Results. The pattern of portal and peripheral plasma insulin concentrations in normal conscious dogs was described elsewhere[1,3] as well as plasma glucose values. Shortly after the anesthesia was administered to dogs the levels of portal insulin fell to their lowest points in all 4 dogs and their amplitude was dramatically decreased. This change prevailed for about 30 min after the administration of anesthesia. Then there appeared to be a tendency to restaure the original pattern of insulin release (fig.).

Discussion. The results of this experiment suggest the pattern of basal pulsatile insulin release in dog can be manipulated by general anesthesia (nembutal). This suggestion is supported by the fact that both the portal insulin concentrations in every particular dog and the averaged values (fig.) reached their lowest point shortly after the administration of anesthesia and remained there, with reduced amplitude and frequency, for approximately 30 min. The standard errors of averaged portal insulin values within the mentioned 30-min interval are several times smaller than those before or after. This shows that although the individual levels of portal insulin are quite different in various conscious dogs at any particular moment, they become much more uniform after the anesthesia was administered. This suggests the possibility that a primary control of basal insulin release is in the CNS. It would not contradict the experimental evidence submitted by other investigators that electrical stimulation of certain areas of the brain[4] and injections of hypothalamic extracts[5-8] are followed by enhanced insulin release. There is also a possibility of an existence of multiple control of basal pulsatile insulin release.

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Effects of CA on the epididymis of intact, castrated and TP-treated langurs (*Presbytis entellus entellus* Dufresne)

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Summary. Cyproterone acetate (CA) treatment of intact langurs resulted in the disappearance of spermatozoa and regression of epididymal lumen, which can be compared with castration. The antiandrogenic nature of CA was confirmed in castrates treated simultaneously with testosterone propionate.

Cyproterone acetate (CA) is known to compete for androgen receptors in the peripheral target tissues[1]. In rats, subdermal silastic capsule implantation of CA caused functional impairment of the epididymis, thus interfering with the motility and fertilizing ability of spermatozoa[2,3]. The androgen antagonistic nature of CA has been investigated in a non-human primate model (*Presbytis entellus entellus* Dufresne) for the development of an ideal contraceptive for human males. The adult male langurs were acclimatized to laboratory conditions before use. The animals were fed with wheat chapatty (unleavened bread), banana, carrot, onion, potato, guava and soaked bengal gram, and were provided with water ad libitum. 15 male langurs were used and divided into groups of 3 each, as follows:

Group A: controls receiving 5 ml of olive oil on alternate days for 40 days.
Group B: CA (15 mg/kg b.wt i.m.) 3 times a week for a period of 40 days.
Group C: castration. Bilateral castration was achieved through the scrotal route keeping epididymides in situ.
Group D: castration + testosterone propionate. After 10 days of castration 10 mg TP was administered s.c. on alternate days for 30 days.
Group E: castration + CA + TP. After 10 days of castration, animals received 200 mg CA and 10 mg TP/alternate days for a period of 30 days.
Epididymides (groups A-E) were removed surgically under Nembutal anesthesia, cleared of connective tissue and

Changes in epididymis weight and histological measurements after CA treatment, castration, castration + TP and CA in male langur

Group	Treatment	No. of animals	Absolute epididymis weight (g)	Luminal epithelial cell height (μm)		
				Caput	Corpus	Cauda
A	Control	3	0.66 ± 0.2	86.5 ± 5.3	86.3 ± 8.4	92.3 ± 6.4
B	CA (15 mg/kg on alternate days for 40 days)	3	0.36 ± 0.1^{b}	36.6 ± 3.4^{c}	42.6 ± 4.0^{c}	35.2 ± 5.3^{c}
C	Castration	3	0.26 ± 0.1^{c}	20.8 ± 2.3^{c}	54.3 ± 2.9^{c}	52.5 ± 3.3^{c}
D	Castration + TP	3	$0.94 \pm 0.2^{a,***}$	$70.6 \pm 5.1^{c,***}$	$92.4 \pm 5.8^{a,***}$	$83.9 \pm 4.8^{a,***}$
E	Castration + TP + CA	3	$0.45 \pm 0.1^{A,*}$	$32.79 \pm 4.4^{B,**}$	$50.03 \pm 2.8^{B,*}$	$56.05 \pm 3.1^{B,*}$

1. CA treatment (B), castration (C) and castration + TP (D) compared with controls (A): [a]Nonsignificant; [b]significant at 5% level; [c]significant at 1% level.
2. Castration + TP (D) and castration + CA + TP (E) compared with castrates (C): *Nonsignificant; **significant at 5% level; ***significant at 1% level.
3. Castration + CA + TP (E) compared with castration + TP (D): [A]Significant at 5% level; [B]significant at 1% level.

weighed accurately on a torsion balance. For histological examination a piece of each of caput, corpus and cauda were fixed in Bouin's fixative; paraffin sections were cut at 6 µm and stained with Harris haematoxylin and eosin. Student's t-test for 2 samples was applied in comparing means[4].

