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Angiopathies in the equine endometrial biopsy – a marker for extrauterine vascular lesions?

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Summary

Endometrial, myometrial and extrauterine vessels of 13 juvenile mares, 53 adult non-pregnant mares, 11 adult pregnant mares (two of which had a rupture of the uterine artery), and 4 post-parturient mares were investigated by means of histology and immunohistochemistry. The vessels of juvenile mares did not show any alterations. The endometrial vessels of the adult non-pregnant mares, on the other hand, were characterized by mild to moderate panelastofibrosis or panfibroelastosis. The myometrial vessels revealed lesions of the same quality, but to a higher degree in one third of the mares. In the extrauterine vessels (arteria and vena uterina, ramus cranialis of the arteria and vena uterina, arteria and vena ovarica of each side) mild to moderate fibrosis and fibroelastosis of the vascular wall predominated. There was a distinct correlation between the degree of arteriosis in the uterine (endometrial and myometrial) and the extrauterine vessels. Based on these findings, the endometrial biopsy is a reliable indicator for extrauterine arterial alterations. The vascular lesions of the pregnant mares in the first half of the pregnancy resembled those of the adult non-pregnant mares. By contrast, the endometrial, myometrial and extrauterine arteries of mares in the second half of pregnancy and post-parturient mares were characterized by a pronounced hypertrophy of the myocytes within the media.

Keywords: mare, angiopathies, extrauterine vessels, peripartal hemorrhage, endometrial biopsy

Angiopathien in der Endometriumbiopsie bei der Stute – Ein Marker auch für extrauterine Gefäßläsionen?

Endometriale, myometriale und extrauterine Gefäße von 13 juvenilen Stuten, 53 adulten nicht graviden Stuten, 11 adulten graviden Stuten (davon 2 Stuten mit einer Ruptur der A. uterina) und 4 Stuten post partum wurden histologisch und immunhistologisch untersucht. Juvenile Stuten wiesen keine veränderten Gefäße auf. Im Vergleich dazu waren die endometrialen Gefäße adulter nicht gravider Stuten durch gering- bis mittelgradige Panelastofibrosen oder Panfibroelastosen gekennzeichnet. Die myometrialen Gefäße zeigten qualitativ vergleichbare Veränderungen, graduell waren sie aber bei einem Drittel der Stuten stärker ausgeprägt. Extrauterine Gefäße (A. und V. uterina, Ramus cranialis der A. und V. uterina, A. und V. ovarica beider Seiten) zeichneten sich vorwiegend durch gering- und mittelgradige Fibrosen oder Fibroelastosen der Gefäßwand aus. Es konnte eine deutliche Korrelation bezüglich der quantitativen Veränderungen zwischen den uterinen (endometriale und myometriale) und den extrauterinen Arteriosen gefunden werden. Ein Rückschluss von endometrialen Angiosen, die mittels Uterusbiopsie erfassbar sind, auf extrauterine Arterienalterationen ist daher mit hoher Wahrscheinlichkeit möglich. Stuten in der ersten Trächtigkeitshälfte zeigten Gefäßveränderungen vergleichbar denen adulter nicht gravider Stuten. Dagegen wiesen Stuten in der zweiten Trächtigkeitshälfte sowie post partum eine deutliche Hypertrophie der Myozyten in der Media von endometrialen, myometrialen und extrauterinen Arterien auf.

Schlüsselwörter: Stute, Angiopathien, extrauterine Gefäße, peripartale Hämorrhagie, Endometriumbiopsie

Introduction

In routine investigations of endometrial biopsies of the mare, degenerative alterations of the blood vessels, varying in quantity and quality, occur with a frequency of 80% *(Schoon et al., 1997)*. According to *Runge (1995)* they are equally distributed within the whole endometrium. Normal vessels are only seen in young, up to five- year old, maiden mares *(Kriesten, 1995)*. The majority of arterial and venous angioses are characterized by a mild to moderate increase of collagenous and elastic fibres in the intima, media and adventitia. Severe and destructive vascular lesions are rare and only present in multiparous mares with more than five foalings *(Schoon et al., 1997)*. The incidence and degree of angioses increases with the number of parturitions, independent of the age of the mare *(Schoon et al., 1997; 1999)*. In contrast to detailed investigations of endometrial vascular alterations, morphological studies on the large arteries supplying the uterus (referred to as "extrauterine vessels"), are not available in the mare to date. In cows a gravid sclerosis of the large uterine arteries is described histologically as a thickening of the intima and a lamination of the membrana elastica interna *(Ahlborn, 1920; Kamiya and Daigo, 1989)*.

