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# Cavernous smooth muscle changes during penile erection and sympathetic stimulation

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We studied the cavernous smooth muscle of eight dogs in the flaccid state, during erection induced by cavernous nerve stimulation or papaverine injection, and during sympathetic stimulation or after epinephrine administration. Histologic staining and electronic microscopy demonstrated cavernous smooth muscle relaxation during erection. The characteristic smooth muscle contraction in the flaccid state was enhanced by sympathetic stimulation or intracavernous epinephrine injection. Cavernous smooth muscle relaxation is a major factor in the erectile process.

Keywords: smooth muscle, cavernous tissue, papaverine injection, sympathetic stimulation.

In the 17th century, de Graaf[1] induced penile erection by arterial perfusion with water and concluded that erection results from increased arterial flow. He also postulated that venous occlusion is a prerequisite. About a century later, Langguth[2] reported that the expansion of the penile tissue with erection is an active phenomenon. With the progress in microscopic techniques, Kölliker, from his histologic studies of 1852[3], inferred that the cavernous bodies are capable of active relaxation and contraction — later confirmed by Eckhard[4] in his classic 1863 neurophysiologic studies in dogs.

In recent years, more sophisticated techniques have been used to investigate the hemodynamics of penile erection[5-8]. Although increased arterial flow[7] and decreased venous drainage[8,9] have been demonstrated, cavernous smooth muscle relaxation has been deduced only indirectly. Indeed, as recently as the first World Congress on Impotence in 1984, the very existence of smooth muscle relaxation remained controversial. The purpose of this study was to confirm, histologically and via electron microscopy, differences of the cavernous smooth muscles in the contracted, flaccid and erect states.

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## Materials and methods

In eight mongrel dogs, weighing 26.8 to 39.3 kg, cuff electrodes were implanted around the cavernous nerves and the sympathetic trunks (at the level of L5) for electrical nerve stimulation as previously described[8]. Needles (21-gauge) connected to Statham transducers (Mod. P 23 BC) were placed proximally in both cavernous bodies for pressure recording. Three 19-gauge scalp-vein needles were inserted bilaterally at the mid point of the corpora. The cavernous nerves were stimulated three times (1.2 V, 20 Hz, pulse duration 1 ms, stimulation time 1 min), separated by 10-min intervals, followed by three stimulations of the sympathetic trunks (2.5 V, 20 Hz, pulse duration 1 ms, stimulation time 1 min). This stimulation protocol was then repeated.

After the parasympathetic and sympathetic nerve stimulations were shown to be effective in inducing and abolishing erection, the aorta was clamped proximal to the bifurcation. To minimize distension artifacts of the cavernous tissue during perfusion, the cavernous bodies were cut distally, proximal to the os penis. Before saline perfusion, the dogs were treated as follows: in two, the cavernous nerves were stimulated for 30 seconds; in another two the sympathetic nerves were stimulated for 30 seconds; in one dog each, papaverine (10 mg; Lilly) or epinephrine (1 mg; Abbott) was injected into both corpora; and two control dogs received no treatment.

Through the intracavernous scalp vein needles and, simultaneously, a 16-gauge needle in the inferior aorta, we perfused normal saline (37°C) for 10 seconds to wash out the erythrocytes followed by sodium cacodylate-buffered (0.15 M) Bolar's fixative (2 per cent paraformaldehyde and 0.75 per cent glutaraldehyde) at room temperature. The inner section (about 0.5 cm thick) of the mid-portion of the corpora cavernosa was cut out and immersed in Bolar's fixative. After overnight storage at 4°C, pieces of cavernous tissue (about 2 $mm^3$) were cut out and processed for electron microscopy. The remaining tissue block was put in 10 per cent formalin for 3 days and processed for light microscopy (hematoxylin and eosin and trichrome).

All values are expressed as the mean ± SD unless otherwise indicated. Statistical analysis was performed with Student's *t*-test.

