Table II. Hemagglutinin production by *C. albicans* infected with DNA of PyV

Cells, counts Incubation, 37 °C	Inoculum/System	Mortality %	Budding %	Final titer Distribution	Serolog. tests Increase
Infected[a]: 2.19×10^6 cells/ml 4 h, complete M	Py-DNA 0.5 ml	3.52	7.44	*625 HAU* M: 60% C: 40%	HI: posit. (1:8) 625×
Infected[b]: 2.69×10^6 cells/ml 4 h, defined M	Same	4.53	7.39	*1075 HAU* M: 58% C: 42%	HI: posit. (1:16) 1075×
Infected[c]: 2.66×10^6 cells/ml 4 h, complete M	Same + 50 mg Urethan	3.03	8.91	*590 HAU* M: 59% C: 41%	HI: posit. (1:16) 590×
Infected[d]: 2.19×10^6 cells/ml 4 h, defined M	Same + 50 mg Urethan	3.41	8.00	*1135 HAU* M: 55% C: 45%	HI: posit. (1:32) 1135×

[a] Exp. 74-A: 0.5 ml PyV-DNA + 0.3 ml yeast, approximately 10^6 cells, 6 min interaction at 2 °C, then reincubated with 50 ml growth medium for 4 h at 37 °C. Further processing like Table I. [b] Similar to above, but with medium 1415_9 + 0.15 *M* sucrose. [c] Exp. 74: Similar to 74-A[a] but 50 mg Urethan in the growth medium or [d] in medium 1415 + 0.15 *M* sucrose. Polyoma DNA was extracted with hot phenol and 1 *M* NaCl., ether and N_2 and did not give HA and HI reaction before the inoculation of Candida (OD_{260} was 0.026/0.3 ml and was infectious to mouse embryo cells).

effect of the carcinogen. Investigations in vitro are scarce or irrelevant[13,14], although a virus activation theory was put forward to explain Urethan carcinogenesis[15]. Its effect on the nucleic acid metabolism of the host, in agreement with others[16], is doubtful. The slight virus production by Urethan in Candida-Py-DNA assays may not be significant. The tumorigenic action of Urethan was thought to be connected with its slow evacuation and insufficient metabolism in young mice[17]. The dose was chosen on basis of in vivo data[15,16]. In our assays Urethan stimulation was observed only in defined medium[9] and sucrose, lacking macromolecules. The high amino acid, vitamin and carbohydrate content of this mixture may be the enhancing factor in virus production of Protista[3], further increased by Urethan through some unknown mechanism. The alkalinity cannot be a cause, since adjusting complete medium to pH 7.6 had no similar effect[8]. HA test was used for the quantitation of PyV. This was not taken as synonimous with infection, although a good correlation was demonstrated between HA and infectivity[3,5,7]. Serologic findings underline these results, especially with Py-DNA, which gave negative reactions before inoculation, but after incubation. HA and HI tests became positive, suggesting the production of Py-virion[3,4].

Zusammenfassung. Das onkogene Polyomavirus kann sich im Pilz *C. albicans* vermehren und die Virusausbeute wird durch Urethanzugabe erhöht.

E. Kovács and G. Kolompár[18]

Department of Surgery, Faculty of Medicine, University of Toronto, Toronto 5 (Canada), 2 June 1969.

[13] R. A. C. Foster, F. H. Jokson and V. K. Miller, J. gen. Physiol. *33*, 1 (1949).
[14] S. Kawamoto, N. Ida, A. Kirschbaum and F. Taylor, Cancer Res. *18*, 725 (1958).
[15] J. Berenblum, Acta Un. int. Cancr. *20*, 893 (1964).
[16] A. M. Kaye and N. Trainin, Cancer Res. *26*, 2206 (1966).
[17] S. Mirvish, G. Cividali and I. Berenblum, Proc. Soc. exp. Med. *116*, 265 (1965).
[18] We are very grateful to Mr. G. M. Healy of the CMRL, University of Toronto, for the generous supply of media and to Mr. B. Bucz for his technical help in this work supported by a grant of the National Cancer Institute of Canada.

Experimental Brain Tumours in Dogs

Brain tumours have been induced by different methods in mice, rats and rabbits[1]. But experimental neurosurgery demands brain tumours in animals larger than rodents. Recently we succeeded in producing such neoplasms in dogs after administration of 1-methyl-1-nitrosourea (MNU). MNU was introduced into experimental neuro-oncology by Druckrey et al.[2].

