The influence of acute hypophysectomy (series II) and acute hypophysectomy + homogenate of neurohypophyses injected i.p. (series III) on the urine output (V), sodium excretion ($U_{Na}V$), glomerular filtration rate (GFR) and tubular rejection fraction for sodium (TRF_{Na}) as compared to the non-hypophysectomized rats (I)

Period	Time (min)	I	II	III		
		Non-hypox ($n = 5$)	Hypox ($n = 5$)	Hypox + neurohypophyses i.p. ($n = 5$)	P I:II	P I:III
			V (µl/min)			
1	0– 20	2.94 ± 0.45[a]	2.94 ± 0.65[a]	3.78 ± 0.66[a]	ns	ns
2	20– 40	35.35 ± 5.68	9.03 ± 1.11	43.75 ± 6.19	< 0.002	ns
3	40– 60	32.94 ± 3.67	9.91 ± 1.48	32.33 ± 5.06	< 0.001	ns
4	60– 80	21.04 ± 4.73	8.09 ± 2.02	7.77 ± 2.12	< 0.05	< 0.05
5	80–100	14.97 ± 3.26	6.61 ± 1.68	3.84 ± 0.85	ns	< 0.05
			$U_{Na}V$ (µEq/min)			
1	0– 20	0.06 ± 0.01	0.08 ± 0.03	0.08 ± 0.02	ns	ns
2	20– 40	6.13 ± 0.99	0.41 ± 0.11	8.54 ± 1.38	< 0.001	ns
3	40– 60	6.81 ± 1.10	0.77 ± 0.23	7.76 ± 1.29	< 0.001	ns
4	60– 80	3.73 ± 0.89	0.26 ± 0.10	1.85 ± 0.54	< 0.01	ns
5	80–100	2.58 ± 0.64	0.41 ± 0.24	0.77 ± 0.26	< 0.05	< 0.05
			GFR (ml/min)			
1	0– 20	1.37 ± 0.19	0.97 ± 0.21	1.83 ± 0.26	ns	ns
2	20– 40					
3	40– 60	1.59 ± 0.16	1.04 ± 0.16	1.34 ± 0.18	< 0.05	ns
4	60– 80	1.47 ± 0.17	0.84 ± 0.11	0.91 ± 0.27	< 0.02	ns
5	80–100	1.34 ± 0.15	1.02 ± 0.20	0.94 ± 0.49	ns	ns
			TRF_{Na} (%)			
1	0– 20	0.04 ± 0.02	0.07 ± 0.03	0.03 ± 0.01	ns	ns
2	20– 40					
3	40– 60	3.16 ± 0.50	0.55 ± 0.10	4.02 ± 0.42	< 0.001	ns
4	60– 80	1.94 ± 0.52	0.29 ± 0.08	1.49 ± 0.17	< 0.001	ns
5	80–100	1.59 ± 0.54	0.35 ± 0.24	0.88 ± 0.26	ns	ns

[a] Means ± S.E. The infusion was given in the 2nd urine-sampling period. All values were calculated per 1 g of kidney weight.

besides its possible effect on the sodium transport[10], also play a role in causing the renal haemodynamics to promote sodium excretion during the extracellular fluid volume expansion.

Zusammenfassung. Es wird gezeigt, dass die Natrium- und Wasserausscheidung hypophysektomierter Ratten durch ein Hypophysenhinterlappenextrakt korrigiert werden kann. Es handelt sich dabei nicht um ADH und das natriuretische Prinzip scheint auch vom Oxytozin verschieden zu sein.

B. LICHARDUS and J. PONEC[11, 12]

Institute of Experimental Endocrinology, Slovak Academy of Sciences, Kramáre, Limbová ul., Bratislava (Czechoslovakia), 28 February 1972.

[10] J. H. CORT and B. LICHARDUS, in *Regulation of Body Fluid Volumes by the Kidney* (Eds. J. H. CORT and B. LICHARDUS, S. Karger, Basel 1970), p. 1.

[11] The present results and conclusions were discussed in detail by one of the authors (B. L.) in his Purkynje Lecture on 'Interaction of hormonal and non-hormonal mechanisms of the body fluids volume regulation' at the XIXth Meeting of the Czechoslovak Physiological Society, held in Prague on January 26–28, 1972.

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Period of Teratogenic Vulnerability of Rat Embryo to Induction of Hydrocephalus by Tellurium

Congenital communicating hydrocephalus has been produced in the offspring of rats fed metallic tellurium throughout or during part of the gestational period[1–4]. The objective of this work was to delineate the precise period of teratogenic susceptibility of the embryo to tellurium by limiting the maternal administration of the metal to single injections on specific days of gestation.

