

separate, threads become progressively longer and thinner. Our previous study⁶ has shown that when the polar migration of chromosomes is nearly complete, the cytokinetic ring of microfilaments begins to form between daughter cells. Although spindle microtubules tend to disorganize and disappear in other parts of the cells, they persist and may even increase in number in the region of the cytokinetic ring. By late telophase, daughter cells are somewhat elongated towards the base of the neuroepithelium. Whether this elongation is active or passive is not yet clear. Nevertheless, the cytoplasmic mass flows basally until daughter cells remain connected only at their apical corners by a short cytoplasmic bridge (= thread) filled with spindle microtubules and enveloped by the cytokinetic ring (figure 3). The present study also shows that small cytoplasmic granules and vesicles contribute to the formation of an electron-dense midbody (figures 2 and 3). The fact that the midbody is usually found in close association with the cytokinetic ring (figures 2 and 3) suggests that the constricting effect of furrow microfilaments may trap small cytoplasmic granules and vesicles and press them between the microtubules within the forming thread. Arnold¹¹ has suggested that a) the cytokinetic ring itself cannot completely pinch apart the 2 daughter cells and b) final cell separation occurs at the midbody. Confirmation of this view has proved to be difficult due to the rapidity of the separation event. However, we have often found threads split at the

level of the midbody (figure 4). Some of the longer threads, which show rather abrupt bending, often possess additional electron-dense regions (figure 5) and may be broken in more than one place. This finding further supports the idea that midbodies form as a result of trapping of cytoplasmic material, although we cannot yet rule out the possibility that multiple separation points are due to breakage during tissue processing.

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The effect of Valium® anaesthesia on the radiosensitivity of the skin of the mouse foot¹

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Summary. Valium® anaesthesia significantly reduces the effect of large single doses of X-rays on the mouse foot skin as compared with Nembutal® anaesthesia. The radioprotective action of Valium may be attributed to a direct effect on the cells of the skin.

Radiobiological studies on the effects of ionizing radiation on normal or malignant tissues often necessitate general anaesthesia of the animal in order to position it accurately in the radiation beam. Most of these experiments are carried out on mice which are anaesthetized by an i.p. injection of sodium pentobarbitone (Nembutal®) causing a general anaesthesia of about 60 min duration. A recent single-dose study of the radiation-induced skin reaction^{3,4} with negative pions at low dose-rate (0.2–0.3 gray/min) resulted in long irradiation times of up to 5 h; for that reason pentobarbitone had to be replaced by diazepam (Valium®) which allows the immobilization of the mice during 5–6 h. In this paper we report on the effect of diazepam on the radiation sensitivity of the mouse foot skin.

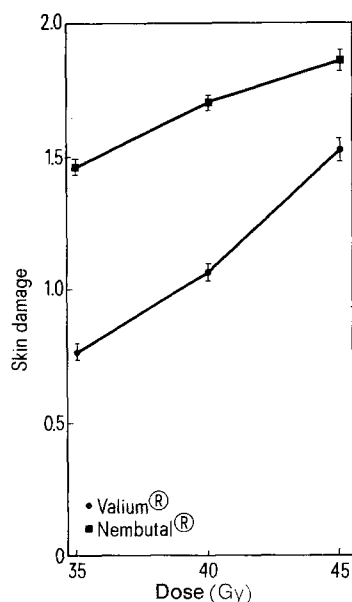
Materials and methods. The experiment was carried out on female NMRI mice weighing 23–26 g at the time of the irradiation. The anaesthesia was performed either with 30 mg/kg diazepam or with 70 mg/kg sodium pentobarbitone; the drugs were injected i.p. 5–8 min before the irradiation. The X-rays (35, 40, 45 gray) were delivered by a Picker unit (250 kVp, 0.9 mm half-value layer in Cu, 2.5 gray/min). The method for assessment of the skin damage and for the presentation of the results has been published in full detail elsewhere⁵. Briefly, the skin reaction on the irradiated foot was scored daily by 2 independent observers and recorded on an arbitrary scale.

As an index of skin damage the average of all daily means

of observations (day 8–30 post irradiation) on each dose-group was calculated and plotted against the radiation dose.

