0022-5347/86/1351-0142$02.00/0
THE JOURNAL OF UROLOGY

Vol. 135, January
Printed in U.S.A.

THE ULTRASTRUCTURE OF THE ERECTILE TISSUE IN PRIAPISM

M. A. SPYCHER* AND D. HAURI

From the Departments of Pathology and Urology, University Hospital Zurich, Switzerland

ABSTRACT

The ultrastructure of erectile tissue from the corpora cavernosa penis of patients suffering from stasis priapism and high-flow priapism has been studied. Trabecular interstitial edema was confirmed as the first reaction of the tissue to the hemodynamic impairment. At the cellular level trabecular smooth muscle cells were found to be the first affected by the altered environmental conditions. Their reaction consisted of structural and functional transformation to fibroblast-like cells. Severe cellular damage and widespread necrosis were not seen in high flow priapism; such damage existed in stasis priapism, but only when the priapic episode lasted more than 24 hours. Blood clot formation within the cavernae and destruction of the endothelial lining occurred in stasis priapism lasting over 48 hours. At this time trabecular inflammation became conspicuous and most of the smooth muscle cells were either transformed to fibroblast-like cells or had undergone necrosis. This stage was not reached in high flow priapism, a fact supporting the view that high flow priapism is a more benign and prognostically more favorable form of priapism. Massive smooth muscle cell transformation and the loss of contractile trabecular elements may play an important role in the evolution of irreversible erectile failure following stasis priapism persisting longer than 24 hours.

Priapism is caused by impaired hemodynamic conditions in the corpora cavernosa of the penis. Due to hitherto unknown mechanisms persistent blood stasis leads to stasis priapism (SP). It has been shown by cavernosography, however, that blood flow is maintained or even increased in some cases of priapism, called high-flow priapism (HFP).[1] In HFP the penis is less rigid than in SP and also causes less pain and discomfort to the patient. Prognostically, HFP has proven to be significantly more favorable than SP as far as the post-priapic erectile potency is concerned.[2] During blood stasis, O_2 tension and pH are rapidly reduced in the corpora cavernosa. Although this raises blood viscosity considerably,[3,4] clot formation is not reported to occur within the first days after onset of priapism.[5] It is widely accepted that blood stasis in priapism causes trabecular edema which accounts for the initiation of erectile tissue fibrosis. However, morphological studies of trabecular tissue response to a hypoxygenated environment are few[1,5] and only a little interest has been shown in the microanatomy of the normal human penis until recent years.[7-13] The present study was undertaken to establish the structural changes in the tissue of the cavernous bodies during priapism using both light and electron microscopy. An attempt was made to determine the early pathological alterations which occur in the clinical condition known as priapism.

MATERIALS AND METHODS

Tissue samples of the corpora cavernosa penis of 22 males were examined in the present study. Eleven patients suffered from priapism and eleven from other penile disturbances making surgical intervention necessary, the latter serving as a contrast group (table 1, A and B). Blood gas values and intracavernosal blood pressure were not determined in either group but cavernosography was performed in the priapic patients. Small tissue samples were taken at different sites according to surgical necessities, but most often near the distal end of the cavernous bodies. The tissue was fixed in buffered glutaraldehyde, postfixed in osmium tetroxide, dehydrated in graded ethanols and propylene oxide, and subsequently embedded in Epon 812. Semithin sections were stained with methylene blue azur A, thin sections with uranyl acetate and lead citrate. The sections were examined in a Philips EM 400 T/HM and a JEOL 100CX electron microscope.

TABLE 1A. *Priapic group*

Case No.	Preoperative Status	Age	Duration of Priapism	Type of Priapism†	Erectile Potency°	Case Situation (See Table 2)
1	traumat. priapism	28	5 mo.	high-flow	+	b)
2*	idiop. priapism relapse	23	24 hr.	stasis	+	d)
3	idiop. priapism	54	14 days	high-flow	±	b)
4	idiop. priapism	60	12 hr.	stasis	+	c)
5	idiop. priapism	29	3 wk.	stasis	±	f)
6*	idiop. priapism relapse	23	18 wk.	stasis	+	f)
7**	postsurg. priapism	53	6 wk.	undeterm.	−	f) or b)
8	idiop. priapism	44	48 hr.	stasis	±	e)
9	idiop. priapism	39	days (?)	undeterm.	−	prob. f)
10	idiop. priapism relapse	62	24 hr.	stasis	+	e)
11	idiop. priapism relapse	58	12 hr.	stasis	−	d)

* Same patient (cases 2 and 6).
** Same patient as case 16 in table 1*B*.
† Type of priapism determined by cavernosography.
° Erectile potency according to patient's statement.