In clinical investigations on the extrauterine arteries carried out by means of transrectal Doppler ultrasound, *Bollwein et al. (1998)* and *Mayer (1999)* observe an increase in the uterine blood flow in the arteria uterina of the mare at early diestrus and early estrus, as well as a decrease just before and after the ovulation. *Bollwein et al. (1999)* and *Woschee (1999)* describe a continuous increase in uterine blood flow during pregnancy from the 11th week onwards, without any significant differences between the arteria uterina of the gravid and non-gravid side. Investigations of *Stolla and Bollwein (1997)* and *Blaich et al. (1999)* revealed that mares suffering from moderate to severe endometrial alterations have a significantly higher vascular resistance compared to those with absent or mild endometrial alterations. These new sonographic methods are not reliable indicators for patients with a risk of peripartal hemorrhage due to altered extrauterine blood vessels. It is well-known that

especially in older, multiparous mares in the last third of their pregnancy or during parturition the large uterine arteries may rupture, resulting in intraabdominal, mostly fatal bleedings *(Rooney, 1979; Lofstedt, 1993; Rooney and Robertson, 1996)*. Histologically, these ruptured blood vessels and the contralateral vessels, manifest a multifocal, moderate to severe fibrosis and elastosis of the intima as well as a considerably thinner tunica media *(Rooney and Robertson, 1996)*.
The aim of this study was to attempt a histomorphological and immunohistochemical characterization of endometrial, myometrial and extrauterine vascular alterations and to determine whether there is any correlation between the findings of the extrauterine and the endometrial and myometrial blood vessels (referred to as "uterine vessels"). As a consequence, the endometrial biopsy is a potentially important diagnostic tool in the detection of high-risk patients for peripartal hemorrhage.

Material and methods

Tissues from 81 mares of differing age and breed were collected at the Institut für Veterinär-Pathologie, Universität Leipzig during routine necropsies from 1998 to 2000. The mares were grouped according to age and stage of reproduction (tab. 1). There were two deaths in group 3 following a rupture of the arteria uterina.

Tab. 1: Age and number of the mares within the groups 1–4

Alter und Anzahl der Stuten innerhalb der Gruppen 1–4

group	characterization	age (years)	average age (years)	number (n = 81)
1	juvenile mares	< 2	0.5	n = 13
2	adult non-pregnant mares	2 - 24	10.0	n = 53
3	pregnant mares (1.-9. month)	3 - 18	8.7	n = 11
4	mares 1-4 days post partum	14 - 19	16.3	n = 4

From each genital tract cross sections of the uterus (both cornua and corpus) and bilateral samples of the following vessels were taken: arteriae and venae uterinae, ramus cranialis of the arteriae and venae uterinae, arteriae and venae ovaricae (referred to as "extrauterine arteries and veins"). The tissues were fixed in 4% formalin and routinely embedded in paraplast. The sections were stained with Hematoxylin–Eosin and a modified Constantine`s Picro-Sirius Red *(Grüninger, 1996)*. Repre-sentative samples were investigated immunohistochemically with antibodies against vimentin, desmin, α-smooth muscle actin (α-sma), collagen IV and laminin using the peroxidase anti-peroxidase-technique.
The quality of the vascular lesions was classified (hyperplasia of the intima, elastosis, fibrosis, elastofibrosis, fibroelastosis and alterations of the membrana elastica interna) and graded semiquantitatively according to *Grüninger (1996)*.
The uterine and extrauterine vascular changes of the mares in group 2 (adult non-pregnant mares, n = 53) were compared statistically using a vascular degeneration index (VDI). The VDI is the sum of the scores of the membrana elastica interna (MEI), the intima (I), the media (M) and the adventitia (A) (tab. 2 to 4).

