Arch Gynecol Obstet (1998) 262: 1–26

Archives of
Gynecology
and Obstetrics

Reviews

The Mayer-Rokitansky-Küster syndrome

An analysis of its morphology and embryology
Part I: morphology

K. S. Ludwig

Department of Anatomy, University of Basel, Pestalozzistrasse 20, CH-4056 Basel

Received: 12 June 1997 / Accepted: 24 March 1998

Abstract. The histological appearance of the rudimentary uterus, endometrium, uterine tube, Gartner's duct, round ligament, vagina and ovary is described in ten case of the MRK syndrome. When the layout of the pelvic contents of patients with this syndrome is compared with that of a normal embryo of 20 mm CRL (stage 20), the following conclusions may be drawn. The MRK syndrome can be regarded as resulting from the cessation of development of the Müllerian duct, which in this condition extends only as far as its attachment to the caudal mesonephric ligament, the round ligament. The adjacent structures beyond this point, which include the connecting strand and smooth muscle bundles dorsal to the bladder and vaginal rudiment, are derivatives of the Wolffian duct or Gartner's duct respectively. Our findings suggest that this syndrome is due to a deficiency of the estrogen and gestagen receptors. This deficiency may inhibit the further development of the embryonic Müllerian duct and account for the subsequent faulty differentiation of its existing elements. It is still undecided why, in cases of the MRK syndrome, development of the Müllerian duct ceases at the attachment of the caudal mesonephric ligament (later the round ligament). Further research is necessary to answer this question.

Key words: Mayer-Rokitansky-Küster syndrome – Histology – Wolffian (Gartner's) duct – Müllerian duct – Embryological malformation

Introduction

A female genital tract in which vaginal aplasia is accompanied by duplicated solid uterine horns constitutes the Mayer-Rokitansky-Küster syndrome, or MRK syndrome [11]. The uterine horns are bulbous at the insertion of the round ligament, and from here extend medially behind the bladder, where they are covered by a fold of peritoneum. This fold is known as the primitive broad ligament, and within it the horns may remain separate or become joined together. The subsequent con-

Correspondence to: Prof. Dr. K. S. Ludwig

necting strand consists of fibrous and muscular tissue and is generally thought to represent the anlage of a rudimentary cervix. The uterine tubes are either normally developed or hypoplastic, but the ovaries produce a normal endocrine pattern [11]. In cases where the syndrome is unilateral, the opposite side develops a uterus unicornis with a normal vagina (the "uterus unicornis cum cornu rudimentario et vagina simplex" of Kussmaul [20]).

The MRK syndrome was first reported by Mayer [25], who simply called it "uterus bipartitus". This term was adopted by Rokitansky [34], Kussmaul [20] and other authors, regardless of the variability of the malformation, i.e. the number of genital organs involved and the presence or absence of a lumen in the uterine rudiment. In his review of the literature, Küster [21], coined the term "uterus bipartitus solidus rudimentarius cum vagina solida", which again fails to take into account the large number of variations encountered. We prefer to follow the recommendation of Hauser and Schreiner [11], and have described this combination of abnormalities as the Mayer-Rokitansky-Küster syndrome, in spite of the opinions of other authors [4].

The MRK syndrome appears to be the result of retardation in development of the Müllerian duct. The ovaries function normally, as shown by the presence of corpora lutea [3, 9, 11, 21, 36, 40, 42, 44]. The amount of gonadotrophins and ovarian hormones secreted is as usual [11, 44]. All authors have emphasised the normal external appearance of these women, in spite of the severe malformation of their internal genital organs. The chromosomal sex (karyotype) is always female [9, 11, 32, 44].

Although there have been numerous reports of the MRK syndrome in the literature, only a few authors have illustrated certain of the morphological characteristics (Mayer [25] Table VIII, Fig. 2 and Table IX, Fig. 2; Rokitansky [34] Table I, Fig. 1; Küster [21] p 695, Fig. 3 and Table VII, Fig. 1; Büttner [3] p 227, Fig. 11; Hauser und Schreiner [11] p 382, Fig. 2; Gardó et al. [6] p 75, Fig. 2). Küster ([21] p 697, Fig. 4) is the only author who has illustrated a histological section, showing the muscular arrangement of the uterine rudiment.

The development of the genital system is closely associated with that of the urinary system, and many authors have described combined malformations affecting both systems [1, 4, 8, 9, 11–14, 29, 32, 39, 42, 44]. Rokitansky mentioned a case of "uterus unicornis sinister cum cornu rudimentario dextro" in which the right kidney was absent ([34] p 46).

The aim of this study is to present ten cases of the MRK syndrome and, in the first part, to give an anatomical and histological description of the material collected at operation. In the second part, the formal embryogenesis of the syndrome will be described, and discussed in terms of the development of the Müllerian and Wolffian ducts.

Materials and Methods

Organ samples were removed at operation from ten patients aged from 16 to 39 years. A list of these organs is given in Table 1.

The tissues were fixed immediately after dissection in Bouin's or Carnoy's solution, or in a modified Davidson's solution [19]. The material was then embedded in paraffin, cut into 7 µm serial sections and stained alternately with HE, Azan or Pasini, PAS and resorcin gentian violet azocarmine naphthol green (RGAN).

Measurements given in this paper were taken from the serial sections.

Table 1. MRK Syndrome: Data on reported cases (material available for analysis)

No.	MRK Syndrome	Ovary*	Rudimentary uterine horn	Gartner duct	Details of the dissected material
1	bilateral	+	lumen present	–	Rudiment of tube attached to uterine horn
2	bilateral	+	lumen present	present	Fimbriae and ampulla of tube, isthmus attached to uterine horn/ round lig./vaginal biopsy
3	bilateral	++	solid	present	Fimbriae and rudimentary tube/ connecting strand/vaginal biopsy
4	bilateral	++	solid	present	Round ligament attached to uterine horn
5	bilateral	++	solid	–	Rudiment of tube and parts of round lig. and connecting strand attached to uterine horn
6	bilateral	+	solid	–	Tube with fimbriae
7	bilateral	+	solid	present	Fimbriae and ampulla of tube/ parts of round lig. and connecting strand attached to uterine horn
8	unilateral left	+ left	solid	–	Ampulla of the left tube Fimbriae of left tube attached to ovary
9	unilateral right	++	solid	–	Ampulla of right tube
10	unilateral left	+ left	solid	–	–

* Excision: unilateral +, bilateral ++

Results

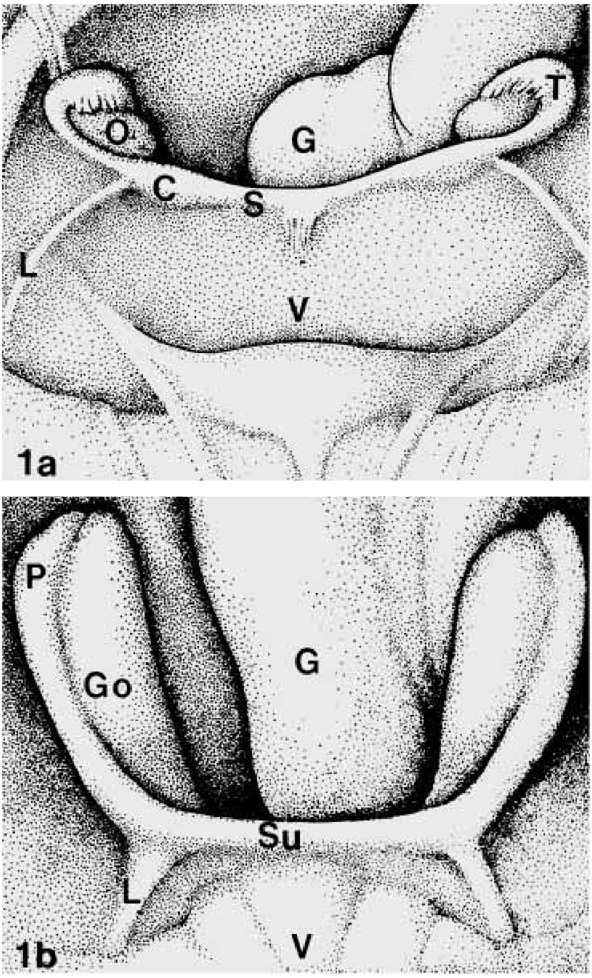
Description of the local macroscopic anatomy (Fig. 1a, 2a)

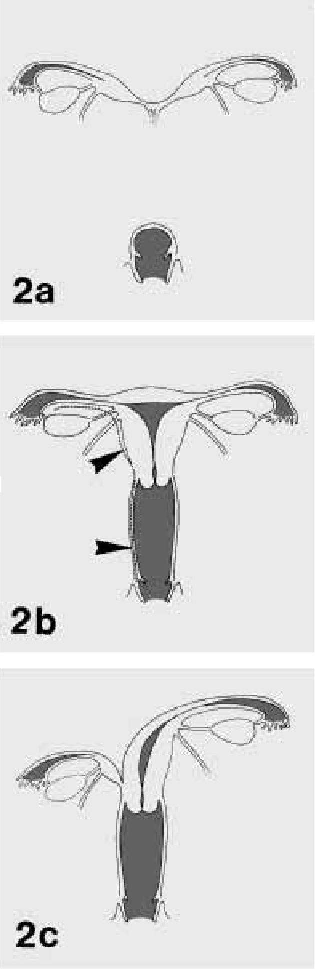
On either side there is an ovary, to which the fimbriae and infundibulum of the Fallopian tube are attached. These enclose the ovaries dorsally, laterally and ventrally. At the site of attachment of the round ligaments, the tubes continue into the bulbous rudiments of the uterine horns. These bilateral rudiments are joined together medially by the connecting strand. Both the uterine rudiments and connecting strand lie within a peritoneal fold that arises in the frontal plane from the dorsal wall of the bladder. Behind this fold lie the rectouterine (Douglas) pouch and the rectum. Medially, where the two connecting strands arise, a more compact connective tissue plate may develop.

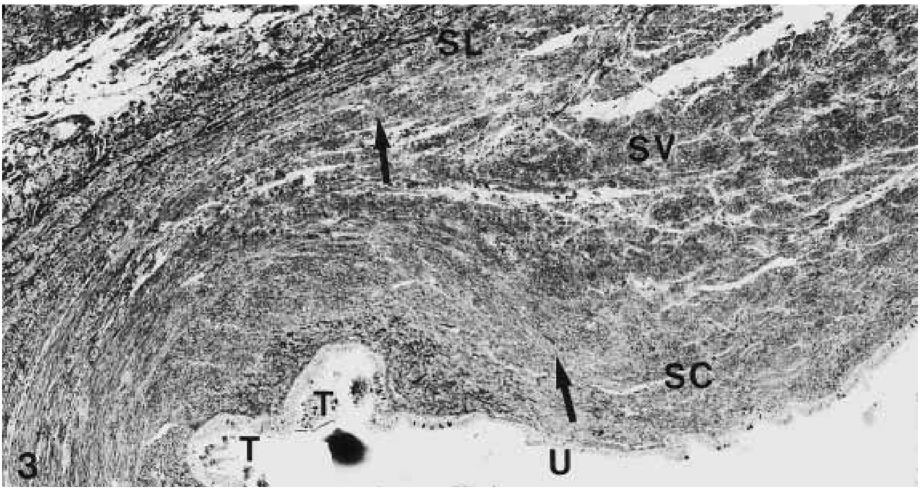
An example of the MRK syndrome is depicted diagrammatically in Fig. 2c. If a rudimentary uterine horn has developed in the cranial region of the cervix of a uterus unicornis, the uterine tube and the ovary itself show the same characteristics as in the typical MRK syndrome.