Accepted for publication July 26, 1985.
* Requests for reprints: Department of Pathology, University Hospital, CH-8091 Zurich, Switzerland.

TABLE 1*B*. *Contrast group*

Case No.	Preoperative Status	Age
12	potent, correction surgery	33
13	potent, cancer of penis	45
14	posttraumatic impotency	34
15	impotency of vascular origin	57
16*	impotency of vascular origin	53
17	impotency of vascular origin (diabetic)	60
18	impotency of vascular origin following X-ray therapy of lymphoma	39
19	posttraumatic impotency	45
20	impotency due to spinal paralysis	36
21	impotency due to multiple sclerosis	38
22	idiopathic impotency	50

* Same patient as case 7 in table 1*A*.

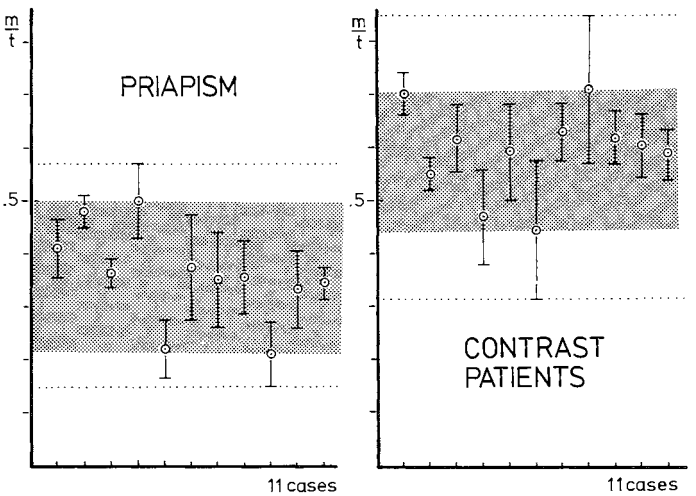


FIG. 1. Morphometry of trabecular edema. M over t quotients (m/t) in priapism and in contrast group (see text). Points represent mean values, bars = ± 1 standard deviation, shaded area = range of the means, and dotted lines = highest and lowest values of standard deviations. Number of fields of view tested per tissue sample: no. = 5. M/t values of contrast patients ranged between 0.45 and 0.70 and those of patients with priapism between 0.22 and 0.55.

Morphometric analysis was carried out at the light microscopic level using semithin sections and histological sections (HE and/or van Gieson stain as a control). The quotient m over t (m/t; m = smooth muscle fiber bundles, t = trabeculae) was determined by measuring the total length of the trajectories of a test-line system passing through either structure at a constant optical magnification. Measurements were made using a KONTRON MOP AM-03 system.

RESULTS

The first reaction of the cavernosal tissue to hemodynamic impairment in priapism was the formation of trabecular interstitial edema which varied in extent according to different factors such as duration and severity of stasis flow-type and the patient's constitution. Morphometrically the edema was manifest as a clear drop of the mean m/t quotient (fig. 1), lower values indicating a more pronounced edema. Values below 0.4 were found to represent a higher risk of postpriapic erectile impotency.

In the early stage of priapism (around 12 hours after onset) and in patients suffering from a priapic relapse of short duration (less than 12 hr), the tissue alterations were insignificant. They consisted of sporadic minor cavernal endothelial defects, sometimes with thrombocytes adherent to the exposed basement lamina, and occasional lymphocytic infiltration of the trabecular tissue. The trabecular smooth muscle cells (SMC) were apparently unaltered (fig. 2). No blood clot formation occurred at this stage of priapism.