## Results

In the following, the results of the study are given as mean values + SD of the eight animals. The mean baseline intracavernous pressure of 18 ± 4.2 cm $H_2O$ rose with cavernous nerve stimulation to a mean erectile pressure of 145 ± 10.9 cm $H_2O$. After cessation of stimulation, the pressure returned to baseline within 4 to 6 min. Sympathetic stimulation induced a brief pressure rise of mean 9 ± 0.8 cm $H_2O$, which returned to baseline immediately upon cessation. When the sympathetic trunks were stimulated in the full erection state (induced by cavernous nerve stimulation), a symmetrical hump-like rise in pressure for 5 to 8 seconds resulted, followed by an immediate fall.

In each cavernous body, three arterial sections of the above described cavernous area were measured. The diameter of the cavernous artery (Fig. 1), as measured by light microscopy, was 0.81 ± 0.21 mm in the flaccid state; this increased to 1.72 ± 0.27 mm after cavernous nerve stimulation and decreased to 0.43 ± 0.11 mm after sympathetic stimulation. The difference between the flaccid and stimulated diameters was statistically significant ($P<0.05$); however, when the arterial diameters after cavernous nerve stimulation and papaverine treatment or after

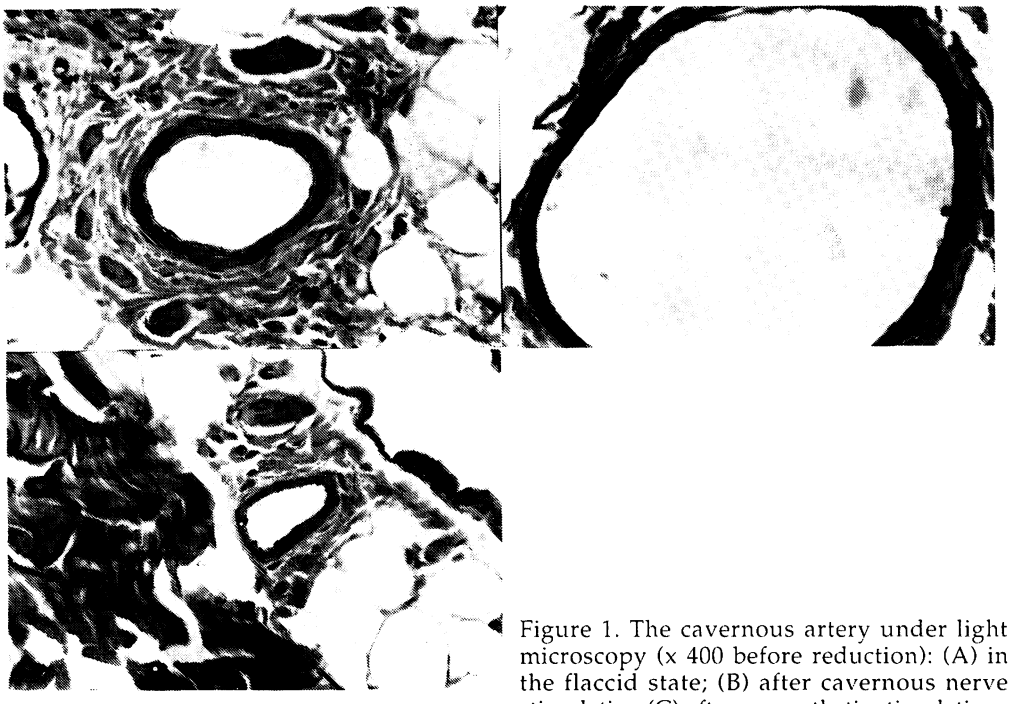


Figure 1. The cavernous artery under light microscopy (x 400 before reduction): (A) in the flaccid state; (B) after cavernous nerve stimulation;(C) after sympathetic stimulation.

sympathetic stimulation and epinephrine treatment were compared, the differences were not significant.