Results. The foot skin of 2 series of mice, of 3 dose-groups each, has been irradiated with single doses of X-rays. In the first series Nembutal was used as the anaesthetic, whereas in the second series the anaesthesia was performed with Valium. The figure shows the skin damage as a function of the radiation dose. At each dose the Valium series manifests a significantly lower level of skin damage as compared with the reference series ($p < 0.01$, Mann-Whitney-U statistics). A dose modification factor (DMF) of about 0.8 has been estimated from the 2 curves by comparing the doses which produce a skin damage index of 1.5. This DMF value below unity illustrates the decreased radiosensitivity of the skin when diazepam is used as an anaesthetic.

Discussion. It has been reported that pentobarbitone has no significant influence on the radiosensitivity of the mouse foot skin^{6–8}. Thus, from the present data it can be concluded that Valium can induce radioprotection of the skin. Psychotropic drugs (Valium®, Librium®) elicit hypothermia in mice and exert a radioprotective effect against lethal wholebody doses of X-rays⁹. Hypothermia has been found both in Valium- and Nembutal-treated^{10,11} animals. The depression of the core temperature was significantly more pronounced in the mice treated by Nembutal¹⁰. It therefore seems probable that hypothermia represents a concomitant



The effect of Valium® anaesthesia on the radiation induced skin damage as compared to the Nembutal® anaesthesia. Skin damage: average skin reaction over 22 days \pm SEM. The radiation dose is expressed in gray: 1 gray (Gy) = 100 rad.

effect rather than a main cause of the radioprotection. The radioprotective action of Valium could also be attributed to other indirect physiological changes which ultimately may alter the tissue oxygenation. It is generally accepted that a reduction of oxygen supply diminishes the radiosensitivity of a tissue. In several pharmacological studies involving different animal species it has been shown that Valium potentially decreases the oxygen supply of the tissues by lowering the arterial blood pressure¹²⁻¹⁴, by decreasing the heart frequency¹³ or by depressing the respiration¹⁵.

But analogous findings are also known to be produced by Nembutal, which as a potent cardiodepressor in mice, for example, causes a fall in blood pressure to about 50% of the resting value¹¹.

Since neither the hypothermia nor the potentially decreased oxygen supply seems to be an unequivocal cause of the radioprotective effect, a direct action on the irradiated cells of the skin cannot be excluded and is therefore suggested.

In the case of a selective action on normal tissues, the Valium-induced radioprotection would be of clinical interest in certain radiotherapeutic procedures. Further investigation, especially on malignant tissues, is necessary before any conclusion concerning clinical application can be made.

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Caveolated cells observed in the duodenal glands of the white-tailed deer

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Summary. This study reports the presence of caveolated cells in the duodenal glands of the white-tailed deer. Caveolated cells have not been observed previously in the duodenal glands of other species studied to date.

Although widely distributed the caveolated cell is thought to be limited to derivatives of the entoderm. They are not numerous and are reported to make up less than 1.0% of the epithelial cells in the intestinal glands of the descending colon¹. Caveolated cells have been observed in the mucosa of the small intestine² and colon³ of the mouse and in the gastric mucosa of man, dog⁴, and the opossum⁵. Caveolated cells also have been reported in the epithelium lining the bile duct and gall bladder^{6,7} as well as in the trachea⁸ and alveoli of the lung⁹.

Materials and methods. Portions of the proximal duodenum of 5 white-tailed deer (*Odocoileus virginianus*) were taken for study. All animals were from the central Missouri area and all appeared healthy and free of disease. Tissues were fixed for 4 h at 0°C in 3.5% glutaraldehyde buffered in 0.1 M phosphate to a pH of 7.4. They were washed in buffer, osmicated in 1.0% osmium tetroxide at 0°C for 2 h,

passed through propylene oxide, infiltrated with and embedded in Epon 812. Thin sections of this material were cut, mounted on uncoated grids and stained with uranyl acetate and lead citrate. The sections were examined in a Phillips 300 electron microscope operated at 60 kV.

Results and discussion. Caveolated cells were observed scattered with the epithelium of the duodenal glands of the white-tailed deer. The cells appear pear-shaped, exhibit a narrow apex that protruded slightly into the lumen and have a wide base (figure 1). Like the remainder of epithelial cells comprising the duodenal glands, they are limited basally by a delicate basal lamina. The apex is held in close apposition to neighboring epithelial cells by tight junctions and desmosomes are found along the lateral cell membranes. The caveolated cells exhibit longer microvilli than adjacent epithelial cells and their cytoplasm is characterized by bundles of filaments that extend from the core of