TUMOUR INHIBITORY TRIAZENES.
D. E. V. Wilman, Chester Beatty Research Institute, London.

5-(3, 3-Dimethyl-1-triazeno) imidazole-4-carboxamide (DIC) is a well known antitumour agent undergoing clinical trial. It has the disadvantage of being very photosensitive. The related aryltriazenes, however, do not decompose in this fashion although they are acid labile, to an extent dependent on the ring substituents.

In the case of 1-aryl-3, 3-dialkyltriazenes, the ring substituents have no marked effect on the activity towards the TLX5 lymphoma. Replacement of both methyl groups by ethyl or isopropyl groups leads to inactivity, where as if only one is replaced activity is retained. Microsomal metabolism experiments suggest that this is due to enzymic dealkylation to form the monoalkyl derivative.

Metabolism of 1-aryl-3-methyl-3-alkyltriazenes gives the monomethyltriazeno. Monomethyltriazenes are more acid labile and the activity of this metabolite is dependent on its half-life and hence the ring substituent. The dialkyltriazenes probably act as a slow release form of the monoalkyl metabolite, which is the active species.

THE ROLE OF ALKALINE PHOSPHATASE IN THE RELEASE OF \textit{p}-HYDROXY ANILINE MUSTARD FROM ITS PHOSPHATE CONJUGATE. P. Workman, J. A. Double and C. R. Ball, Department of Cancer Research, University of Leeds.

Para-hydroxy aniline mustard phosphate (AM-O-phos) was among the esters of \textit{p}-hydroxy aniline mustard (AM-OH) synthesized with the aim that such conjugates would exhibit a specific cytotoxic effect, \textit{via} the release of AM-OH, towards tumours containing high levels of the appropriate deconjugating enzymes (Bukhari, Everett and Ross, \textit{Bioch. Pharmac.}, 1971, 21, 963). Subsequently AM-O-phos was shown to be a substrate for selected phosphatases (Ball and Double, \textit{Bioch. Pharmac.}, 1974, 23, 3173). In this work the cytotoxicity of AM-O-phos in HeLa culture was studied in relation to the phosphatases of this cell line. The results are consistent with the view that the uptake of AM-OH is dependent on the activity of alkaline phosphatase, of the carcinoma placental type, located in the plasma membrane. No such dependence on acid phosphatase activity was observed. The cell culture model has also allowed the importance of extracellular phosphatase activity to be assessed.

HORMONES IN BREAST CANCER PATIENTS ON TAMOXIFEN. M. P. Golder, M. E. A. Phillips, M. Baum, K. Griffiths, D. R. Fahmy, J. M. Henk, V. Jones and P. E. Preece, South Wales and Monmouthshire Radiotherapy Centre, Velindre Hospital, and Tenevus Institute for Cancer Research, Department of Surgery, Welsh National School of Medicine, Cardiff.

Tamoxifen (20 mg) has been given twice daily to 30 consecutive post-menopausal women with advanced breast cancer. Progesterone, oestriol and estriol stimulating hormones have been assayed on plasma taken before and at regular intervals during treatment. By the criteria of Forrest \textit{(in Clinical Management of Advanced Breast Cancer)}. Eds. Joslin and Gleave, Cardiff: Alpha Omega Alpha Publish-
ing Co. 1970), between 30 and 40% had objective remissions.

Pre-treatment levels of prolactin were variable, and were not changed by treatment, whether or not remission occurred. Pre-treatment levels of oestradiol varied less, but were also substantially unchanged in all patients during treatment. Growth hormone showed no consistent response. In most patients in whom regression of disease was observed, values of luteinizing and follicle stimulating hormone did not vary, but in the majority of non-responders, gonadotrophin levels were lowered.

METABOLIC ABNORMALITIES IN TUMOUR BEARING ANIMALS. K. C. Calman and R. A. McAllister, Department of Clinical Oncology, Western Infirmary, Glasgow.

Twenty-four hours after implantation of the TLX-5 lymphoma in CBA mice, the CoA content of liver was significantly reduced ($P < 0.001$). Significant reductions in the CoA content continued up to the seventh day, when the animals were in a moribund state. The citrate content of liver showed no further significant increases until the seventh day. Significant reductions in energy content (ATP, ADP, AMP) of these livers did not occur until 6 days after implantation.

Control experiments in which normal CBA mice were challenged with i.p. injections of normal CBA spleen cells, or with spleen cells from A strain mice, showed no change in the CoA or citrate content of liver. No decrease in CoA was noted in starvation experiments.

These results indicate that serious metabolic abnormalities occur in the non-involved organs of tumour bearing animals and these may be related to the development of cachexia.

UPTAKE OF $^{67}$GALLIUM BY NORMAL LACTATING MAMMARY GLAND AND BY TUMOURS IN THE DOG. A. T. Yoxall and L. N. Owen, Department of Clinical Veterinary Medicine, University of Cambridge.

Following intravenous injection of $^{67}$Ga it is known that there is a concentration of the isotope in several tumours and in a few normal tumours, including lactating mammary gland. Investigations in the lactating bitch have shown that $^{67}$Ga and $^{45}$Ca were taken up by the mammary tissue at the same rate and that the isotopes reached similar levels in both plasma and milk. The isotopes were found to be associated with calcium binding proteins in milk. It was not possible to show any correlation between $^{67}$Ga and $^{45}$Ca uptake in a transmissible venereal tumour.

A preliminary study to investigate if there is any association between the “leakiness” of tumour blood vessels as determined by the uptake of $^{125}$I-albumin and $^{67}$Ga in a melanoma has produced equivocal results.

THE PROGNOSIS FOLLOWING SURGICAL EXCISION OF CANINE MAMMARY CARCINOMATA. D. E. Bostock, Department of Clinical Veterinary Medicine, University of Cambridge.

Spontaneously arising canine mammary carcinomata may be of value as models in immunotherapeutic trials for breast cancer in women, but before their full potential can be exploited their behaviour following surgery alone must be known.

For this reason, 227 bitches from which histologically confirmed mammary carcinomata had been excised were followed up. Only 43% of these animals were eventually destroyed as a result of the original tumour but the accuracy of the prognosis could be improved by histologically sub-dividing the tumours. Papillary and tubular adenocarcinomata carried the most favourable prognosis, the median survival times being 12 and 90 weeks. Dogs with solid carcinomata had a medial post surgical survival time of 44 weeks whereas for those with anaplastic carcinoma it was only 11 weeks. Clinical immunotherapeutic trials will thus be concentrated on dogs with the latter tumour types.

Since most dogs die from their tumour within 12 months of surgery it should be possible to evaluate the effect of post surgical immunotherapy sooner than would be possible with a similar trial in man.

AUTORADIOGRAPHY OF EHRLICH ASCITES TUMOURS TREATED WITH SOYBEAN TRYPsin INHIBITOR IN VIVO. P. Whur and H. Koppel, Cell Biology Unit, Marie Curie Memorial Foundation, Oxted and B. Weatherhead, Depart-