Br. J. Cancer (1980) **42,** 900

HYPERPHAGOCYTOSIS AND THE EFFECT OF LIPOPOLYSACCHARIDE INJECTION IN TUMOUR-BEARING MICE

J. W. B. BRADFIELD*, T. WHITMARSH-EVERISS†, D. B. PALMER†,

R. PAYNE* AND M. O. SYMES†

*From the Departments of *Pathology and †Surgery, The Medical School, Bristol*

Received 28 March 1980 Accepted 21 August 1980

Summary.—(AxT6)F_1 hybrid mice received s.c. transplants from (AxT6)F_1 mammary carcinomas. At 1, 2 or 4 weeks after tumour transplantation, the mice were bled to obtain plasma and then challenged with 25 μg *E. coli* lipopolysaccharide (LPS) endotoxin i.v. The mice were killed 24 h later, further plasma was obtained and their liver ratios and spleen ratios were determined. A similar procedure was

MATERIALS AND METHODS

(A female × CBA(T6) male) F_1 hybrid mice bred in the Department of Surgery by crossing highly inbred A/Mi and CBA-HT6 mice, also maintained in the Department, were used throughout the study.

Two mammary carcinomas (referred to as

shown by the oxidized form, and the decrease in the absorbance at this wavelength provides

The levels of ornithine carbamoyl transferase (OCT) were measured by the method of Vassef (1978). OCT, an enzyme confined almost exclusively to the liver mitochondria, catalyses the reaction: Carbamoyl phosphate + L-ornithine = L-citrulline + phosphate. To

calculated, following an analysis of variance on the total data, by using a common variance

There was a significant rise in liver ratio in animals bearing Tumour 1 for 4 weeks

chromatic nuclei both in clumps and singly within sinusoids. It was not clear whether these were tumour cells or enlarged macrophages.

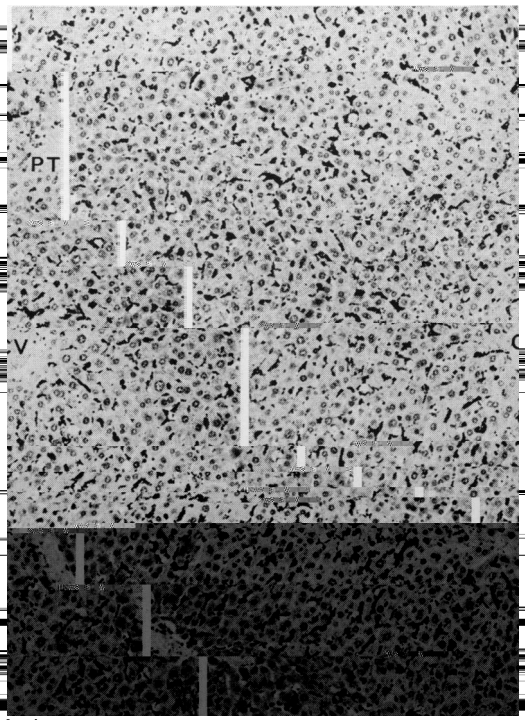
Hepatic damage during clearance of blood borne endotoxin by activated hepatic

passage of Tumour 1 or 2

To obtain values for the plasma AST and OCT before injection of LPS, mice were bled from the eye in groups of 5, with pooling of plasma from the mice in a given group, prior to determination of enzyme levels. It was found that the enzyme concentrations were unaffected

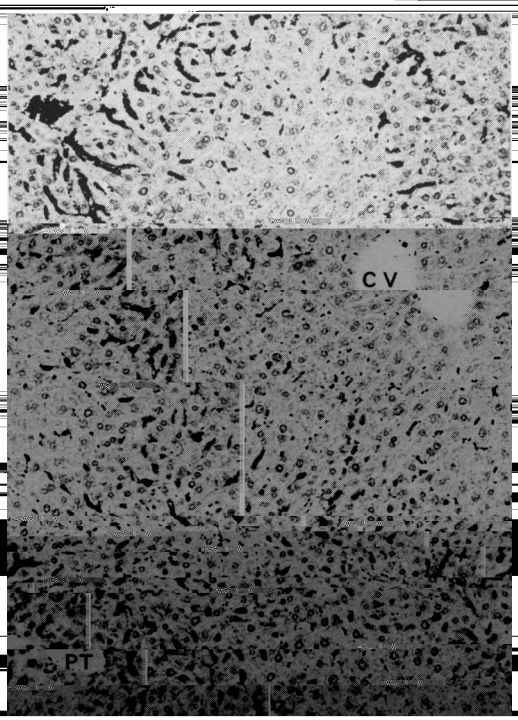
FIG. 1.—Uptake of ^{51}Cr-SRBC by liver and

bearing second-passage transplants of either Tumour 1 or Tumour 2 for 1 or 2 weeks, showed a similar increase in AST levels. In contrast, injection of LPS into mice bearing 4-week tumours (either 1 or 2) caused a significantly greater increase in AST levels. This suggested that LPS clearance caused more hepatocellular damage in animals with 4-week tumours.



The comparable results for the OCT levels are shown in Table III. Again, injection of LPS into non-tumour-bearing animals caused a significant rise in OCT

mice bearing either Tumour 1 or Tumour 2



macrophage precursors in the marrow of C3H mice during the growth of C3H mammary-tumour transplants. This was observed after 4 days of tumour growth, but the response was no longer seen at 2 weeks. Otu *et al.* (1977) measured marrow phage chemotaxis and *in vivo* RES clear-

age, as the liver is the main site of endotoxin clearance from the bloodstream

It is of interest that there was no evidence for an increased hepatoxicity of

1967). Minimal hepatocellular damage without histological evidence of overt liver necrosis has been documented during Kupffer-cell endocytosis of LPS (Ruiter *et al.*, 1980) and other particles (Bradfield

mice in that the basal levels of AST and OCT were similar in both groups. There is, however, no way of judging the sensitivity of this assessment.

The degree and mechanism of hepato-

T.W.E. is supported the by Bristol and Weston Health District (Teaching) and R.P. by the Medical Research Council

cells by macrophages from tumor bearing mice. *J. Natl Cancer Inst.*, **55**, 971.

[illegible] M. (1970) [illegible]

disease. In *Progress in Liver Disease*. Vol. 6. Ed. Popper & Schaffner. New York: Grune & Stratton

BALIS, J. U., RAPPAPORT, E. S., GERBER, L., MAGAREY, C. J. & BAUM, M. (1970) Reticuloendo-