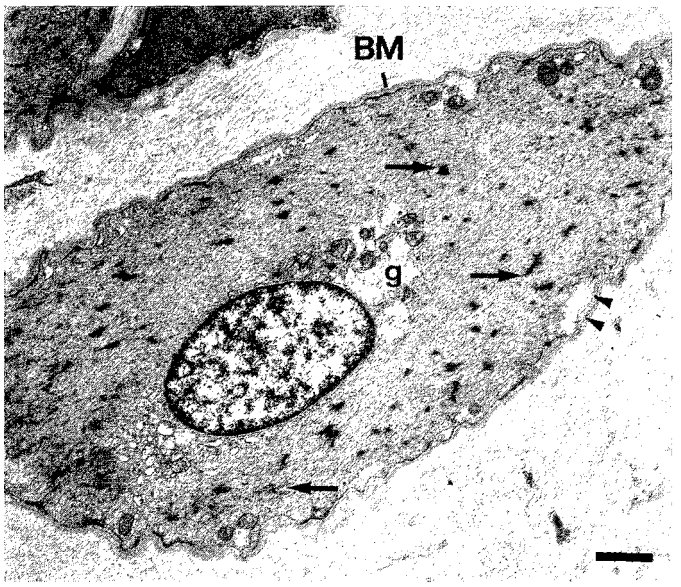


FIG. 2. Normal trabecular smooth muscle cell (SMC) surrounded by distinct basement membrane (BM). Cytoplasm contains densely packed filaments with dense bodies (arrows), sparse organelles at cell periphery and on either side of nucleus, and small glycogen areas (g). Plasma membrane shows marked pinocytotic activity (arrow heads) (× 8,000). Bar = 1 μm.

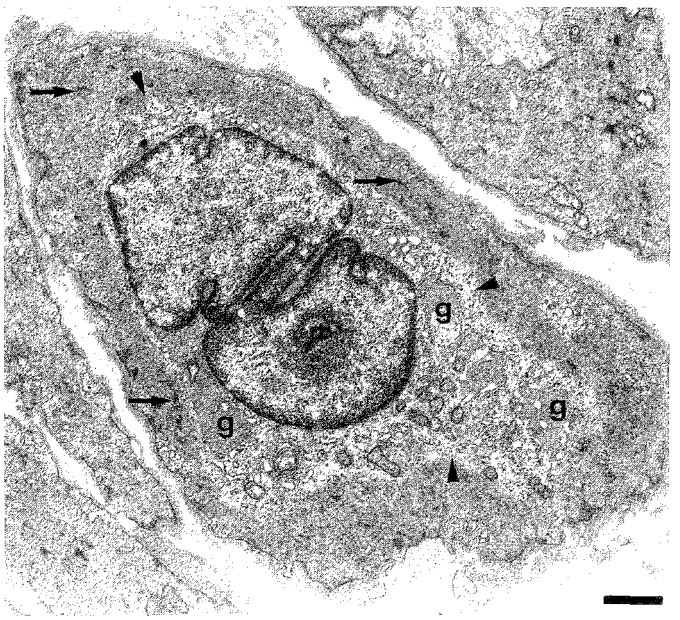
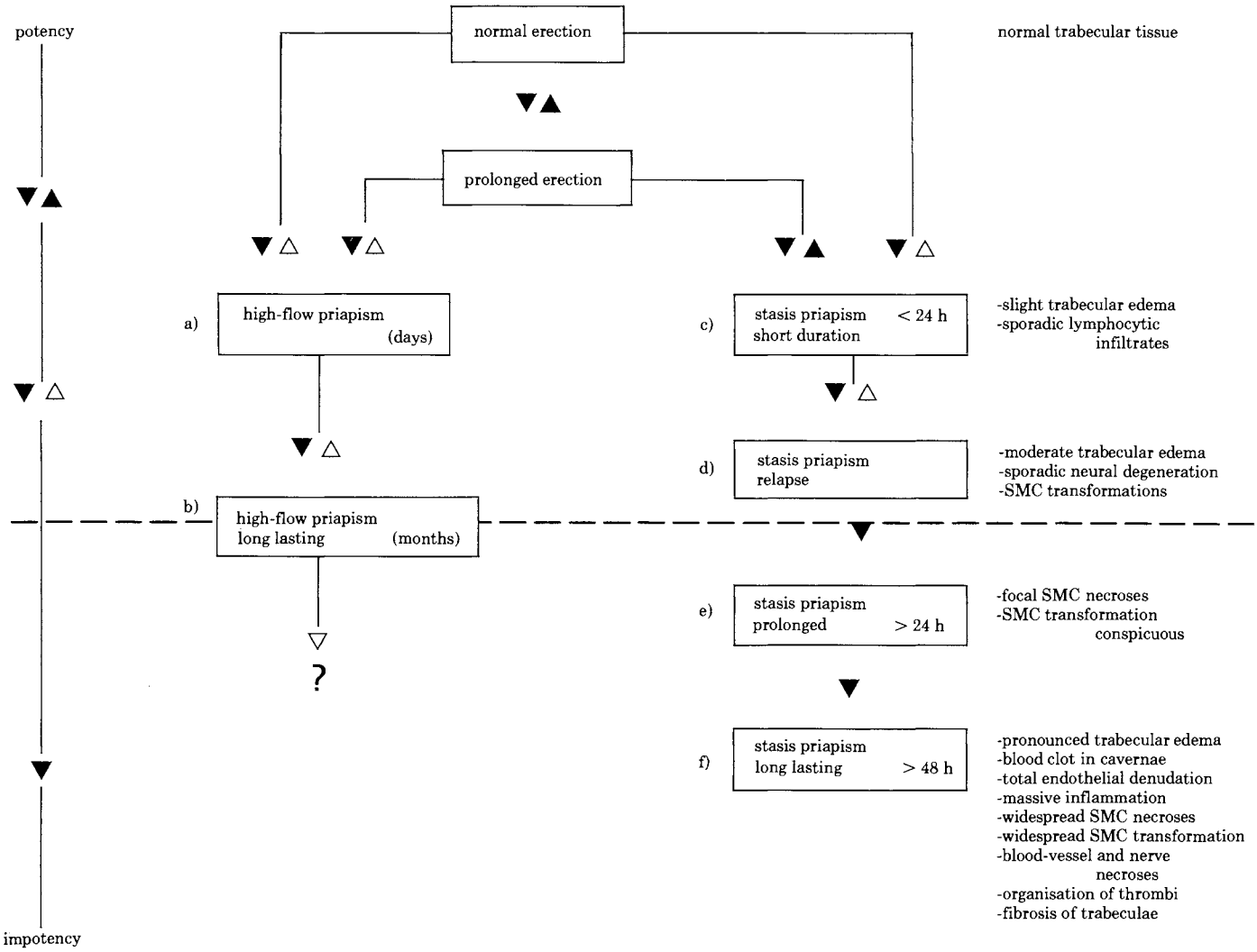