Description of the local embryological structure

Fig. 1b illustrates the local embryological situation at stage 20 (ovulation age approximately 51 days, CRL 18–22 mm according to O'Rahilly and Muecke [31])


O
G
T
C
S
L
V
1a
P
Go
G
Su
L
V
1b


2a
2b
2c


SL
SV
SC
T
T
U
3

of a case which resembles the situation of the MRK syndrome. On either side a gonad (Go) lies on the mesonephros. The urogenital fold (P), containing the Wolffian duct medially and the Müllerian duct laterally, is attached to the lateral wall of the gonad. At this stage the Müllerian duct has only just reached the round ligament at the caudal pole of the mesonephros [24, 31].

Medial to the insertion of the round ligament, the two urogenital folds unite to form the urogenital septum (Su; formerly known as the "tractus genitalis" or "genital cord") [23, 28], which is a frontally orientated double fold of peritoneum: the anlage of the broad ligaments. These are attached to the dorsal wall of the bladder (V) and at this stage contain only the Wolffian ducts. Behind the urogenital septum the entry of the primitive pelvic peritoneal pouch can be seen. In stage 20 the pouch extends as far as the anlage of the pelvic diaphragm, below the opening of the Wolffian ducts into the urogenital sinus.

Comment

The description of our cases of the MRK syndrome agrees with those reported in the literature [3, 8, 11, 21, 25, 34]. In the general discussion we shall refer to this region again and discuss it further, together with the probable etiology of the MRK syndrome.

The rudiment of the uterine horn: its muscular structure

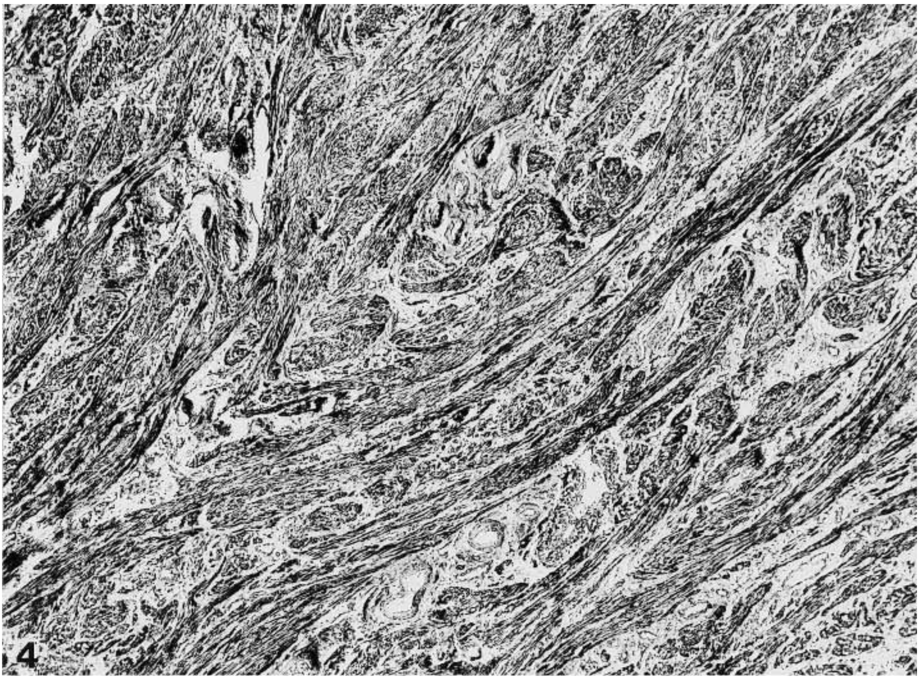
The rudiment of the uterine horn is club-shaped. The tube and the round ligament are inserted into it laterally. The rudiment tapers in a medial direction and joins the connecting strand.

In cases 1 and 2 the rudiment contains a slit-like lumen into which the tube itself opens (Fig. 3). In the other 8 cases the uterine rudiment is solid. Its length var-

Fig. 1. **a** Drawing showing the anatomy of the pelvis in a case of bilateral MRK syndrome. From photographs of G. A. Hauser taken during operations and my personal notes. **b** Sketch showing pelvis of an embryo at stage 20 (ovulation age approx. 51 days, CRL ca. 18–22 mm according to O'Rahilly and Muecke [31]) taken from personal reconstructions and the models of Keibel [17]. The Müllerian ducts, situated in the urogenital fold, have reached the caudal pole of the mesonephros. *C* rudimentary uterine horn; *G* gut; *Go* gonad; *L* round ligament of the uterus; *O* ovary; *P* urogenital fold; *S* connecting strand; *T* Fallopian tube; *Su* urogenital septum; *V* dorsal wall of bladder

Fig. 2 a–c. Diagrams of a normal female genital tract and 2 types of the MRK syndrome. **a** Bilateral MRK syndrome (uterus bipartitus rudimentarius solidus seu partim excavatus, Vagina rudimentaria). **b** Normal situation (Uterus virgineus, Vagina simplex). The *dotted line* (*arrow heads*) on the left indicates the sites where rudiments of the Wolffian duct can be found. *c* Unilateral MRK syndrome (uterus unicornis cum cornu rudimentario [solido seu partim excavato], Vagina simplex)

Fig. 3. Opening of the tube (*T*) into the lumen of the rudimentary uterine horn (*U*). The muscle layers of the tube gradually merge with those of the uterus (*arrows*). The stratum vasculare of the uterus (*SV*) can be found between the stratum longitudinale (subserosum) (*SL*) and the stratum circulare (*SC*), the true muscle layer of the Müllerian duct (case 2). ×64


4


SL
5a


SL
5b

ies between 7 and 11 mm, with an average of 10 mm. It is oval in cross-section and measures approximately 12×9.4 mm.

The wall of the rudimentary horn is made up of bundles of muscle fibres and contains numerous blood vessels (Fig. 3–5). The muscle bundles in the subserosa are mainly longitudinal (Fig. 3, 5) and continue into the same layer of the Fallopian tube and the outer muscular layers of the round ligament (Fig. 5b). The deeper muscle bundles in the subserosa (Fig. 5a) penetrate the adjacent vascular layer to form a dense network of fibres between the blood vessels (Fig. 4). No other tissue layers were observed in the solid uterine rudiments. In cases 1 and 2, where a slit-like lumen is present, the innermost circular muscle layer of the tube continues into a similar layer in the uterus which lies just below the endometrium (Fig. 3). Muscle bundles run between here and the vascular layer.

Comment

Both descriptions given in the literature for a solid uterus rudiment [3, 21] correspond with our findings. In cases where the uterus rudiment possesses a lumen, the wall structure looks similar to a normal uteruswall as mentioned by Werth and Grusdew [46], Wetzstein [47] and Wetzstein and Renn [48].

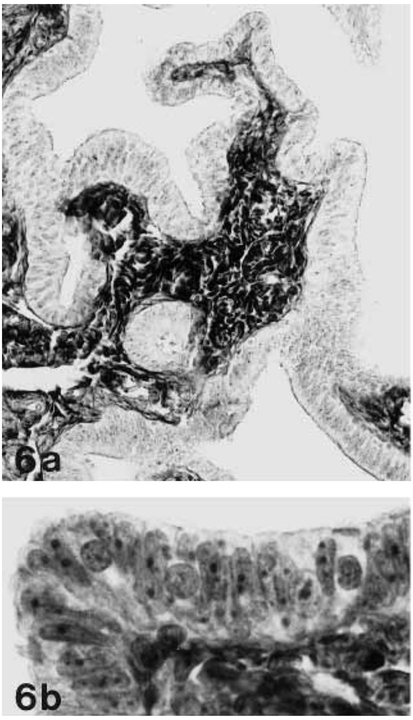
The rudimentary uterine horn: endometrium

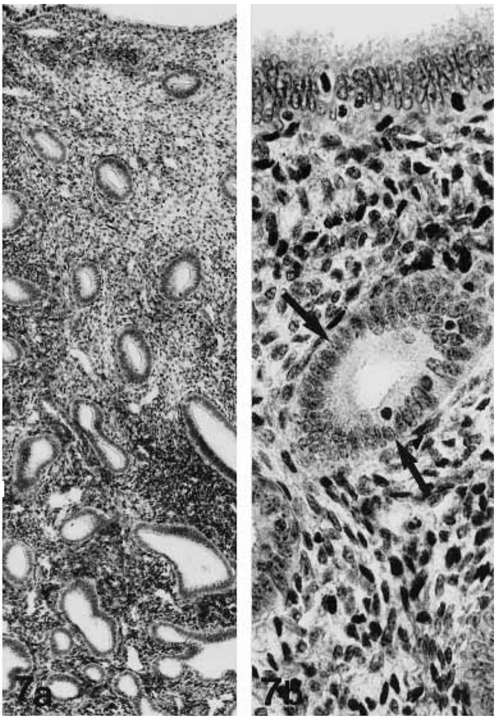
The endometrium in case 1 (Fig. 6): The mucosa shows primary and secondary folding. The lamina propria consists of coarse connective tissue fibres and contains numerous small vessels. No glands can be seen. The epithelium is pseudostratified, with some of the cells bearing kinocilia and some having bulging apices (Fig. 6b). The epithelium shows only slight staining (Fig. 6a).

