AN EARLY DIFFERENTIAL EFFECT OF CADMIUM ON THE SCROTAL AND CONTRALATERAL CRYPTORCHID TESTES IN THE RAT

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Summary. Cadmium chloride at a dose level of 0.5 mg/100 g body weight exerted a differential deleterious effect on cryptorchid and contralateral scrotal testes in the same rat. The degenerative changes occurring in the cryptorchid testis 72 hr after cadmium administration were almost comparable to those found after ligation of the spermatic artery for 72 hr and were highly significant compared to those found in the scrotal counterpart.

It has been established by many workers that cadmium causes a severe testicular degeneration in most mammals with scrotal testes (Pařízek, 1957; Kar & Das, 1960; Gunn, Gould & Anderson, 1963) but that birds, which have a different testicular localization and vasculature, are not affected (Chiquoine, 1964; Guthrie, 1964). No definite conclusion has so far been reached on whether temperature regulating mechanisms or abnormalities of vasculature are the principal cause of the lesions. This paper describes part of our experimental findings dealing with the possible mode of action of cadmium in the impairment of testicular physiology.

Laboratory-bred male rats weighing 130 to 140 g were used. Fifty rats were made unilaterally cryptorchid (ULC) by surgical means, and unilateral ligation of the spermatic artery was effected at laparotomy in a further group of fifteen rats. Two hours after ULC, twenty-five of the fifty rats were given a subcutaneous injection of 0.2 ml of a solution of CdCl_2 in 0.9% saline at a dose level of 0.5 mg/100 g body weight. Rats were killed at 24, 48 and 72 hr after initiation of the experiments, i.e. CdCl_2 injection or ligation of the spermatic artery. Experiments with UCL and CdCl_2 were extended to 120 and 144 hr. The testes from each rat were removed, trimmed of adhering tissue and weighed. One testis was kept for histological examination in order to compare the degree of degeneration with the change in weight.

The experimental data obtained are summarized in Table 1. The untreated ULC rats did not show any significant differences between the cryptorchid and scrotal testes in terms of weight and histology at 24, 48 or 72 hr, but differences in weight between the cryptorchid and scrotal testes were observed at 120 and 144 hr. The testis associated with a ligated spermatic artery showed a slight but

TABLE 1
DIFFERENTIAL EFFECTS OF CADMIUM CHLORIDE ON SCROTAL AND CRYPTORCHID TESTES AND THE EFFECT OF UNILATERAL LIGATION OF A SPERMATIC ARTERY IN RATS

Treatment	Weight of the testes in mg (mean $\pm$ S.E.)					
	24 hr	48 hr	72 hr	120 hr	144 hr	
	<i>Surgically manipulated</i>	<i>Surgically manipulated</i>	<i>Surgically manipulated</i>	<i>Surgically manipulated</i>	<i>Surgically manipulated</i>	<i>Scrotal</i>
ULC control	1365.3 $\pm$ 18.5 (Cryptorchid)	1300.0 $\pm$ 95.7 (Cryptorchid)	1266.7 $\pm$ 72.6 (Cryptorchid)	967.5 $\pm$ 19.73 (Cryptorchid)	941.5 $\pm$ 25.5 (Cryptorchid)	1115.0 $\pm$ 43.5
ULC + CdCl ₂	1410.0 $\pm$ 20.8 (Cryptorchid)	1053.3 $\pm$ 73.3 (Cryptorchid)	830.0 $\pm$ 53.8* (Cryptorchid)	772.0 $\pm$ 35.83* (Cryptorchid)	757.5 $\pm$ 35.7 (Cryptorchid)	752.5 $\pm$ 34.2
ULLSA	1338.0 $\pm$ 38.7 (Ligated)	1187.8 $\pm$ 39.9 (Ligated)	816.0 $\pm$ 82.1* (Ligated)	—	—	—

ULC = unilateral cryptorchidism; ULLSA = unilateral ligation of spermatic artery.

* Highly significant value compared to that of the contralateral control.

insignificant gain in weight compared to its contralateral control by 24 hr. After 48 hr ligation, both the experimental and contralateral control testes weighed almost the same but, after 72 hr, the experimental testis weighed significantly less ($P < 0.001$) than its intact control. The histological changes at the end of 24 hr included a typical haemorrhagic appearance with increased basiphilia of the spermatogenic elements and early hydropic degeneration of the interstitium. After 48 hr, the tubules of the testis were almost sperm free and the rest of the spermatogenic elements were pycnotic. By 72 hr, the lamina propria showed marked tortuosity and there was a reduction in the tubular diameter. The changes found in the cryptorchid testis of rats treated with CdCl_2 were identical with those found after ligation of the spermatic artery but the contralateral scrotal testis was not much affected. Severe haemorrhagic changes were only seen in the ULC testis 72 hr after CdCl_2 administration. The initial hydropic degenerative changes evident in the scrotal testis between 48 and 72 hr after CdCl_2 injection were much less intense than those in the contralateral cryptorchid testis.

These experiments show that cadmium, in a dose which has little effect on the scrotal testis, can cause considerable impairment of the contralateral cryptorchid testis with 72 hr. Unilateral occlusion of a spermatic artery by surgical ligation gives almost identical results. Among the recorded effects of cadmium, testicular hypertension (Schroeder, 1964), vascular damage (Pařizek, 1957; Gunn *et al.*, 1963; Chiquoine, 1964), decreased blood flow (Waites & Setchell, 1966) and aspermatogenesis (Pauffer & Foote, 1969) are well documented. The physiological purpose of the scrotal sac in most of the mammalian species appears to be to maintain the temperature of the testis by means of the pampiniform plexus at a cooler level than the abdominal temperature in order to facilitate spermatogenesis. It has been suggested that cadmium impairs this cooling mechanism by damaging the cells of the pampiniform plexus and thus inducing degenerative changes in the testis similar to those accompanying cryptorchidism (Turner, 1966). No difference was observed, however, between the intrascrotal and contralateral cryptorchid testes 72 hr after ULC in the present experiments. Pronounced regressive changes in the cryptorchid testis compared with the scrotal counterpart within 72 hr of cadmium injection does not entirely support the suggestion that the action of cadmium is mediated through the pampiniform plexus. It has been shown that administration of cadmium temporarily increases the temperature of the scrotal testis but also reduces the temperature of the cryptorchid testis (Johnson, Gomes & Van-Demark, 1970). In our experiments, typical cadmium-induced haemorrhagic changes were only evident in the contralateral cryptorchid testis. This was probably due to augmentation of the action of cadmium on the vasculature of the cryptorchid testis compared with its intrascrotal counterpart. An increased rate of incorporation of tritiated lysine has been reported in the cryptorchid testis (Davis, 1965; Ferlit & Davis, 1966). The successful reversal of a cadmium-induced testicular lesion by reserpine has been observed in some preliminary experiments at 72 hr (testicular weight on the cryptorchid side = 1051.1 ± 27.0 versus scrotal side = 1065.0 ± 30.5). This effect may be the result of catecholamine depletion from the central and peripheral tissues. It has been also noted

that the differential effects of cadmium between the scrotal and cryptorchid testes persist up to 120 hr. After this period, both testes show a similar degree of degeneration (Table 1). Further experiments are in progress to elucidate the cause of the differential effects of cadmium.

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