FIG. 3. Beginning transformation of SMC in patient suffering from stasis priapism relapse. Filamentous mass is reduced to small rim at cell periphery (arrows) while organelle-containing cytoplasm is significantly enlarged (arrow heads; g = glycogen) (× 8,000). Bar = 1 μm.

A significant change in trabecular ultrastructure was observed in SP lasting 12 to 14 hours, in priapism relapsing several times and in HFP of prolonged duration (days) (table 2). Still, endothelial damage was minimal and fibrin clots were not seen in the cavernal lumina. The trabecular smooth muscle cells (SMC), however, showed a beginning cytoplasmic transformation distributed focally. The perinuclear portion of cytoplasm, normally a small area containing mitochondria, profiles of endoplasmic reticulum, ribosomes and components of the Golgi apparatus was strikingly increased in size, thus displacing the reduced mass of contractile filaments to the periphery (fig. 3). In addition to the transforming cells, scattered necroses of

TABLE 2. *Schematic synopsis of priapic states with respect to flow type, duration, reversibility and ultrastructural findings*



Interrupted line stands for hypothetical "point of no return" (see text).
▼ ▲ = reversible, ▼ △ = limited reversibility, ▼ = irreversible.
Letters a–f indicate localization of cases in table 1A.

SMC and single nerve fibers were noticed although they were few in number. The pattern of damage observed in the two patients with medium to long-lasting HFP (days to weeks) did not differ from that seen in this category of SP. Despite the long duration of HFP (five months in one patient!), the m/t quotient did not fall below 0.4.

In SP of prolonged duration (24 to 48 hours) widespread cavernal endothelial destruction and exposure of the basement membrane with subsequent thrombocyte adherence were observed but still no blood clots plugged the cavernae (fig. 5). Transformations as well as necroses of SMC, however, became conspicuous.

When blood stasis persisted longer than two days in long lasting priapism, thrombus formation was found in most of the cavernal lumina, these usually being distended. In most instances their endothelial lining was missing. The trabecular tissue appeared densely infiltrated by inflammatory cells, mainly granulocytes. The majority of SMC either underwent necrosis (figs. 6, 7) or were seen in various states of transformation into fibroblast-like cells (figs. 4, 8). Transition stages between SMC and fibroblast-like cells exhibited both features

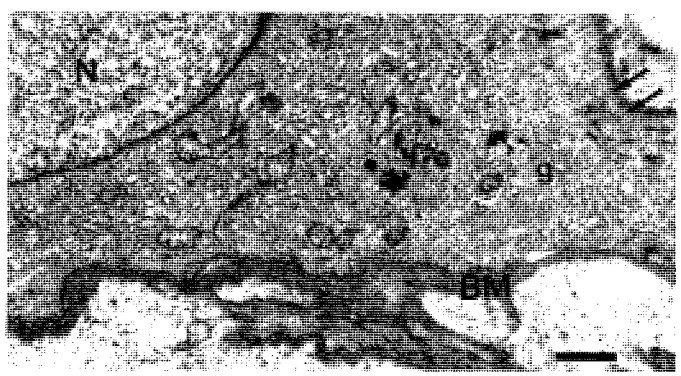


FIG. 4. Advanced stage of SMC transformation in patient suffering from long-lasting stasis priapism. Micrograph shows part of cell exhibiting features of SMC and of fibroblast-like cells. Cell is surrounded by distinct basement membrane (BM). In areas where filaments and dense bodies are still present, marked pinocytotic activity is observed (arrows). Cytoplasm contains abundant organelles and small glycogen accumulations (g). Chromatin is evenly distributed within nucleoplasm (N) (× 9,100). Bar = 1 μm.

