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Changes in the Small Blood Vessels of the Adult Human Testis in Relation to Age and to Some Pathological Conditions

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Summary. A total of 91 postmortem fresh human autopsy testes were examined, using microangiography and histology. Histologically 70 of them were classified as normal. Incomplete spermatogenic arrest was found in 5 testes; 10 testes showed progressive tubular fibrosis and 6 were completely hyalinized. In general, the microvascular architecture remained stationary during the whole adult life. The intratesticular end arteries had a peculiar spiralling course irrespective of the age of the subject. Focal hyalinization of tubules was seen in 56% of the normal testes, becoming more common with increasing age. These regions showed fewer capillaries both in microangiography and in histology. Thickening of the intratesticular arterial walls was found histologically in 59% of the normal testes, in 90% of the testes showing progressive tubular fibrosis and in all totally hyalinized testes. Testes with totally hyalinized tubules showed severe vascular changes in both microangiography and histology. It is suggested that vascular alterations play a part in the pathogenesis of testicular fibrosis.

Zusammenfassung. Insgesamt 91 postmortem Hoden wurden histologisch und mikroangiographisch untersucht. 70 Hoden wurden als normal klassifiziert. Unvollständige Spermiogenese-Hemmung wurde in 5 Hoden gefunden, in 10 Fällen war eine progressive Fibrose der Tubuli zu finden und 6 Hoden waren total atrophisch. Hauptsächlich die mikrovasculäre Architektur bleibt das ganze postpubertale Leben hindurch konstant, und die Spiralisierung der intratesticularen End-Arterien ist unabhängig vom Alter. Herdförmige hyaline Umwandlungen wurden in 56% der normalen Hoden gefunden. Die Frequenz dieser Umwandlungen nimmt mit steigendem Alter zu. In diesen fibrosierten Herden waren weniger Capillaren sowohl histologisch als mikroangiographisch erkennbar. Arterielle Wandveränderungen wurden in 59% von normalen, in 90% von Hoden, die progressive Fibrose der Tubuli aufwiesen, und in allen total atrophischen Hoden gefunden. Sowohl mikroangiographisch als histologisch waren die Arterienveränderungen in der letztgenannten Gruppe erheblich. Die Befunde lassen darauf schließen, daß die vasculären Veränderungen eine besondere Rolle bei der Fibrosierung des Hodens spielen.

With increasing age numerous changes have been found to appear in the human testis. The activity of the spermatogenesis decreases; the tunica propria of the seminiferous tubules thickens and changes are also detectable in the interstitial tissue (Tillinger, 1957; Bürgi and Hedinger, 1959). It is a familiar observation that the histological picture of the postpuberal human testis is uneven and that some abnormal seminiferous tubules can be detected in all testes (Kyrle, 1920). Extensive alterations are found in the "senile atrophic" testis, in which all the seminiferous tubules are hyalinized (Bürgi and Hedinger, 1959; Heinke and Doepfmer, 1960).

Some very brief comments in the earlier literature note that the testicular small arteries show arteriosclerotic changes (Koopmann, 1936; Tonutti *et al.*, 1960). Heinke and Doepfmer, 1960 suggested that most advanced degeneration of the seminiferous tubules is seen near the

sclerotic arteries. Very recently, Hatakeyama *et al.* (1966) observed that arteriolar "hyalinosis" is a common feature in the arterioles of the human testis. The architectural organization of the microcirculation in the normal human testis was recently thoroughly investigated in this laboratory (Kormano and Suoranta, 1971 a). While the gross vascular pattern of the adult testicular arteries was found to show no age-related changes (Kormano and Suoranta, 1971 b), the local degenerate areas, generally observed in the ageing testes, may in fact be more related to changes at the microcircular level. The present study was therefore carried out to reveal any age changes in the intratesticular microvasculature. Special attention was paid to a possible relation between histologically detectable degenerate areas and microangiographically observable changes in the small intratesticular end-arteries.

Material and Methods

103 scrotal testes were extirpated from 54 fresh cadavers. The age distribution of the material is seen in Table 1. The testes of 32 cadavers were obtained postmortem following accidents, suicides or some acute illness, usually before autopsy (in the Department of Forensic Medicine, University of Helsinki). The rest of the material was taken from hospital patients who had suffered a more or less chronic illness before death (mainly from II Department of Pathology, University of Helsinki). The subjects were selected only on the basis of the freshness of the cadavers (time between death and preparation of the specimens varied from 2 hours to 3 days).

Table 1. *Distribution of the material*

Age group	Number of normal/ all testes	Number of testes/autopsies	Acute death
20–29	14/16	16/9 (+ 1 deep frozen)	8
30–39	4/4	4/3	3
40–49	11/15	15/9	6
50–59	12/15	15/9 (+ 2 deep frozen)	4
60–69	13/15	15/8	5
70–79	15/20	20/10	5
Over 80	1/6	6/3	1
Total	70/91	91/51 (+ 3 deep frozen)	32

The testis, epididymis and whole spermatic cord were extirpated together. The testicular artery was cannulated and 10% suspension of fine-grain barium sulphate (Micropaque, Damancy & Co.) in saline was injected under a controlled pressure of 120–150 mm Hg for 2–3 hours. Some additional testes were also filled from the venous side. Three testes were deep-frozen after injecting contrast material and frozen 2 mm sections were microangiographed according to the method of Kormano (1969) to reveal any aberrations of microvascular architecture due to fixation. The injected specimens were radiographed in contact with a fine-grain X-ray film (Microtex, Kodak). In 91 testes satisfactory filling of the vessels was obtained and accepted for further analysis. The testes were fixed in Bouin's solution for 5 days and embedded in paraffin wax.

For high-resolution microangiography 0.5 mm to 2 mm transverse sections, usually 4 sections from each testis, were cut. These were radiographed in contact with a high-resolution emulsion (Maximum Resolution Plate, Kodak). A Siemens

AG Cu 3 ö X-ray tube, equipped with a copper target and beryllium window, was used for microangiography. The X-ray tube was run at 35 kV and 10 mA, the focus-to-film distance being 120 cm, and the exposure time was 3.5 hours. The high-resolution plates were developed in Gevaert 209 A developer for 7 min. 10 μ sections were cut between each microangiographed section and stained by the PAS-hematoxylin and Weigert-van Gieson methods for histologic examination. Serial sections were cut from selected microangiographed sections and stained by the same methods.