Tab. 2: Scores of the intima (I), media (M) and adventitia (A) for calculation of the vascular degeneration index (VDI)

Bewertung für die Intima (I), Media (M), Adventitia (A) für die Berechnung des Gefäßschädigungsindex (VDI)

Degree of deposition of elastic and/or collagen fibres in the intima (I), media (M) and adventitia (A)	Score
none	0
mild	1
moderate	2
severe	3

Tab. 3: Scores of the membrana elastica interna (MEI) of extrauterine arteries for calculation of the vascular degeneration index (VDI)

Bewertung für die Membrana elastica interna (MEI) extrauteriner Arterien für die Berechnung des Gefäßschädigungsindex (VDI)

Description of the membrana elastica interna (MEI) of extrauterine arteries	Score
continuous	0
mildly discontinuous	0,5
moderatly discontinuous	1
severely discontinuous	1,5
not visible	2

Tab. 4: Scores of the membrana elastica interna (MEI) of uterine arteries for calculation of the vascular degeneration index (VDI)

Bewertung für die Membrana elastica interna (MEI) uteriner Arterien für die Berechnung des Gefäßschädigungsindex (VDI)

Description of the Membrana elastica interna (MEI) of uterine arteries	Score
continuous	0
discontinuous	1
not visible	2

In cases of destructive alterations of the media, the score of the media was multiplied with the factor d = 2.

$$VDI = MEI + I + (M \times d) + A$$

The extrauterine VDI is defined as the mean score of the VDI of all extrauterine arteries examined per mare. The degree of the arterial alterations was classified according to the calculated VDI (tab. 5). The statistical calculation was done by means of SSPS 10 statistical program with crosstabulation and the chi"-test by Person.

Tab. 5: Classification of the arterial lesions according to the calculation of the vascular degeneration index (VDI)

Einstufung der Arterienveränderungen nach dem berechneten Gefäßschädigungsindex (VDI)

Degree of arterioses	Scores of the VDI
none	0 - 1
mild	> 1 - 5
moderate	> 5 - 9
severe	> 9 - 14

Results

Group 1 (juvenile mares, n = 13)

Uterine and extrauterine vessels of juvenile mares were characterized as follows:

Arteries
The intima consists of a scant stratum subendotheliale with few, fine collagenous fibres, sporadic spindle cells and a fine, regularly undulating membrana elastica interna (MEI). The media is formed by numerous circularly arranged myocytes and fine collagenous and sporadic elastic fibres. The adventitia is mainly composed of fine, loosely arranged, collagenous fibres intermingled with elastic fibres and isles of myocytes (fig. 1).

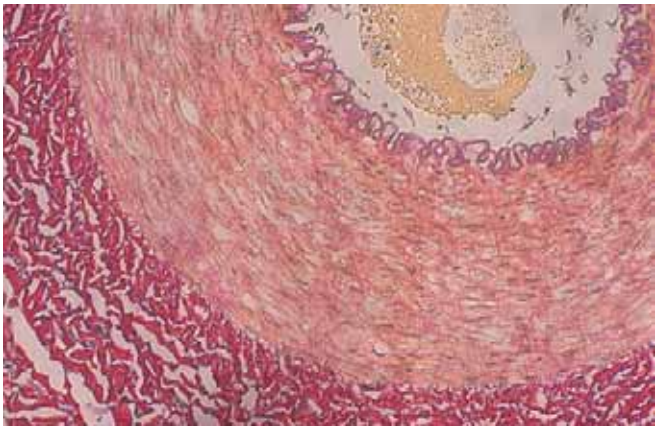


Fig. 1: Intact arteria uterina dextra, juvenile 8-month-old mare (Picro-Sirius Red stain, magnification 62.5x)

Unveränderte Arteria uterina dextra, 8 Monate alte juvenile Stute (Pikro-Sirius Rot-Färbung, Vergrößerung 62,5x)

Veins
The stratum subendotheliale of the intima can not be distinguished from the media and a membrana elastica interna is absent. Media and adventitia consist of fine, mainly collagenous and sporadic elastic fibres with intervening myocytes.
The vessels of juvenile mares showing these characteristics are defined as "normal".

Group 2 (adult non-pregnant mares, n = 53)

Qualitative changes of uterine and extrauterine arteries and veins
Endometrial, myometrial and extrauterine arteries and veins show variable deposits of collagenous and elastic fibres in the whole vessel wall combined with various degenerative changes of the myocytes (fig. 2).

