MUP from uranium treated animals in agarose and also by immunoelectrophoresis using antisera to MUP did not differ from control urine. The elution pattern of MUP from control and normal urine on G 200 did not differ as detected by immunodiffusion of the fractions eluted.

Discussion. Renal damage has been associated with changes in the chemical composition of GBM and alterations in urinary basement membrane like glycoproteins[5,6,8,11–17]. Alterations in the chemical composition of GBM have been demonstrated in nephrotoxic nephritis[5,15–17], aminonucleoside nephrosis[6,11,12] and in cyclophosphamide[8] and corticosteroid[18] treated animals. Similar alterations have been found in urinary GBM like glycoproteins in the same conditions[5,6,8,17]. These findings suggest that urinary GBM like glycoprotein can reflect basement membrane injury.

In the present study uranium poisoning was associated with a 50% increase in excretion of major urinary glycoprotein in the rat. The reason for the increased MUP is unclear. The possibility that increased MUP is a nonspecific effect of proteinuria is unlikely as the MUP peak precedes the peak of proteinuria. The changes in urine MUP may reflect the morphologic changes in the GBM seen in uranium poisoning[9,10]. Increased MUP excretion could also be the result of damage to the tubular basement membrane[19].

Résumé. Les effets de l'uranium sur l'excrétion de la glycoprotéine urinaire principale du rat ont été étudiés chez 10 animaux. La principale glycoprotéine urinaire augmente de 50% dans les 24 h qui suivent l'administration de l'uranium.

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Decrease of Litter Size and Fetal Monoamines by 6-Hydroxydopamine in Mice

There is a rich sympathetic innervation in the female genital organs including the tubae and ovaries of many mammalian species[1]. In the ovaries of cats[2] and women[3], it is higher than in other reproductive organs. In tubes the sympathetic innervation may play a role in the motility[1], in the ovaries its physiological role is still more obscure. Because 6-hydroxydopamine rather specifically destroys the peripheral sympathetic nerve endings[4], it seemed appropriate for the studies on the role of this innervation.

Methods. Young adult female Albino Swiss mice weighting 25–35 g were used. The dose of 6-hydroxydopamine (6HD) (Fluka AG, Buchs) was either 50 + 50 mg/kg i.p. in two following days and then 50 mg/kg i.p. twice a week, or 100 + 100 and 75 mg/kg, respectively. Controls were injected with saline. Vaginal smear was taken daily for determining the effect on the estrus cycle. After about 3 cycles the female mice were put together with males for mating. Each female was kept together with 2 different males. A group of mice were killed before delivery and the rest some days after it. Ovaries, tubes, kidneys, hearts and brains were promptly frozen in liquid nitrogen, for fluorescence microscopy. Of iris a stretch preparate was immediately made and dried at the room temperature. Tubes and ovaries were freeze-dried for 3 days. The preparations for fluorescence microscopy was made according to ERÄNKÖ[5] and FALCK and OWMAN[6]. Noradrenaline (NA) and 5-hydroxytryptamine (5HT) were determined spectrophotofluorometrically recording to MILLER et al.[7].

Results. Neither the higher or lower dose had significant effect on the estrus cycle. The treated mice became pregnant at best nearly as well as the controls, but the litter size was smaller (Table II). 6HD treatment through the pregnancy decreased the NA content not only in the mother but also in the fetus and newborn mice. 5HT contents did no change significantly. (Table I and II).

Discussion. The results show that 6HD decreases the litter size in mice. The mechanism of this is not known. The decrease of NA content in the tissues of fetal and newborn mice indicates that 6HD is able to tranfer into the fetus, and thus a direct embryotoxic effect is possible. Other possibilities are changes in the uterine and placental circulation due to the direct vasoconstricting sympathomimetic action of 6HD and the sympatholysis, changes in tubal motility including the utero-tubal sphincters or the expulsion of ova.

Our preliminary results in rats suggest an abortive mechanism due to the sympatholysis[8] Rabbits, however, did not seem to become pregnant at all after 6HD treatment.

Antiadrenergic drugs have been used to block ovulation in mammals as well as in birds[9,10]. Partly these effects may be of central origin[11], but this seems not to be the case in

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Table I. Effect of 6HD on the NA and 5HT content (μg/g of tissue) in nonpregnant mice and pregnant mice and their fetuse

