

simple Bayesian form of analysis, 69% accuracy overall was achieved in predicting survival time (with 80% accuracy in those patients who survived over 2 months) and accuracy in predicting an objective response was 82%, and 72% for a subjective response.

These results suggest that: (i) it is possible in most patients to predict response using simple clinical parameters and analysis; (ii) this can be done in routine practice quickly and easily; and (iii) such a system—if implemented widely—might be of significant benefit to individual women suffering from breast cancer.

p-FLUOROPHENYLALANINE (pFPhe) AND MITOSIS: INHIBITION AND RECOVERY OF DIVISION IN HELA CELLS. D. N. WHEATLEY AND J. Y. HENDERSON. Department of Pathology, University of Aberdeen.

pFPhe inhibits the entry of HeLa cells into division; this effect is known to require incorporation of the amino-acid analogue into protein (Wheatley and Henderson, *Nature, Lond.*, 1974, 247, 281). Analysis of the proteins containing pFPhe made by HeLa cells on polyacrylamide disc gel electrophoresis systems showed excellent agreement with the Phe proteins. The turnover of pFPhe proteins also compared closely with that of the Phe proteins both at 37°C and 40°C.

When pFPhe is removed from the culture medium, cells recover their normal $G_2 \rightarrow M$ progression in a cycle related manner after a delay period which depends on both the concentration and length of pFPhe exposure. After careful analysis of conditions permitting recovery, it would appear that a highly labile protein or group of proteins is involved which can only suppress mitosis when pFPhe is maintained at "physiological" levels. At slightly elevated temperature the inhibitory action is accentuated.

A COMPARISON OF CHEMICAL AND MICROBIOLOGICAL METHODS FOR ESTIMATING ALKYLATING AGENT CONCENTRATION. S. M. TOOGOOD, P. WORKMAN, C. R. BALL and R. C. GARNER. Department of Cancer Research, University of Leeds.

Three methods of estimating alkylating agent concentration have been compared,

initially using aniline mustard as a model compound: (i) inactivation of *E. coli* B; (ii) reaction with 4-p-nitrobenzyl pyridine (Epstein *et al.*, *Anal. Chem.*, 1955, 27, 1435) and (iii) formation of a ³⁵S-thiazan derivative (Connors, T. A. *et al.*, *Biochem. Pharmac.*, 1972, 21, 1309).

Quantitation of the latter in a reproducible manner has proved difficult and sensitivity is not as great as expected. Greatest biological sensitivity amongst DNA repair deficient strains of *E. coli* B was shown by *uvrA* *extrA* and *uvrA recA* mutants. Surprisingly, a triple mutant *polAuvrAextrA* was less sensitive to both aniline and nitrogen mustards, the reverse being true for methyl methane sulphonate.

The microbiological method is more sensitive than either chemical method, particularly for the more reactive drugs such as p-hydroxyaniline mustard and nitrogen mustard, and more readily applied in some instances. The method has enabled drug adsorption to albumin to be studied. Identification and estimation of alkylating agents and their metabolites in biological fluids should be made possible using this technique.

PREDICTION OF RESPONSE TO ANTIHORMONE TREATMENT USING AN *IN VITRO* TEST FOR DEPENDENCE OF HORMONES. H. SALIH, I. DE SOUZA, H. FLAX, K. NEWTON and J. R. HOBBS. Tumour Biology Group, Westminster Hospital Medical School.

In vitro hormone dependence has been defined by detecting enhanced pentose shunt activity in 24 h cultures of freshly biopsied human breast cancers after known hormones have been added to the culture medium. Four hormones (oestrogen, androgen, prolactin, growth hormone) have been implicated in half of the 300 breast cancers, and these could not be assessed adequately by the previous methods of studying urinary patterns of androgen excretion or measuring binding to receptors in homogenates. The clinical response of 40 patients to antihormonal treatments revealed: (1) 9/9 oestrogen dependent tumours responding to antioestrogens; (2) 6/7 androgen dependent tumours responding to antiandrogenic measures; (3) 5/6 prolactin - growth hormone dependent tumours responding to satisfactory hypophysectomy; (4) 3/3 prolactin dependent

tumours failed to respond because prolactin was not abolished; (5) 2/2 oestrogen dependent tumours got worse on oestrogens; (6) 2/2 androgen dependent tumours got worse on testosterone; (7) 10/11 *in vitro* independent tumours failed to respond. The *in vitro* test thus gave a correct prediction in 37 of 40 patients.