CA administration to intact langurs (group B) resulted in a significant decrease in epididymis weight ($p < 0.05$). Castration alone (group C) caused a significant decrease in epididymal weight ($p < 0.01$, table). TP administration to castrates (group D) resulted in a significant rise in the weight of epididymis ($p > 0.01$). Simultaneous administration of CA and TP to castrates (group E) did not show any significant change in epididymal weight when compared with castrates (table). In CA-treated langurs the tubular lumina of the epididymis were devoid of spermatozoa. Stereocilia were scanty and the epithelial lining had regressed ($p < 0.01$, table). Development of massive intertubular stroma was evident with an apparent reduction in tubule size (fig. 1 and 2). Castration alone (group C) caused a significant decrease in epithelial cell height and an apparent reduction in tubular dimensions (table). These changes reversed to normalcy after TP treatment (group D) where an increase in epithelial cell height was observed. Tubules appeared normal with columnar epithelium; stereocilia were present. Simultaneous administration of CA and TP to castrates (group E) revealed a significant reduction in tubule size with regressed epithelium.

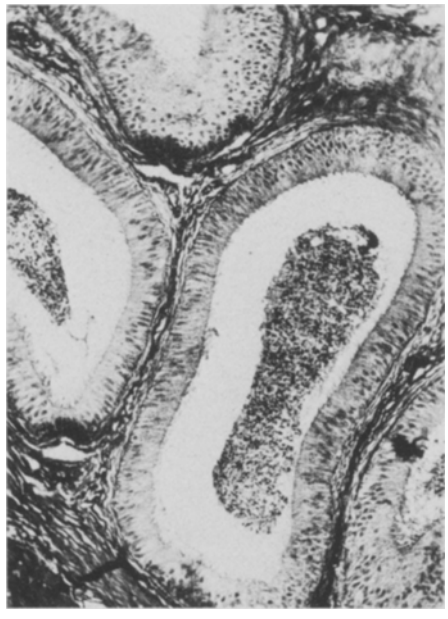

Figure 1. Cauda epididymis of control langur (group A) showing columnar epithelium and packed spermatozoa. × 100.

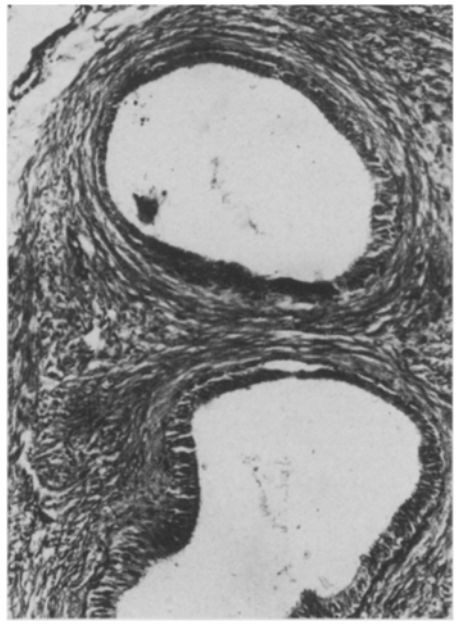

Figure 2. Cauda epididymis of CA-treated langur (group B). The epithelium is regressed and the lumen is devoid of spermatozoa. A massive increase in intertubular stroma is seen. × 100.

The antiandrogenic nature of CA has been stressed[5-7]. CA administration to intact langurs resulted in a significant decrease in epididymis weight parallel to the findings of Schenk et al.[8] and Back et al.[5], who suggested that since plasma testosterone levels were not depressed below normal values, accessory sex organ regression evidently resulted from the local antiandrogenic action of the drug. Castration resulted in a marked reduction of epididymidis weights which were maintained by TP therapy, confirming the findings of Setty et al.[6] and Rastogi et al.[7] who observed similar results in rhesus monkeys and mouse respectively. No significant change in epididymides weights of castrates treated with CA and TP simultaneously suggests that CA competitively inhibited the action of TP.

Treatment of intact langurs resulted in absence of spermatozoa and regressed epithelium of the epididymis[3,5,9]. Arora-Dinakar et al.[10] stated that the absence of spermatozoa impaired hormonal homeostasis responsible for the incorporation and utilization of protein-bound androgen. Prakash et al.[11] observed ultrastructural changes in principal and clear cells of epididymis after CA treatment; this was indicative of an impairment in the absorptive and secretory functions. Castration alone caused a reduction in tubule size with regressed epithelium and a loss of luminal contents accompanied by a pronounced increase in the intertubular connective tissue. The histological features were restored to normalcy following TP therapy[6,7], suggesting androgen sensitivity of the epididymis. The antiandrogenic nature of the drug was seen in castrates following simultaneous administration of CA and TP. CA antagonised the action of TP as seen in decreased epithelial cell height and tubule diameter, and loss of stereocilia[7]. These findings led us to speculate that CA interferes with the action of TP and impairs structural and secretory activites of the epididymis in *Presbytis* langurs.

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