Results

Histological Findings and their Classification

The general appearance of the testis was studied using the histological sections, usually six from each testis. Special attention was paid to the local degenerative areas. The evaluation of the seminiferous tubules was carried out according to previous authors (Heller *et al.*, 1952; Tillinger, 1957; Tonutti *et al.*, 1960; Heinke and Doepfmer, 1960; Girgis *et al.*, 1969). No attempt was made to determine the stages of the cycle of the seminiferous epithelium (Clermont, 1966). Activity of the germinal epithelium was determined mainly according to Tillinger (1957), and it was evaluated as normal when at least 3/4 of the tubules exhibited what the examiner considered to be, both quantitatively and qualitatively, a normal spermatogenesis for a given age.

Only a marked decrease or increase in the number of Leydig cells was regarded as pathological. The cytological appearance of Leydig cells was examined only cursorily.

Unavoidably, division of the material into qualitative subgroups is somewhat arbitrary, and depends on the experience of the examiner, but in this study the criteria were constant following a second examination period six months later. The pathological changes in the testes were classified in the present study into the following categories (Table 4): 1) Mainly epithelial damage, including spermatogenic arrest; 2) progressive tubular fibrosis (Engle, 1947) with focal epithelial damage and tubular hyalinization involving more than 1/4 of the histological sections examined; 3) total or almost total tubular hyalinization.

The number of testes studied in each age group is shown in Table 1. Altogether 70 testes were histologically normal. Incomplete spermatogenic arrest, mainly at primary spermatocyte level, was observed in five testes (Fig. 3). 10 testes showed progressive tubular fibrosis. Focal hyalinized areas and variable amounts of epithelial damage were found in all of them, although every testis in this group also had normal looking areas (Fig. 19). Six testes were completely hyalinized.

Age Changes in the Histology and Vascularization of the Normal Testes

General Histological Features. The spermatogenic activity and the height of the epithelium decreased with increasing age (Fig. 10). The wall of the seminiferous tubules was thickened and the tubular diameters were often decreased. Capillaries were occasionally found in the tunica propria, as described earlier (Kormano and Suoranta, 1971a). This was unrelated to the thickening of the tubular wall. In all testes local degenerations were found in some degree, varying from slight lowering

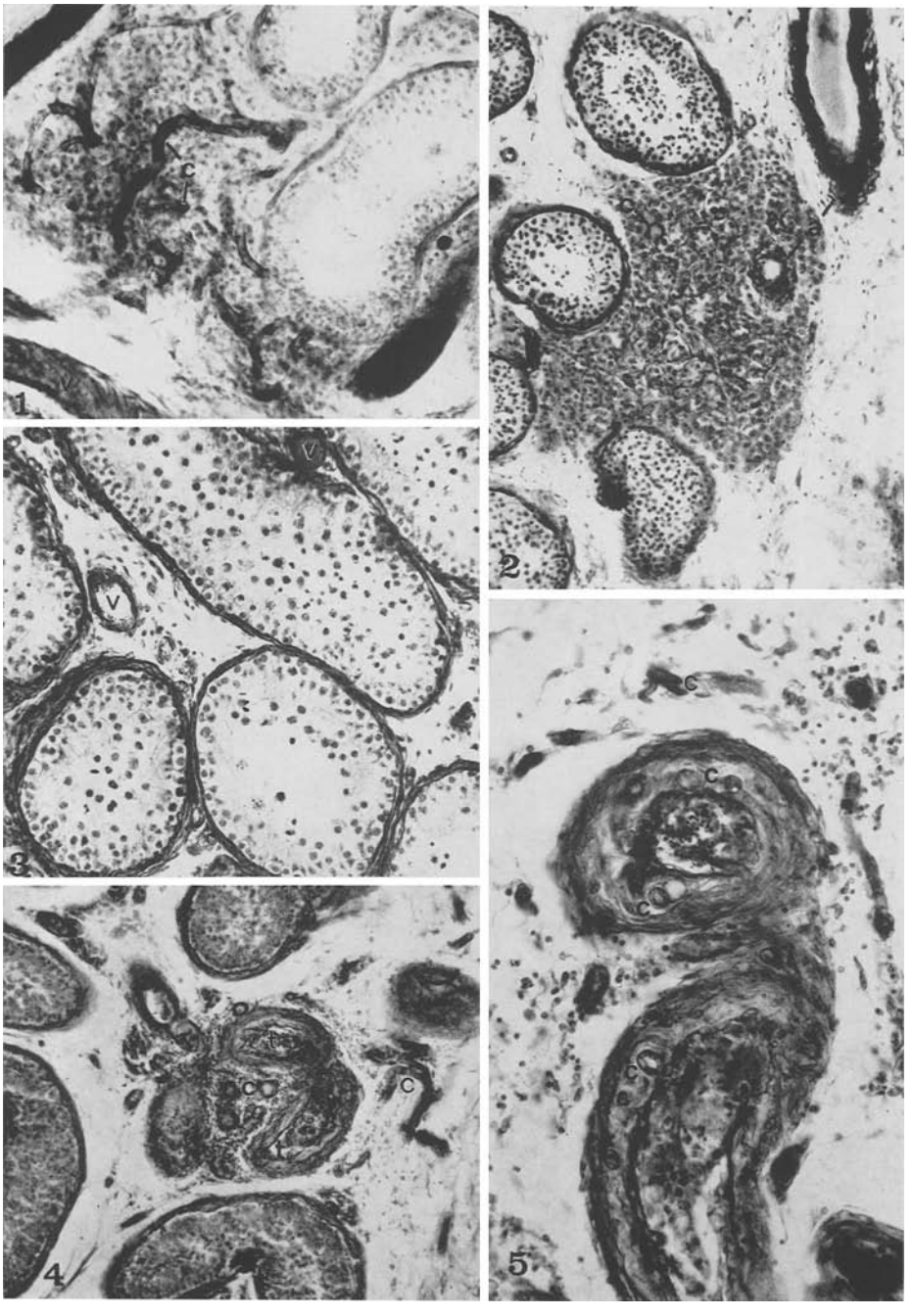


Fig. 1. Focal Leydig cell cluster with rich capillary supply. The whole testis shows incomplete spermatogenic arrest (*c* capillary, *v* vein) (56 y.). PAS-hematoxylin-stained 10 μ section. ×130