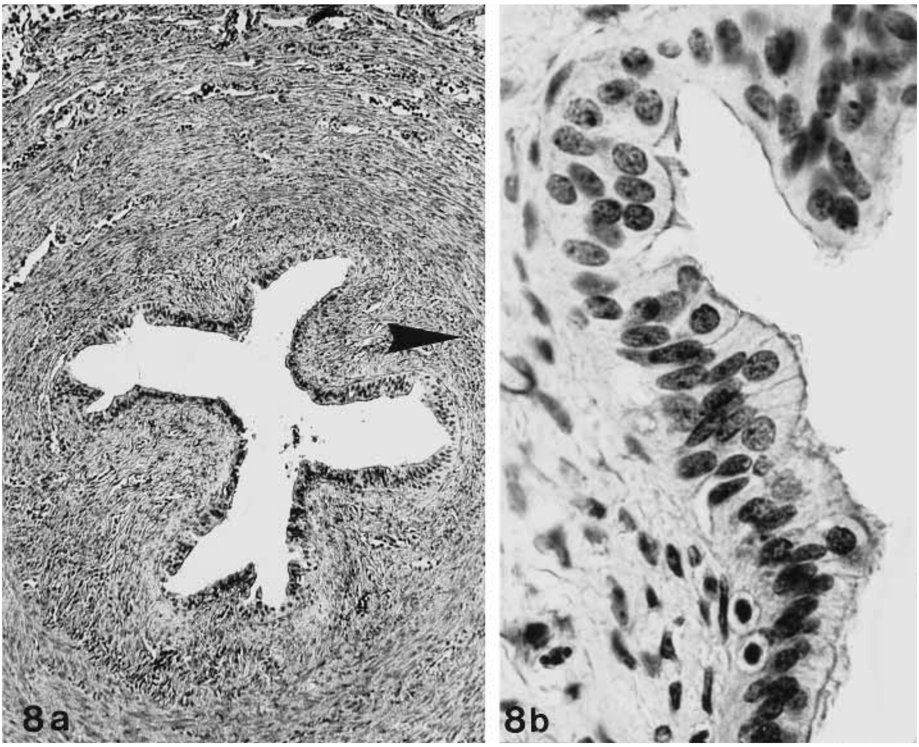
The endometrium in case 2 (Fig. 7): The slit-like lumen is bounded by two walls, a roof and a floor. The Fallopian tube ends in the roof region of the uterine horn, and both are lined by the same pseudostratified epithelium (Fig. 3). The floor of the lumen has a typical endometrial structure (Fig. 7). The epithelium is cylindrical or pseudostratified, the glands, which often branch, reach through the whole depth of the lamina propria into the superficial layers of the myometrium. There is a single layer of glandular epithelium. It contains many mitotic figures and shows a small lighter region between the cell bases and the nucleus. The cell apices are filled with granular material, and the lumina of the

Fig. 4. The stratum vasculare of the muscle layers of the rudimentary uterine horn. The muscle bundles form an irregular three-dimensional network (case 10). ×64

Fig. 5a, b. The outer muscular layers of the uterine rudiment. **a** The longitudinal muscle bundles of the subserosa (*SL*) are sectioned obliquely, with their transition into the disorganised muscle bundles of the stratum vasculare (*arrows*). Adjacent to these some blood vessels (*arrow heads*) can be seen (case 2). ×64. **b** The muscle bundles of the stratum longitudinale (subserosum) (*SL*) blend with the round ligament. Adjacent to the stratum subserosum, a layer of loose connective tissue with blood vessels and numerous small muscle bundles can be seen (*arrow heads*). This layer of connective tissue is connected with the stratum vasculare of the uterus and the central part of the round ligament (case 4). ×64


6a
6b


7a
7b


8a
8b

glands are wide and contain occasional secretory material. No hemosiderin is to be seen in any of the cells.

Fallopian tube (Tuba uterina)

No measurements are available for the Fallopian tubes, because only fragments were at our disposal. Fimbriae, infundibulum and part of the ampulla with a lumen were usually present. The lumen often terminates before the tube reaches the rudimentary horn. In cases where the uterus contains a hollow space the entire tube possesses a lumen.

The muscular layers exhibit the usual structural arrangement. In the ampulla these layers are thin and consist of inner circular and outer longitudinal fibres. In the isthmus some longitudinally orientated muscle bundles lie adjacent to the mucosa. Next to these, there is a thick circular layer and then a massive layer of trellis-like muscle bundles (Fig. 8a, 11). The outermost muscle bundles are predominantly longitudinal. The tube is surrounded by peritoneum.

Some of the oviducts investigated possess a normal funnel-shaped infundibulum and an ampulla (Fig. 9), while others are rudimentary in structure. This is particularly clearly seen in the formation of the mucosa, where true folding is lacking and only small ridges of the lamina propria, covered by a cylindrical pseudostratified epithelium, have developed (Fig. 10a). Lining the indentations between the ridges there is only a single layer of cuboidal epithelium (Fig. 10a, 11). In the distal part of the ampulla, the mucosa normally shows 4 distinct longitudinal ridges,with an occasional smaller one (Fig. 8a, 11). The epithelium is pseudostratified on the ridges but only cuboidal in the crypts (Fig. 8b).

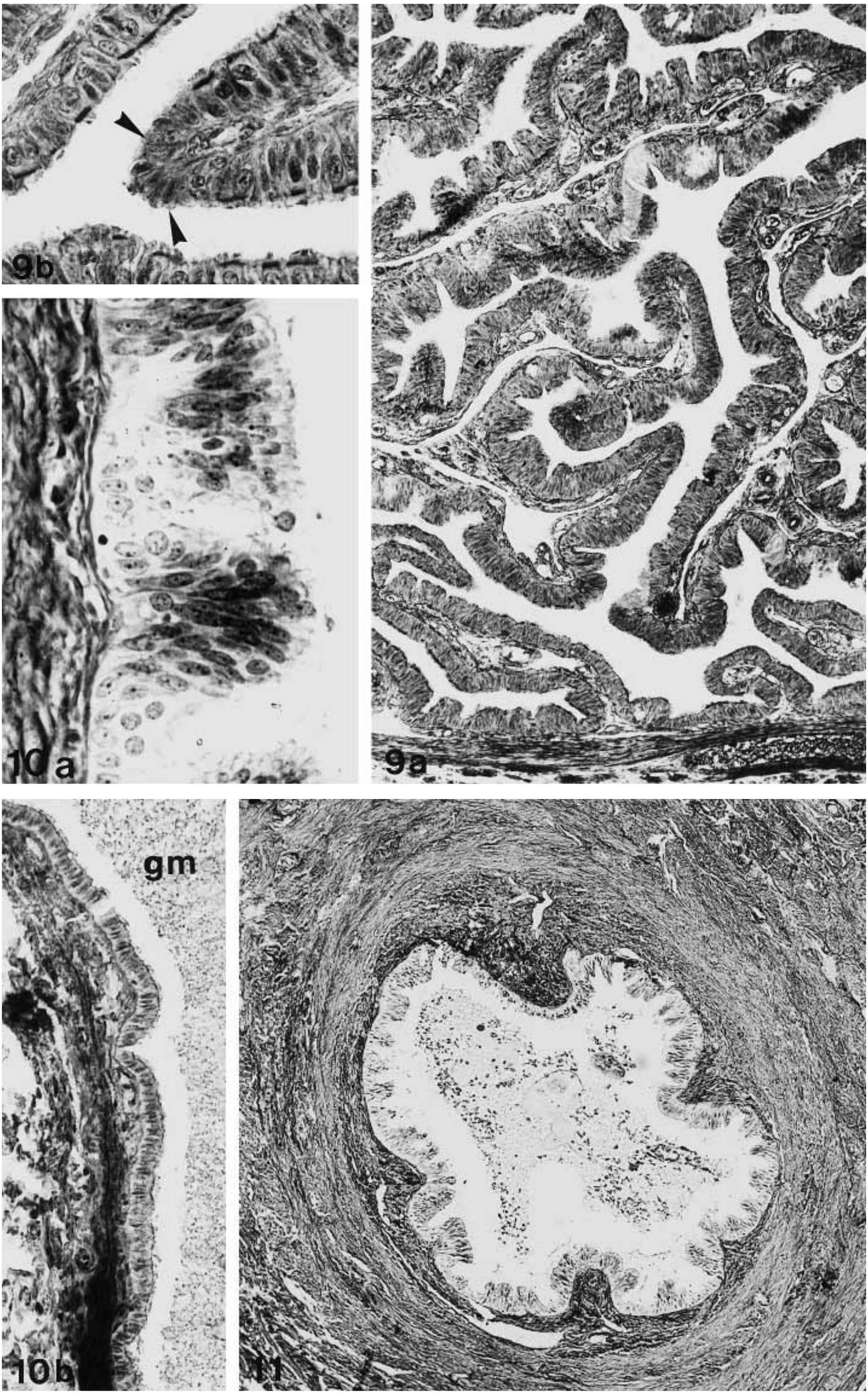
In case 3, where the oviduct ends blindly, only a few indentations are present (Fig. 8). In case 2, however, both indentations and ridges are so numerous that the pseudostratified cylindrical epithelium appears to form clusters (Fig. 10a, 11).

In case 6 only the funnel-shaped infundibulum is present, together with a short stretch of the ampulla. The ridges in the upper part of the ampulla are covered by clusters of pseudostratified cylindrical epithelium (Fig. 10a), whereas the

Fig. 6a, b. Endometrium of the uterine rudiment (case 1). **a** The surface is sinuous, but no true glands are present. The epithelium is only lightly stained. ×160. **b** Some of the epithelial cells bear kinocilia. ×640

Fig. 7a, b. Endometrium of the uterine rudiment (case 2). **a** The surface is smooth. Numerous tubular glands extend from the epithelium down as far as the muscular layers. The tips of the glands are often forked, the glandular lumen is slightly distended and contains traces of secretory products. ×60. **b** The surface consists of a pseudostratified epithelium with high mitotic activity. The columnar glandular epithelium also shows numerous mitoses. The cell apices contain granular inclusions. The nuclei lie more towards the base, and between the nuclei and cell base a small light region can be seen (arrows). ×300

Fig. 8a, b. Structure of the Fallopian tube (case 3). **a** The transverse section shows four primary folds, giving the lumen a starlike appearance. The epithelium is pseudostratified and of irregular height, varying between 1–3 cell layers. The outer zone of the lamina propria contains individual longitudinal muscle bundles (*arrow head*) adjacent to a massive layer of circular muscles which is surrounded by a zone of loose vascular connective tissue. ×75. **b** Detail of the epithelium: it is sinuous and bears kinocilia. ×640


9b
10 a
9a
gm
10 b
11

floor contains a thin muscular layer, and the lumen is filled with mucoid granular material. In this lower part the mucosa is not folded (Fig. 10 b) and is covered by cylindrical epithelium. Many cells bear kinocilia and others are of the secretory type (Fig. 10 b).

Comment

No histological descriptions are to be found in the literature, but two types of MRK tube are mentioned. One of these is hypoblastic in character [11] and the second, which is otherwise normal, ends blindly [3, 21]. These findings are in general agreement with our own results. The structure of the hypoblastic oviducts corresponds with fetal stages as described by Wendeler [45].

Gartner's duct (GD)

During normal development the caudal portions of the Wolffian ducts may persist close to the myometrium of the uterus and the muscular wall of the vagina. These are referred to as Gartner's duct or canal (Fig. 2 b).

The position of the GD relative to the uterine rudiment in the MRK specimens is as follows.

