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Congenital anomalies of the reproductive organs

by

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Interest in congenital malformations dates back to the dawn of history but it is only during the past few decades that research workers from all over the world have begun to investigate this problem on a scientific basis. The recent interest in congenital malformations is due to the fact that 15% of all perinatal deaths is due to developmental anomalies. This increase in the percentage of deaths due to congenital malformations should not be interpreted to mean a proportionate rise in the incidence of malformed children in recent years. On the contrary, recent advances in antibiotics, immunology and preventive medicine have brought about a sharp decline in the number of perinatal deaths from other causes so that the percentage of deaths from congenital malformations has shown a relative increase.

It is known that only a small proportion (1-3%) of all live births show developmental abnormalities. Of these, some of the anomalies could be detected easily at birth while others, however, pass unrecognised for a variable number of years. It is rather unfortunate that a majority of malformations pertaining to the reproductive system belong to the latter category and hence one has to be vigilant if abnormalities of the reproductive system are to be detected early.

When one examines a large number of defects belonging to a particular system or organ, it will soon be evident that there is always a gradation leading from the normal to the grossly abnormal. This would imply that both normal and abnormal developments differ neither in principle nor in character. Consequently, a knowledge of normal embryology of the reproductive organs is essential for the understanding and interpretation of the various anomalies which may occur in the reproductive system. A brief account of the development of the uterus, vagina, hymen and female external genitalia is given below before an attempt is made to explain their malformations.

Embryology

Most of the organs belonging to the urogenital system owe their origin to the mesoderm of the intermediate cell mass (intermediate mesoderm) (Fig. 1) while others are derived partly or wholly from the urogenital sinus or from the mesoderm surrounding the sinus. The development of only some of the reproductive organs will be described below.

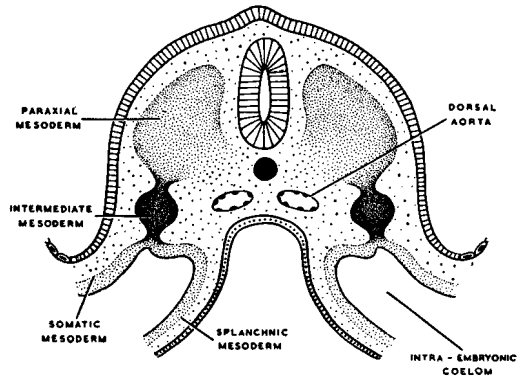

Fig. 1. Transverse section of a somite embryo to show the intermediate mesoderm. (Adapted from Medical Embryology by Langman).

Development of the uterus and vagina

In embryos of about the 10 mm. C.R. lenth, the two paramesonephric ducts commence their formation as invaginations of the coelomic epithelium. The lips of the grooves fuse resulting in the formation of bilateral ducts (Fig. 2) whose cranial extremities open into the peritoneal cavity. The formation of the ducts continues in a caudal direction and the two ducts fuse with one another at about the 20 mm stage in what is

known as the urogenital septum. At this stage, three different portions of the paramesonephric ducts could be observed: (1) cranial vertical segment (2) intermediate horizontal segment and (3) caudal vertical segment (Fig. 3). Of these, the cranial vertical and the intermediate horizontal segments are known to give rise to the fallopian tubes while the caudal vertical segment gives rise to the utero-vaginal canal. At about the 40 mm stage, the body of the uterus could be distinguished from that portion which is destined to give rise to the cervix. The lower end of the vertical segment of the utero-vaginal canal forms the solid Mullerian tubercle (Fig. 4A). In embryos of about 60 mm stage two bilateral swellings known as the sinovaginal bulbs make their appearance at the posterior portion of the lower part of the urogenital sinus (Fig. 4B). The sinovaginal bulbs enlarge and fuse with one another across the midline and cranially with the solid Mullerian tubercle. With further growth of the sinovaginal bulbs, the original utero-vaginal canal is carried in a cranial direction.

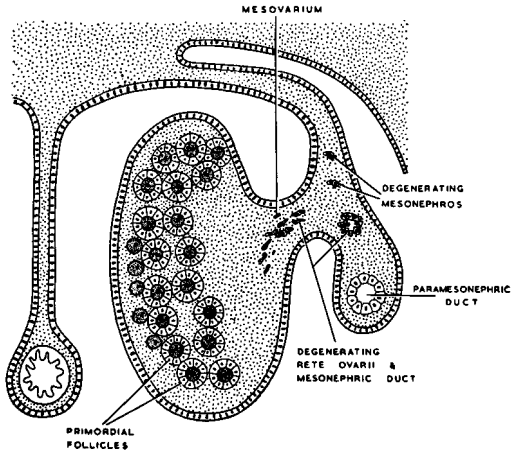

Fig. 2. Transverse section of embryo to show differentiation of the paramesonephric duct and ovary, (Adapted from Human Embryology by Hamilton, Boyd & Mossman).

