axo-axonal synapses may exist between adrenergic and cholinergic nerves. Whilst muscle is present at the bases of the guinea-pig atrioventricular valves, histology shows that the more distal portions contain only fibrous and connective tissue, yet still possess both adrenergic and cholinergic nerves. It is possible the function of the adrenergic nerves is to monitor the cholinergic nerves, but they far outnumber these nerves in this site. A further possibility is that they are en route to the ventricles, but this is unlikely since their morphology is typical of terminal axons. In the case of the pulmonary valve, no cholinergic nerves are present and using the light microscope the valve appears to consist solely of fibrous and connective tissue. A rich adrenergic plexus is also present in this valve. Since no obvious effector site has been demonstrated it is possible these adrenergic nerves may be serving an afferent function. Alternately they may be influencing nerves not demonstrated by cholinesterase techniques. As GOSLING and DIXON[1] point out, further evidence on this problem can come only ultrastructural investigations, and it is hoped to proceed with these in the near future.

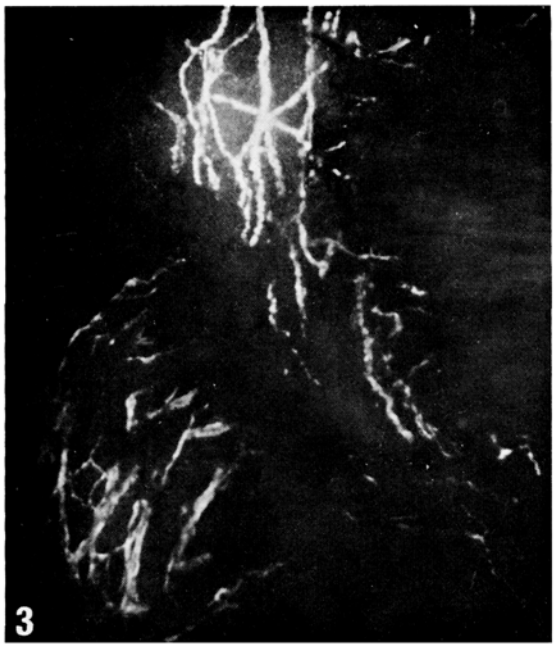

Fig. 3. Pulmonary valve cusps processed to demonstrate catecholamine activity. The adjacent section showed no AChE activity in similar sites.

Résumé. Des plexus fluorescents de nerfs dans les valvules du cœur du Cobaye sont décrits. Bien que du tissu musculaire et des nerfs cholinergiques fussent présents dans les valvules atrioventriculaires, les nerfs adrénergiques de la valvule pulmonaire ne se rapportaient qu'au tissu connectif fibreux. Puisque dans cette situation il n'y a pas d'emplacement effecteur évident ou que ces nerfs influencement des nerfs dont la présence n'est pas révélée par des techniques de cholinesterase ou qu'ils sont de caractère afférent.

R. H. ANDERSON[7]

Department of Anatomy, The University, Manchester M13 9PL (England), 29 March 1971.

[7] Acknowledgment. The author thanks Prof. G. A. G. MITCHELL for his continued interest.

The Target Period During Fetal Life for the Production of Tellurium Hydrocephalus

The morphological anomalies in present congenital malformations are determined by the type and amount of the in-jurious agent, and by the particular moment (target pe-riod) of injury to the embryo and fetus[1,2].

Injuries to the conceptus during embryonic life – the organogenetic period – result in malformed organs (i.e., the nondivision of the telencephalon resulting in holoprosencephaly). Injuries during fetal life, when the formed organs are increasing their bulk, result in anomalies of growth such as absence or small or large gyri, porencephaly. Small doses of tellurium fed to gestating rats during their pregnancy, will result in the birth of hydrocephalic offspring in 50 to 100% of pregnancies[3–5]. The present report concerns the time of the target period for the production of tellurium-induced hydrocephalus in rats.

The diet given to the rats in the present experiments, consisted of 2.5 g of metallic tellurium (Fisher Company) added to 1 kg of normal rat food (Purina diet). The amount of this food given to and usually eaten per rat per day was 20 g (therefore containing 50 mg of tellurium). One group of 20 animals, was fed the tellurium diet every day of gestation (21 days) and 12 of them gave birth to litters containing an average of 8 animals, 6 of which were hydrocephalic. The experiments were divided into 2 types, the 'period insult' and the 'single insult'. The purpose of these experiments was to detect and define the particular period – the target period-during intrauterine development when the fetal rats were more susceptible to tellurium and consequently more likely to be hydrocephalic at birth. For the purposes of these studies, the 21-day-period of gestation was divided into 3 periods, the 1st period was from day 1 to day 9 inclusive, that is until the appearance of the neural plate, the 2nd period was from day 10 to day 15, the organogenetic period, and the 3rd period was from day 16 to 21.

The first experiment was named the 'period insult' because the tellurium diet was fed to the pregnant rats every day of 1 of the 3 gestative periods. Therefore 1 group of 20 pregnant rats received the tellurium diet every day of the 1st period, another group of 20 received it during the 2nd period and a 3rd lot received it during the last

[1] L. MURPHY, in *Teratology* (Eds. J. G. WILSON and J. WARKANY; University of Chicago Press, Chicago, Ill. 1965).
[2] S. DUCKETT, in *Brain Damage in Children* (Ed. P. BLACK; Williams and Wilkins. Baltimore, in press).
[3] F. GARRO and A. PENTSCHEW, Arch. Psychiat. Neurol. *206*, 272 (1964).
[4] W. F. AGNEW, F. M. FAUVRE and R. H. PUDENZ, Expl. Neurol. *21*, 120 (1968).
[5] S. DUCKETT, Expl. Neurol. *31*, 1 (1971).

period. 12 rats fed during the 2nd period gave birth to hydrocephalic rats. The average litter numbered 9, 5 of which were hydrocephalic. None of the animals in the 1st and 3rd periods gave birth to hydrocephalic animals.

