of this resistance may illuminate critical sites of the cell–carcinogen interaction.

Cells treated in vitro with N-methyl-N-nitrosourea, MNU, exhibited malignant transformation and were ten-fold more resistant to MNU toxicity than previously treated normal cells. Transformation and resistance were related and dose dependent. MNU resistant cells were twice as resistant to methyl methanesulphonate toxicity and ten-fold more resistant to the toxic effect of thymidine, compared with normal cells.

Resistance to MNU and thymidine could not be explained by reduced incorporation, as measured by the uptake of the respective radioactively labelled compound. The cross resistance suggested similar sites may be involved in MNU and thymidine toxicity. (Studies performed at the Paterson Laboratories, Christie Hospital, Manchester.)

INHIBITION OF THE EFFECTS OF METHYLCHOLANTHRENE BY VITAMIN A AND VITAMIN A ANALOGUES, Ilse Lasnitzki and De Witt S. Goodman, Strangeways Research Laboratory, Cambridge.

Retinol and retinoic acid have been shown to inhibit carcinogenesis in vitro and in vivo but their possible clinical use may be limited by their high toxicity. Vitamin A analogues without the biological properties of the natural vitamin may serve as substitutes. The influence of two analogues, α-retinoic acid and anhydroretinoic acid, on the effect of methylcholanthrene was examined in mouse prostates grown in vitro and compared with that of retinol and retinoic acid.

The carcinogen alone induced extensive epithelial hyperplasia and dysplasia. All four compounds, applied at various dose levels, were highly active in inhibiting this effect. At the highest concentration they almost totally suppressed the hyperplasia, at the lowest concentration retinoic acid and anhydroretinoic acid were the most effective inhibitors. Mechanisms involved in the antagonism have been investigated.

IMMUNOGENICITY OF EMBRYONIC ANTIGENS ASSOCIATED WITH CHEMICALLY INDUCED RAT TUMOURS, R. W. Baldwin and B. M. Vose, Cancer Research Laboratories, University of Nottingham.

Chemically induced rat hepatomata and sarcomata express neoantigens at the cell surface which are also detectable on mid-gestation rat embryo cells. These antigens are revealed by the cytotoxicity of serum and lymph node cells from multiparous female rats for embryo and tumour cells by serum from these animals. Since the multiparous rat becomes sensitized to these antigens, they are immunogenic when expressed on embryo cells in the pregnant host. Immunization of syngeneic rats with mid-gestation rat embryo cells failed, however, to elicit immunity to challenge with hepatomata or sarcomata. Also, lymphoid cells from multiparous rats were ineffective for adoptively transferring tumour immunity. These studies are discussed in connection with the view that the tumour specific rejection antigens on these tumours differ from the tumour associated embryonic antigens.

"WILD" TYPE ANTIGENS OF SARCOMATA INDUCED BY A NATURAL AMINE SARCOMA VIRUS (MSV-FBJ), David B. Jones and Michael Moore, Charles Salt Research Centre, The Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry.

MSV-FBJ is a C-type murine oncornavirus which induces primitive mesenchymal sarcomata of long latency in mice. The agent was originally isolated from a spontaneous murine osteosarcoma and is of demonstrated "wild" type antigenicity.

Transplantation rejection techniques have demonstrated a tumour associated antigen common to all cells transformed by MSV-FBJ and also present on cells infected with "wild" type Gross leukaemia virus. The specificity was absent from cells transformed by the "non-wild" type isolate MSV-Harvey (MSV-H).

Serum from mice immunized against MSV-FBJ sarcoma cells reacted in the indirect membrane immunofluorescence test with both MSV-FBJ sarcoma cells and Gross antigen bearing cells, but not with the membrane of MSV-H cells. Further, aged C57BI serum specifically reactive with cellular rather than virion specificities of Gross virus infected cells reacted with MSV-FBJ sarcoma cells. Identification of antigens on the surface of MSV-FBJ sarcoma cells which were not also present on "wild" type antigen-bearing tumours could not be achieved by absorption techniques.
By complement fixation, murine oncorna-

virus group specific antigen was identified in

crude extracts of MSV-FBJ sarcomata to-
gether with soluble antigens of type specificity.

