Nottingham.

Chemically induced and spontaneously arising rat tumours express embryonic antigens, which are also demonstrable on embryo cells taken between 14 and 16 days of gestation. The expression of tumour associated embryonic antigens may be a common feature of malignant transformation since these antigens are present on tumours which lack demonstrable levels of tumour specific rejection antigens. Also, unlike the tumour rejection antigens associated with chemically induced tumours, they show cross-reactivity, especially between tumours of the same histological type. This suggests that the tumour associated embryonic antigens, which differ from other embryonic products such as α-fetoprotein in being immunogenic in the autochthonous host, may be appropriate markers for immunodiagnostic assays. This is further emphasized by studies to be discussed, showing that homogeneous preparations of soluble embryonic antigen can be isolated readily from tumour cytoplasmic fractions, indicating the possibility of utilizing defined reagents in immunoassays for monitoring circulating tumour antigen.

CORRELATION OF SERUM LEVELS OF HEPATOMA D23 ANTIGEN, ANTIBODY AND IMMUNE COMPLEXES WITH GROWTH OF TRANSPLANTED TUMOURS. M. R. Price and J. G. Bowen. Cancer Research Campaign Laboratories, University of Nottingham.

Hepatoma D23 antigen has been monitored in the serum of tumour bearing rats using an antibody inhibition assay based upon membrane immunofluorescence methods for detecting antibody in tumour immune sera. Simultaneously, levels of tumour specific antibody in sera of tumour bearing rats were analysed by their direct membrane immunofluorescence staining with hepatoma D23 cells. Applying these techniques, it has been established that during the early stages of subcutaneous growth of hepatoma D23 in syngeneic rats there is significant shedding of tumour specific antigen into the circulation. This is then depressed after a period of between 10 and 14 days tumour growth, at which time circulating tumour specific immune complexes are detectable. Finally, antibody can be detected. These observations are relevant to current views that cell mediated immunity to tumour cells can be blocked by interaction of antibody or immune complexes with tumour cells or by antigen inhibition of effector cells. Furthermore, these model studies indicate the importance of designing immunochemical assays for diagnostic and prognostic purposes during tumour therapy.

THE GROWTH OF SPONTANEOUS MELANOMA ALLOGRAFTS IN IMMUNOSUPPRESSED NEONATAL DOGS. G. R. Betton and L. N. Owen. Department of Animal Pathology, University of Cambridge.

Clinical cases of melanoma in the dog have provided tumour cells for transplantation as fresh cell suspensions, cells stored in a frozen state and tissue culture cell lines. Tumour growth has been achieved in 18 of 36 cases
using intravenous or subcutaneous routes in newborn dogs under immunosuppression with anti-lymphocyte serum. Intravenous injections of tumour cells resulted in miliary nodules in the lungs and heart in as little as 3 weeks. Melanoma of the subcutis with metastases in some cases followed subcutaneous inoculation. Regression has been observed following cessation of ALS treatment. Normal cells have not produced tumours but melanoma cell cultures have retained this characteristic of malignancy.

NUCLEAR PROTEIN METABOLISM DURING ONE-DOSE URETHANE CARCINOGENESIS. C. F. FARNSWORTH and M. GRONOW. Department of Cancer Research, University of Leeds.

Treatment of 7–9 day old B6AF1 mice with a single carcinogenic dose of urethane, at 1.2 mg/g body weight resulted in an immediate decrease in liver DNA synthesis reaching a maximum at about 8–12 h after injection, the rate of synthesis returning to normal after 48 h.

Of the nuclear proteins, the non-histone protein fraction showed a significant decrease in specific activity 8 h after injection, and an increase in specific activity 24 h after injection. Histone and residual proteins did not show any significant changes.

The proteins present in the non-histone protein fraction were analysed by isoelectric focusing electrophoresis. The gels of treated and control samples showed similar gel patterns but with a much denser band appearing in the treated sample having a pI of 7.4.

Histone and residual protein fractions were also analysed by electrophoresis and showed no difference between treated and control samples.

STUDIES RELATED TO THE CARRIER PRINCIPLE IN THE DESIGN OF CYTOTOXIC DRUGS. M. SZEKERKE. Research Group for Peptide Chemistry, Hungarian Academy of Science, Budapest.

With the aim of rationalizing the design of peptide-type carriers attached to cytotoxic drugs, attention was focused on the mechanism of carrier function. The interaction of model peptides with nucleic acids was analysed by following the thermal denaturation profiles.

Complex formation with DNA reflects adequately the differences in the anti-tumour activity of diastereoisomer α- and γ-glutamyl melphalan derivatives. The changes of Tm-values of poly I : C-peptide complexes are in marked contrast to the behaviour of the complexes of DNA with the same peptides. No differences were detected in the ultraviolet absorption spectra (25°C) of DNA in the presence of peptides, while with N-aminoacyl D-glucosamine derivatives interactions are indicated by spectral shifts.

Both for carrier activity and DNA interaction there seem to exist precise structural requirements for peptides.