The 2nd experiment was named the 'single insult' experiment because it consisted of giving 20 g (50 mg tellurium) of the tellurium diet on only 1 day of the experiment to each animal so that 21 such groups of 5 animals represented the 21 days of gestation. Normal food was given on all the other gestative days. 3 animals died during the experiment and 72 animals gave birth to an average of 8 offsprings. There were no hydrocephalic animals.

Discussion. It is concluded that 2,500 ppm of metallic tellurium added to a normal diet of a gestating rat every day during the period extending from the 10th to the 15th days of gestation in the rats will result in hydrocephalic offsprings in the majority of the litters. This period of gestation is the target period of most drug-induced congenital malformations in the rat[1,6]. The tellurium absorbed by the mother reaches the fetal brain within minutes, and presumably causes an arrest of maturation of the telencephalic vesicles, which consequently present as hydrocephalus at birth.

Résumé. Le terme de «target period», qui peut se traduire par période-cible, signifie la période de grossesse la plus sensible aux effets nocifs d'un agent tératogène. Le présent travail situe chez le rat la période-cible du tellure entre les 10e et 15e jours de la grossesse.

S. Duckett, A. Sandler and T. Scott

Department of Neurology and Pathology, Jefferson Medical College of the Thomas Jefferson University, Philadelphia (Pennsylvania, 19107, USA), 25 February 1971.

6 S. Duckett and K. A. O. Ellem, Expl. Neurol., in press (1971).
7 This work is supported by grant No. NS 8891-01 from the U.S. Public Health Service.

Catecholamine-Containing Nerves in the Submucosa of the Ureter

During an investigation into the arrangement and innervation of smooth muscle in the rabbit renal calix and pelvis[1], nerves containing catecholamine were observed in the submucosa. Histochemical demonstration of monoamines in nerves is regarded as indicative of their effector role; these substances have not been reported as being present in afferent nerves. That monoamine-containing nerves existed in the submucosa of the upper urinary tract suggested the need to investigate their distribution in more detail in the hope that it might prove possible to demonstrate the presence or absence of probable effector target sites in this region. This report presents the results of preliminary studies on catecholamine-containing submucosal nerves in a variety of species.

Adult rabbits, rats and guinea-pigs were killed by a blow to the head; the kidney, together with the proximal half of the ureter were then removed. Each kidney and the attached ureter was placed on a cryostat chuck and plunged into either isopentane or propane previously cooled in liquid nitrogen. Cryostat sections were prepared and processed for tissue catecholamines according to the method of Spriggs et al.[2] using paraformaldehyde at 70.4% relative humidity. Adjacent sections were fixed in formalin and stained using Massons trichrome technique for routine histology. Paraformaldehyde-treated sections were examined using a Zeiss photomicroscope fitted with a Wotan HBO 200W mercury vapour lamp in combination with excitor filter BG12/4 mm and barrier filter GG9/1 mm.

Fluorescent nerves were observed in the submucosa of the renal pelvis and ureter in all the specimens examined. Other than in the submucosa of the calix (where very few nerves were detected) regional differences in submucosal innervation in the pelvis or ureter were not apparent. Relatively large fluorescing nerves were observed adjacent to the muscle coat extending into the submucosa. Finer branches continued towards the epithelium, some of which were closely related to the basal layer (Figure 1). The relative thickness of the tissue sections prevented positive identification of nerves penetrating the epithelial basement membrane. However, catecholamine-containing nerves were not observed in the deeper layers of the epithelium proper. In addition to the nerves described above, others were identified in the submucosa lying adjacent to small arteries (Figure 2). These nerves accompanied the vessels and were arranged in a plexiform fashion on the external aspect of the muscular media. Fluorescent nerve cells or chromaffin cell bodies have not been seen in any of the preparations.

The relationship between catecholamine-containing nerves and small arteries has been well documented in a variety of tissues, including the ureter[3]; the present results endorse this association in the submucosa of the

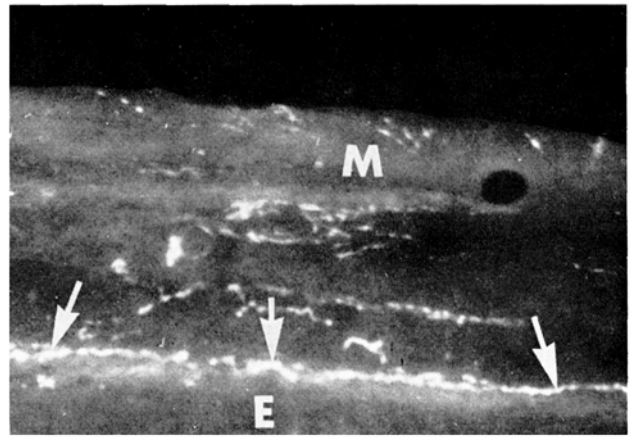

Fig. 1. Longitudinal section through the guinea-pig ureter showing fluorescing nerves (arrows) adjacent to the epithelium (E). Other nerves are observed in the muscle coat (M).

1 J. A. Gosling and J. S. Dixon, Am. J. Anat. *130*, 393 (1971).
2 T. L. B. Spriggs, J. D. Lever, P. M. Rees and J. D. P. Graham, Stain Tech. *41*, 323 (1966).
3 A. Elbadawi and E. A. Schenk, Am. J. Anat. *126*, 103 (1969).