The assessment of hypospadias

J.F.A. van der Werff

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Van der Werff, J.F.A.

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The assessment of hypospadias

De vaststelling van hypospadie

Proefschrift

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ek is geen profeet nie
ek is een dinges

(Breyten Breytenbach, 1972)

voor mijn ouders:

J.F.A. v.d Werff, 12/6/1922 -15/3/1978
A.A. v.d. Werff- Veerkamp, 5/10/1922 - 11/10/1990

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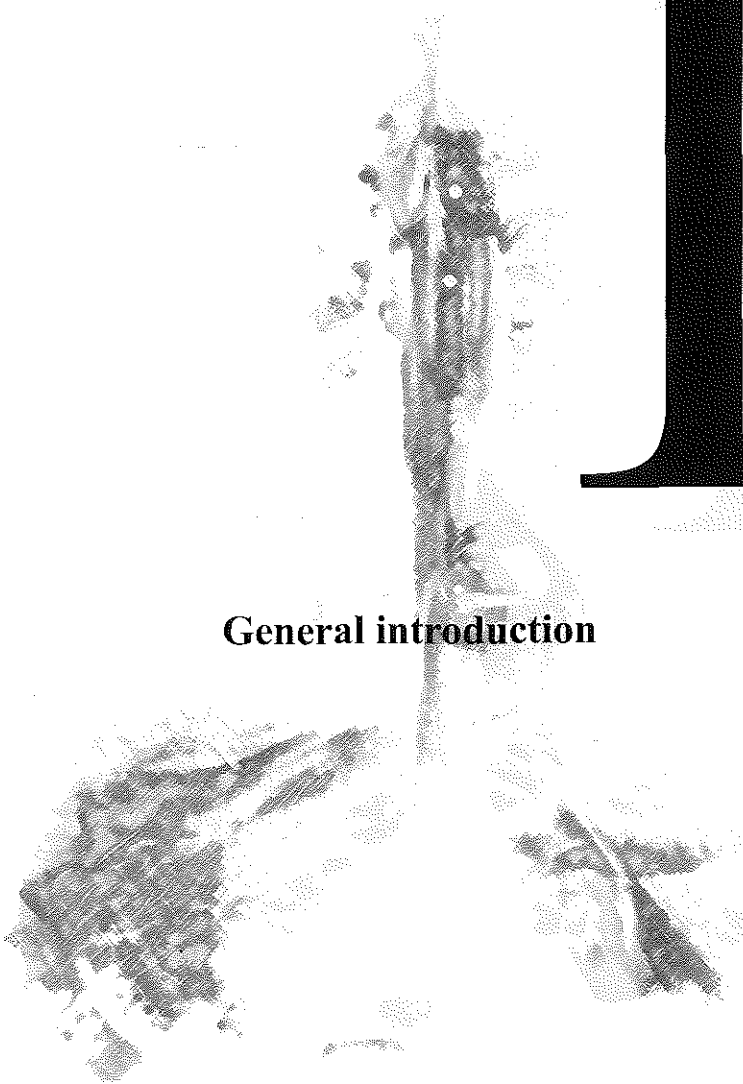

General introduction

Υποσπαδιας εστι παθοζ εφ ου η βαλανος εφειλκυσται.η εστι παθοζ εφ ου η βαλανος αποκειται και το της ουρηθρας τρημα υποκειται.

Galenus (130-200 AD)

Definition, incidence, aetiology and embryology

Hypospadias is a congenital anomaly involving the anterior urethra that can affect both men and women. The deformity is characterised by a dystopia of the external orifice of the urethra and can be associated with a curvature of the penile body in male subjects. The incidence of hypospadias in men is estimated as one in two to three hundred live male births and seems to be increasing although it varies according to the registration system used, geographical area and racial influences [1].

The precise aetiology of this anomaly remains unclear, although certain risk factors can be assessed. For instance, hypospadias is known to cluster in families but little else is definitive about the genetics involved in its aetiology and it still seems to be a multifactorial anomaly [2-6]. Early exposure to progestins in utero during organogenesis also appears to be of influence in the development of hypospadias with a twofold relative risk [7]. Because of the sporadicness of this exposure and hypospadias it is, however, difficult to demonstrate a definitive association [3]. Another factor held responsible as a possible cause of hypospadias is a local vascular insufficiency of the embryo during pregnancy [8].