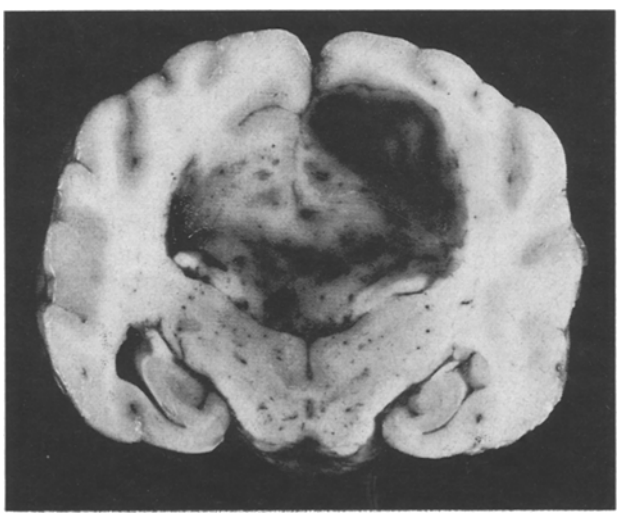
Ten mongrel dogs, aged 4 months to 3 years, received 20 mg MNU/kg body weight monthly by i.v. injections of freshly prepared solution of MNU in sterile physiologic saline with phosphate buffer (pH 4.2). 4 dogs developed brain tumours (Table). Histologically the tumours resemble intracerebral sarcomas or multiforme glioblastomas. All of them show signs of malignancy: infiltrative

Pathological findings after monthly i.v. injections of 1-methyl-1-nitrosourea

No. and sex	Body weight at start of the experiment (kg)	Total number of injections	Total absolute dosis of MNU (g)	Survival time after first injection (days)	Pathological findings In the central nervous system	In other organs
1 Male	11.6	12	3.392	315	Brain tumour of the left frontal lobe (size: $2 \times 2 \times 1.5$ cm)	—
2 Male	9.5	15	4.040	423	Brain tumour of the corpus callosum and adjacent white matter (size: $3 \times 2.5 \times 2$ cm)	Multiple sarcomas of the lungs and spleen and of lower thoracal vertebrae
3 Female	10.5	16	4.274	426	Brain tumour of the right frontal lobe (size: $1 \times 0.5 \times 0.5$ cm)	Sarcomas of the heart, spleen, intestine and both the lungs
4 Male	10.5	15	4.234	405	Brain tumour of the right temporal lobe (size: $1 \times 0.5 \times 0.5$ cm)	—
5 Male	12.0	12	4.088	326	—	Multiple malignant hemangioendotheliomas of the heart and the lungs
6 Male	10.0	4	1.000	102	—	Non-specific granulomatous inflammation of the lungs and the kidneys
7 Male	5.0	11	1.150	292	Brain abscess	Phlegmona of the leg, septicopyemia with multiple abscesses
8 Female	6.6	11	2.152	349	Multiple cerebral hemorrhages	Hemorrhagic diathesis of unknown origin
9 Female	7.0	12	2.890	316	Multiple cerebral hemorrhages of unknown origin	—
10 Female	7.0	18	4.100	494	Perivascular proliferation of reticular cells and histiocytes	Multiple sarcomas of the lungs, the spleen and the heart

growth, nuclear polymorphism, atypical mitoses, immature blood vessels, areas of necrosis and hemorrhages. In 4 dogs other organs were afflicted by multiple separated tumours. They are composed of undifferentiated, elongated mesenchymal cells or they form irregular vascular spaces, lined by endothelial cells. The capillary-like vessels are surrounded by clusters of undifferentiated mesenchymal cells with cellular polymorphism. These sarcomas and malignant hemangioendotheliomas are similar to tumours obtained with MNU in rabbits[3]. We consider the tumours in different organs as an expression of a systemic neoplastic process and not as metastases from a single blastomatous focus.

Our preliminary results indicate the possibility of producing primary brain tumours in adult dogs and open new aspects for experimental neurosurgery. The exact determination of the histogenesis of the cerebral neoplasms will be the subject of further investigations.



Dog No. 2; brain tumour with destruction of the corpus callosum and adjacent parts of the hemispheres.

Zusammenfassung. Durch wiederholte i.v. Injektionen von gelöstem Methylnitrosoharnstoff werden bei 4 Hunden intrazerebrale Geschwülste induziert. Damit ist der Beweis erbracht, dass dieser Stoff nicht nur bei Nagetieren, sondern auch bei grösseren Säugetieren Geschwülste des Zentralnervensystems verursachen kann.

R. WARZOK, J. SCHNEIDER, D. SCHREIBER and W. JÄNISCH

Pathologisches Institut, Medizinische Akademie, Erfurt (DDR), 6 October 1969.

[1] W. JÄNISCH and D. SCHREIBER, *Experimentelle Geschwülste des Zentralnervensystems* (VEB Gustav-Fischer-Verlag, Jena 1969).
[2] H. DRUCKREY, S. IVANKOVIC and R. PREUSSMANN, Naturwissenschaften *51*, 144 (1944).
[3] D. SCHREIBER, W. JÄNISCH, R. WARZOK and H. TAUSCH, Z. ges. exp. Med. *150*, 76 (1969).