Table 2. *Changes observed in normal testes*

Age group	Number of testes	Focal hyalinization	Leydig cell clusters	Inflammatory cell infiltrations	Hernia like protrusions	Vascular changes in histology	Glomerular loop formations in microangiography	Total number of testes with changes
20–29	14	3	3	1	—	2	—	6
30–39	4	2	—	3	1	3	1	3
40–49	11	8	4	1	3	6	—	7
50–59	12	5	8	4	1	8	—	9
60–69	13	8	9	8	4	10	1	12
70–79	15	12	5	4	3	11	5	15
over 80	1	1	1	1	—	1	—	1
Total	70	39	30	22	12	41	7	53

of the spermatogenic activity to complete hyalinization of the tubules. The degenerative areas were more clearly observed at the periphery of the testes.

Relation Between Focal Degenerated Areas and Capillary Supply. In 39 testes, classified as normal, areas of totally hyalinized seminiferous tubules (5 to 20 tubules in each area) were found, increasing in frequency with age (Table 2). No special features were found by microangiography in the end arteries supplying the degenerate areas (Fig. 6). However, in hyalinized areas the terminal arterioles and capillaries were not filled and distended as completely as elsewhere in the same testis. The intertubular and peritubular capillary networks were poorly organized and the capillary bed was sparse (Figs. 6 and 7). These features were better visible in microangiography than in histology.

Most of the clusters of Leydig cells found in a total of 30 normal testes usually had a rich capillary supply (Fig. 1). Some poorly vascularized nodules contained 5–10 Leydig cells in clumps, which were surrounded by connective tissue (Fig. 2).

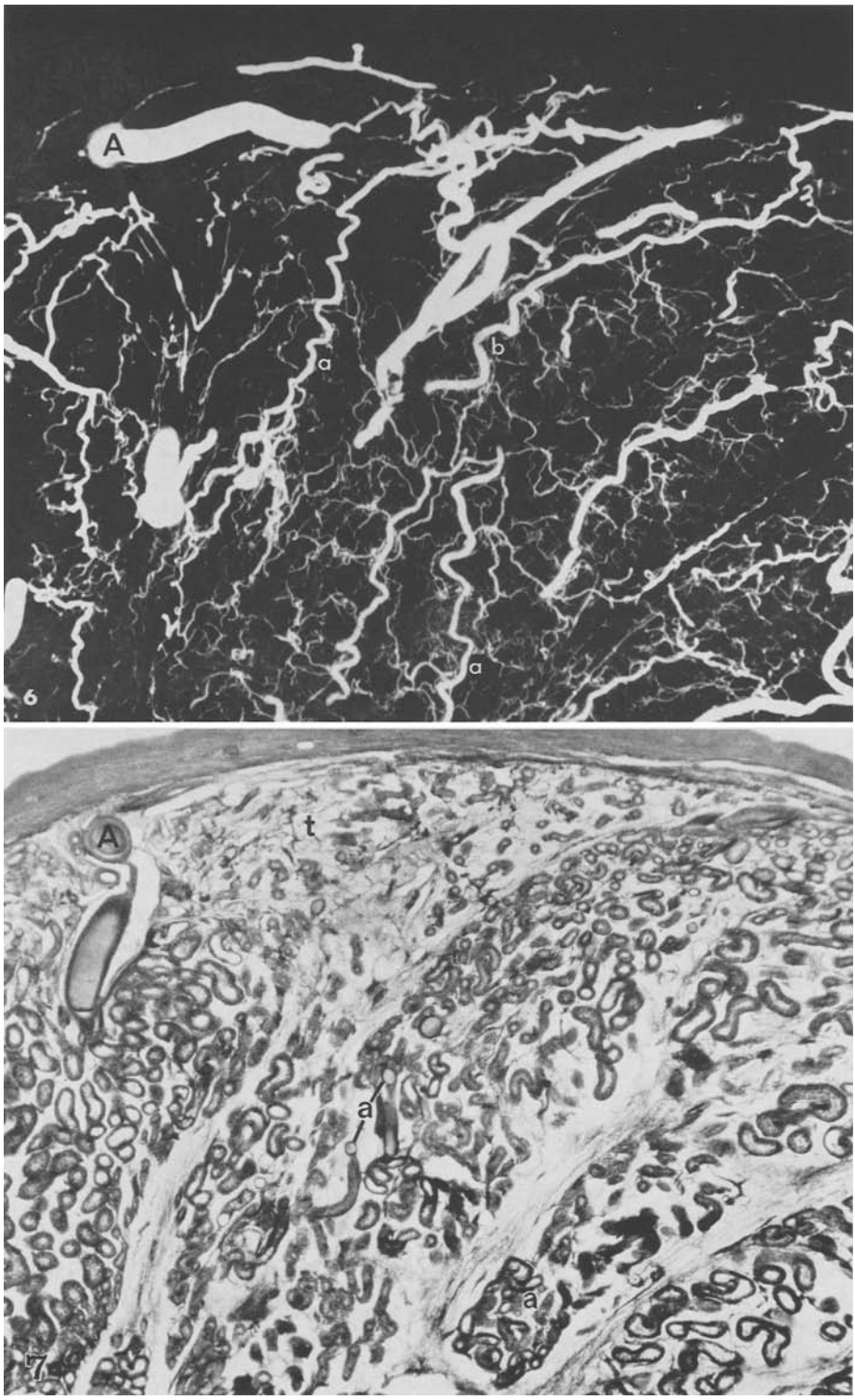
Focal inflammatory cell infiltrations were found in 22 normal testes (Table 2). This kind of reaction was usually around degenerating tubules (Fig. 4). Only a few spermatogenic cells and sometimes multinucleate giant cells and inflammatory