The morphogenesis of the male external genital system and therefore the hypospadias deformity as well, have been the subject of controversy in the past [9-11]. Glenister, a lecturer at the Charing Cross Hospital Medical School in London, contributed a substantial amount of knowledge on the development of the male external genital [9,12,13]. His general concept of the embryogenesis of the male anterior urethra has had very little opponents in the literature. Some details, such as the formation of the glandular part of the urethra or the onset of preputial development, are challenged by others [14-18]. Searching for cellbiological mechanisms like cell proliferation and apoptosis, responsible for normal development of the male genital system, it is striking to find nothing on this subject in the literature.

Treatment

Although the goals of treatment of hypospadias have not changed (straight penis, terminal meatus with good function and cosmesis), for centuries this treatment has posed surgeons major problems. Dieffenbach has been credited to be the founder of modern hypospadias

repair although his technique failed [19]. Several attempts were made at the end of the 19th century to solve the problems in hypospadias repair. Nevertheless, a quotation by Russell gives an indication of the standard of care in those days [20]: " It has been suggested that in view of the hopelessness of providing the subject with an effective sexual organ, it would be a wise and humane proceeding to perform castration in childhood." Obviously he was discussing the more severe type of hypospadias, but it clearly shows that progress had not been tremendous. From the beginning of the 20th century, three French schools of hypospadias surgery came to blossom, all with different techniques. Duplay introduced two techniques, based on parallel incisions on the penile skin to provide flaps to form a tube, which was covered by undermining of penile skin [21, 22]. Nové-Josserand [23] used a free skin graft tunnelled through the glans and Ombrédanne utilised a buttonhole incision in the preputial skin to cover the neo-urethra and ventral shortage of skin after orthoplasty [24]. From the American front, Blair [25] is to be credited to be the forerunner of Byars' wellknown technique of orthoplasty and urethroplasty [26]. Other important surgeons in the first half of the 20th century were Denis Browne, Ormond Culp and Reed M. Nesbit [27-29]. By the time we reach the late nineteen fifties, already more then 150 techniques used for urethroplasties were described and progress in success rates was slow. Testimony to this slow progression are two citations from that era:

"..... In conclusion, hypospadias is a fascinating and challenging surgical problem, the more so because poor results are so obvious that they cannot be overlooked." This statement of historical interest was put down on paper by Creevy in 1958 who reviewed the literature on operative techniques for hypospadias and their results [30].

" ... It is unlikely that there ever will be complete agreement as to how and when congenital chordee and hypospadias should be corrected." (Culp [28]).

As stated, at the end of the nineteen fifties results following hypospadias repair were not satisfactory, with urethrocutaneous fistula, meatal stenoses, residual curvature and calculi from hair bearing urethral skin posing a lot of problems. It is therefore probably not without coincidence that in 1964 three young plastic surgeons in Holland separately published their thesis on the treatment of hypospadias [31-33]. Heybroek presented a modification of Ombrédanne's technique called the Groningen method of hypospadias repair for distal hypospadias [31]. The fistula rates with this technique were twelve percent for distal hypospadias and thirty to fifty percent for more proximal cases. Roldaan and Nicolai in 1989 presented their results with this technique [34]. No other reports on this procedure are available from the literature. From Utrecht, Lamaker published a thesis on the use of a Duplay orthoplasty and a Denis Browne urethroplasty as well as a "new" technique [32]. The only thing new about Lamakers' technique was the undermining of the skin flaps covering the buried skin strip. He presented a fistula rate of seventy percent for the "old" Denis Browne repairs, whereas his modification showed fistulas in twenty-five percent of patients. But, fistulas from this 'new' technique were more difficult to treat. No additional reports in the literature can be found on this technique. Van der Meulen from

Rotterdam introduced a truly new technique or better yet a philosophy on hypospadias repair [33]. He made an analysis of the possible factors responsible for postoperative complications in hypospadias surgery and suggested solutions to solve these problems. The rotation of dorsal skin as a well vascularised flap by using a backcut, avoiding superposition of suture lines, adequate release of curvature, using drainage instead of urinary diversion, simple noncompressing dressings and staged repairs when necessary were all part of this philosophy. His treatment was based on embryological insights [9, 33]. Numerous papers on his techniques have been written since, including the results of other surgeons using his techniques, midterm follow up and psychosexual adjustment of his own patients [35-46].