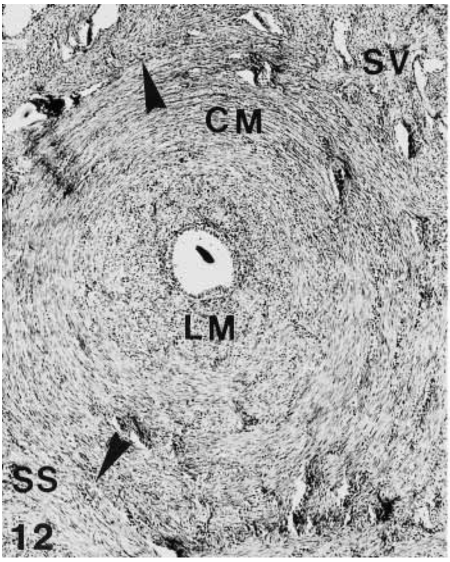
The duct runs in a nearly longitudinal direction, parallel to the muscle bundles of the tela subserosa (Fig. 17 a), and is separated from the true muscular tunic of the uterine rudiment by the stratum vasculare (Fig. 12–14). Its diameter lies between 0.5 and 0.7 mm. The lumen, which contains traces of mucus (Fig. 13 a) in a more or less condensed state (Fig. 12), is round or slightly oval. The diameter is about 120 μm (50–200 μm). The shape of the lumen may vary within short distances and the walls are often undulating (Fig. 16 a–d). In these regions the muscular fibres are not strictly orientated in one direction, but cross each other. The border between it and the stratum vasculare is always quite distinct.

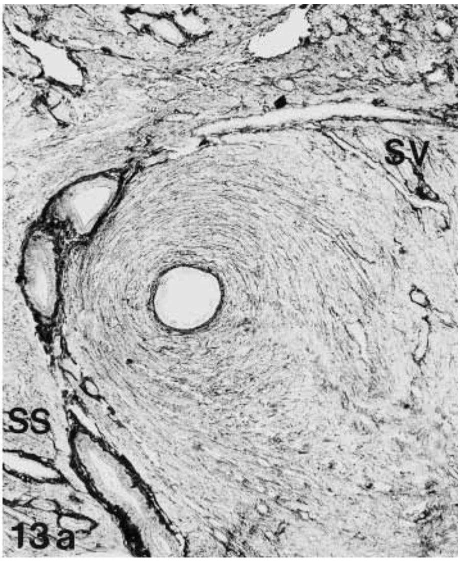
The epithelium rests on a distinct basement membrane and its height varies between 12.5 and 25 μm. It is, depending on the height, either simple columnar or pseudostratified. The cells of the simple columnar epithelium are very narrow, and

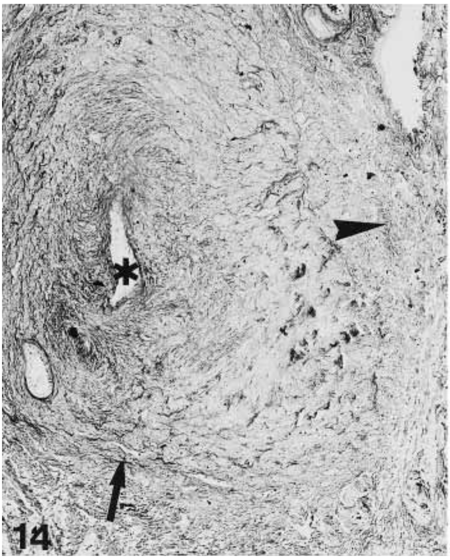
Fig. 9 a, b. Fallopian tube, ampulla (case 9). **a** The folds of the mucosa look the same as in a normal tube. ×60. **b** The epithelium consists of ciliated cells, secretory cells with bulging apices (*arrow heads*) and a few peg cells. ×400

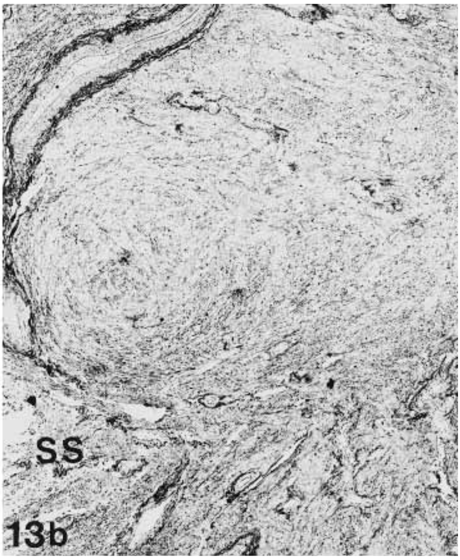
Fig. 10 a, b. Fallopian tube (case 6). Only a few fimbriae and a short ampulla-like portion have developed. **a** The “ampulla” exhibits only reduced, simple folds. The pseudostratified epithelium shows clusters of high columnar cells, only a few of which bear kinocilia. Most of the cells bulge and contain vacuoles in the apex. ×400. **b** Longitudinal section through the caudal end of the “ampulla”, which is filled with granular material (gm). The epithelium is only single-layer and columnar, consisting predominantly of ciliated cells and few secretory cells. ×160

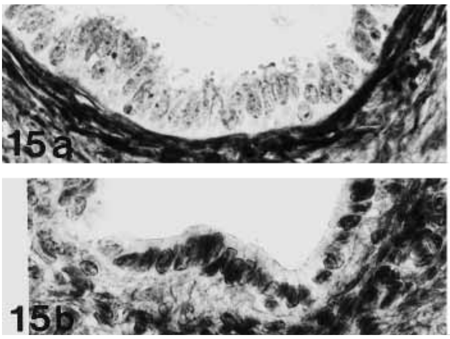
Fig. 11. Transverse section through the caudal part of the ampulla of a Fallopian tube (case 1). The mucosa shows signs of five folds. The epithelium varies in height from single-layer to pseudostratified. Many cells are ciliated. The lumen contains cell detritus and remnants of fragmented eggs (compare Fig. 29), granulosa cells and macrophages, all embedded in a jelly-like substance. ×64

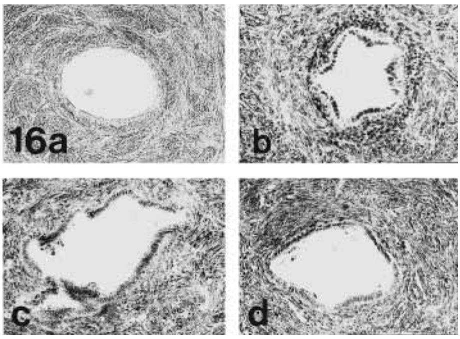

SV
CM
LM
SS
12


SV
SS
13a


*
14


SS
13b


15a
15b


16a
b
c
d

the nucleus is an elongated ovoid lying near the apex (Fig. 15 a). This nuclear arrangement leaves the cell base only slightly stained (Fig. 16). The apex is either smooth or bears stereocilia (Fig. 15, 16), sometimes kinocilia. If the height of the epithelium exceeds 20 μm, it is always pseudostratified and ciliated.

The GD contains three muscular layers. The inner layer is predominantly longitudinal, and lies next to a massive layer of circular fibres. An additional outer longitudinal layer joins the muscles of the stratum vasculare and those of the tela subserosa (Fig. 12, 13 a, b).

In case 7 the GD stretches over the distal end of the uterine rudiment into the connecting strand (CS). Within the transitional area the circular muscles of the GD cross over to the longitudinal muscles of the CS (Fig. 17 a).

In case 2 the duct is not fully canalized. About 1/3 of its length is solid (Table 2), although the typical muscular tunic persists even though a lumen is lacking (Fig. 13 b). The GD is clearly demarcated from the stratum vasculare of the uterine rudiment.

In case 4 the GD exhibits yet another peculiarity (Fig. 14). Towards the distal end two lumina can be recognized, one round the other oval in section. A comparison of the serial sections reveals that the oval duct appears to be a blind branch of the main duct, and both lumina are lined by the same type of epithelium. The muscular arrangement around the two ducts is not typical for a GD. The inner longitudinal muscle layer has no crossing fibres, instead there are many small blood vessels running between the two ducts. A circular muscle layer surrounds them and indicates the boundary of the stratum vasculare of the uterine rudiment, since the outer longitudinal muscle layer is also missing.

Fig. 12. Transverse section through a Gartner duct (case 3). The lumen contains condensed material and is bordered by a regular single-layer epithelium. The thin lamina propria is surrounded by a layer of longitudinal muscle bundles (*LM*) These bundles cross over into a massive layer of circular muscle (*CM*) and then into an outer layer of longitudinal muscle bundles (*arrow heads*). The latter run into the muscles of the stratum vasculare uteri (*SV*) or of the stratum subserosum (*SS*). ×48

Fig. 13 a, b. Transverse section through a Gartner duct (case 2). **a** The duct is round, with pseudostratified epithelium. Its tunica muscularis is clearly separated from the stratum vasculare uteri (*SV*) and the stratum subserosum (*SS*) ×48. **b** The section is taken from an area approximately 0.5 mm caudal to Fig. 13 a. The duct is solid, with no lumen or epithelium. The typical arrangement of the muscular layers is still the same. A stratum longitudinale subserosum (*SS*) with small vessels can be seen. ×48

Fig. 14. Transverse section through the ampulla of a Gartner duct (case 4). The lumen of the main duct is slit-like and irregular in shape (*asterisk*), that of the accessory duct is oval. The muscle layers which enclose both ducts do not exhibit the typical three-layered structure, but form a network. These muscular layers are distinctly separated from those of the uterus (*arrow*) and subserosa (*arrow head*). ×48

Fig. 15 a, b. Different types of epithelia can be found in the Gartner ducts. **a** The epithelium is pseudostratified and columnar with basal cells. The cell apices are bulging and contain secretory granules. The lumen contains some secretory material (case 2). ×400 **b** The epithelium varies between single-layer and pseudostratified (case 7). ×400

Fig. 16 a–d. Transverse sections through different regions of the Gartner duct (6.2 mm long) of case 7 showing the changes within short distances from cranial to caudal. **a** round, **b** starlike, **c** slit-like, irregular, sinuous (ampullary region), **d** roundish. ×80

Table 2. Cases in which Gartner's duct was present

Case Nr.	Length of uterine rudiment in mm	Length of the Gartner duct in mm
2	ca. 7	0.9 (ca. 0.3 mm solid, without lumen)
3	ca. 9.5	2.7
4	ca. 10.9	0.9 (0.35 mm with two lumina, 0.2 mm solid)
7	ca. 15	5.3*

* The last section of the histological series still shows a fully developed GD which reaches into the attached CS (Fig. 17a). Its total length must therefore be distinctly longer than shown in Table 2

Comment

GD are generally assumed to be present in about 20% of adult women, a figure based upon only two small series of cases: 8 out of 40 [33] and 12 out of 54 [26]. Sneeden [38] found GD remnants in only about 7% of his hysterectomy material (15 out of 216 cases), but he believes that many may have remained undetected.

This is very much less than the high percentage of GD remnants found in our material, where 4 out of 10 (40%) showed such remnants – twice as many as described in normal women. The same observation was made by Meyer [26], who noticed a similar increase in the amount of GD tissue in cases of uterine malformation.