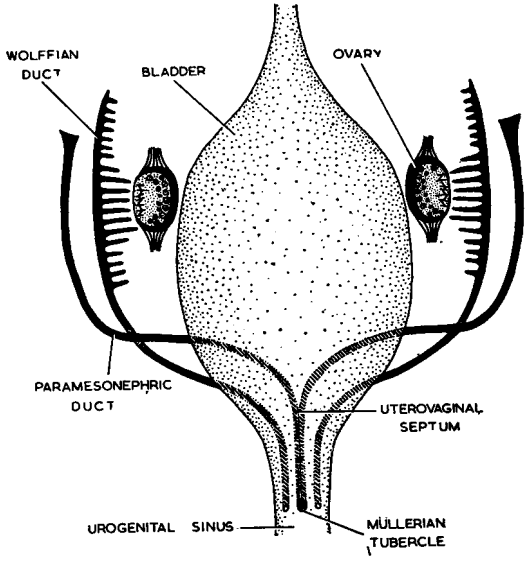

Fig. 3. Ventral view of the developing paramesonephric ducts which lie behind the urogenital sinus. (Adapted from Langman).

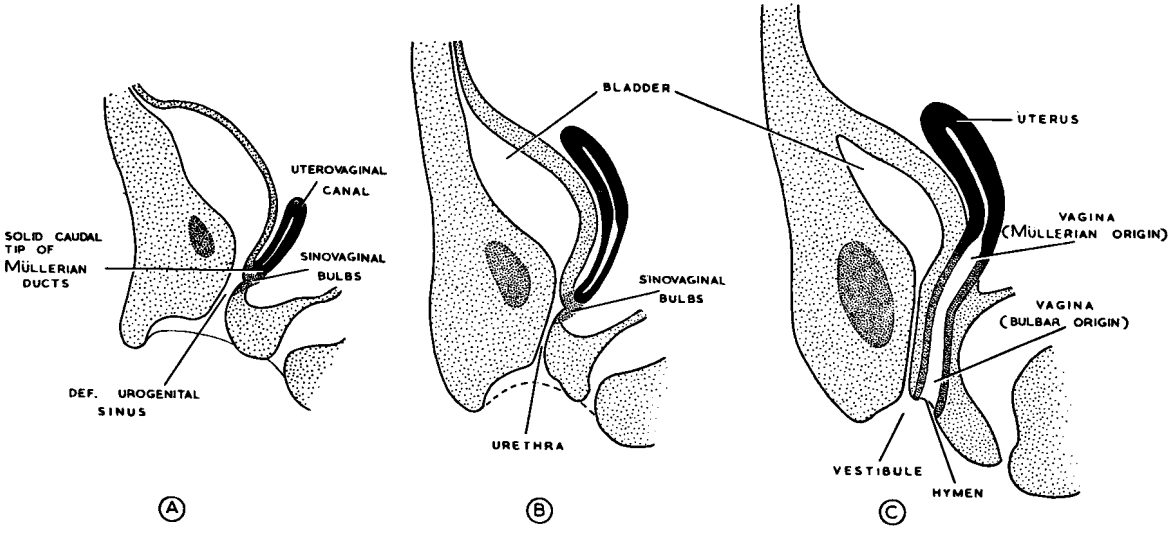

Fig. 4. Stages in the development of the vagina. (Modified from various sources).