Although everything had been tried before (skin grafts, rotation flaps, advancement, meatal based flaps, one stage repairs, two stage techniques, etc.), the last forty years of this century have been overwhelmed with "new" techniques or modifications, even better sutures, more delicate tissue handling, etc. [47]. For clearness we shall focus on those techniques that have had followers in the literature and leave the one-day fly techniques for what they are. Although Backus and DeFelice [48] stated that: " ...there is general agreement that the chordee correction and the urethroplasty should be carried out as separate operations...", the main characteristic of the techniques of the last four decades was their strive for one stage repairs in all forms of hypospadias. Browsing the literature, it is difficult to tell who was first with what. Reading a chapter written by Hodgson [49], he states that both Hodgson (first) and Asopa (second) started using a rotated inner face island flap from the prepuce. With this, Hodgson is to be credited for either a defective memory or lack of knowledge of his own technique, because he did not *rotate* his flap but instead used a *buttonhole* to transfer the preputial skin to the ventral side as many surgeons did in that era [50,51]. He did not use a backcut so his flap was still attached and therefore by definition was not an island flap. In contrast, Asopa [52] did use a backcut in the preputial skin to *rotate* his dorsal inner lining flap. When we turn to a paper by Harris [53], he claims to have developed a preputial island flap in England at the same time Asopa did in India. One thing can be agreed upon regarding the preputial island techniques: it was Duckett who popularised their use by presenting an enormous number of patients [54,55].

Apart from preputial island flaps, free grafts where frequently used in the last forty years. Devine and Horton [56] started publishing their results and Bracka founded his two stage technique with free skin grafts on a survey of his teachers' bad results [57,58].

Another issue that regained interest was the matter of closing the glans in hypospadias repair [59,60]. At the same time it has again become more fashionable to either restore or save the prepuce for cosmetic reasons [34]. Concerning postoperative care, circular dressings (silastic foam) and suprapubic diversion were reinvented, although the decline in Public Health budgets forced some surgeons to perform day care surgery without the use of urinary diversion on patients with hypospadias [61,62].

If we try to value the merits of the advances made in hypospadias surgery by a single

technique or a single surgeon, we should assess the following: is the presented technique new or is the modification essential, was a sufficient number of patients treated by this method, are the results predictable and reproducible (in other words, are there reports on the same technique by other surgeons), are data available on the short-term and long-term outcome of this particular technique ?
The techniques of Ombrédanne, Denis Browne, Duplay and Mathieu in particular have been used and evaluated at long-term by a number of surgeons [63-69]. Other techniques that were reviewed at long-term follow up but did not have any followers in the literature are those by Culp and Harris [70,71]. The techniques advocated by Duckett for correction of mild hypospadias (MAGPI procedure) and the more severe types (transverse preputial island flaps and onlay island flaps) have been globally used and reported although long-term results still have to be awaited [72-75].