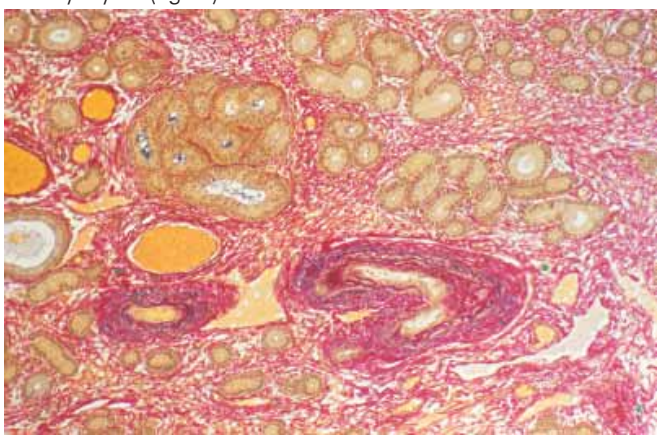


Fig. 2: Endometrial arterioles with moderate panelastofibrosis, adjacent to a dilated venule, stratum glandulare, 14-year-old nonpregnant mare (Picro-Sirius Red stain, magnification 62.5x)

Endometriale Arteriolen mit mittelgradiger Panfibroelastose, daneben eine dilatierte Venule, Stratum glandulare, 14-jährige nicht gravide Stute (Pikro-Sirius Rot-Färbung, Vergrößerung 62,5x)

Degenerative changes of the arterial intima are characterized by a lamellation of the membrana elastica interna and deposits of collagenous and elastic fibres. In arteries with moderate to severe intimal elastofibrosis or fibroelastosis the MEI cannot be identified (fig. 3). The accumulation of acid mucopolysaccharides around the MEI is more prominent in the extrauterine arteries than in the uterine arteries and correlates positively ($p < 0.0001$) with the degree of alterations in the MEI (fig . 4). In extrauterine arteries a mediafibrosis (depositions of collagenous fibres) predominates, whilst within the media of nearly all uterine arteries there is a noticeable increase of both collagenous and elastic fibres. Destructive alterations of the media, characterized by a severe accumulation of collagenous and elastic fibres and a loss of myocytes, may occur in uterine as well as in extrauterine arteries (fig. 3).
Fibroelastosis of the adventitia is present in extrauterine and in uterine arteries whereas in extrauterine arteries fibrosis of the adventitia is more frequent. Elastosis of the adventitia is a rare finding, sporadically occurring in uterine arteries.
Uterine phleboses are characterized by mural elastofibrosis or fibroelastosis. Destructive alterations (dysplasia of the media,

an accumulation of numerous elastic fibres affecting the outer vascular layers near the adventitia) are mainly observed in myometrial veins (fig. 5). Extrauterine veins show a lamellar thickening of the media and adventitia due to fibrosis or fibroelastosis.

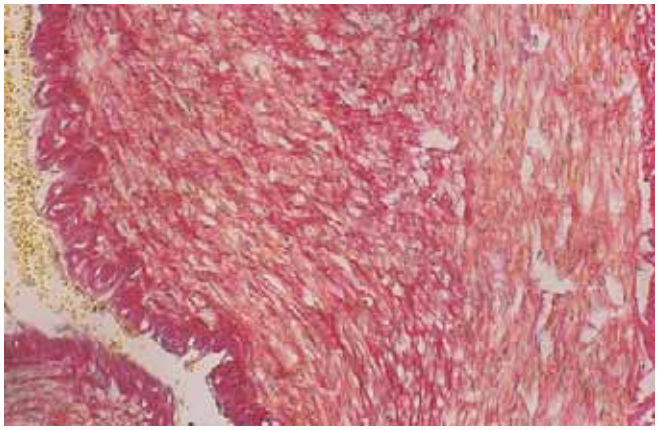
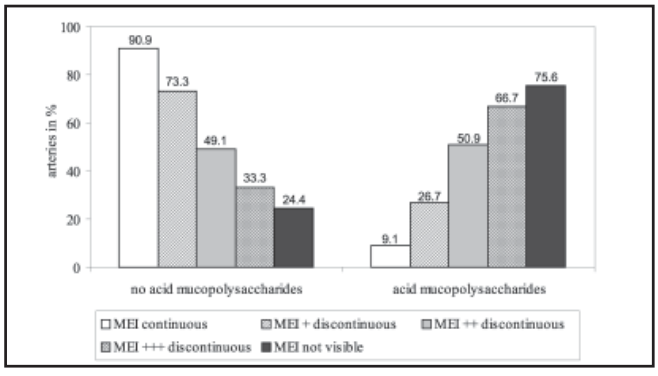