The cavernous spaces (Fig 2) were diminished after sympathetic stimulation, when compared with the flaccid state, but markedly distended after cavernous nerve stimulation.

With electron microscopy, the cavernous smooth muscle cells (Fig. 3) were contracted after sympathetic stimulation or epinephrine injection, when compared with the flaccid state; after cavernous nerve stimulation or papaverine injection, their appearance was relaxed, ie increased length and decreased diameter. The shape of the smooth muscle nuclei was congruent with the contour of the cell: after sympathetic stimulation or epinephrine injection, they were undulating, signifying active contraction as opposed to passive contraction by perfusion or inappropriate treatment of the tissue; after cavernous nerve stimulation or papaverine injection, they were markedly elongated with reduced cross-sectional diameters.

## Discussion

The study presented suggests that there is a considerable difference of the arterial diameter during sympathetic stimulation, the flaccid state and the erect state. The data are statistically significant, but due to the small number of the groups this does not necessarily seem to be biologically significant. Nonetheless, the arterial diameters measured in the three different states are so different that at least the assumption of an increasing arterial diameter with erection and a decrease in diameter during sympathetic stimulation is justified. These experimental data are

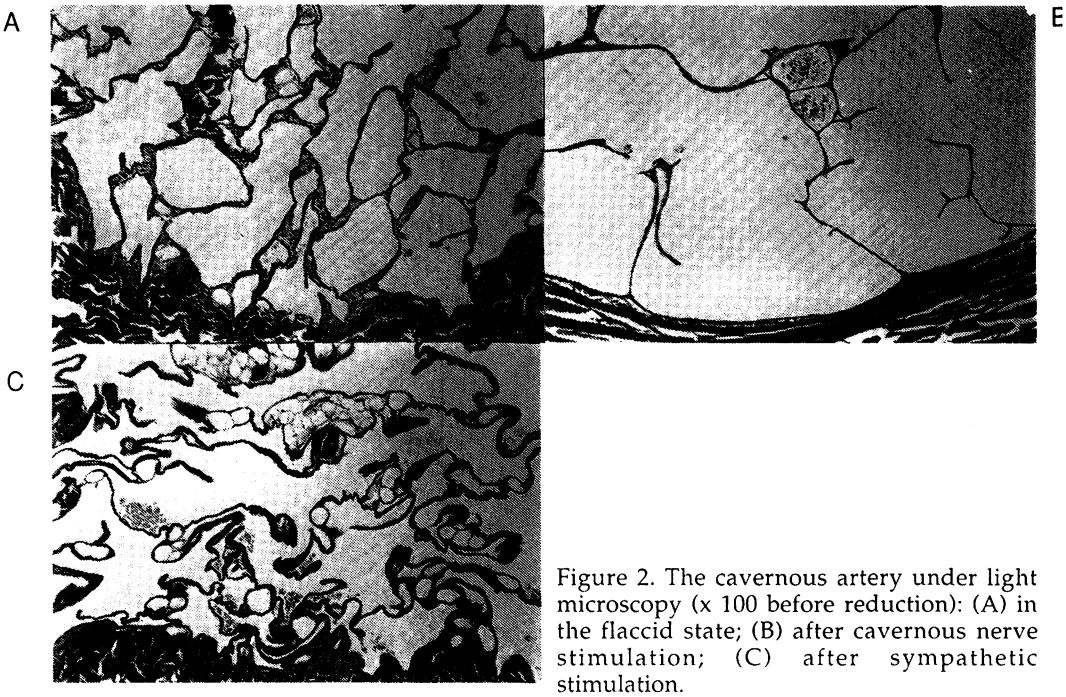


Figure 2. The cavernous artery under light microscopy (x 100 before reduction): (A) in the flaccid state; (B) after cavernous nerve stimulation; (C) after sympathetic stimulation.

supported by many clinical pulsed Doppler examinations, showing a significant increase in the cavernous arterial diameter after the induction of erection by vasoactive drugs[12].