Fig. 5

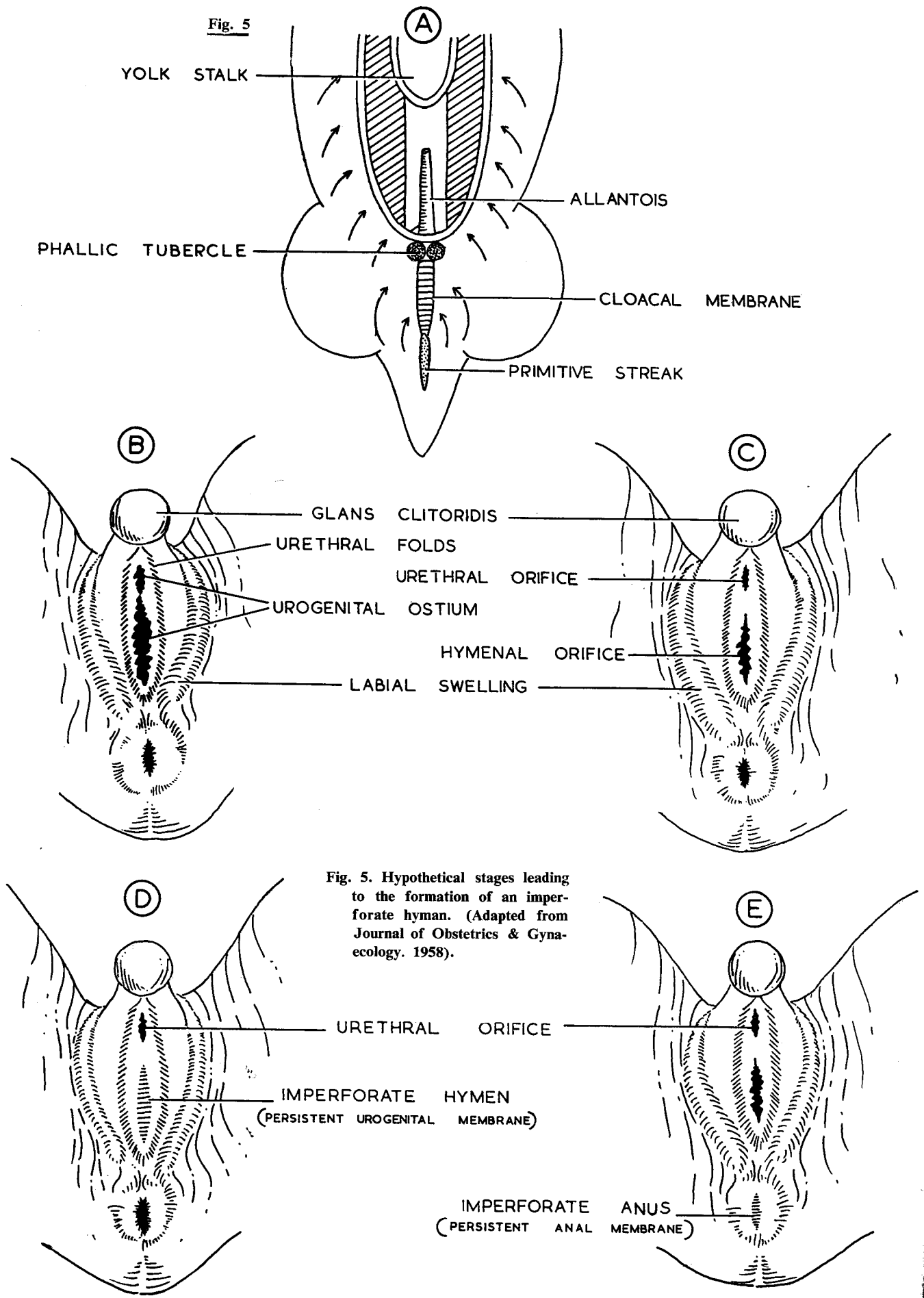

Fig. 5. Hypothetical stages leading to the formation of an imperforate hyman. (Adapted from Journal of Obstetrics & Gynaecology. 1958).

While the development of the uterus from the fused Mullerian ducts is generally accepted, there is still considerable controversy on the development of the human vagina. Thus Bloomfield & Frazer (1927) and Hunter (1930) believe that the whole length of the vagina is formed from the fused Mullerian ducts whereas Mijsberg (1924) thinks that the vagina is formed in part from the mesonephric ducts. However, Hart (1911) is of the opinion that the epithelium of the mesonephric ducts contributes to the formation of the entire vagina. A third group of investigators, on the other hand, have denied the possibility of any contribution from the mesonephric ducts in the development of the vagina. For example, Koff (1933) describes the upper four-fifths of the vagina as arising from the Mullerian tubercle and the lower one-fifth from the fused sinovaginal bulbs whereas Meyer (1934-1938) says that the proliferation of cells from the dorsal wall of the urogenital sinus (sinovaginal bulbs of Koff) gives rise to the epithelial lining of the entire vagina. This view is supported by the recent investigations of Bulmer (1957) on the development of the human vagina.