Fig. 3: Moderate fibrosis of the intima and destructive mediafibrosis, membrana elastica interna indistinguishable from newly produced fibres, loss of myocytes caused by the accumulated collagenous fibres, arteria uterina sinistra, 21-year-old nonpregnant mare (Picro-Sirius Red stain, magnification 62.5x)

Mittelgradige Intimafibrose und destruierende Mediafibrose, Membrana elastica interna nicht von zugebildeten Fasern zu unterscheiden, Myozytenschwund durch eingelagerte kollagene Fasern, Arteria uterina sinistra, 21jährige nicht gravide Stute (Pikro-Sirius Rot-Färbung, Vergrößerung 62,5x)

Degree of endometrial and myometrial vascular alterations
In 69.8% of the mares angiopathies of varying degree and quality are diagnosed (tab. 6). Endometrial and myometrial arterioses are manifest as mild to moderate panfibroelastosis (51.2 %) or panelastofibrosis (44.9 %) with (15–20%) or without a destructive character. Only 2.9% of the arteries investigated show a mild panfibrosis. The arterioles are mostly characterized by a mild panelastofibrosis (57.1%). Sporadically a panfibroelastosis occurs (8.6 %). In the arterioles of one third of the mares (34.3 %) exclusively changes of the adventitia, either as perielastosis or as perielastofibrosis, are observed.



+ mild ++ moderate +++severe

Fig. 4: Occurrence of acid mucopolysaccharides in the intima of extrauterine arteries depending on the degree of lesions of the membrana elastica interna (MEI) in the adult non-pregnant mares

Vorkommen von sauren Mukopolysacchariden in der Intima extrauteriner Arterien in Abhängigkeit zum Grad der Veränderungen an der Membrana elastica interna (MEI) bei den adulten nicht graviden Stuten

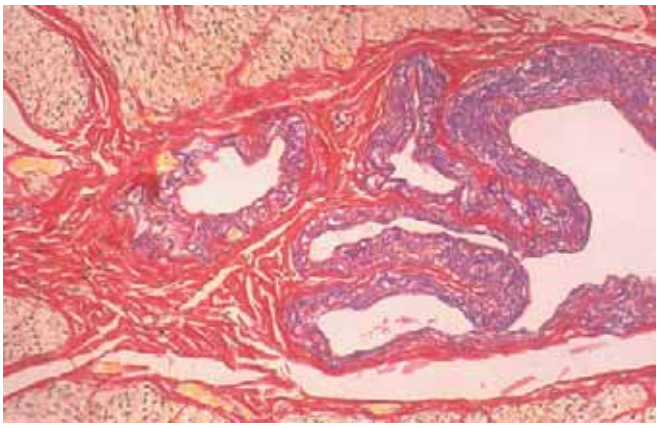


Fig. 5: Myometrial vein with severe destructive panelastofibrosis: deposits of numerous elastic and sporadic collagenous fibres in media and adventitia, dysplasia of the media, 21-year-old non-pregnant mare (Picro-Sirius Red stain, magnification 62.5x)

Myometriale Vene mit hochgradig destruierender Panelastofibrose: zahlreiche elastische und wenige kollagene Fasern in Media und Adventitia, Dysplasie der Media, 21-jährige nicht gravide Stute (Pikro-Sirius Rot-Färbung, Vergrößerung 62,5x)

In uterine veins a panelastofibrosis (87.0%) dominates. 17.9% of the cases reveal a destructive character mostly involving the myometrial veins. Only sporadically are panfibroelastosis (6.5%), panelastosis (2.6%) and panfibrosis (2.6%) present in veins. Alterations of the venules are rare, with only one incident of a mild perifibrosis in the endometrium. In the myometrium of five mares mild degenerative lesions (perifibrosis n=4, perielastofibrosis n=1) of the venules are visible.