Hardly any data on the length of the GD are available. Meyer [26] found a complete duct running from the epoophoron to the parametrium in a single case out of 160. Normally the duct is found only in the form of short tubes or cysts. Huffman [16] depicts in his Fig. 3 possible locations of GD remnants, but gives no measurements of the length.

According to Rieder [33], Meyer [26] and our own investigations, the GD is always located below the longitudinal muscular bundles of the tela subserosa, and separated from the true muscle of the uterine horn by the stratum vasculare.

Rieder [33] found the diameter of a complete GD to be about 0,5–1 mm, which is in agreement with our findings.

The muscular tunic with its typical three layers is described by Rieder [33] and Meyer [26], whereas Horstmann and Stegner [15] do not mention the innermost longitudinal muscle layer. The observation that an additional solid part, still surrounded by a typical muscular tunic, may be present at the distal end of the GD (cf. our cases 2 and 4) was also reported by Rieder [33] and Meyer [26]. The latter described a GD in a rudimentary left uterine horn from a case of uterus unicornis dexter. This duct possessed a true tunica muscularis, which consisted of a thin internal longitudinal muscle layer, a slightly broader circular layer and an outer longitudinal muscle layer connected with the stratum subserosum and the stratum vasculare. The GD runs from the distal end of the rudimentary horn to the cervix of the uterus unicornis. In this section, which measures about 5 mm in length, the duct is surrounded only by longitudinal muscle fibres. This arrangement of the muscle layers corresponds with our case 7, where the location of the GD within the connecting strand is described.

Rieder [33] and Meyer [26] both described cases where the GD contained two lumina (cf. our case 4). The irregularly shaped lumen and the altered arrangement of the muscle fibres, as in our case 7, were also observed by Meyer [26] and Huffman [16]. Both authors consider, as we do, that this part of the duct is in fact an ampulla.

According to Meyer [26], Gartner's duct is covered by a simple epithelium or a simple/pseudostratified epithelium of 16 to 18.5 µm in height. Rieder [33] does not mention either kinocilia or stereocilia. According to Horstmann and Stegner [15], the covering epithelium of the GD is either cylindrical (sometimes bearing kinocilia) or flat, or even multilayered. In our cases no flat or multilayered epithelium was found, but stereocilia were regularly encountered.

If, as in our case 4, the distal part of the GD develops an ampulla, it may continue as a solid strand (but still with a three-layered tunica muscularis) and end in the longitudinal muscle layer of the tela subserosa. These longitudinal muscle bundles run caudally within a double fold of peritoneum to become attached to the dorsal wall of the bladder [25, 34]. According to these authors, the left and right bundles meet to form a single strand which reaches the rudimentary vagina.

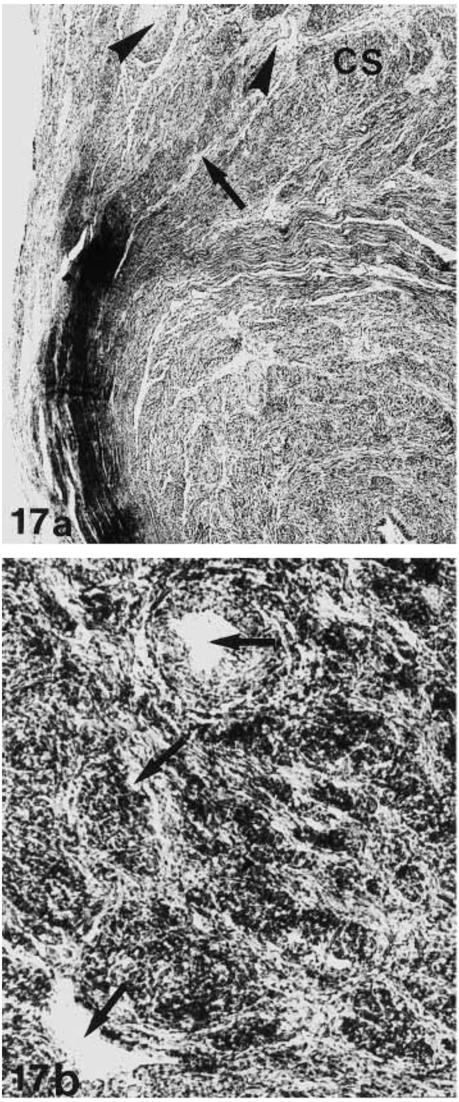
If an ampulla is present it is normally situated near the lower part of the cervix [16, 26, 33]. Further down, the GD enters the vaginal wall, and it can be concluded that, caudal to the ampulla, only parts of the vagina are represented. For this reason, any tissue detected in the extension of the rudimentary uterine horn behind the bladder should not be regarded as part of an extraperitoneal uterus [21] or a cervix [11].

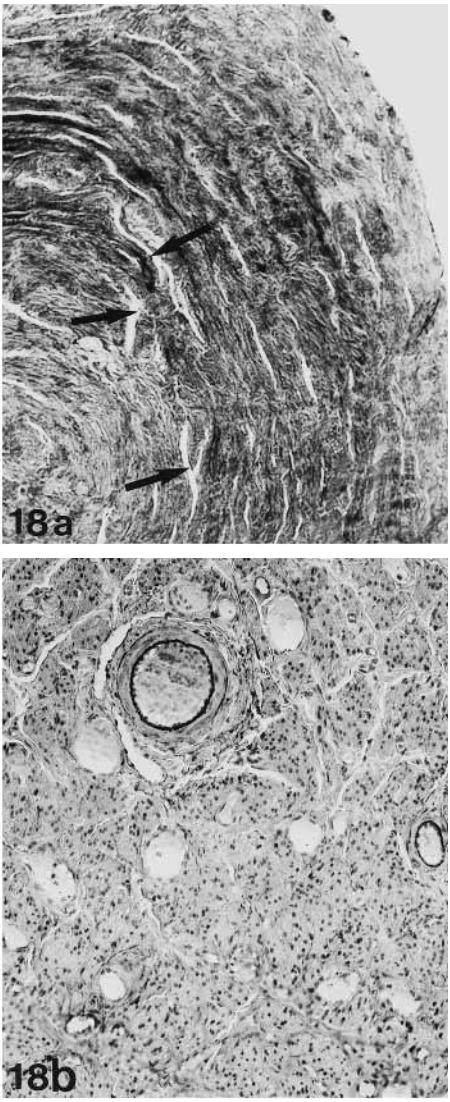
The connecting strand (CS)

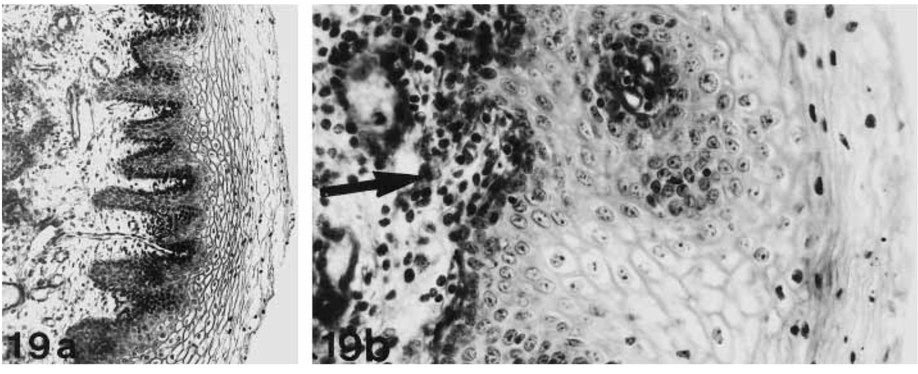
The CS extends from the caudal pole of the uterine rudiment to the dorsocaudal wall of the bladder within a peritoneal fold described as the “ligamentum latum” by Rokitansky [34]. It consists of smooth muscle bundles of varying thickness clearly separated from each other by connective tissue (Fig. 17). A few large blood vessels lie within this connective tissue and run parallel to the muscle bundles (Fig. 17a), while small vessels branch irregularly between the muscular tissue (Fig. 17b). The muscle bundles of the CS gradually join with those of the tela subserosa, a few of them reaching the stratum vasculare of the uterine rudiment. If a GD is present within the CS, it runs between these two muscular layers and passes over to join the rudimentary uterine horn (Fig. 17a). The CS does not possess a definite shape. It is hardly to be described as an “organ”, and is not clearly separated from the surrounding tissue – in particular, the numerous smooth muscle bundles within the ligamentum latum.

Comment

Mayer [25] describes the CS as a band which runs between the two layers of the peritoneum and consists of a fibrocellular mass with numerous blood vessels, but without any duct with an epithelial lining (p 545/46). Rokitansky [34] desribed it as a flattened, firm and fleshy cord, merging into cellular tissue, through which muscle fibres run (. . . einem abgeplatteten, soliden, fleischigen Strang, der in ein wie von Fleischfasern durchzogenes Zellgewebe übergeht), while Kussmaul [20]


CS
17a
17b


18a
18b


19a
19b

mentions the CS as a combination of connective tissue and muscle fibers. Our findings seem to be in general agreement with these descriptions.

Round ligament of the uterus

The round ligament of the uterus originates at the corner of the utero-tubal junction, runs along the linea terminalis, passes through the inguinal canal and is inserted into the labium majus. In transverse section the round ligament is indeed round (or oval) in shape and distinctly demarcated from its surroundings.

The segments of ligaments available for this description were taken from the utero-tubal junction of the rudimentary uterine horn, and are only about 2 cm long. The ligament has a coat of longitudinally running densely packed bundles of smooth muscle (Fig. 18a) which encloses an axial zone containing fibrous material (Fig. 18b). This central region of the ligament contains numerous blood and lymph vessels of varying diameter, which run parallel to the longitudinal muscle fibres (Fig. 18b). At the insertion of the ligament near the uterine horn its muscular covering opens out like a funnel to unite with the muscle fibers of the tela subserosa of horn (Fig. 5b) and tube. The fibrous axial zone is connected to the stratum vasculare of the uterine horn (Fig. 5b).

Comment

The proximal third of the round ligament consists mainly of smooth muscle fibres and blood vessels [11, 35, 37, 41]. The axial zone, together with its muscle fibres and vessels, joins the stratum vasculare, and the muscular coat is connected with the stratum subserosum of the uterus [35, 41]. These observations are in agreement with our own findings.