CHANGES IN RESPONSE TO CHEMOTHERAPEUTIC AGENTS DURING THE LIFE HISTORY OF MONOLAYER CULTURES OF A MOUSE TUMOUR CELL LINE. P. R. TWENTYMAN and N. M. BLEEHEN. Academic Department of Radiotherapy, Middlesex Hospital Medical School, London.

At the previous meeting of the Association, we described how EMT6 mouse tumour cells become less sensitive to bleomycin as they pass from exponential growth into plateau phase. This result was the opposite of that reported by other workers using Chinese hamster cells. Detailed investigation of the proliferation kinetics of our EMT6 cell line has revealed that the plateau phase may be subdivided into early plateau (with a pulse labelling index of 25% and considerable cell loss) and late plateau (with a labelling index of <5% and little cell loss). Sensitivity to bleomycin is indeed reduced during early plateau (compared with exponentially growing cells), but in late plateau the sensitivity becomes greater than that in exponential cells. Sensitivity to a number of other chemotherapeutic agents has also been investigated in cultures of various ages.

THE EFFECT OF WHOLE BODY HYPERTHERMIA IN ADVANCED CANCER. R. T. PETTIGREW, C. M. LUDGATE and A. N. SMITH. Department of Anaesthetics and Department of Clinical Surgery, Western General Hospital and University of Edinburgh.

The anaesthetized patient is immersed in molten wax at 50°C. This reverses the normal physiological processes of heat loss. A 5°C rise is achieved in one hour and maintained for 3-4 h. Fifty-five patients with advanced cancer have been heated to 41.8°C and the tumour response assessed by criteria which include relief of pain, weight gain, serial biopsy changes and evidence of tumour

regression. One group (45 patients) was treated by hyperthermia alone; sarcomata and gastrointestinal tract tumours were the most responsive (8 in 11); an intermediate group, skin and lung tumours, was less so (6 in 16); a third (mainly genito-urinary), the least (0 in 14). The addition of chemotherapy to hyperthermia in 10 patients raised the proportion regressing from 11 in 23 (48%) to 7 in 10 (70%). Occasional complications were mild superficial burns, tracheitis, ventricular fibrillation and disseminated intravascular coagulation.

ANALYSIS OF THE ANTIMETASTATIC ACTION OF THE ANTIMITOTIC AGENT ICRF 159. K. HELLMANN, S. E. JAMES and A. J. SALSBUY. Imperial Cancer Research Fund, London.

ICRF 159 inhibits metastases from the spontaneously metastasizing Lewis lung carcinoma (3LL) without markedly impeding the growth of the primary implant. It has previously been proposed that this antimetastatic action of ICRF 159 is due to the inhibition of malignant cell release from the primary tumour consequent upon normalization of the tumour blood vessels by the drug. Lung "metastases" due to intravenous injection of 3LL cells should therefore be unaffected by ICRF 159 administration. This was not, however, found to be the case.

When primary tumours were excised up to 6 days following implantation, secondary growths were not apparent in the lungs at 21 days. Treatment of primary tumours for the first 6 days by 30 mg/kg ICRF 159, at a time therefore when no circulating malignant cells would have been present, produced an almost complete inhibition of metastases. Thus, under these conditions the antimetastatic action cannot be ascribed to an effect of the drug on 3LL cells in the blood stream.

A COMPARISON OF THE CELL KILLING IN THE MOUSE AFTER EXPOSURE TO FTORAFUR AND TO 5-FLUOROURACIL. L. M. VAN PUTTEN, L. K. J. KRAM-IDSENGA and M. PIJPERS-DE BRUIN. Radiobiological Institute TNO, Rijswijk, Holland.

Ftorafur (N-1-(furanidyl)-5 fluorouracil) was compared with 5-fluorouracil (5-FU) in mice. The LD₅₀ and the slopes of the dose-effect curves for killing of L1210 leukaemia