Degree of the extrauterine vascular alterations
82.4% of extrauterine arteries show accumulations of collagenous and elastic fibres, varying in degree (47.8%: mild, 31.7%: moderate, 2.9%: severe). Panfibroelastosis (65.3%) and panfibrosis (26.1%), partially destructive (16.2%) are present quite frequently. Destructive panelastofibroses (1.2%) and mild fibroses of the intima (7.4%) are rare findings.
In 73.8% of the extrauterine veins a mild to moderate phlebosis is present. The veins are mainly characterized by mural fibrosis (74.2 %), less frequently a mural fibroelastosis occurs (22.6 %) and only one vein shows a mild panelastofibrosis.

Comparison of uterine and extrauterine arterioses by means of the calculated vascular degeneration index (VDI)
Frequency and degree (VDI) of the endometrial, myometrial and extrauterine arterioses are presented in fig. 6.

Endometrial versus myometrial arterioses
Uterine specimens without degenerative endometrial arterioses are associated with unchanged myometrial arteries in 94.7% ($p<0.0001$). If endometrial arteries show mild lesions, the myometrial arteries are affected too (mild: 35.3%, moderate:

64.7%; p 0.0001). Moderately changed endometrial arteries always correlated with myometrial arterioses (moderate: 93.3%, severe: 6.7%; p<0.0001).

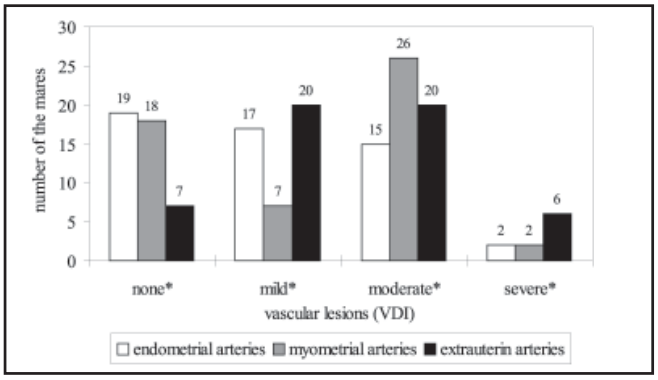


Fig. 6: Frequency and degree (VDI) of the endometrial, myometrial and extrauterine arterioses in the adult non-pregnant mares. (* VDI = 0–1: „none"; VDI > 1–5: „mild", VDI > 5–9: „moderate", VDI > 9–14: „severe")

Häufigkeiten und Grad (VDI) der endometrialen, myometrialen und extrauterinen Arteriosen bei den adulten nicht graviden Stuten. (VDI = 0–1: „unverändert"; VDI > 1–5: „geringgradig", VDI > 5–9: „mittelgradig", VDI > 9–14: „hochgradig")*

Endometrial versus extrauterine arterioses

Only 36.8% of the mares with normal endometrial arteries simultaneously reveal unchanged extrauterine arteries. In 63.2% of the mares without changes of the endometrial arteries, mild degenerations of the extrauterine arteries are observed (p< 0.0001). If the endometrial arteries are mildly altered, there are always extrauterine arterioses (mild: 47.1%, moderate: 47.1%, severe 5.8%; p<0.0001). Mares with moderately damaged endometrial arteries show moderate (73.3%) or severe (26.7%) alterations of the extrauterine arteries (p<0.0001).

Group 3 (pregnant mares, n = 11)

Alterations of uterine vessels

Three of the seven mares examined in the first half of the pregnancy (3; 5 and 10 years old) have intact uterine vessels. The remaining four mares, aged between 6 and 12 years, reveal vascular lesions consisting of mild to moderate fibroelastosis (arteries) and elastofibrosis (veins), consistent with the alterations in the non-pregnant mares. The vessels of the mares in the second half of pregnancy (n=4), however, contain less elastic and collagenous fibres. Only two of them (>14 years) manifest a mild panelastofibrosis of the uterine arteries and veins and a perielastosis of the arterioles. The larger myometrial arteries and veins are characterized by a prominent hypertrophy of the myocytes, especially in the adventitia and less pronounced in the media. In older mares (>8 years; n=3) a loose configuration with a partial loss of the concentric arrangement of the myocytes and sporadic deposition of acid muco-polysaccharides are visible in the media of arterial vessels.

Alterations of extrauterine vessels

Extrauterine vessel alterations of mares in the first half of the pregnancy are identical in quality and quantity to those of the adult non-pregnant mares.