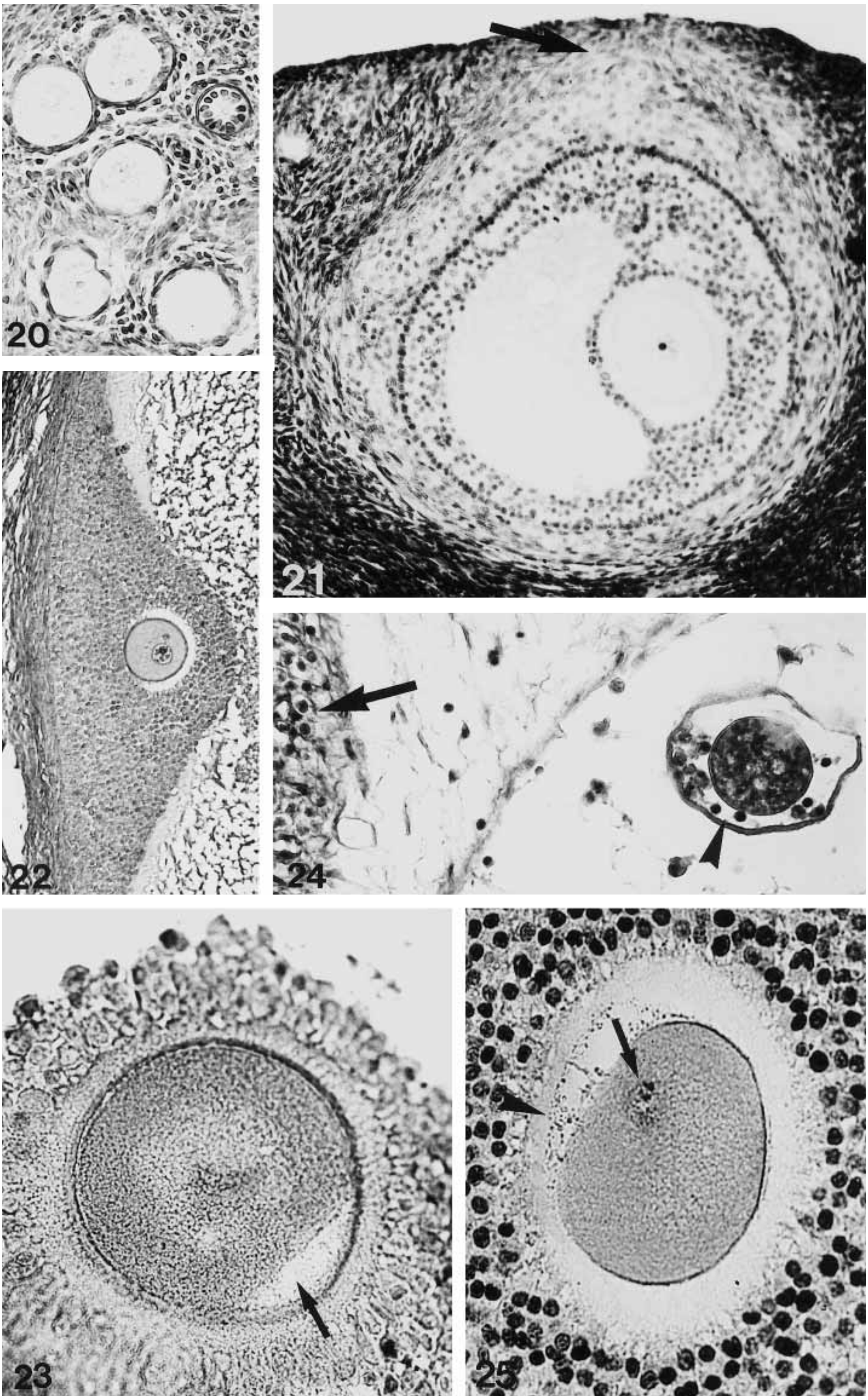
The rudimentary vagina

In patients with the MRK syndrome, the vagina, which is normally a thick-walled fibromuscular tube running from the uterus to the outside of the body, is only present in a very rudimentary form.

Fig. 17 a, b. Connecting strand (case 7). **a** Section through the connecting strand (*CS*) with its parallel longitudinal muscle bundles. These continue into the outer longitudinal muscle layer of the Gartner duct (*arrow*). Blood vessel (*arrow head*). ×52. **b** Oblique section through the connecting strand muscle bundles showing that they are enclosed in connective tissue, with blood vessels of varying diameter (*arrows*) running parallel to the muscle bundles. ×120

Fig. 18 a, b. Round ligament of the uterus. **a** Longitudinal section through the surface, showing parallel muscle bundles and distended vessels (*arrows*) (case 4). ×120. **b** Transverse section through the central region of the ligament. The longitudinal muscle bundles and the blood vessels run parallel to each other (case 2). ×120

Fig. 19 a, b. Mucosa of rudimentary vagina (case 2) **a** The mucosa consists of a typical stratified squamous epithelium resting on a papillate lamina propria. ×80. **b** In this region of the lamina propria an infiltration of leucocytes can be seen (*arrow*). Some have migrated through the epithelium. ×300


20
21
22
24
23
25

It is often little more than a shallow invagination of the skin at the normal site of the vaginal orifice. In some cases, however, the vagina may be represented by an introitus, a hymen and a blind sac of up to 3 cm in length. The mucosa is thrown into folds and consists of a stratified squamous epithelium resting on a highly papillate lamina propria (Fig. 19a). The arrangement of the cells corresponds to the description of the basal, parabasal, intermediate and superficial layers of the normal vagina wall (Fig. 19a). The outer layers are flattened and appear to store glycogen. There is not much evidence of desquamation in the material available, but some infiltration and migration of leucocytes seems to be taking place (Fig. 19b).

The ovary

Resting primary oocytes surrounded by one layer of flat or cuboidal follicular cells can be observed in all the ovaries examined (Fig. 20). The oocytes possess a large nucleus with a distinct nucleolus and several micronuclei. Some of them show signs of atresia, the cytoplasm is vacuolated and the pycnotic nuclei hardly visible (Fig. 20).

Small tertiary follicles in their first phase of growth are regularly seen. The follicular epithelium consists of 3–4 layers. A cumulus oophorus is associated with an oocyte which has increased in size, and a thin zona pellucida and corona radiata are present (Fig. 21). Surrounding the basal lamina of the follicle, the theca interna consists of concentrically arranged elongated cells, covered by cells which are more epithelioid in type. Circumscribed areas of the theca interna may protrude into the theca externa. Both the thecae in this area are pressed towards the tunica albuginea, causing the surface of the ovary to bulge (Fig. 21).

Antral follicles in the second resting phase are fairly numerous, their diameters measuring about 3–5 mm. The cumulus oophorus is well developed (Fig. 22).

In case 2 a preovulatory follicle about 12 mm in diameter and with 10–12 layers of follicular cells, many still undergoing mitosis, is present. The oocyte has finished its first meiotic division and has extruded the first polar body. The chromo-

Fig. 20. Six primary follicles in the cortex of an ovary. ×252

Fig. 21. Small tertiary follicle. The theca interna shows a zone of increasing thickness below the surface epithelium of the ovary (*arrow*). ×160

Fig. 22. Cumulus oophorus of a tertiary follicle of approximately 4 mm in diameter. ×100

Fig. 23. Secondary oocyte in a Graafian follicle (diameter 12 mm) shortly before ovulation. The first polar body (*arrow*) is only faintly stained in comparison with the more granular cytoplasm of the oocyte (case 2). ×400

Fig. 24. Follicular atresia: A hypertrophic and hyperblastic theca interna can be seen (*arrow*) covered by loose mesenchyme-like connective tissue. Degenerating granulosa cells are present in the former cavum folliculi. A multinucleated oocyte and some lymphocytes can be seen within a swollen zona pellucida (*arrow head*). A macrophage is attached to the zona pellucida by a cell process. ×300

Fig. 25. Early atresia of a Graafian follicle. The oocyte is beginning to divide (*arrow*). The zona pellucida is either thickened (*arrow head*) or starting to dissolve. Many of the granulosa cell nuclei are pycnotic. ×375

somes are not yet arranged in the plane of the metaphase plate of the second meiotic division (Fig. 23). The follicle appears to be almost at the point of ovulation, as indicated by the presence of a stigma on the surface of the ovary.

Most of the antral follicles undergo atresia. At the beginning of follicular atresia the membrana granulosa and the cumulus oophorus disintegrate, revealing large spaces between the cells. The granulosa cells have pycnotic nuclei and the oocyte, together with the zona pellucida, shrinks. Between the latter and the cells of the corona radiata there is a space containing granular material (Fig. 25). The zona is thickened in some regions and breaking down in others (Fig. 25). The oocytes may even divide parthenogenetically. Fig. 25 shows an oocyte preparing to divide, as indicated by the arrangement of chromosomes and asters.

In the later stages of atresia the cells of the theca interna become markedly hyperplastic and hypertrophic (Fig. 24). Loose connective tissue growing into the follicle pushes the thickened basal membrane towards the centre of the former cavum folliculi. The liquor folliculi contains necrotic granulosa cells and macrophages which may become attached to the thickened zona pellucida by long cellular processes (Fig. 24). The zona surrounds the remnants of the oocyte and also some additional round cells. The oocyte itself may divide parthenogenetically or increase its number of nuclei before finally disappearing (Fig. 24).

Corpora lutea are present in all the ovaries investigated. Some are active, while others repesent different stages of regression or the final formation of corpora albicantia.

Three typical examples are present in our material.

- In case 5a a fully developed, typical corpus luteum can be seen. The main bulk is formed by the large, more intensely stained polyhedral lutein cells of the granulosa (Fig. 26a, b). The smaller, only lightly stained lutein cells of the theca have also proliferated. The basement membrane has disintegrated and these cells, together with blood vessels, are spreading between the layers of the granulosa to form a close meshed endocrine microvascular network. Loose connective tissue fills the former antral space (Fig. 26a).
- In case 1a corpus luteum showing the first signs of regression can be seen. Its age is about 16 days, or 2–3 days into the following cycle. Beneath the capsule and along the larger blood vessels clusters of hypertrophic cells of the theca can

