attached to the nuclear membrane. Otherwise, apart from the occasionally observed alignment of homologues and the well-known association of acrocentrics and perhaps other chromosomes including the X and chromosome 1 with the nucleolus, it is not known whether the interphase chromosomes bear a consistent or nonrandom relationship to one another or to other nuclear structures. The important question of the extent to which aneuploidy, and in particular the presence of a large chromosome, results in a disorganisation of the nucleus cannot therefore be answered. The striking configuration of protrusions - projections in otherwise smoothly-outlined nuclei - signals a change in the normal pattern at least as far as the nuclear membrane is concerned, but whether this in itself is of any significance in relation to the function of the cell is unknown.

It is possible that lagging of the abnormal chromosome at anaphase is at least a contributory factor in the formation of protrusions; prominently protruding chromosome arms were seen in anaphases and telophases, as well as metaphases, in histological sections of a variety of malignant tumours[12] and a carcinoma in situ of the cervix uteri[13] known to have large abnormal chromosomes.

Protrusions serve as useful indicators of an aneuploid clone having a large abnormal chromosome and, although not per se indicative of malignancy, may thus (depending on the circumstances) provide evidence of a neoplastic condition.

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Hyperosmolar coma as etiological factor in the CNS radiation syndrome of rats

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Summary. Supralethal dose of whole-body or trunk but not head-irradiation in rats induced hyperosmolar coma accompanied by hypernatremia and hyperkalemia. This clinical entity has presented the symptoms of the CNS radiation syndrome with a characteristic short survival time.

The CNS radiation syndrome (CNS-S) is characterized by neuropathological symptoms such as ataxia, hyperirritability, convulsions, coma and by short survival time[2]. Although these symptoms appear indicative of CNS involvement, the pathophysiological sequence leading to lethality does not appear to be exclusively related to CNS injury. Observations on different species show that CNS-S can be induced after a supralethal dose delivered to the whole body but that the same dose is insufficient when only the head is irradiated[3]. Even when CNS symptoms are present after head-only irradiation, survival time is significantly longer than animals that received an equivalent dose to the whole body. The reason for this phenomenon remains to be elucidated and this was the object of our experiment.

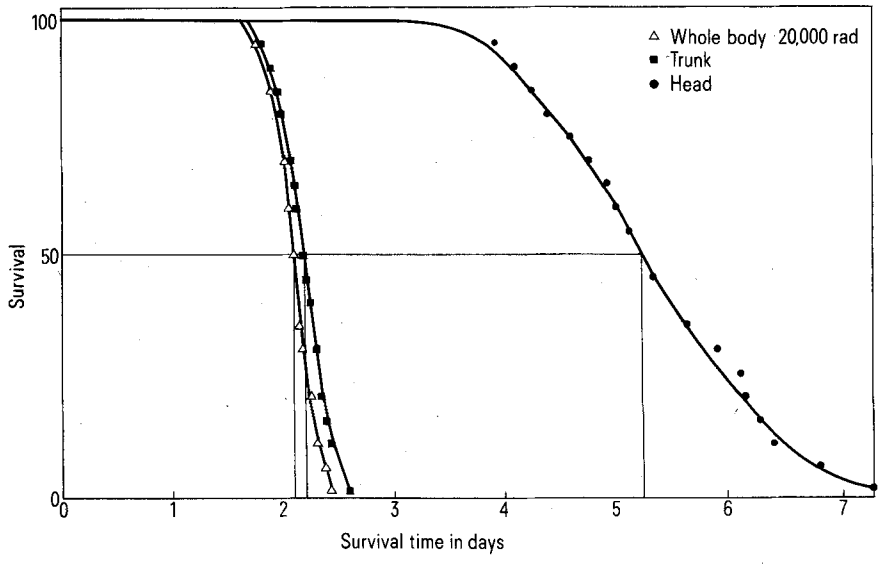
Material and methods. Animals. Young, mature 12-week-old male albino rats weighing about 280–290 g were used in this study. Standard Purina rat chow and water was available ad libitum throughout the experiment. The experimental protocol contained the following studies: 1. Survival time of whole-body, head-only and trunk-only irradiated animals after 20,000 rad exposure (20 animals in each group). 2. Study of blood constituents (plasma osmolality, plasma electrolytes and hematological values) at 48 h after 20,000 rad irradiation in whole-body, head-only or trunk-only exposed rats. In the control group, the sham-irradiated animals were similarly handled but not exposed (20 animals in each group).