It is also remarkable that during the early foetal stages, the entire length of the vagina is occluded by a solid epithelial plate. Subsequently the epithelium proliferates but this is usually preceded by proliferation of the mesoderm surrounding the epithelial vaginal plate. The proliferation of the epithelial plate is followed by degenerative changes which commence at the cranial and caudal ends of the plate so that by about 150 mm stage the cervix becomes distinguishable from the vagina. The process of canalisation of the vaginal plate becomes complete in foetuses of 200 mm (Fig. 4C).

Development of the hymen

There are also diverse views on the formation of the hymen. Pozzi (1884) postulated that the hymen and vagina must be developed from two different sources since cases have been reported in which a well-marked hymen was present in the absence of a vagina. Bloomfield & Frazer (1927) and Hunter (1930) believed that the hymen was the result of a "true inversion" of the posterior wall of the urogenital sinus produced by the bulbar lower end of the vaginal epithelial plate. According to Koff (1933), the hymen is the partition between the dilated and canalized sinovaginal bulbs and urogenital sinus. Meyer (1938) found that the opening of the vagina occurred quite independent of the hymen, which might or might not be formed when the vagina opened into the posterior diverticulum of the urogenital sinus. He was of the opinion that the lateral portions of the hymen were formed by the infoldings of the lateral walls of the urogenital sinus, while the posterior part of the hymen was formed as a result of pressure by the plunger-like process of the vaginal cord on the dorsal diverticulum of the sinus.

Development of the female external genitalia

It is clear from Fig. 5 that the labial folds which surround the urogenital ostium give rise to the labia majora while the urethral folds which remain unfused in the female, form the labia minora. The clitoris is developed from bilateral swellings which first make their appearance in the infraumbilical region of the embryo. These swellings subsequently fuse to form the genital (phallic) tubercle which constitutes the primordium of the clitoris.

Explanation of Anomalies

The various anomalies of the reproductive organs, the development of which has already been outlined earlier, can be grouped under the following categories:

Uterine anomalies such as uterus bicornis, uterus unicornis, uterus didelphys with double vagina, etc.

Atresia of cervix and vagina.

Vaginal septa and imperforate hymen.

Recto-vaginal fistula.

Entry of ureter into vagina.

Uterine anomalies

Most of the uterine anomalies are explicable on the basis of an arrest of development. Lack of fusion in a localised area or along the whole length of the Mullerian ducts can account for anomalies such as uterus bicornis, while a failure of fusion of the bilateral sino-vaginal bulbs can

give rise to double vagina. If the latter condition is accompanied by a failure of fusion of the Mullerian ducts it would then result in uterus didelphys with double vagina.

Atresia of cervix and vagina

In the absence of any direct observations on the critical stages of embryos with these malformations there are two possible ways of explaining these anomalies. One is to attribute the anomaly to an arrest of development of a particular segment of cervix or vagina at an early stage and the other is to postulate a localised mesodermal hypertrophy which could prevent the normal development of the affected segment.

Vaginal septa and imperforate hymen

The aetiology of transverse vaginal septa is easily explicable on the hypothesis of a failure of fusion of the two parts of the vagina developed from the Mullerian ducts and the sinovaginal bulbs respectively although it is by no means certain that the vagina is normally developed from these two parts. However, this view is inadequate to explain the occurrence of other varieties of septa described by Monie and Sigardson (1950). Moreover, acceptance of the theory of nonfusion would also imply that the two portions of the vagina arising from the Mullerian tubercle and the urogenital sinus respectively, vary in different cases of cryptomenorrhoea since the obstructing membrane which forms the boundary between the two portions is found at varying distances from the vaginal introitus.

Secondly, if the persistence of the epithelial vaginal plate is regarded as the causative factor in the formation of the various types of septa within the vagina, then it must be admitted that epithelial cells of the vaginal plate are capable of transforming themselves into connective tissue and muscle which were found in the obstructing membrane in some cases (Kanagasuntheram and Dissanayake, 1958). It is therefore, thought that some other factor, such as an abnormal proliferation of the mesoderm surrounding the vaginal plate might be responsible for the formation of vaginal septa whether these be horizontal, saggittal or oblique. It is, of course, well known that mesodermal tissue can become converted into muscular and connective tissue elements which are present within the septa.