In the intima of the arteries of all mares in the second half of the pregnancy a mild to moderate fibrosis or fibroelastosis is observed. The membrana elastica interna is divided into delicate fibres and compared to the mares in the first half of pregnancy the amount of acid mucopolysaccharides is increased. The changes of the media are characterized by a vacuolation of the myocytes and a simultaneous accumulation of acid muco-polysaccharides, hypertrophic myocytes and a mild to mode-rate fibrosis. The concentric arrangement of the myocytes is disturbed by the vacuolation of the media in those mares older than eight years (n=3). The adventitia is enlarged and edematous showing a mild fibrosis. Especially at the end of the pregnancy the adventitia contains hypertrophic smooth muscle cells.

Extrauterine phleboses of pregnant mares are present as mild to moderate fibrosis or fibroelastosis as consistent with those of adult non-pregnant mares.

Because of the differing quality between the lesions of the media, particularly in the second half of the pregnancy, a quantitative comparison of the uterine and extrauterine arterioses is impossible.

Histopathological findings in mares with a rupture of the arteria uterina (n = 2)

Two mares, one with a rupture of the arteria uterina sinistra (18 years, 10th month of pregnancy), the other with a rupture of

Tab. 6: Frequency of uterine angioses in adult non-pregnant mares

Häufigkeiten der bei den adulten, nicht graviden Stuten auftretenden uterinen Angiosen

	arteriae		arteriolae		veins		venulae	
Degree of angioses	endometrium	myometrium	endometrium	myometrium	endometrium	myometrium	endometrium	myometrium
none	n = 19	n = 18	n = 24	n = 22	n = 17	n = 16	n = 52	n = 48
mild	n = 16	n = 7	n = 20	n = 27	n = 23	n = 8	n = 1	n = 5
moderate	n = 17	n = 27	n = 9	n = 4	n = 13	n = 26	-	-
severe	n = 1	n = 1	-	-	-	n = 3	-	-

the arteria uterina dextra (15 years, 8th month of pregnancy, fig.7) reveal a moderate fibrosis of the intima, a prominent lamellation of the membrana elastica interna and a destructive fibrosis of the media in the ruptured artery as well as in the remaining extrauterine arteries. These findings are consistent with the character and the degree of alterations occurring in the vessels of those pregnant mares older than eight years in the second half of their pregnancy.

Group 4 (mares 1 to 4 days post partum, n = 4)

Uterine vascular alterations
Irregularly widened lumina and a mild fibrosis or fibroelastosis of the media and adventitia of the arteries and larger veins are typical findings for the post-parturient mares. Large amounts of acid mucopolysaccharides are present in the stratum suben-dotheliale of most endometrial arteries. The myocytes of the media are extremely hypertrophic in the uterine arteries.

Extrauterine vascular alterations
Except for an even more prominent hypertrophy of the smooth muscle cells within the media and adventitia, the findings are consistent with those of the second half of pregnancy.
The alterations of the extrauterine veins are in accordance to those of adult nonpregnant mares.

Immunohistochemistry

Expression of vimentin, desmin and a-smooth muscle actin (α-sma)
The endothelial cells and the fibrocytes express vimentin. The higher the degree of fibrosis or fibroelastosis, the more vimentin-expressing cells are visible in the stratum subendotheliale and the media, independent of the state of pregnancy. In all mares a co-expression of desmin and α-sma can be demonstrated in the myocytes of the media and adventitia. An increasing degree of fibrosis or fibroelastosis is correlated with a higher number of cells in the stratum subendotheliale, showing a co-expression of desmin and α-sma. Additionally, one third of these cells co-expresses vimentin. An increasing accumulation of fibres in the media is matched by a decrease in the number of desmin and α-sma co-expressing cells and an increase in the number of vimentin expressing cells.

Expression of laminin and collagen IV
The subendothelial basement membrane of normal arteries is detectable as a fine, continuous lamella using antibodies against laminin and collagen IV. The basement membrane of the myocytes is visible as a fine network particularly in the media. As the degree of arterioses increases the subendothelial basement membrane is more irregular and lamellated whilst the basement membrane of the myocytes becomes cloudy and more indistinct.

