portion of the synthesis curves (RNA: first 10 min incubation, DNA: 15 min). Although RNA synthesis was significantly more depressed in 10% DMSO than was DNA ($p < 0.001$), the inhibition of nucleic acid synthesis, in general, did not appear to be selective. It is of interest to note that, in both cases, removal of the drug by washing resulted in a significant overshoot in synthetic activity.

An etiologic relationship between the results presented herein, and previous studies on RNA-dependent processes has not been established. Where the inhibitory effect of DMSO is acute, it is doubtful if RNA mediation plays an important role. Conversely, these data may relate to the mechanism of DMSO action on cell proliferation, such as the reversible inhibition of fibroblast growth in culture[4], its effect on fetal development in vivo[9,10], and its ultrastructural effects on ribosomes[3].

Zusammenfassung. Es hat sich gezeigt, dass Dimethyl-Sulfoxid (DMSO) die RNA-Synthese in Sarkom 180 Tumorzellen in vitro hemmt. In 15% DMSO betrug die Syntheserate nur 7% der Kontrolle. Diese Hemmung war leicht reversibel durch einfaches Entfernen des Wirkstoffes durch Auswaschen der Zellen mit Tyrodes-Lösung. Nach Entfernung des DMSO wurde eine leicht erhöhte Aktivität der Synthese beobachtet. Die Angaben wurden mit der Kinetik der Hemmung von DNA-Synthese verglichen und ihre möglichen Beziehungen zu anderen Wirkungen von DMSO beschrieben.

R. F. HAGEMANN

Cellular and Radiation Biology Laboratories, Allegheny General Hospital Pittsburgh (Pennsylvania 15212, USA), 21 July 1969

Antitumor Activity of an Aqueous Extract of *Amanita phalloides* Fr.

It was previously shown, by electron microscopic examination, that the earliest evidence of a structural damage caused by non-lethal doses of the total extract of *Amanita phalloides* Fr. occurs in the nucleus and nucleolus, and that it is in these structures that the changes begin to regress; the signs of damage in the cytoplasm and its regression occur after nuclear changes[1,2]. Since these lesions seem to indicate that the *Amanita phalloides* extract interferes with the metabolism of the nucleic acids, experiments were performed to determine if such an extract might have an antitumour activity in rats.

Materials and methods. Wistar strain albino rats of both sexes, weighing about 200 g were used. Yoshida ascites tumour AH 130 was inoculated i.p. (0.3 ml of a liquid containing about 15×10^3 tumour cells in 1 mm^3). An aqueous extract of fresh mushrooms was prepared. The material previously lyophilized was diluted with saline just before use. This solution was injected i.p. (1.5 mg/200 g of body wt.). Preliminary controls had shown that this dose was not lethal for rats. In control animals the same amount of saline was given.

The action of pure α-amanitine (0.5 mg/200 g i.p.) and of an extract enriched in phalloidine (30% of phalloidine) were also tested. These substances were kindly supplied by Prof. TH. WIELAND from Heidelberg. The ascites tumour cells were also examined after incubation in vitro at 37 °C respectively with total mushroom extract, pure α-amanitine and phalloidine extract.

Experimental. 1st Group. 7 rats in which the ascites tumour cells had been inoculated 2 days before, were injected with *Amanita phalloides* extract. All these animals died 24 h later.

2nd Group. 19 rats were inoculated with ascites tumour cells. In 10 of these animals the aqueous extract of *Amanita phalloides* was injected at the same time. The 9 control animals died in 2 weeks with ascites. None of the treated animals died, nor did they develop ascites.

3rd Group. Reduced quantities of the *Amanita phalloides* extract were given in different groups of 3 rats each. The inhibitory activity of the extract during the transplantation of the tumour was present with doses of 0.75, 0.5 and 0.3 mg. When 0.15 mg of *Amanita phalloides* extract was given, an ascites developed, but 2 days later than the controls.

4th Group. 9 rats, in which the *Amanita phalloides* extract inhibited the growth of the tumour, were inoculated again after 10–15 days with the same dose of tumour cells. The animals did not develop ascites.