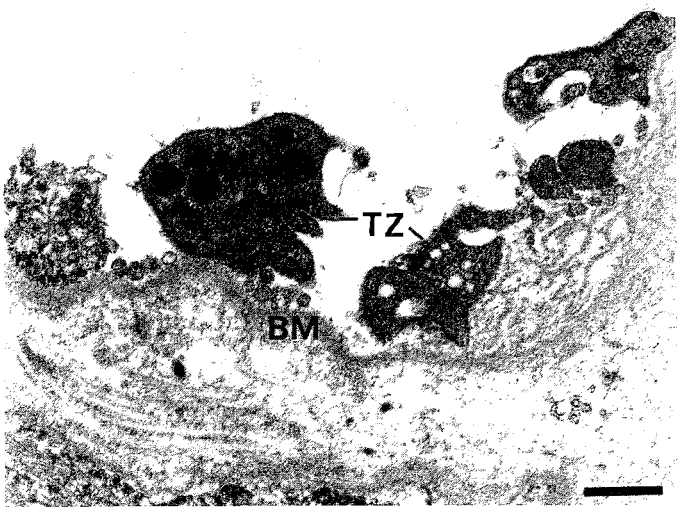


FIG. 5. Cavernal lining in prolonged stasis priapism. Endothelial covering is missing. Thrombocytes (TZ) are seen adhering to denuded basement membrane (BM) (× 11,500). Bar = 1 μm.

FIG. 6. Necrotic trabecular SMC in long lasting stasis priapism. Necrotic tissue is invaded by neutrophil granulocyte (PMN) (× 3,500). Bar = 1 μm.

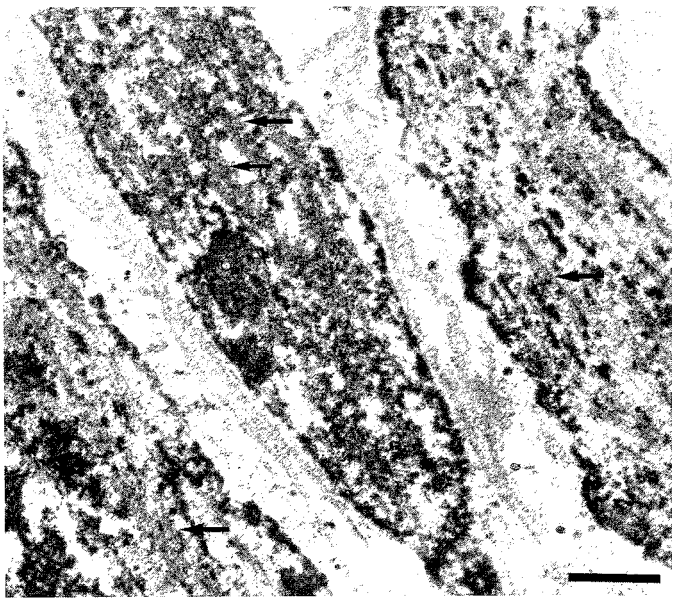


FIG. 7. Higher magnification of necrotic SMC from same preparation as fig. 6. Myofilaments are clumped (arrows) and organelles are no longer discernible (× 11,600). Bar = 1 μm.