Discussion

Endometrial arteries and veins of adult non-pregnant mares investigated in this study show mild to moderate panfibroelastoses and panelastofibroses, as consistent with the descriptions of *Kriesten (1995)* and *Grüninger (1996; 1998)*. The myometrial vessels are characterized by the same quality of alterations, with a greater prominence in one third of the mares. Alterations in the extrauterine arteries are mainly classified as fibroses or fibroelastoses. The degree of changes is the same as that of the uterine arterioses in two thirds of the cases investigated and higher in one third of the mares. The more prominent alterations of the myometrial and extrauterine vessels compared with the endometrial vessels may possibly be due to a higher hemodynamic stress, since according to *Grüninger (1996)*, hemodynamic and hormonal changes may be causes of endometrial angioses. Histological and Doppler ultrasonographic studies of the arteria uterina (*Blaich, in press)* demonstrate that an increasing degree of fibrosis in arteries is accompanied by an elevated vascular resistance and therefore a reduced uterine perfusion.
The continuous increase in uterine blood flow during pregnancy, measured by Doppler ultrasound *(Bollwein et. al, 1999; Woschee, 1999)*, is associated with histological changes only in the late stages of pregnancy. The mares in the first half of pregnancy do not show any differences compared to the non-pregnant mares either regarding the uterine or the extrauterine arteries. The vessels of mares in the second half of pregnancy, however, reveal prominent vascular signs of disorganization, mainly affecting the media of the uterine and extrauterine vessels. In post-parturient mares the alterations of the vessels investigated are even more distinct. The postpartal structural disorganization in the endometrial vessels is interpreted as a result of an increased contractility of the myocytes *(Wrede, 1999)*.
It is interesting that alterations of the extrauterine arteries of mares in the second half of pregnancy (> 8 years) and post-parturient mares are similar to those with ruptured arteries. These histopathological findings in arteries, ruptured during the late pregnancy, are in agreement with the observations of *Rooney and Robertson (1996)*.
According to *Lofstedt (1994)* causes of vascular ruptures are an increased intravascular pressure, stretching of the vessels by the weight of the fetus and the uterus predisposed by the degenerative vascular lesions.
In general, all mares with uterine angiopathies also manifest extrauterine vascular lesions. Because of the close correlation between uterine and extrauterine alterations and the representativeness of the endometrial biopsy *(Runge, 1995)*, the diagnostic importance of angiopathies in uterine biopsies should be reevaluated. A further unfavourable influence on fertility *(Kriesten, 1995)*, a decreased perfusion of the endometrium due to a reduced lymphatic drainage *(Schoon et al., 1994)* and a contribution to the pathogenesis of the endometrosis *(Grüninger et al., 1996; 1998)* have been discussed as consequences of endometrial angioses. In accordance with *Schoon et al. (1997)* an inclusion of angioses into the categorization of *Kenney and Doig (1986)* is recommended.

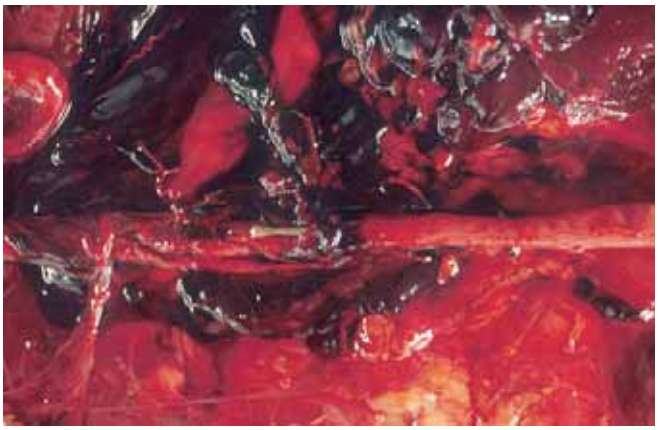


Fig. 7: Rupture of the arteria uterina dextra, 11 cm ventral of the branching off the arteria iliaca externa, 15-year-old mare, 8th month of pregnancy

Ruptur der A. uterina dextra, 11 cm ventral des Abganges von der A. iliaca externa, 15-jährige Stute, 8. Trächtigkeitsmonat

It is concluded that the histopathological findings of the vessels in the endometrial biopsy are reliable markers for inferring the status of the extrauterine arteries. Older multiparous mares with moderate to severe endometrial angioses diagnosed in endometrial biopsy can be identified as risk patients for fatal ruptures of extrauterine vessels during late pregnancy or birth.

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