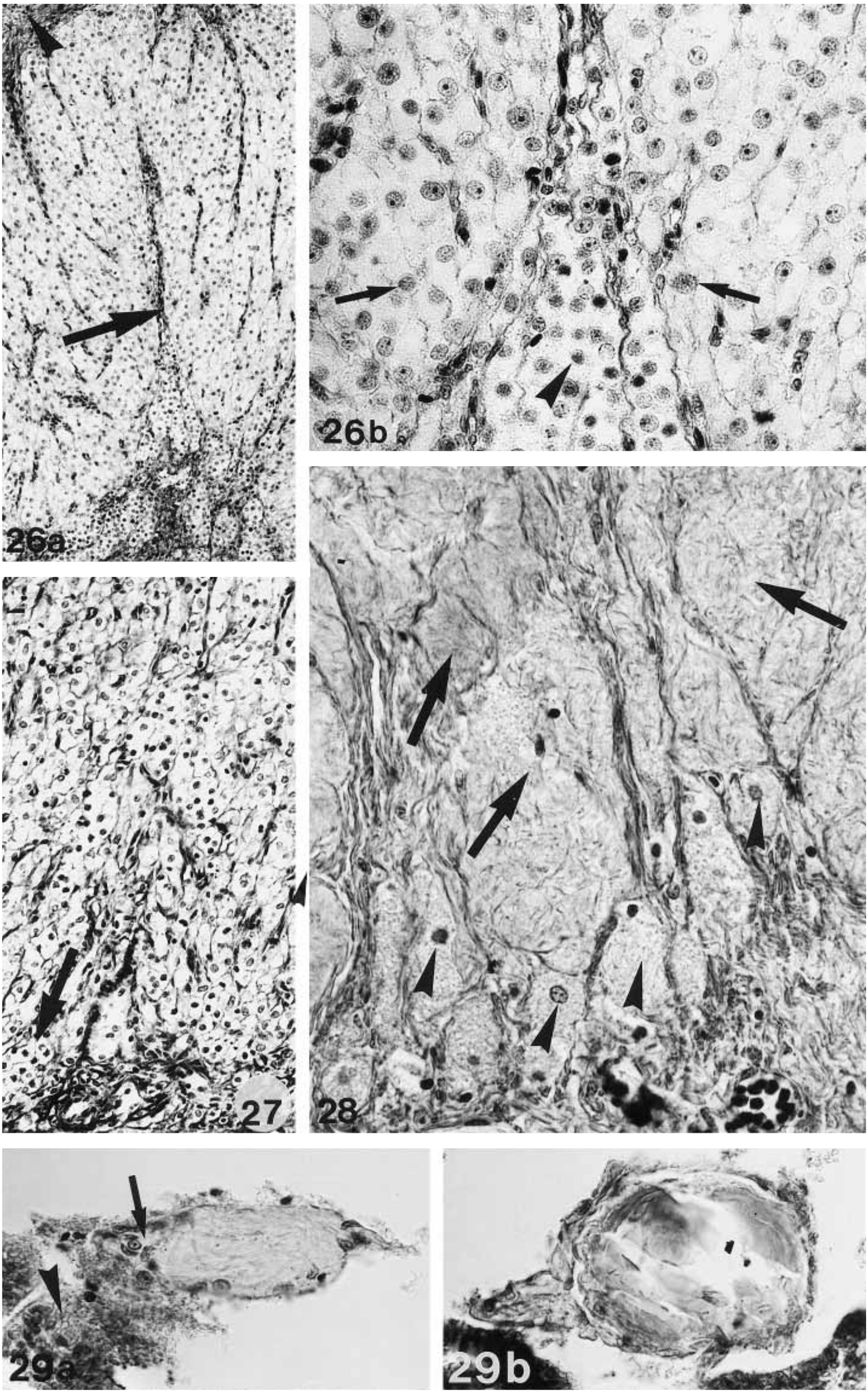
→

Fig. 26a, b. Active corpus luteum from case 5. **a** Groups of theca lutein cells growing beside sprouting blood vessels (*arrow*) between the granulosa lutein cells. Fibrin clot (*arrow head*). ×75. **b** In the centre theca lutein cells (*arrow head*) are situated alongside the blood vessels. Granulosa lutein cells can be seen on both sides of these (*arrows*). ×300

Fig. 27. Regressing corpus luteum (case 1). The granulosa lutein cells have a vacuolated cytoplasm (loss of lipids) and pycnotic nuclei. Theca lutein cells (*arrow*). The age is approximately 16 days, i.e. 2–3 d into the following cycle. ×160

Fig. 28. Late regression stage of the corpus luteum (case 8). The granulosa cells are completely hyalinised (*arrows*). The theca lutein cells are swollen and vacuolated because of loss of lipids (*arrow heads*). ×400

Fig. 29a, b. Fallopian tube, ampulla with disintegrating oocytes (case 7). **a** The cytoplasm of the oocyte is hyalinised. There are still some granulosa cells (*arrow*) and macrophages attached to the zona pellucida. Tubal epithelium (*arrow head*). ×320. **b** An oocyte with fragmented cytoplasm. ×300


26a
26b
27
28
29a
29b

be recognized (Fig. 27). These cells have pycnotic nuclei and a lightly stained cytoplasm. Some of the cells of the granulosa exhibit a vacuolated cytoplasm because of lipid extraction during the histological preparation. Their nuclei are pycnotic and do not have the distinct nucleoli of the stage of bleeding, and some show early signs of hyalinisation.

– The corpus luteum in the ovary of case 7 has largely regressed and has an estimated age of about 60 days. This corresponds approximately with the 18th day of the next cycle but one (Fig. 28). There is a distinct increase in the number of pycnotic lutein cells of the theca (Fig. 28), whereas those of the granulosa are mostly hyalinised and lack nuclei.

Proof that ovulation can take place in patients with the MRK syndrome is provided by the numerous degenerated eggs sometimes found inside the Fallopian tube (Fig. 11, 29). Strangely enough, these eggs are not found in the caudal end of the rudimentary tube (case 7) or in the rudimentary uterus itself (case 1), but always in the ampulla. The eggs are roundish or oval, with major axes of 86–140 μm and minor axes between 39 and 78 μm. The cytoplasm is hyalinised and fragmented.

The 2 degenerating eggs in the tube of case 7 (Fig. 29) lie about 260 μm apart. The more cranial still has some granulosa cells attached to the zona pellucida (Fig. 29a), and both egg cells are surrounded by macrophages.

Comment

All stages of follicular development, corpora lutea and forms of atresia were found in the ovaries investigated. These findings confirm that the processes observed in these ovaries are the same as those in normal women of reproductive age [22, 43]. The analysis of the hormonal status also confirms the fact that these patients have functionally normal ovaries [11].

Corpora lutea have been mentioned in several reports, but only four authors have published any histological observations [3, 7, 27, 40], and only 1 of these has attempted to correlate the histological findings with the stage of the menstrual cycle [3].

It is not clear why the degenerating eggs have in both cases been found in the ampulla of the tube and have not been transported towards the uterus. Although it is obvious that unfertilized eggs are kept back and resorbed on the spot and only fertilized eggs are carried onwards, the signals that initiate transport are still unknown.

General discussion

The MRK syndrome is usually considered to result from retarded development of the Müllerian duct [11]. This development – both of the duct itself and its prospective coat – is extended only up to (or slightly beyond) the attachment of the round ligament, where it ends in a muscular swelling: the rudimentary uterus or uterine horn. This rudiment is located in the cranial and lateral region of a peritoneal fold which was identified with the broad ligament by Rokitansky [34], an identification later confirmed by Küster [21]. This fold, becoming gradually lower, elongates medially towards the dorsal wall of the bladder to fuse with the same fold on the opposite side. Its dorsal lamina is homogeneous and forms the ventral border of the rectouterine (Douglas) pouch.

Except for the presence of the muscular uterine rudiment, this situation is more or less identical with that seen in an embryo at stage 20 (ovulation age approximately 51 days, CRL 18–22 mm according to O'Rahilly and Muecke [31]). The peritoneal fold described above (the so-called ligamentum latum in the MRK syndrome) is known as the urogenital septum in the normal embryo. Its cranial border encloses the mesonephric duct [23, 24, 28]. At the point where the urogenital septum joins the dorsal wall of the bladder anlage, the Wolffian ducts turn caudally and run together, parallel to each other, to follow the anlage of the bladder and urethra as far as their openings into the urogenital sinus on both sides of the Müllerian tubercle. The tubercle is already clearly visible at this stage, long before the Müllerian ducts have reached the area [5, 23].

The blastemata of both the coverings and muscular walls of the Wolffian ducts are in contact with each other and with those of the bladder, primitive urethra and urogenital sinus [24]. There is therefore a solid plate of tissue between the rectouterine pouch and the pelvic parts of the urinary system. As soon as the mesonephric duct develops a muscular coat, beginning in the fourth month of pregnancy [46], it is known as Gartner's duct (GD) in the female sex.

Longitudinal muscle bundles develop in the subserosa of the peritoneal cavity of pelvis, especially in the region of the urogenital septum, and cover over the enclosed organs [18, 46]. These subserosal longitudinal muscles, together with the muscular bundles of the Wolffian duct, form, even when the epithelium is degenerate, a fibromuscular structure (. . . fleischfaserige Gebilde – Rokitansky [34]), which Kussmaul ([20] p. 71, Fig. 31) described as a cellular tissue through which muscle fibres run, and which emulates the appearance of a uterine body (von Fleischfasern durchzogenes Zellgewebe, welches die Form eines Gebärmutterkörpers nachahmt). Küster [21] denies that the MRK syndrome is due to an anomalous underdevelopment of the Müllerian duct, and appears to follow the interpretation of Kussmaul [20] by supposing that its fibres (Müller'schen Fäden) proliferate as solid strands which extend as far as the urogenital sinus and develop their lumen later. In cases where no lumen is formed and the epithelium degenerates, some development of muscular bundles still takes place. Küster ([21], p. 697/98) classified these anomalies in terms of the scheme published by Winckel [49], believing that the malformation develops during the period in which the Müllerian ducts fuse to form a solid filament in the area of what will later be the boundary between vagina and uterus. In modern terms this area corresponds to the urogenital canal.

Küster [21] overlooked the fact, already recognised in the contemporary embryological literature, that the Müllerian ducts already possess a lumen as they grow. This comes to an end immediately proximal to the solid growing tip [10, 28]. We therefore conclude that in cases of the MRK syndrome it must be impossible to find elements of the Müllerian duct distal to the rudimentary uterine horn.

Küster [21] admitted that he was only familiar with Winckel's article [49] through a citation. That accounts for the fact that he missed an important sentence which runs ". . . in considering the development of the [Müllerian duct] an organ which is by no means unimportant has so far been totally ignored; namely, the Wolffian duct" (daß man bei der Deutung ihrer Genese bisher ein Organ ganz außer acht gelassen hat, welches sicher keine kleine Rolle dabei spielt: ich meine den

Wolff'schen Gang – Winckel [49], p. 1553). Hauser und Schreiner [11] adopted Küster's misinterpretation.

Our results do not confirm either the latter or the description by Meyer [26]. Gartner's duct may extend beyond the distal end of the uterine rudiment and may reach into the CS. It gradually loses its typical muscular tunic and only a few longitudinal bundles remain. If, as in our case 4, the distal part of the GD develops an ampulla with a lumen, the adjacent segment may turn into a solid strand with a three-layered tunica muscularis ending in the longitudinal muscle layer of the tela subserosa. These longitudinal muscle bundles lie caudally in a peritoneal fold and become attached to the dorsal wall of the bladder, as described by Mayer [25] and Rokitansky [34]. According to these authors, the bundles from either side meet here to form a single strand reaching as far as the vaginal rudiment.

In cases where an ampulla is present it is situated near the lower part of the cervical region [16, 26, 33]. Further down, the GD joins the vaginal wall. It may therefore be concluded that, caudal to the ampulla, only elements of the vagina are to be found. Tissue remnants detected in a continuation of the rudimentary uterine horn behind the bladder cannot be regarded as parts of an extraperitoneal uterus [21] or its cervix [11, 20].

Our histological pictures of the rudimentary uterine horn, endometrium, Fallopian tube, round ligament, Gartner's duct and ovaries confirm the few descriptions given in the literature. They have already been discussed in the individual sections.