Fig. 2. Poorly vascularized Leydig cell cluster, cells in small clumps surrounded by connective tissue. In general the testis is normal, although spermatogenesis is locally arrested and shows sloughing (*a* artery, *c* capillary) (64 y.). Weigert v. Gieson-stained 10 μ section. ×80

Fig. 3. Incomplete spermatogenic arrest mainly at primary spermatocyte stage. Tubular walls slightly thickned (*v* small vein) (62 y.). Weigert v. Gieson-stained 10 μ section. ×170

Fig. 4. Degenerating tubules (*t*) are surrounded by inflammatory cells and many blood vessels. Tubules are slightly shrunk and progressive tubular fibrosis is seen in other parts of the testis (*c* capillary) (58 y.). PAS-hematoxylin-stained 10 μ section. ×80

Fig. 5. Adjacent area of the same section as in Fig. 4. Two degenerated tubules with thickened walls, penetrated by some capillaries (*c*). Round cells surround the tubules, cell debris, but no blood vessels, are seen in their lumina. ×270



Figs. 6 and 7

Table 3. *Spiralization of the intratesticular arteries*

Age group	Average number of arteries studied	Number of straight arteries	Intensity of spiralization (loops/mm)	
20–29	630	51	centripetal 155/58	= 2.67
			centrifugal 83/53	= 1.56
30–39	240	3	centripetal 47/25	= 1.88
			centrifugal 17/9	= 1.88
40–49	600	0	centripetal 127/59	= 2.11
			centrifugal 89/40	= 2.23
50–59	780	7	centripetal 294/168	= 1.75
			centrifugal 216/134	= 1.61
60–69	540	5	centripetal 274/150	= 1.83
			centrifugal 158/95	= 1.66
70–79	600	3	centripetal 138/62	= 2.29
			centrifugal 111/55	= 2.02

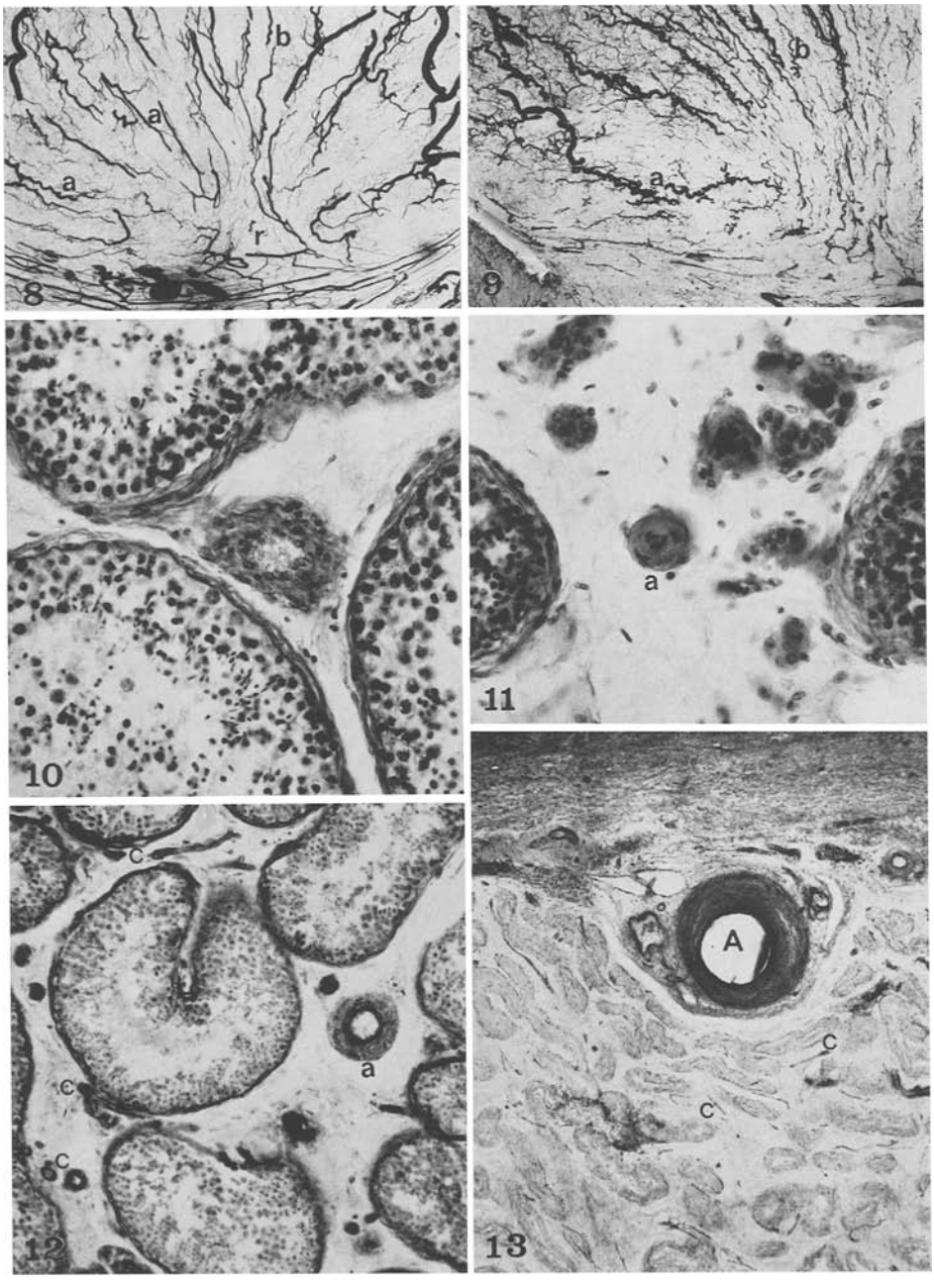
cells were seen in their lumina. These areas had an increased and more distended capillary supply (Fig. 5). Hernia-like protrusions as described by Hatakeyama *et al.* (1962) were observed in 12 normal testes, with no relation to blood vessels.