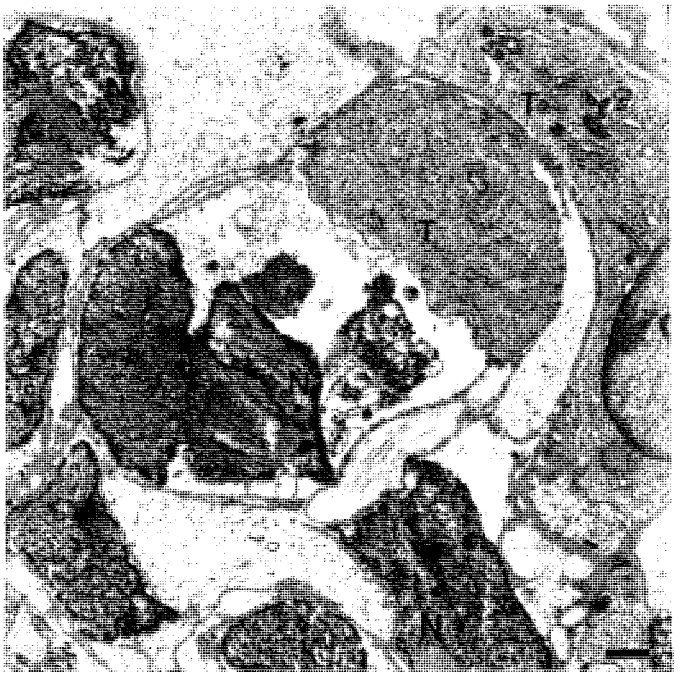


FIG. 8. Long lasting stasis priapism. Necrotic (N) and transformed (T) SMC are seen in same trabecular fiber bundle (× 5,500). Bar = 1 μm.

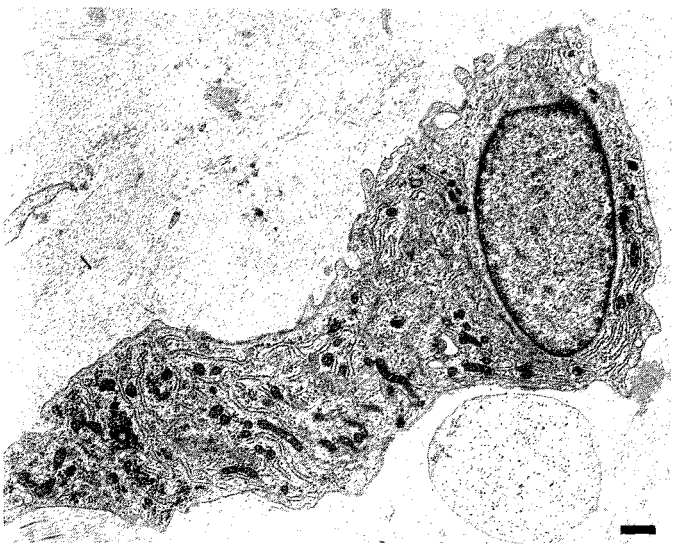


FIG. 9. Fibroblast-like cell of cavernal tissue in long lasting stasis priapism. After full transformation SMC has adopted fibroblast-like appearance and it has often escaped its basement membrane confinement. Cell is rich in organelles and it may hardly be distinguished from connective tissue fibroblasts unless remnants of SMC features including myofilaments, dense bodies, pinocytotic activity, basement membrane and glycogen accumulations (g) are seen. Compare fig. 4. (× 4,500). Bar = 1 μm.

of SMC such as filaments, dense bodies, pinocytotic activity and basement lamina, and features of fibroblastic cells which mainly consist of a cytoplasm containing numerous organelles (fig. 4). Fully transformed SMC were devoid of contractile filaments. They were still surrounded by the basement lamina (fig. 8) or they had apparently escaped their basement membrane envelope and had adopted a fibroblast-like shape (fig. 9).

In long-lasting stasis priapism, basement membrane sheaths were occupied by either necrotic SMC or fibroblast-like cells (fig. 8) or they were empty. Fibroblast-like cells were never

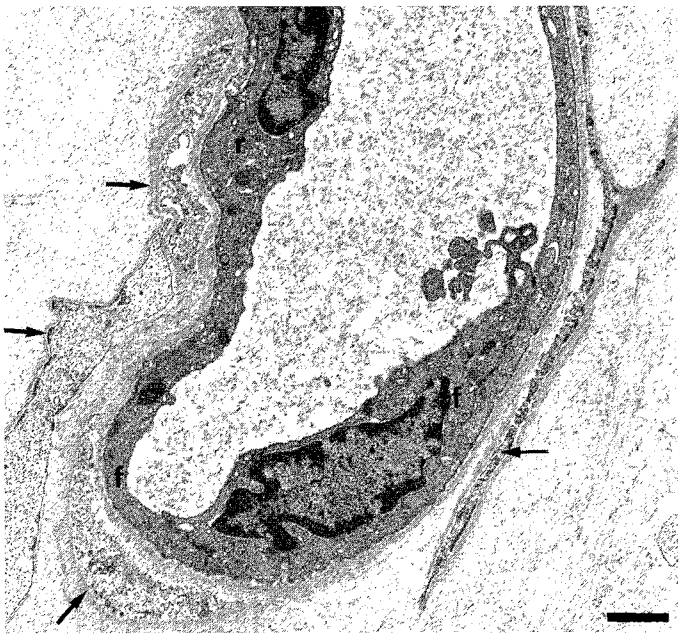


FIG. 10. Viable trabecular blood capillary in long-lasting stasis priapism. Endothelial cells are rich in filaments (f) and in ribosomes (r). Pericytes surrounding capillary tube are necrotic (arrows) (× 8,500). Bar = 1 μm.