Irradiation. Rats were placed into individual Lucite restraining cages and were exposed to 30.5±0.5 MeV electrons from the AFRRI[4] high energy electron Linear Accelerator (LINAC). The primary reason for using the LINAC was the ability to obtain effective shielding. The significant parameters were 3.75 pulses/sec and 8.9 rad/pulse. The pulse width was about 0.9 μsec, giving an instantaneous dose rate of about 9.9 Mrad/sec. About 2000 pulses of

Table 1. Alterations of the hematological parameters of head-, trunk-, and total body-irradiated rats at 48 h after exposure of 20,000 rad

	No. of rats	Hematocrit	Red blood cells $\times 10^3$	White blood cells	Platelets $\times 10^3$
Control, sham-irradiated	20	44.5±2.5	6.360±1.056	6.413±952	1.012±215
Head-irradiated	20	46.9±1.3	5.687±730	5.274±1.298	1.239±174
Trunk-irradiated	20	42.4±1.6	5.388±472	948±413*	263±100*
Whole-body-irradiated	20	41.3±2.6	6.581±830	493±159*	244±73*

Asterisks are representing significant changes to the control group, $p<0.001$.



Survival curve of head-, trunk- and whole body-irradiated rats after exposure of 20,000 rad.

Table 2. Alterations of plasma osmolality and electrolytes of head-, trunk-, and total body-irradiated rats at 48 h after exposure of 20,000 rad

	No. of rats	Plasma osmolality (mOsm/l)	Plasma electrolytes Na^+ (mEq/l)	K^+ (mEq/l)
Control, sham-irradiated	20	311.5±1.7	144.6±2.2	4.2±0.5
Head-irradiated	20	326.4±3.5*	142.5±2.5	3.9±0.4
Trunk-irradiated	20	358.8±8.9*	153.1±2.8*	5.1±0.4*
Whole-body-irradiated	20	394.7±14.9*	161.9±8.9	7.7±1.4*

Asterisks are representing significant changes compared to the control group, $p < 0.001$.

electrons were needed to deliver the desired doses to the animals.

Results and discussion. Whole-body supralethal dose of radiation in rats has led to a characteristically rapid death of the so-called CNS-S but when only the head was exposed to the same radiation dose, the survival time was significantly prolonged. Similar results have been found in other species of mammals such as dogs[5] and monkeys[6] after a superlethal dose of radiation to the head. In rats, however for some unknown reason, the upper limit of the radiation range to induce the gastrointestinal radiation syndrome is 10,000 rad[7] with a survival time of about 4 days. Therefore to obtain a clearly distinguishable CNS radiation syndrome, the radiation dose had to be increased up to 20,000 rad. The survival curves of the whole-body and partially irradiated groups are presented in the figure. In contrast to the considerably longer survival time of the head-irradiated animals the trunk-irradiated rats had the same short survival time as in the case of whole-body exposure. The characteristic clinical symptoms of the CNS-S have been manifested and the animals rapidly become comatose and died around 48 h postirradiation. Although the head-irradiated rats were also ataxic, sensitive to audiogenic stimuli and have exhibited typical 'head-drop' position they were not comatose until at least one day prior to death.

The biological effectivness of shielding was verified by obtaining the hematological values. Table 1 shows that after head exposure at 48 h postirradiation, the RBC, WBC and platelet counts were within the normal physiological values. Whole-body and trunk irradiation resulted in a dramatic decrease of the WBC and platelet counts with the exception of the RBC. Table 2 shows that the plasma osmolality for all groups were significantly elevated at 48 h postirradiation. The greatest increase, however, occurred after whole-body irradiation. The possible tissue degradation products induced by this high dose of radiation might act as toxic agents and/or induce increased plasma solutes (osmolality). So far no such toxic product has been identified or related to radiation toxicity[8]. The tremendous plasma osmolality increase was mainly due to hypernatremia and hyperkalemia. This plasma hyperosmolality could cause rapid dehydration of the CNS with a concomitant increase in intracellular solute concentration[9] and coma and convulsions may ultimately occur. Hyperkalemia can also cause life-threatening cardiac arrhytmias, which may begin to appear at serum concentrations as low as 5.6 mEq/l.

This etiology is probably restricted to rodents because in other species a similar clinical CNS-S might be induced at much lower radiation doses without the manifestation of generalized cell destruction.

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