Arterial Supply of the Testicular Parenchyma. Early subendothelial lesions of the arterial walls were not found, partly due to distension of the blood vessels after contrast infusion. Thickening of the vessel walls was detected in 41 normal testes increasing with age in both small (luminal diameter 12–50 μ, vascular wall thickness 12–50 μ) and larger (luminal diameter 50–250 μ) arteries (Table 2). Both centripetal and centrifugal branches of testicular arteries were involved and the thickening was composed of cellular elements and/or "hyaline" deposits (Figs. 10 to 12). Not all arteries in the same testis were involved.

Coiling was detected most extensively in the centripetal and centrifugal but also in the main arterial branches (Figs. 8 and 9). I could not find any correlation between the intensity (measured as loops/mm) of the coiling and age (Table 3). Actually, it is very difficult to determine the characteristics of the arterial spiralling, as also observed by Hassler (1965). The most extensive form of spiralization, in which the loops of the spiral artery are in contact with each other, the "glomerular loop formation" (Figs. 17 and 18; Hassler, 1969), was seen only exceptionally in the testicular parenchyma (7 times; Table 2), but more often in arteries outside the testis, especially in the epididymis and in the tunica vaginalis

Fig. 6. Microangiogram of a 1 mm section of a normal testis showing spiralled course of centripetal (*a*) and -fugal (*b*) arteries. Disorganized and poorly filled capillaries are seen in the upper part of the picture (*A* a main branch of testicular artery). ×15

Fig. 7. Adjacent section of the same testis as in Fig. 6. An area of degenerating tubules (*t*) is found under tunica albuginea, corresponding the area with pathological vasculature seen in Fig. 6. Two normal spiral arteries (*a*) in the middle of the picture (*A* the same main branch as in Fig. 6) (39 y.). Weigert v. Gieson-stained 10 μ section. ×15



Figs. 8 and 9. Microangiograms of testes from 25-year old (Fig. 8) and 52-year old (Fig. 9) subjects prepared using the frozen section technique. Many straight arteries running either centripetally (*a*) or -fugally (*b*) near the rete (*r*) testis of the younger subject. Almost all arteries in testis of the older subject have spiralled course. In the latter photomicrograph the rete testis (*r*) occupies the right side of this picture. ×4

testis. Table 3 shows the number of straight centripetal and centrifugal arteries in each age group. The frequency of these arteries decreased from 8% in the age group 20–29 to about 1.0% in all older persons. No relation was observed between the spiralization of the arteries as seen in microangiography, and the arteriolar "hyalinosis" as seen in histology. The arterial branches running either in the connective tissue septae or in the looser testicular parenchyma were identically spiralled.

Microvascular Supply of the Pathological Testes

Brief autopsy diagnosis and observations of the pathological testes are given in Table 4.

Mainly Epithelial Damage. Incomplete spermatogenic arrest at spermatozyte stage was found in each of the 5 testes (Table 4; Fig. 3). Microangiography did not show any special feature in these testes as compared with those of the normal group.

Progressive Tubular Fibrosis. This group consisted of 10 testes. A common feature was fibrosis of the seminiferous tubules, which included more than one fourth of the histological examined area. Variable histological changes of the arteries were found in 90% of these testes. The microvascular supply showed features similar to the smaller hyalinized areas of the normal testes, e.g. less dense and irregular terminal arteriolar and capillary beds (Figs. 18 and 19). Occasionally, the diameters of the arteries supplying the degenerating areas were also smaller (Fig. 18), but the gross vascular pattern of testicular arteries was normal (Fig. 16).

Hyalinized Testes. Only in two of the six hyalinized testes some tubules had lumina with few Sertoli and spermatogenic cells (Table 4). All six testes showed arterial changes; in five testes this was graded as severe and involved almost all branches (Fig. 13). The gross vascular pattern of totally hyalinized testes was completely different from the normal testicular vessels (Figs. 14 and 15). The main branches of testicular artery were thinner and irregular, and it was even impossible to differentiate between centripetal and centrifugal branches. Further, the coiled course of the arteries was irregular or even absent. The filling of smaller vessels and the organization of the microvascular bed was very poor (Fig. 13).

Fig. 10. Endothelial cell proliferation in a small thickened testicular artery of a 64-year old subject. The testis shows normal spermatogenesis for the age apart from some sloughing. Weigert v. Gieson-stained 10 μ section. ×260

Fig. 11. Normal testis with homogeneously thickened arterioles (*a*). Leydig cells are situated in small clumps. Tunica propria is slightly thickened and tubules shrunk (age 47). Weigert v. Gieson-stained 10 μ section. ×260

Fig. 12. More PAS-positive material than usual is seen subendothelially in a thickened arterial (*a*) wall. The testis shows normal spermatogenesis for the age (62), except some sloughing (artifactious ?) (*c* capillary). PAS-hematoxylin-stained 10 μ section. ×80