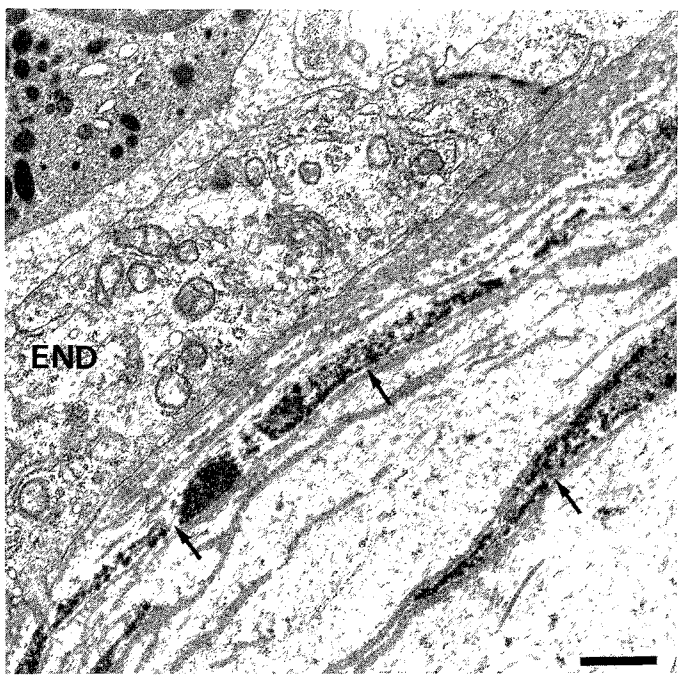


FIG. 11. Viable cavernal endothelium in long lasting priapism. Apparently intact endothelial cell (END) covers cavernal lining but subendothelial SMC are necrotic (arrows) (× 10,000). Bar = 1 μm.

observed undergoing necrosis. Clearing of necrotic SMC by invading phagocytes occurred only sporadically.

Nerve fibers, their terminal varicosities and blood capillaries were also affected by the extensive tissue necrosis. However, in all the samples examined the coexistence of necrotic tissue and living vascular structures was remarkable. Many of the trabecular capillaries showed an intact endothelium although their pericytic cells were disintegrated (fig. 10). We also observed normal-looking cavernae lined by intact endothelial cells next to areas of necrosis (fig. 11).

DISCUSSION

Priapism in its classical form is thought to be caused by total or subtotal blood stasis within the corpora cavernosa of the penis. Arteriography and cavernosography have, however, demonstrated that rigidity of the cavernous bodies can persist although blood flow through the erectile tissue is apparently normalized or even increased.[1,14] This type of priapism has been termed high-flow priapism. It differs from stasis priapism in that the penis keeps a more elastic consistency and does not cause pain. Normal erectile potency can be restored by surgical intervention even after a very long duration of high-flow priapism.[1,14] Persisting stasis priapism on the other hand is known to result in erectile tissue fibrosis and functional failure unless surgically treated within about 24 hours from onset.[1,3,15] According to our morphometric analyses trabecular edema was established in both types of priapism, although it was less pronounced in the high-flow type. Since priapism is assumed to evolve from normal erection[1,3] one can speculate that interstitial edema representing a physiological reaction of the trabecular tissue to the altered hemodynamic conditions may be a normal feature of erection. This assumption, however, cannot be proven, since tissue from normal erect corpus cavernosum is not available. After cessation of stimulation and restitution of blood flow the tissue would return to its normal state. Under unfavorable circumstances such as in priapism, however, the edema could persist or even be intensified and thus lead to or accompany cellular damage.

The first cells affected are shown to be the SMC rather than cavernal endothelial cells. SMC reaction apparently consists of the attempt of the cells to be activated and transformed into non-contractile fibroblast-like cells which seem to be more resistant to the altered environment in priapism. Similar SMC modifications have been reported to occur in the media wall of blood vessels under various conditions, among others reduced O_2-tension and altered wall pressure.[16-18] Since transformed SMC are mobile and capable of collagen and elastic fiber synthesis, we assume that they play a significant role in the evolution of postpriapic erectile tissue fibrosis.