The formation of an imperforate hymen is regarded here as an entirely distinct anomaly from vaginal septa just described. The normal embryology of the hymen is unfortunately insufficient to reconcile with the observations that a normal hymen may be present in the complete absence of a vagina, and that the hymen may be imperforate, cribriform, absent or may even extend around the urethral orifice. Consequently, a hypothetical explanation has been advanced by Kanagasuntheram and Dissanayake (1958) who consider that the imperforate hymen is explicable on the same basis as an imperforate anus (Fig. 5). They believe that the abnormal hyperactivity of the primitive streak is responsible for the invasion of mesodermal cells into the urogenital or anal membrane which consequently does not undergo dissolution as it normally does when it is not reinforced by mesoderm.

Recto-vaginal fistula

This anomaly seems to be a recapitulation of the normal condition found in lower vertebrates in which a cloaca persists. A cloaca is also present during early stages of the human embryo till a mesodermal urorectal septum grows down to separate the hind gut from the urogenital sinus (Fig. 6). If the urorectal septum fails to wall off the rectum from the urogenital sinus, the former will open into that part of the urogenital sinus which subsequently gives rise to the vagina (Fig. 7) However, the postition of

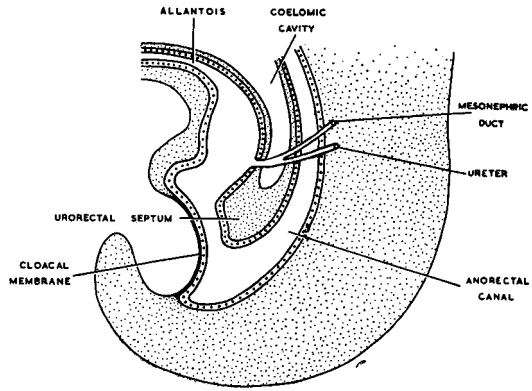

Fig. 6. Sagittal section of an embryo showing the cloacal membrane and the urorectal septum. Note the ureter arising from mesonephric duct. (Modified from various sources).

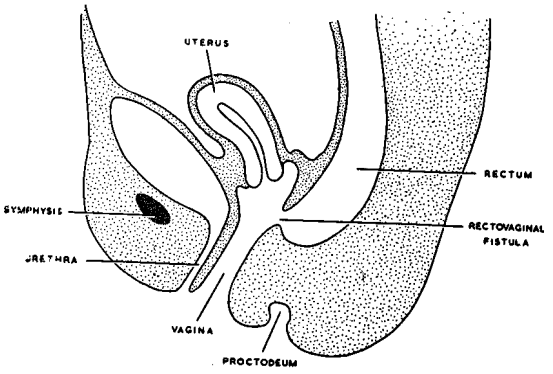

Fig. 7. Diagram illustrating the formation of a recto—vaginal fistual. (Adapted from Langman)

the rectal opening into the vagina is variable and this variability has been discussed in greater detail by Paul and Kanagasuntheram (1956).

Entry of ureter into vagina

The ureter is normally an outgrowth from the mesonephric duct which opens at first into the cloaca and subsequently into the urogenital sinus when the urorectal septum completes the division of the cloaca (Fig. 6). The mesonephric duct is later absorbed into the primitive bladder and the ureter thus acquires a separate opening into the bladder. If, however, there is a failure of absorption of the mesonephric duct into the wall of the bladder, the duct will then carry the ureter along with it and would open into that part of urogenital sinus which is later destined to form the vagina.

A knowledge of the congenital anomalies of the reproductive organs is not one of academic interest only, but it does, for example, help the clinician to give a fairly accurate forecast of the results of a pregnancy occurring in a patient with a bicornuate uterus. Causes of congenital malformations are, in general, ascribed to genetic and environmental factors. It is also generally accepted that about 10% of all malformations are due to genetic causes and another 10% to environmental factors while the majority of anomalies are said to be the result of complex interactions between genetic and environmental systems. It is not altogether clear whether anomalies of the reproductive organs are due to genetic imcompetencies or to environmental changes although the environmental hazards experienced by the fertilized ovum in its journey through the fallopian tube towards the uterus and subsequent to its implantation inside the endometrium are well known. Although anomalies of the reproductive organs in contrast to most other congenital defects occur during foetal stages when the embryo has passed its zenith of differentiation processes, whether subtle and invisible changes which affect later processes of growth and differentiation already pre-exist during early embryonic stages still remains a mystery to us.

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