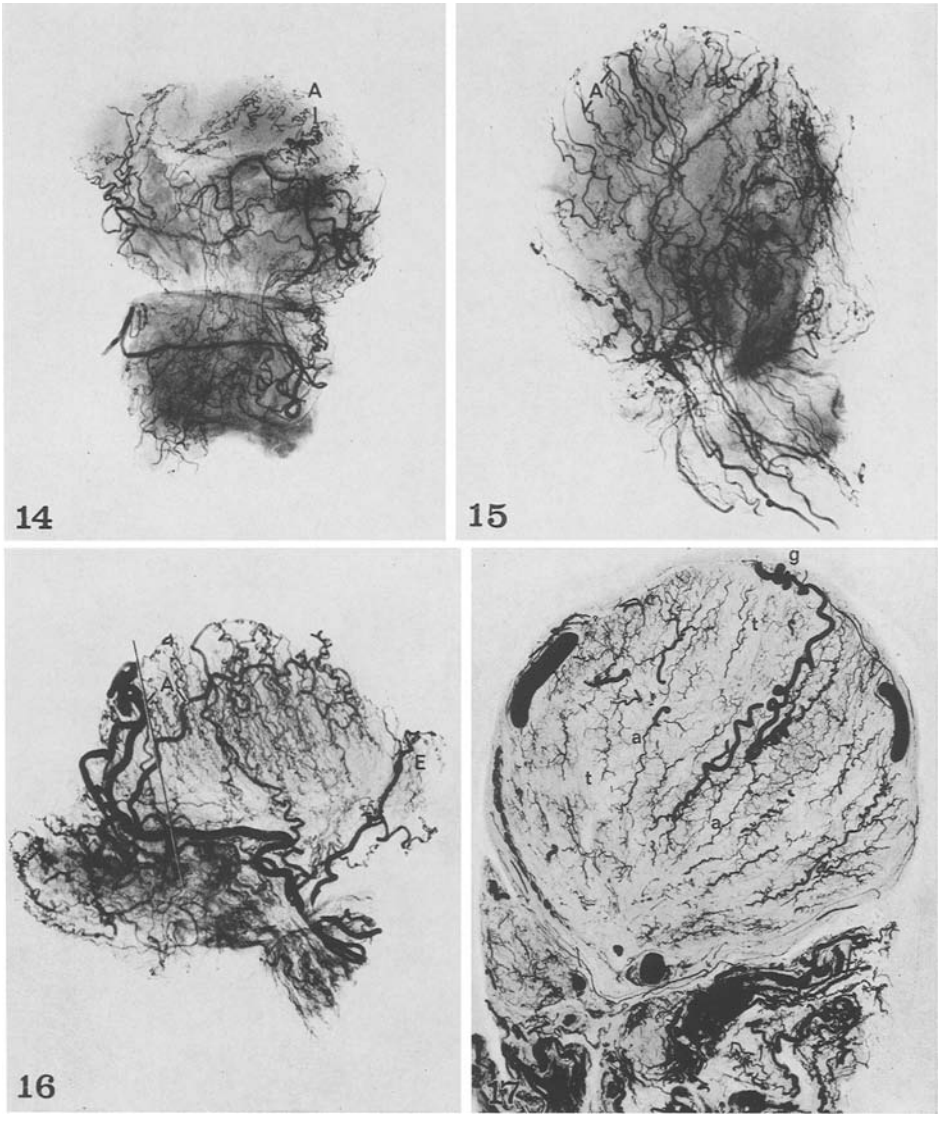
Fig. 13. A thickened main branch of testicular artery (*A*) is seen under tunica albuginea. The testis is completely hyalinized. PAS-positive capillaries (*c*) are scanty. The gross vascular pattern of the same testis is shown in Fig. 15 (age 93). PAS-hematoxylin-stained 10 μ section. ×40

Table 4. *Changes observed in pathological testes*

Ages and autopsy diagnosis	Seminiferous tubules	Leydig cells	Inflammatory infiltrations	Hernia-like protrusions	Vascular changes in histology	Glomerular loop formations in micro-angiography
		Mainly epithelial damage: (5 testes)				
21 y. Rejection of kidney transplant (usual rejection therapy) Hypert. heart d. (H.H.D.); Cardiac failure	*Both testes*: Incomplete spermatog. arrest (I.S.A.) at spermatocyte stage; Diameters decreased	normal	none	none	none	none
56 y. Myocardial fibrosis (M.F.) and H.H.D.; Acute alcohol intoxication (A.A.I.)	*A*: I.S.A. at spermatocyte stage; 6 focal hyalinized areas (F.H.A.) (5–20 tubules each)	normal	5 focal areas (F.A.)	2	none	none
	B: Same; 4 F.H.A.	2 clusters	4 F.A.	1	slight	[a]
62 y. Arteriosclerotic heart d. (A.H.D.); A.A.I.	*A*: I.S.A. at spermatid stage; 1 F.H.A.	normal	none	1	none	[a]
Total:		1	2	3	1	—
		Progressive tubular fibrosis: (10 testes)				
42 y. M.F.; Coronary occlusion (C.O.)	*A*: 1/7 with lumen and some spermatogenic cells; 6/7 hyalinized	several large nodules	5 F.A.	1	slight	none
48 y. Cerebral glioma; Bronchopneumonia (B.p)	*A*: 3/5 with Sertoli cells only; 1/5 hyalinized; 1/5 normal; Diameters decreased; Walls thickened	marked diffuse and nodular increase	3 F.A.	none	moderate	none
	B: 2/4 hyalinized; 1/4 Sertoli cells only; 1/4 normal; Diameters decreased; Walls thickened	same	13 F.A.	2	severe	none
49 y. Malignant lymphoma with metastases	*A*: 3/4 hyalinized; 1/4 with lumen and some spermatogenic cells[b]	2 clusters	4 F.A.	none	moderate	2

Ages and autopsy diagnosis	Seminiferous tubules	Leydig cells	Inflammatory infiltrations	Hernia-like protrusions	Vascular changes in histology	Glomerular loop formations in micro-angiography
58 y. B.p.	*A*: 1/4 hyalinized; 1/4 I.S.A.; Diameters decreased; Walls thickened	(Interstitial fibrosis)	9 F.A.	1	slight	none
64 y. A.H.D.; Subdural hematoma; A.A.I.	*A*: 1/4 hyalinized; 1/4 I.S.A.[b]	3 clusters	none	none	none	none
74 y. M.F.; C.O.	*A*: 2/3 hyalinized; 1/3 I.S.A. Walls thickened[b]	1 cluster	1 F.A.	1	moderate	none
82 y. M.F.; C.O.	*A*: 1/4 hyalinized[b]	normal	1 F.A.	3	moderate	none
88 y. B.p.	*A*: 1/2 hyalinized	normal	none	none	slight	[a]
	B: 1/3 hyalinized	normal	8 F.A.	none	slight	several
Total:		6	8	5	9	2
		Hyalinization: (6 testes)				
72 y. Thrombosis of the internal carotid arteries	*A*: Total hyalinization	normal	none	none	severe	none[c]
	B: Total hyalinization	4 clusters	3 F.A.	none	severe	none[c]
75 y. Adenocarcinoma of the pancreas with metastases	*A*: 5 tubules with some spermatogenic cells	1 cluster; diffuse increase	none	none	severe	none[c]
	B: 20 tubules with some spermatogenic cells	3 clusters; diffuse increase	none	none	moderate	2[c]
93 y. Polycystic liver; Arteriolar nephrosclerosis; C.O.	*A*: Total hyalinization	7 clusters	none	none	severe in all arteries same	none[c]
	B: Total hyalinization	3 clusters	none	none		none[c]
Total:		5	1	0	6	1