In previous studies[2] the daily oral intake of tellurium by pregnant rats producing hydrocephalic offspring was 15.4 mg/kg as measured in metabolism cages. This dose was used as a rough guide in preliminary experiments designed to establish a teratogenic dose level using parenterally administered tellurium. Female Long Evans rats from our own inbred colony were bred and the morning of appearance of sperm was taken as day zero of pregnancy. Finely pulverized metallic tellurium (Merck, Darmstadt, Germany) suspended in olive oil was injected i.p. or i.m. into pregnant rats in single doses on specific days of gestation. These preliminary experiments demonstrated that an i.m. maternal injection of 13 mg/kg tellurium on day 9 of gestation resulted in hydrocephalic offspring with few fetal deaths. This dose of tellurium

Gestational insult period in rats by i. m. injection of tellurium

Gestation day injected	No. maternal injection	Deliveries (%)	Total offspring born	No. offspring examined	No. fetal resorptions[a]	Hydrocephalus	Hydrocephalus (%)
7	10	80	55	33	26	1	3.0
8	8	63	33	22	26	0	0
9	11	100	104	75	—	14	18.6
10	6	83	38	32	10	10	31.0
11	7	86	53	51	11	0	0
12	5	100	44	37	—	0	0
13	5	80	35	27	9	0	0
Totals	98	—	362	277	82	25	—
Control[b] (9–13)	12	100	109	94	—	1	1.1

[a] Due to the prolonged (10 day) postnatal observation period only those animals failing to deliver by day 22 of gestation were examined for uterine resorption sites. [b] Moderate ventricular dilatation was observed in 1 control animal following olive oil injection on day 9.

was accordingly administered by i.m. injection to 5–10 pregnant rats for each day of gestation from 7–13. 2 or 3 pregnant controls were injected with single doses of olive oil for each day of gestation from 9–13.

Tellurium-induced hydrocephalus is usually postnatal and grossly apparent only 5–6 days after birth[1,2]. For this reason the dams were allowed to deliver and the offspring observed closely for 10 postnatal days at which time they were sacrificed and fixed in Bouin's solution. After 10 days to 2 weeks fixation, the newborn pups were serially sectioned and examined for hydrocephalus and other defects according to a previously described method[5]. Those animals exhibiting increased ventricular dilatation at autopsy were classed hydrocephalic. Due to the prolonged postnatal observation, only those mothers failing to deliver were autopsied and examined for fetal resorption sites the day following the predicted delivery.

Results are shown in the Table. It is apparent that the embryonic period of teratogenic susceptibility to tellurium falls on day 9 and 10 of gestation since with one exception, hydrocephalus occurred following maternal injections only during this period. In view of the demonstrated persistence of tellurium in tissues due to protein binding[6], the single incidence of hydrocephalus following day 7 injection may have been due to a delayed effect of residual tellurium. We attribute the occurrence of hydrocephalus in one control animal to a spontaneous malformation. Spontaneous hydrocephalus in the order of 1% incidence has been reported for other rat colonies[7,8]. Malformations other than hydrocephalus were not observed. These findings agree in part with the report of DUCKETT et al.[4] that hydrocephalus was observed in offspring of rats fed tellurium from day 10–15 but not in the gestational periods of days 1–9 nor 16–21. These authors were not able to produce hydrocephalus by 'single insult', i.e., feeding 50 mg tellurium on a single day of gestation. The induction of hydrocephalus on days 9 and 10 of gestation by i.m. injections but not by oral administration on single days probably indicates better absorption of the metal by the parenteral route.

The teratogenic susceptibility to tellurium thus occurs shortly after germ layer formation and during a period in which most central nervous system anomalies have been reported for this species (day 9–11 of gestation)[9]. Recent experiments in this laboratory (in Teratology) have demonstrated transplacental uptake of ^{127m}tellurium by the developing rat from day 8–21 of gestation using techniques of direct tissue counts and whole body autoradiography. These findings together with the results of the present work establish the presence of tellurium in the rat embryo during the teratogenic period of sensitivity and strongly support the concept of a direct teratogenic effect of this metal on the fetus[10].

Zusammenfassung. Die intramuskuläre Injektion von metallischem Tellur an trächtige Ratten am 9. oder 10. Tag der Gestation führte bei den Jungtieren zu Hydrocephalie. Bei Verabfolgung des Metalls vor oder nach dieser Periode der Embryonalentwicklung konnte die Missbildung nicht beobachtet werden. Das Auftreten der Hydrocephalie nach Verabfolgung von Tellur korreliert somit mit der «empfindlichen Phase» der ZNS-Entwicklung bei der Ratte.

W. F. AGNEW and EILEEN CURRY

Huntington Institute of Applied Medical Research, 734 Fairmount Avenue, Pasadena (California 91105, USA), 29 May 1972.

[1] F. GARRO and A. PENTSCHEW, Arch. Psychiat. NervKrankh. *206*, 272 (1964).
[2] W. F. AGNEW, F. FAUVRE and R. H. PUDENZ, Expl. Neurol. *21*, 120 (1968).
[3] S. DUCKETT, Expl Neurol. *31*, 1 (1971).
[4] S. DUCKETT, A. SANDLER and T. SCOTT, Experientia *27*, 1064 (1971).
[5] M. BARROW and W. F. TAYLOR, J. Morph. *127*, 291 (1969).
[6] W. F. AGNEW and J. T. CHENG, Toxicol. Appl. Pharmacol. *20*, 346 (1971).
[7] B. L. O'DELL, J. R. WHITLEY and A. G. HOGAN, Proc. Soc. exp. Biol. Med. *69*, 272 (1948).
[8] J. GILLMAN, C. GILBERT, I. SPENCE and T. GILLMAN, S. Afr. J. med. Sci. *16*, 125 (1951).
[9] J. G. WILSON, in *Teratology: Principles and Techniques* (Eds. J. G. WILSON and J. WARKANY, Univ. of Chicago Press, Chicago 1965), p. 251.
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