The levels of ovarian and hypophyseal hormones analysed have been recorded as normal [8, 11, 44], which indicates that women with the MRK syndrome have normally functioning ovaries. This fact is confirmed by the appearance of the ovaries described in this paper and the available surgical material [3, 8, 11, 21].

If the functional state of the ovaries is correlated with the activity of the endometrium in our cases 1 and 2, where a rudimentary uterine lumen is present, the following picture emerges.

Case 1: A regressing corpus luteum is present, the epithelium of the endometrium is, however, pseudostratified and lacks mitoses. Its cytoplasm stains only faintly, probably because of the small number of organelles. Under normal circumstances the endometrium should be in a state of desquamation. The endometrium has obviously not responded normally to the hormonal action. It is assumed that receptors for estrogens and gestagens are lacking, and that the epithelial cells have not been stimulated.

Case 2: The ovary contains a Graafian follicle with the first polar body already formed. It is therefore in a state immediately preceding ovulation. The endometrium shows signs of proliferation, but the glandular lumina are already distended and hold some secretory products. The epithelial cells show a fine light zone at the base. This state of development corresponds with that normally seen just before ovulation [30].

It is an interesting fact that no hemosiderin could be detected in the endometrium, confirming that no bleeding or desquamation could have occurred during the previous cycle. This endometrium will not differentiate further into a late secretory stage and no desquamation will take place, again indicating that the endometrium is not responding to ovarian gestagens.

Histogenetic differentiation of the tube requires hormonal stimulation, especially by estrogens, and estrogen receptors have been described on epithelial and stroma cells [2]. The different degrees of differentiation in the normal or hypoplastic Fallopian tubes investigated in this study could be explained by a variation in the number of estrogen receptors on the epithelial cells. Depending on the stage of development of the tube, the lack of receptors at a particular time could lead to the persistence of the embryological or fetal stage described by Wendeler [45].

In contrast to the epithelium of the hypoblastic uterine tubes, the epithelium of the rudimentary vagina reacts normally to the influence of hormones.

Further investigation should help to answer these still open questions.

Acknowledgements. The author is most grateful to Prof. Dr. med. G. A. Hauser, former medical superintendent of the Department of Gynaecology in Luzern, for providing the surgical material. He also supplied me with copies of photographs taken during the operations. Prof. A. Kress' and Dr. J. Steel's work with the English manuscript, the skilful photographic assistance of H. J. Stöcklin, the expert graphic work of L. Stammler and the clever help of the histological technician H. Schaller are gratefully acknowledged.

References

1. Ballowitz E (1895) Über angeborenen, einseitigen, vollkommenen Nierenmangel. Virchows Arch 141: 309–390
2. Boving RL, Peluso JJ, Boving BG (1978) Estrogen binding sites in genital tracts of human female fetuses. Anat Rec 190: 344
3. Büttner O (1909) Zur Lehre von der rudimentären Entwicklung der Müllerschen Gänge. Beitr Geburtshilfe Gynakol 14: 222–238
4. Buttram VC Jr, Gibbons WE (1979) Müllerian anomalies: a proposed classification (an analysis of 144 cases). Fertil Steril 32: 40–46
5. Frutiger P (1969) Zur Frühentwicklung der Ductus paramesonephrici und des Müllerschen Hügels beim Menschen. Acta Anat (Basel) 72: 233–245
6. Gardó S, Papp Z, Árvay A (1971) Gonadal dysgenesis in association with Mayer-Rokitansky-Küster syndrome. Schweiz Z Gynakol Geburtshilfe 2: 73–78
7. Grassner A (1890) Eine seltene Bildungsanomalie der weiblichen Genitalien. Med. Dissertation, Universität Erlangen
8. Griffin JE, Edwards C, Madden JD, Harrod MJ, Wilson JD (1976) Congenital absence of the vagina: the Mayer-Rokitansky-Kuster-Hauser syndrome. Ann Intern Med 85: 224–236
9. Grover S, Solanki BR, Banerjee M (1970) A clinicopathologic study of Müllerian duct aplasia with special reference to cytogenetic studies. Am J Obstet Gynecol 107: 133–138
10. Gruenwald P (1941) The relation of the growing Müllerian duct to the Wolffian duct and its importance for the genesis of malformations. Anat Rec 81: 1–19
11. Hauser GA, Schreiner WE (1961) Das Mayer-Rokitansky-Küster-Syndrom. Uterus bipartitus solidus rudimentarius cum vagina solida. Schweiz Med Wochenschr 91: 381–384
12. Holzbach E (1909) Die Hemmungsbildungen der Müller'schen Gänge im Lichte der vergleichenden Anatomie und Entwicklungsgeschichte. Beitr Geburtshilfe Gynakol 14: 167–221
13. Holzbach E (1910) Zur Genese kombinierter Nieren-Uterus-Missbildungen. Monatsschr Geburtshilfe Gynakol 32: 406–415
14. Hönigsberg M (1902) Ein Fall von angeborener Missbildung des Urogenitaltractes. Monatsschr Geburtshilfe Gynakol 15: 762–771
15. Horstmann E, Stegner H-E (1966) Tube, Vagina und äussere weibliche Genitalorgane. In: Möllendorff W von (Hrsg) Handbuch der mikroskopischen Anatomie des Menschen, vol VII/4. Springer, Berlin Heidelberg New York, S 1–213
16. Huffman JW (1948) Mesonephric remnants in the cerivx. Am J Obstet Gynecol 56: 23–40
17. Keibel F (1896) Zur Entwicklungsgeschichte des menschlichen Urogenitalapparates. Arch Anat Physiol, Anat Abt, S 55–156
18. Keith A (1921) Human embryology and morphology, 4th edn. Arnold, London
19. Klinger HP, Ludwig KS (1957) A universal stain for the sex chromatin body. Stain Technol 32: 235–244
20. Kussmaul A (1859) Von dem Mangel, der Verkümmerung und Verdopplung der Gebärmutter, von der Nachempfängniss, und der Überwanderung des Eies. Stahel'sche Buch- & Kunsthandlung, Würzburg

21. Küster H (1910) Uterus bipartitus solidus rudimentarius cum vagina solida. Z Geburtshilfe Gynakol 67: 692–718
22. Ludwig KS (1968) Zur funktionellen Morphologie des menschlichen Ovariums unter Einwirkung von Oestrogen-Gestagen-Kombinationspräparaten. Gynakol Rundsch 6: 241–251
23. Ludwig KS (1969) Normale Entwickung und Entwickungsstörung des weiblichen Genitales. In: Käser O, Friedberg V, Ober KG, Thomsen K, Zander J (Hrsg) Gynäkologie und Geburtshilfe, vol I. Thieme, Stuttgart New York, S 71–92
24. Ludwig KS (1993) The development of the caudal ligaments of the mesonephros and of the gonads: a contribution to the development of the human gubernaculum (Hunteri). Anat Embryol 188: 571–577
25. Mayer CAJ (1829) Über Verdoppelungen des Uterus und ihre Arten, nebst Bemerkungen über Hasenscharte und Wolfsrachen. J Chir Augenheilkd 13: 525–564
26. Meyer R (1909) Zur Kenntnis des Gartner'schen (oder Wolff'schen) Ganges besonders in der Vagina und dem Hymen des Menschen. Arch Mikros Anat 73: 751–792
27. Muehl G (1902) Rudimentäre Entwickelung von Uterus und Vagina. Med. Dissertation, Universität Greifswald
28. Nagel W (1889) Über die Entwickelung des Urogenitalsystems des Menschen. Arch Mikros Anat 34: 269–384
29. Nation EF (1944) Renal agenesia. A study of thirty cases. Surg Gynecol Obstet 79: 175–181
30. Noyes RW, Hertig AT, Rock J (1950) Dating the endometrial biopsy. Fertil Steril 1: 3–25
31. O'Rahilly R, Muecke EC (1972) The timing and sequence of events in the development of the human urinary system during the embryonic period proper. Z Anat Entwicklungsgesch 138: 99–109
32. Papp Z, Gardó S, Herpay G, Árvay A (1970) Developmental anomalies of the Müllerian ducts. Cytogenetic findings in 28 patients. Schweiz Z Gynakol Geburtshilfe 1: 115–121
33. Rieder C (1884) Über die Gartner'schen (Wolff'schen) Kanäle beim menschlichen Weibe. Virchows Arch 96: 100–130
34. Rokitansky C (1838) Über die sogenannten Verdoppelungen des Uterus. Med Jb Österreich Staates 26: 39–77
35. Schiff EL (1872) Das Ligamentum uteri rotundum. In: kk Gesell der Ärzte (eds) Med Jahrbücher 1872. Braumüller, Wien, S 247–251
36. Schmid-Tannwald I, Girotti M, Hauser GA (1973) Die Formalgenese weiblicher, innerer Genitalaplasien, speziell des Mayer-Rokitansky-Küster-Syndroms. Zentralbl Gynakol 95: 421–428
37. Schröder R (1930) Die weiblichen Genitalorgane. In: Möllendorff W von (Hrsg) Handbuch der mikroskopischen Anatomie des Menschen, vol VII/1. Springer, Berlin, S 329–556
38. Sneeden VD (1958) Mesonephric lesions of the cervix. Cancer 11: 334–336
39. Stirnemann E (1943) Klinische Beobachtungen bei Missbildungen des Uterovaginalkanals. Monatsschr Geburtshilfe Gynakol 115: 187–247
40. Strauch M (1888) Zur Castration wegen functionirender Ovarien bei rudimentärer Entwickelung der Müllerschen Gänge. Z Geburtshilfe Gynakol 15: 138–146
41. Testut L, Latarjet A (1949) Traité d'anatomie humaine, vol 5, 9th edn. Doin, Paris (6e)
42. Turunen A (1957) Über kongenitales Fehlen der Scheide. Ann Chir Gynaecol 46: 125–142
43. Weber W (1969) Zur funktionellen Morphologie des menschlichen Ovariums nach Absetzen von Östrogen-Gestagen-Kombinationspräparaten. Geburtshilfe Frauenheilkd 29: 149– 159
44. Weiser P (1966) Beobachtungen bei Atresie von Uterus und Vagina. Geburtshilfe Frauenheilkd 26: 1388–1394
45. Wendeler P (1895) Die fötale Entwicklung der menschlichen Tuben. Arch Mikros Anat 45: 167–199
46. Werth R, Grusdew W (1898) Untersuchungen über die Entwicklung und Morphologie der menschlichen Uterusmuskulatur. Arch Gynakol 55: 325–413
47. Wetzstein R (1965) Der Uterusmuskel: Morphologie. Arch Gynakol 202: 1–13
48. Wetzstein R, Renn KH (1970) Untersuchungen zur Architektur des menschlichen Myometriums. Anat Anz 126: Erg H 599–600
49. Winckel F von (1899) Über die Eintheilung, Entstehung und Benennung der Bildungshemmungen der weiblichen Sexualorgane. Sammlung klin Vorträge NF Nr. 251/252 (Gynäkologie Nr. 90/91). Breitkopf & Härtel, Leipzig, S 1523–1562