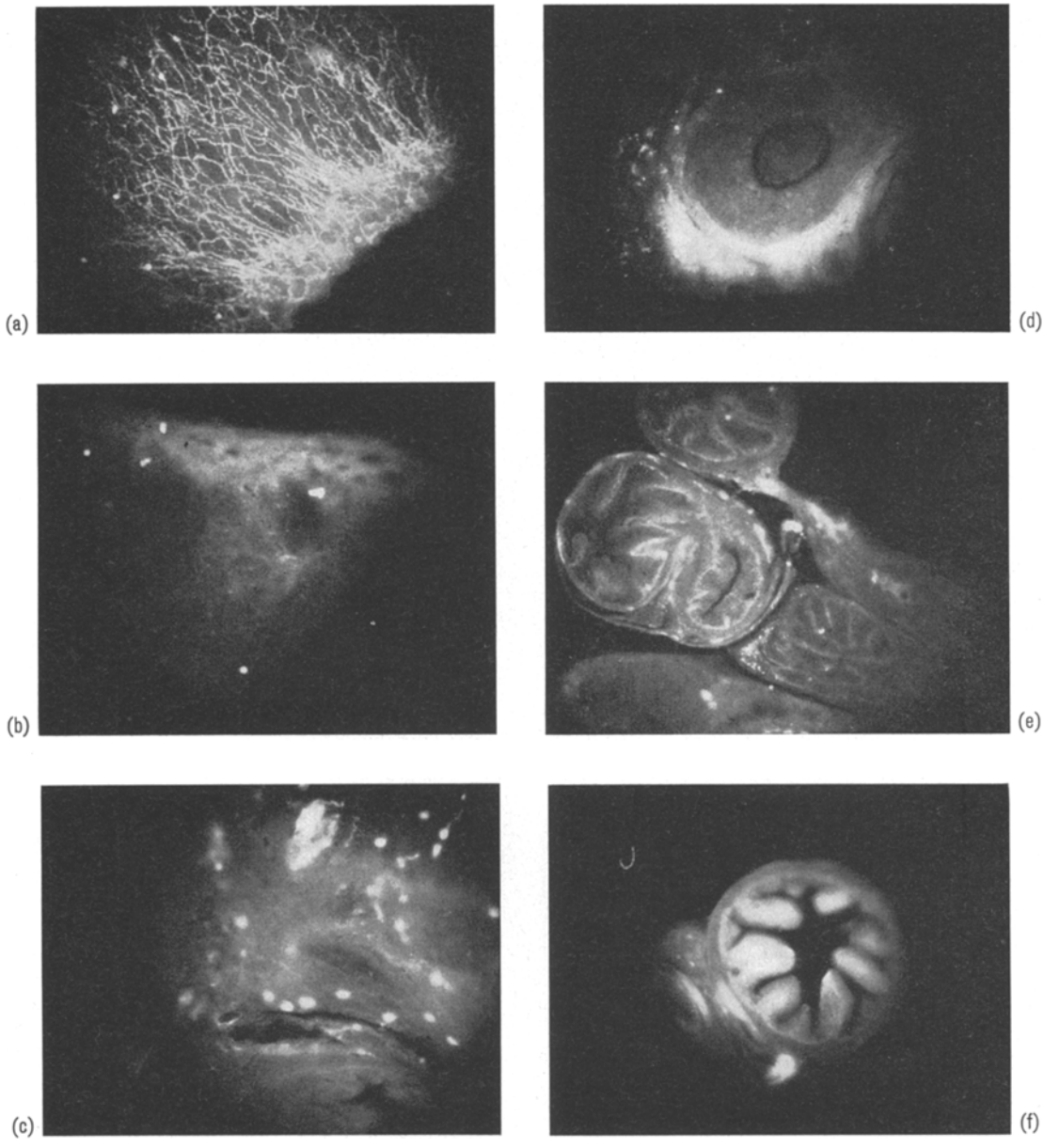
Tissue	NA			5HT		
	Controls	6HD		Controls	6HD	
Nonpregnant mice						
Brain	0.55 ± 0.12	0.40 ± 0.04	$p > 0.05$	1.13 ± 0.10	1.08 ± 0.06	$p > 0.05$
Heart	0.47 ± 0.04	0	$p < 0.001$	0.82 ± 0.25	0.78 ± 0.13	$p > 0.05$
Kidneys	0.76 ± 0.09	0.30 ± 0.03	$p < 0.001$	0.94 ± 0.09	0.90 ± 0.04	$p > 0.05$
Pregnant mice						
Brain	0.61 ± 0.07	0.31 ± 0.07	$0.05 > p > 0.01$			
Heart	0.60 ± 0.10	0.27 ± 0.04	$0.05 > p > 0.01$			
Fetuses, carcass	0.097 ± 0.024	0.036 ± 0.008	$0.05 > p > 0.01$			

Values are means (± SE) of 7 mice, except fetuses which are means of 5 pools (3–6 fetuses each).

Table II. Effect of 6HD on the litter size and tissue NA and 5HT contents (mean ± SE) of the mother mice and the newborns 4–6 days after delivery

	Litter size	NA			5HT		
		Brain	Heart	Kidneys	Brain	Heart	Kidneys
Control mothers	11.7 ± 0.6 (17) $p < 0.01$	0.63 ± 0.06 (8)	1.01 ± 0.08 (8)	0.94 ± 0.19 (3)	0.91 ± 0.001 (3)	0.95 ± 0.001 (2)	0.77 ± 0.095 (3)
6HD mothers	7.4 ± 0.6 (16)	0.56 ± 0.07 (11)	0.59 ± 0.05 (12)	0.63 ± 0.08 (4)	0.83 ± 0.062 (4)	0.81 ± 0.050 (4)	0.64 ± 0.079 (4)
Control newborns		0.31 ± 0.05 (11)	0.85 ± 0.10 (8)		0.51 ± 0.048 (6)	0.69 ± 0.133 (3)	
6HD newborns		0.20 ± 0.02 (12)	0.68 ± 0.08 (9)		0.54 ± 0.066 (7)	0.68 ± 0.102 (4)	

Number of experiments in parentheses.



Fluorescence microscopic pictures of iris of a normal mouse (a), and of a 6HD treated mouse (b), ovaries of a normal mouse (hilus) (C), and of a 6HD treated mouse (a follicle) (d), and tubes of a normal mouse (e), and of 6HD treated mouse (f).

the present study, because the brain NA did not decrease.

Dopamine and noradrenaline are effectively destroyed by the placental monoamine oxidase (MAO)[12] and catecholamine-O-methyl-transferase[13]. 6HD also is a substrate of MAO, though not as good as NA, and thus a part of a large intraperitoneal dose in mice seems to go through the placenta in active form. Some of 6HD may also go through blood brain barrier after a large dose for the same reason. In fetus, however, it can easily reach the brain because the blood brain barrier has not been developed.

Zusammenfassung. 6-Hydroxydopamin, am Muttertier appliziert, geht in den Foetus und reduziert die Wurfgrösse ohne den Östruszyklus zu stören.

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