Aims and structure of the study

In an ideal, but probably Utopian world, operative techniques for congenital malformations are based on the pathoembryology of the disorder involved. This makes knowledge on the normal development of a particular organ system of paramount importance. With this knowledge, a classification system according to the defect in embryogenesis can be built, thereby giving a firm base for differentiated treatment. For hypospadias this all is still illusory.
The aims of this thesis therefore were the elucidation of the normal development of the male anterior urethra and the explanation of the pathoembryology of this region. With this we hoped to be able to propose a classification of the hypospadias deformity. Because van der Meulen based his operative techniques on embryological insights from Glenister [9,33], this gave us the opportunity to investigate his long-term results and to try and travel to Utopia.
In order to study the normal development of the male anterior urethra, a start was made by categorising the collections of embryonic sections (human and mouse) of the Departments of Anatomy in Rotterdam and Leiden, based on the stage of development and sex. Furthermore, important developmental stages for urogenital embryogenesis were microscopically evaluated, specifically paying attention to the occurrence of fusion processes and apoptosis (programmed cell death). Because apoptosis can be difficult to distinguish in older specimens due to the fixation and staining processes used in the past, histologic sections as well as whole mounts of mice specifically marked for programmed cell death with Annexin-V Biotin were studied. The results of these studies were compared with the knowledge on embryogenesis of the urethra from the literature and a hypothesis on the formation of the male anterior urethra was posed (chapter two). Based on this theory of development of the urethra, the literature was searched for the malformations closely related to hypospadias. A lack of consensus in the nomenclature and description of

these anomalies, challenged us to propose a classification for these malformations and hypospadias, which emphasises their similarities and differences, superposed on the pathoembryology of the anterior urethra (chapter three).
Concerning the long-term results of hypospadias repair, it was felt mandatory not only to assess the somatic outcome of patients treated for hypospadias but to establish their psychosexual and psychosocial adjustments as well [46]. For this reason, a start was made to review the patients records of all individuals operated for congenital malformations of the male external genital system at the University Hospital Dijkzigt, the affiliated St. Franciscus Gasthuis and the Sophia's Children's Hospital, together comprising one Plastic Surgery unit in Rotterdam. From this database, the patients operated for hypospadias were selected for further studies. Two surgeons in the unit were responsible for the treatment of hypospadias in the period studied. They both only used their own techniques, described in chapter four, in a prospective but not randomised way, using their respective strategies for urinary diversion and postoperative dressings. Therefore it was possible to compare the complications of both repairs with respect to diversion and dressing techniques (chapter five).
Because the end results of hypospadias repairs can only be assessed after puberty, long-term follow-up studies are of paramount importance. Particularly in the field of hypospadias surgery, trends and fashions seem to be more important then a thorough assessment of problems and possible solutions. Consequently, relatively few reports on the long-term results are available from the literature. From this study, a uroflowmetry assessment of patients operated for hypospadias was made to establish long-term functional results (chapter six). Moreover, patients were reviewed at long-term by using a questionnaire combined with a physical examination. The results of this study for the primary referred patients are given in chapter seven, whereas the outcome for secondary referred patients (hypospadias cripples) is dealt with in chapter eight. All results from these studies were compared with data from relevant literature references.
To stress the importance of all the factors responsible for complications in hypospadias surgery, a chapter with a somewhat higher degree of philosophical content with a general discussion and conclusions finishes this thesis (chapter nine).