5th Group. When the tumour cells were inoculated with pure α-amanitine, the rats showed a cutaneous toxic reaction and all developed ascites and died. The inoculation of an extract enriched in phalloidine in 12 rats inhibited the growth of the tumour in 4 animals. The other 8 rats died with ascites.

6th Group. Experiments in vitro: (a) Controls. After 24 h of incubation at 37 °C most of the tumour cells were still well preserved. (b) Incubation with *Amanita phalloides* extract. After 1 h of incubation, phenomena of nuclear picnosis and initial alterations of the cytoplasm were already present. After 6 h the destruction of the tumour cells was very pronounced and it was complete after 24 h. At this time the normal cells (plasmacells, mesothelial cells, etc.) were still preserved. (c) Incubation with pure α-amanitine. No differences were noted between the cells of this series and the control ones after 1 h, 6 h and 24 h. (d) Incubation with an extract enriched in phalloidine. After 24 h numerous tumour cells were still present and well preserved. However, some cells showed initial signs of nuclear and cytoplasmatic damage. It was observed that only a few cells were completely destroyed.

Discussion. These experiments show that an aqueous extract of *Amanita phalloides* at certain doses inhibits the implantation of the ascites tumour cells; whereas it has no antitumoral activity when given after the development of the tumor. The rats in which the *Amanita phalloides* extract has inhibited the tumour do not develop the tumour even when a second inoculation is performed. This seems attributable to a phenomenon of active immunization, similar to what happens with other experimental techniques (cryolization[3] or irradiation with betatron[4]). The antitumoral activity does not seem linked

1 L. VILLA, A. AGOSTONI and G. JEAN, Experientia *24*, 576 (1968).
2 L. VILLA, A. AGOSTONI and G. JEAN, Sperimentale *117*, 145 (1967)
3 E. BONMASSAR, F. CLEMENTI, S. FERRI, M. G. PAGAN and M. R ZANISI, Archo. ital. Patol. Clin. Tumori *7*, 269 (1964).
4 F. MELAN, C. TESTORELLI and G. TOSI, Archo. ital. Patol. Clin Tumori *11*, 285 (1968).

to the 2 major toxins of this mushroom: the α-amanitine and the phalloidine.

In a recent paper, which we have seen after our experiments were performed, IKEKAWA et al.[5] were able to show an antitumour activity of an aqueous extract of edible mushrooms. The active antitumoral material was suggested by chemical analysis to be a polysaccharide. At this moment we do not know if the antitumoral fraction of the *Amanita phalloides* is also a polysaccharide.

Riassunto. L'estratto totale ecquoso di *Amanita phalloides* Fr., se somministrato in dose non letale, inibisce il trapianto del tumore ascite di Yoshida AH130 nel ratto. Tale attività non dipende nè dalla α-amanitina nè dalla falloidina. I ratti cosi trattati sono immunizzati contro altre inoculazioni di ascite. L'attività inibitoria della *Amanita phalloides* è confermata con ricerche in vitro.

L. VILLA and A. AGOSTONI

Centro di Patologia Molecolare applicata alla Clinica dell'Università di Milano, I-20122 Milano (Italy), 4 August 1969.

[5] T. IKEKAWA, N. UEHARA, Y. MAEDA, M. NAKANISHI and F. FUKUOKA, Cancer Res. *29*, 734 (1969).

Comparative Study by Scanning Electron Microscopy of Synovial Surfaces of Four Mammalian Species

Recent evidence[1] obtained by scanning electron microscopy has shown that the adipose and areolar synovial tissue of man displays a surface pattern in which large numbers of blunt processes of approximately 50 μm diameter cover the macroscopic synovial villi (Figure 1). The shape of these processes, which resemble the tips of a cluster of fingers or the *rubus ideaus* surface, is apparently determined by the underlying fat cells; and dissected adipose tissue (Figure 6) displays a pattern which closely resembles that of the synovial tissue. By contrast, the surfaces of the articular hyaline and fibrocartilages of synovial joints in man and other mammals are covered by numerous shallow pits of approximately 20–40 μm diameter[2–8].