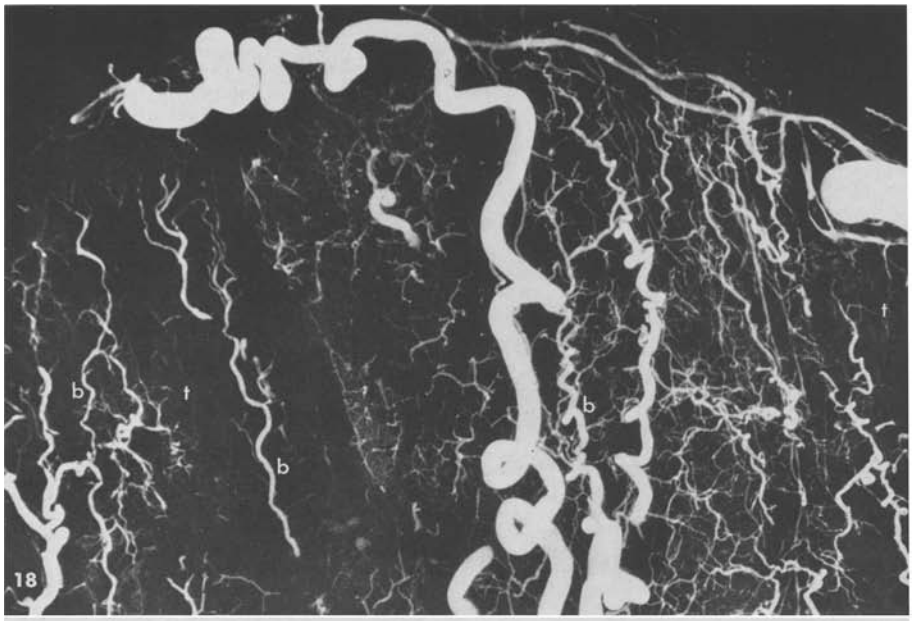
[a] Venography.
[b] The contralateral testis was included in the normal group, because less than 1/4 of the testis was hyalinized.
[c] The gross vascular pattern of the intratesticular arteries was pathologic.



Figs. 14 and 15. The gross vascular patterns of two totally hyalinized testes showing irregular course of the main branches of the testicular artery (*A*). The testicular vasculature is scanty (Fig. 14, age 75; Fig. 15, age 93). ×1,3

Fig. 16. A normal looking gross vascular pattern in a case of a progressive tubular fibrosis of the testis. The testicular artery divides into the main branches (*A*) normally. Caput epididymidis (*E*) is located on the right side and cauda on the left side of the picture. See also the following Figs. (transverse line = section line) (49 y.). ×1,3

Fig. 17. A transverse microangiographed 1 mm section of the same testis as in Fig. 16. Glomerular loop formation (*g*) is seen in the upper pole. In the areas of defective microvascular filling (*t*) the tubules were hyalinized. The luminal shadows of two centripetal arteries (*a*) have an irregular contour. ×3,3



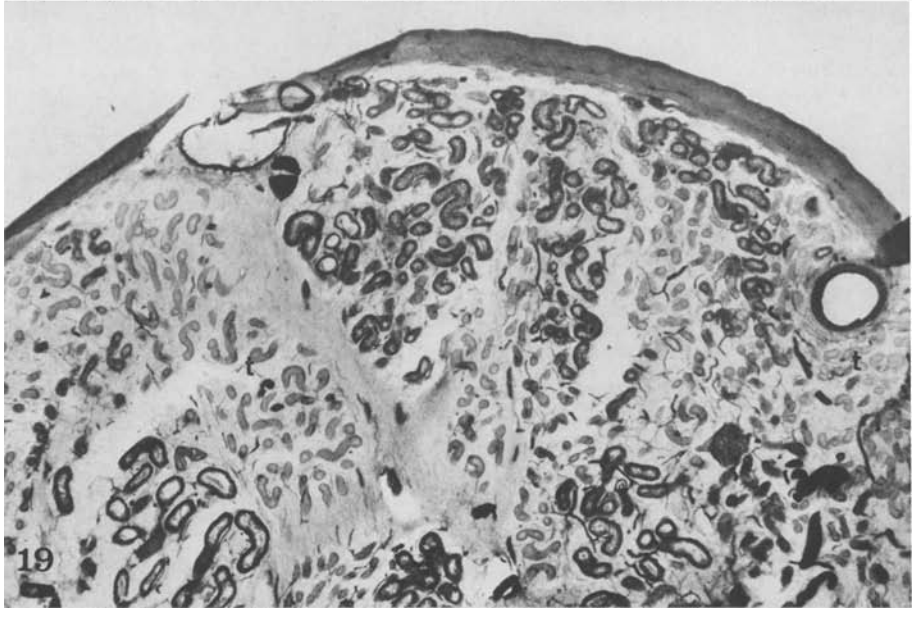


Fig. 18. A higher magnification of the same microangiogram as in Fig. 17 shows poor filling and organization of the microvascular bed on left and right sides of the photomicrograph. The tubules in these areas (*t*) are degenerated (compare following Fig.) and the luminal shadows of the supplying centrifugal arteries (*b*) are narrower than in the middle of the picture. ×13

Fig. 19. Most of the tubules are hyalinized in a histological section of the same area (*t*) as in Fig. 18. PAS-hematoxylin-stained 10 μ section. ×13

Discussion

Many factors are known to influence the filling of a vascular bed by microangiography, such as viscosity and quality of the contrast medium, pressure and length of the injection and time after death (Rubin, 1964; Wendelin and Lindgren, 1970). For these reasons technique must be standardized. Care must be taken in drawing conclusions from vascular changes seen in microangiography, and the histological control sections are necessary. Due to distension of blood vessels light microscopical observation of minimal changes in vascular walls is difficult. Still, the microangiographical picture may be related to the true physiological vascular channel system, although the open functional channels or actual luminal diameters are not distinguishable. In addition, microangiography has the advantage of obtaining a good overall delineation of the vasculature in large tissue blocks and the same preparation is still there for other types of study (Saunders, 1964).