The significance of these antigens in

relation to those previously defined for "wild" type murine leukaemias will be
discussed.

HOST IMMUNE RESPONSES IN

B.C.G. THERAPY OF A RAT OSTEO-

SARCOMA, N. Lawrence and M. Moore,

Charles Salt Research Centre, The Robert

Jones and Agnes Hunt Orthopaedic Hospital,

Oswestry.

The growth of syngeneic grafts of tumour

cells is suppressed when cells are mixed with

B.C.G. before inoculation, or if clinically

established nodules are infiltrated with

microorganisms. Theoretically, three types

of processes operating individually or in

combination might account for this pheno-

menon: (i) non-immune effects; (ii) B.C.G.

immunity and (iii) tumour immunity.

In experiments performed with an immu-
nogenic, chemically induced osteosarcoma,
growth inhibition by B.C.G. was less effective
in rats immunosuppressed by thymectomy
and irradiation than in their immunocom-
petent counterparts. In the study of the

respective roles of immunity to tumour and

B.C.G., the differential radiosensitivity of

primary and secondary immunity permitted

the evaluation of the effect of immunity to

one antigen on a second antigen, to which

primary immunity had been prevented by

interim irradiation.

Evidence will be presented to show that

the host response to B.C.G. is essentially

local and immunological. Tumour out-
growth from B.C.G. tumour cell inocula

occurred with greater frequency in rats

prevented from responding to tumour antigen

than in normal recipients, suggesting that

while local immune reactivity to B.C.G. is a

necessary component of successful tumour

growth inhibition, it is not invariably suf-

ficient.

TUMOUR THERAPY IN DOGS USING

B.C.G., L. N. Owen and D. E. Bostock,

Department of Animal Pathology, School of

Veterinary Medicine, University of Cam-

bridge.

Experimental dogs have been injected

intradermally, intravenously, intrathoraci-


cally and intraperitoneally with percutaneous

B.C.G. vaccine (Glaxo).

Following i.v. injection a patchy inter-

stitial pneumonia has been found with

small granulomata in lungs and liver. There

is lymph node hyperplasia. A small and

 transient rise in temperature occurs.

Dogs with osteosarcoma treated surgically

or by x-irradiation have been injected i.v.

with B.C.G. alone or B.C.G. and autologous
tumour cells. Results are encouraging.

Dogs with lymphosarcoma treated by chemo-

therapy and followed by intravenous B.C.G.

alone have not responded well.

Two dogs, one lymphosarcoma and one

osteosarcoma, had anaphylactic shock after

the second B.C.G. injection and an anti-

histamine drug is now routinely given before

the B.C.G.

IMMUNOLOGICAL MECHANISMS IN

CONTROL OF MALIGNANT DI-

SEASE, C. Bone and R. S. Camplejohn,

Departments of Surgery and Pathology,

University of Newcastle upon Tyne.

Cellular immune mechanisms have often

been implicated as important factors in the

restriction and control of neoplastic pro-

liferation. A study was planned to investigate

the relationship between cellular immunity,

the rate of malignant cell proliferation and

prognosis in 40 patients with carcinoma of

the rectum.

Cellular immunity was measured by

assessing the patients' delayed hypersensit-

ivity responses to 2-4 dinitrochlorobenzene

(DNCB). The proliferation rates of the rectal

carcinomata and the mucosa from which

they arose were measured using an in vivo

stathmokinetic technique (Refsum and Ber-
dal, Tidskr. norske Laegeforen., 1968, 126,

1224).

Each tumour was staged according to its

size and evidence of lymphatic involvement

or metastases. The patients' clinical progress

was followed.

It was found that there was highly signifi-
cant (P > 0-001) relationship between com-
petent cellular immunity and favourable

prognosis. It was also found that the prolifera-
tion rate of the rectal carcinomata was only

half that of the mucosa from which they arose

and growth was due to a diminished cell loss.