Our findings suggest that severity and duration of blood stasis in priapism largely determine whether or not fibrosis and erectile failure will occur. In high-flow priapism lasting for weeks the damaging stimuli (decreased O_2-tension and intracavernal blood pressure) are presumably less pronounced than in stasis priapism. They may be strong enough to trigger SMC transformation but not strong enough to lead to cell destruction. At this stage, restitution to full erectile potency through functional recovery of transforming SMC seems possible. If on the contrary the stimuli exceed a certain threshold value (interrupted line in table 2) as in prolonged (24 to 48 hours) or long-lasting (more than 48 hours) stasis priapism, a majority of SMC may undergo necrosis prior to possible transformation. Blood thrombus formation within the cavernae and extensive endothelial destruction occur at the same time. These areas of trabecular SMC necroses are subsequently invaded by inflammatory cells, transformed fibrolast-like connective tissue synthesizing cells and fibroblasts from viable areas, thus converting the cavernous tissue into scar tissue.

Without regarding the extent of tissue damage, branches of surviving or newly formed blood vessels were always encountered in areas of necrosis, suggesting that the nutritive vascular system remains functional at least to a minor extent.

To our knowledge SMC transformation in the erectile tissue has not been described. Whether it constitutes a specific sequel of priapism or whether it is responsible for erectile impotency of other types remains to be elucidated.

REFERENCES

1. Hauri, D., Spycher, M. A. and Bruehlmann, W.: Erektion und Priapismus — ein neues pathophysiologisches Konzept. Verh. Deutsch. Ges. Urol., **33:** 162, 1982.

2. Bruehlmann, W., Pouliadis, G., Hauri, D. and Zollikofer, Ch.: A new concept of priapism based on the results of arteriography and cavernosography. Urol. Radiol., **5:** 31, 1982.
3. Pryor, J. P.: Priapism. The Practitioner, **226:** 1873, 1982.
4. Martelet, H. G., Janin-Manificat, L., Striffling, V., Bonhomme, J. and Cortet, P.: Le Priapisme leucémique, physiopathologie et approche thérapeutique. Sem. Hop. Paris, **58:** 2511, 1982.
5. Hinman, F. Jr.: Priapism: reasons for failure of therapy. J. Urol., **83:** 420, 1960.
6. Hinman, F.: Priapism: report of cases in a clinical study of the literature with reference to its pathogenesis and surgical treatment. Ann. Surg., **60:** 689, 1914.
7. Tudoriu, Th. and Bourmer, H.: The hemodynamics of erection at the level of the penis and its local deterioration. J. Urol., **129:** 741, 1983.
8. Benson, G. S.: Mechanism of penile erection. Invest. Urol., **19:** 65, 1981.
9. McConnell, J., Benson, G. S. and Schmidt, W. A.: The vasculature of the human penis: a reexamination of the morphological basis for the polster theory of erection. Anat. Rec., **203:** 475, 1982.
10. Bossart, M., Spjut, J. and Scott, B. F.: Ultrastructural analysis of human penile corpus cavernosum, its significance in tumescence and detumescence. Urology, **15:** 448, 1980.
11. Goldstein, A. M. B., Meehan, J. P., Zakhary, R., Buckley, P. A. and Rogers, F. A.: New observations on microarchitecture of corpora cavernosa in man and possible relationship to mechanism of erection. Urology, **20:** 259, 1982.
12. Ruzbarsky, V. and Michal, V.: Morphologic changes in the arterial bed of the penis with aging. Invest. Urol., **15:** 194, 1977.
13. Benson, G. S., Connell, J. A., Lipshultz, L. I., Corriere, J. N., Jr. and Wood, J.: Neuromorphology and neuropharmacology of the human penis. J. Clin. Invest., **65:** 506, 1980.
14. Hauri, D., Spycher, M. A. and Bruehlmann, W.: Erection of priapism: a new physiopathological concept. Urol. Int., **38:** 138, 1983.
15. Stosch, M.: Priapism. Z. Allg. Med., **58:** 1405, 1982.
16. Staubesand, J.: Matrix Vesikel und Mediadysplasie: Ein neues Konzept zur formalen Pathogenese der Varikose. Phlebol. Proctol., **7:** 109, 1978.
17. Feigl, W., Sinzinger, H., Howanietz, L. and Leithner, Ch.: A morphologically different type of smooth muscle cell in the inner media of the splenic artery. Acta Anat., **94:** 617, 1976.
18. Scott, R. F., Jarmolych, J., Fritz, K. E., Imai, H., Kim, D. N. and Morrison, E. S.: Reactions of endothelial and smooth muscle cells in the atherosclerotic lesion. Proc. Second Internat. Symposium on Atherosclerosis. Edited by R. J. Jones. Springer, N.Y., pp. 50–58, 1970.