The testis is known to be highly sensitive to the adequacy of blood supply. Physiologically, an ischaemic period of a few minutes is known to produce a decrease in both spermatogenic (Linzell and Setchell, 1968) and androgenic (Eik-Nes, 1964) activities. It is noteworthy that although blood vessels are confined to the interstitial tissue only, seminiferous tubules are the first to show morphological damage (Oettlè and Harrison, 1952; Steinberger and Tjioe, 1969). The dominance of tubular over interstitial damage is also apparent in the human testis, as shown in the present study. However, since seminiferous tubules are in general more sensitive to various harmful effects, the causal relationship is not at all clear-cut.

The microangiographically and histologically observed changes occurring in the vascular pattern of the human postpuberal testis can be roughly divided into less prominent general changes which are mainly confined to the arterial vessels and into local changes at microvascular level. The most prominent feature, spiralization of the testicular end arteries, was seen in almost all centripetal and centrifugal branches at an early age even in deep-frozen microangiographed testes. Similar changes have been detected in aged and hypertensive human kidney (Ljungqvist, 1963) and in senile brain (Hassler, 1969) as a pathological phenomenon. The spiralization of arteries can also be a normal feature, as in the human endometrium and ovaries (Hammersen and Staubesand, 1961). In the testis the spiralling course of the small arteries was unrelated to histological changes in their walls or to the surroundings of these vessels. Likewise, no relation to age was seen beyond the age of 30. It seems that spiralization of the testicular arteries is a physiological phenomenon, unrelated to the early degenerative changes found in electron microscopy (Hatakeyama *et al.*, 1966). The basic capillary organization remains stationary after puberty in all those areas of the testis which remain functionally active, while distinct changes are visible in the microvascular bed of the degenerated areas. The interstitial tissue of these areas also seems to be inactive, since usually few Leydig cells and blood vessels were found around degenerate tubules. On the other hand, true Leydig cell clusters commonly had a very dense capillary bed.

In some microscopic studies *arteriosclerosis* of the human testis is briefly referred to be common (Koopmann, 1936; Tillinger, 1957; Bürgi and Hedinger, 1959; Heinke and Dopfmer, 1960; Tonutti *et al.*, 1960). Hatakeyama *et al.* (1966) investigated the pathogenesis of arteriolar hyalinosis in human testis and found that almost all adult testes were more or less involved.

Surprisingly, they did not correlate vascular changes to the surrounding structures. In the present study, small arterial and arteriolar thickening was observed in 59% of normal testes, increasing in frequency with age. This agrees with the results of Koopmann (50%, 1936), but not with Fraley and Totten (14%, 1968). The difficulties in light microscopical estimation of changes in small arteries may partly account for the discrepancy.

A few earlier studies (Koopmann, 1936; Bürgi and Hedinger, 1959; Heinke and Doepfmer, 1960) suggest that most advanced vascular changes are seen near the degenerated areas of the testis, although focal tubular hyalinization is not considered an essential feature of the normal human testis (Koopmann, 1936). It could well be a transition stage of total testicular hyalinization. This is supported by the facts that the frequency of focal hyalinotic areas (in 56%) of the normal testes increases with age, and that progressive testicular fibrosis appears more often at an advanced age (Bürgi and Hedinger, 1959). In spite of lacking of histological changes in the blood vessels microangiograms suggested more sparse vascular supply at the capillary level in the hyalinized areas. The most advanced tubular changes were found in the parenchyma under tunica albuginea. These parts of the testis are vascularized by the recurrent centrifugal arterial branches and are situated at the most distal end of arterial supply. Sasano and Ichijo (1969) suggested that the upper pole and the posterior part of the testis are situated at the periphery of arterial supply, and that these parts show advanced senile changes in general. The present results do not agree with the results of Sasano and Ichijo (1969) as regards the localization of testicular damage in relation to vascular supply. Our earlier study of the gross vasculature of the human testis (Kormano and Suoranta, 1971 b) does not support their hypothesis either, because one main trunk occurs only in minority of the testis.

Local damage to the end arteries of the testis in the past may have produced *tubular degenerations*, and it may no longer be possible to find this change by microangiography, because of reparative phenomena like recanalization of the arterial lumina (Brånemark *et al.*, 1968), or washing out the luminal material of the arteries during the infusion. It is thus impossible to draw definite conclusions on the causal relationship between histological alterations of the degenerated tubules and vascular changes seen in microangiography. It seems probable that focal tubular degeneration is at least in part due to microvascular damage. Autoimmune mechanisms could also influence the pathogenesis of the focal lesions (Waksman, 1959; Federlin, 1969). This is supported by the fact that round cell infiltrations were mainly seen around degenerating tubules and more often (80%) in the progressive tubular fibrosis group than in normal testes (31%).

Primary damage in the tubular wall has been considered to play a role in many tubular disorders (Heinke and Doepfmer, 1960), leading to partial or total testicular hyalinization like in orchitis and in hormonal disturbances (Tonutti *et al.*, 1960). Liver diseases can also produce the same histological picture in the testis via altered estrogen metabolism (Albert, 1964). Connection between vascular changes and decreasing androgen production in old age has been likewise suggested (Heinke and Doepfmer, 1960) as an etiological factor in testicular hyalinization. The increasing frequency of vascular changes observable in the present study, with defective microvascular supply of the tubules in the focal degenerative areas of normal testes, frequent arteriolar and small arterial changes in progressive tubular

fibrosis and marked vascular alterations in total hyalinization suggests, however, that the blood vessels are involved in these progressive pathological changes, irrespective of the often unknown primary etiological factor.

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