The evidence presented in this paper demonstrates that a surface pattern of blunt synovial processes similar to that identified in man can be seen in at least 3 other mammals: pig, rabbit and rat. The pattern is therefore presumed to represent a relationship between structure and function common to most mammalian synovial joints.

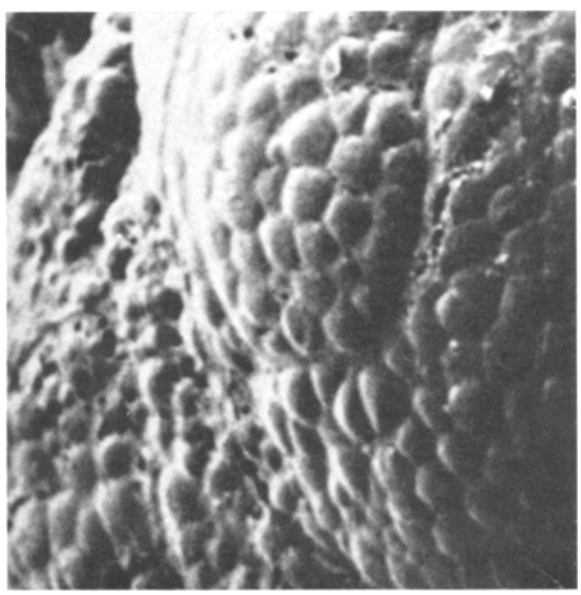

Fig. 1. Human synovial tissue. Broad convex surfaces of synovial villi covered by flat, finger-tip processes of pentagonal shape each measuring approximately 50 μm in diameter. Compare with Figures 3, 4 and 5. × 140.

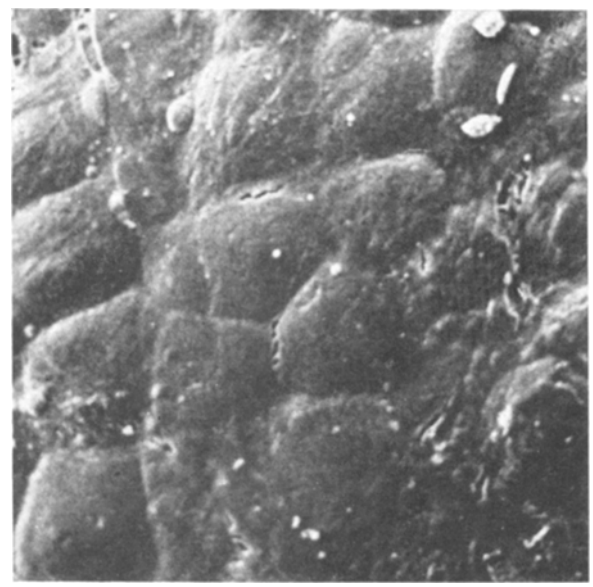

Fig. 2. Human synovial tissue. Field from same specimen seen at higher magnification. Occasional, discrete cells, possibly lymphocytes, seen on synovial surface at upper right. × 1020.

[1] A. GRYFE, D. H. WOODWARD and D. L. GARDNER, Lancet, in *2*, 156 (1969).
[2] P. S. WALKER, D. DOWSON, M. D. LONGFIELD and V. WRIGHT, Ann. rheum. Dis. *27*, 512 (1968); (Proc. Heberden Society, Nov. 1968).
[3] D. L. GARDNER and D. H. WOODWARD, Ann. rheum. Dis., *28*, 470 (1969); (Proc. Heberden Society, Nov. 1969).
[4] J. G. MCCALL, Lancet *2*, 1194 (1968).
[5] D. L. GARDNER and D. H. WOODWARD, Lancet *2*, 1264 (1968).
[6] P. S. WALKER, J. SIKORSKI, D. DOWSON, M. D. LONGFIELD, Ann. rheum. Dis. *28*, 1 (1969).
[7] D. L. GARDNER and D. H. WOODWARD, Ann. rheum. Dis., *28*, 379 (1969).
[8] D. L. GARDNER, A. GRYFE and D. H. WOODWARD, in preparation (1969).