Regarding the cavernous spaces, no quantification of our data was possible due to lack of computer-aided microscopic analysis facilities. Therefore, further studies are necessary for quantification of the amount of smooth muscle and fibrous tissue compared to the space of the cavernous sinusoids in the different states.

Our study demonstrates histologically that canine erection entails a significant increase in cavernous arterial diameter and relaxation of the cavernous smooth muscles, confirming what earlier studies had implied. Although the detumescence phase attracted scientific attention only recently[10,11], Kolliker had already concluded in 1852 that detumescence is likely due to smooth muscle contraction. He also reported that, under certain circumstances (eg application of cold water), the penis can become smaller than in the flaccid state, and "the penis then reaches its most possible smallness and a strange kind of hardness"[3]. We made similar observations after sympathetic trunk stimulation. A rise in the intracavernous pressure was accompanied by a palpable hardening of the cavernous bodies. Similarly, sympathetic stimulation during full erection first resulted in a rise in intracavernous pressure and then abolition of the erection. Microscopy showed that these changes result from cavernous smooth muscle contraction.

Our histologic findings substantiate the assumption that erection is associated with cavernous smooth muscle relaxation. Furthermore, this study demonstrates that contraction of the cavernous smooth muscles beyond that of the flaccid state is possible and can be elicited by sympathetic stimulation.

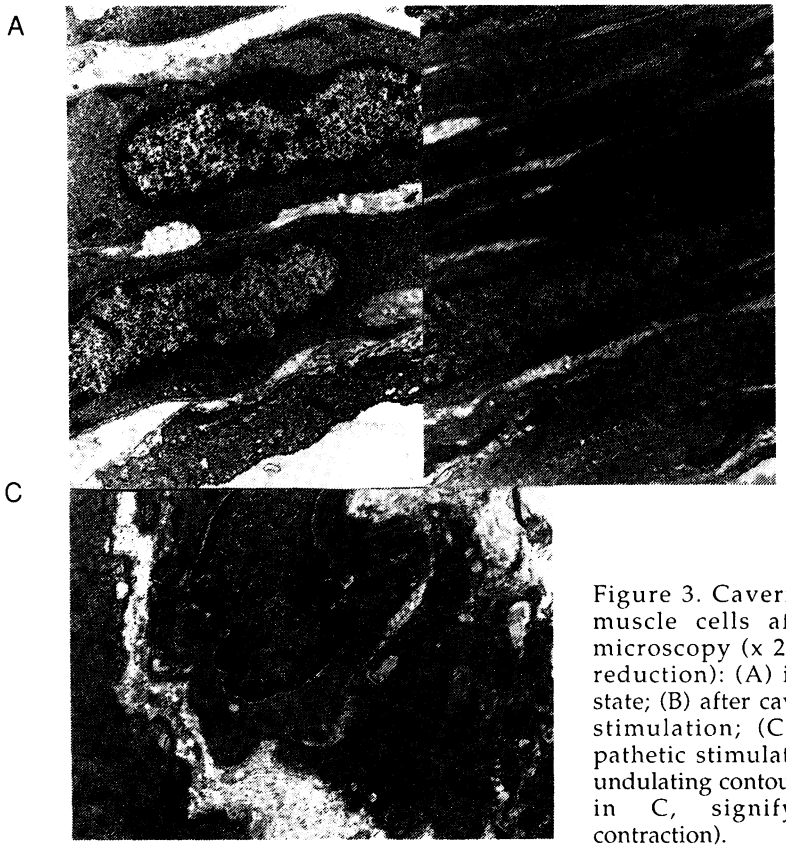


Figure 3. Cavernous smooth muscle cells after electron microscopy (x 22, 700 before reduction): (A) in the flaccid state; (B) after cavernous nerve stimulation; (C) after sympathetic stimulation (note the undulating contour of the nuclei in C, signifying active contraction).

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