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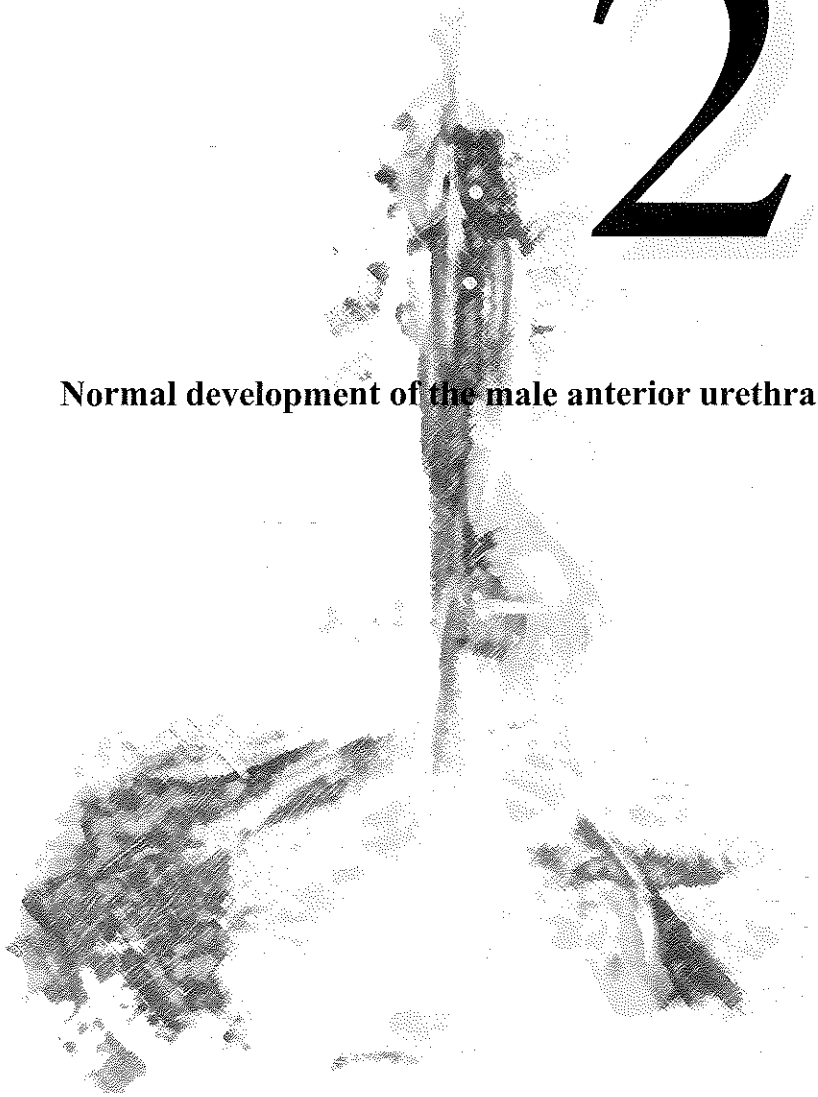

Normal development of the male anterior urethra.

Introduction

Understanding the normal embryonic development is of paramount importance for explaining the pathogenesis of congenital malformations such as hypospadias. Although morphologically the developmental sequence of the male external genital has been studied extensively, several controversies still exist (Kluth et al., '88; Glenister, '54; Hunter, '35; Jones, '10; Rowsell and Morgan ,'87; Spaulding, '21; Kluth et al., '89; Van der Putte, '86; Kluth et al., '95; Van der Putte and Neeteson, '83).

Firstly, the scrotum is said to be formed by fusion of either the genital swellings, labioscrotal swellings or the urethral folds (all seemingly used as synonyms; Glenister, '54; Sadler, '95; Bellinger, '81; Duckett ,'86). Vermeij-Keers et al. ('96), however, disputed this fusion theory by stating that the scrotum develops by a process called merging (Glenister '54).

Secondly, the penile urethra is commonly thought to arise through fusion in the ventral midline of the penile shaft (Glenister, '54; Hunter, '35; Jones, '10; Spaulding, '21) although this is contradicted by reports stating that the urethra is already present before rupture of the cloacal membrane (Kluth et al, '88; Van der Putte, '86).

Thirdly, opinions differ about the formation of the glandular part of the urethra and its orifice. Some authors describe ingrowth of an ectodermal cord from the tip of the genital tubercle to form the glandular urethra (Sadler, '95), whereas Vermeij-Keers et al ('96) believe that fusion of both arms of the genital tubercle followed by the formation and subsequent disruption of an epithelial plate is responsible for development of this part of the urethra. Other reports postulate that both processes (ingrowth *and* fusion together), give rise to the glandular urethra (Glenister, '54).

In contrast to the capacious description of morphogenesis in textbooks and journals (Kluth et al, '88; Glenister, '54; Hunter, '35; Jones, '10; Rowsell and Morgan, '87; Spaulding, '21; Kluth et al, '89; Van der Putte, '86; Kluth et al, '95; Van der Putte and Neeteson, '83; Bellinger, '81; Duckett, '86), control of the basic morphological changes in the developing male external genital, is largely unrevealed in the literature. According to Vermeij-Keers et al. ('83, '90, '96), apoptosis (i.e. programmed cell death) plays an important role in the fusion of swellings and luminisation of tubular structures. Apoptosis is a phenomenon that has been described as early as the late nineteenth century (Clarke and Clarke, '96) and is considered to be important for normal embryonic development (Glücksmann, '51). Many developmental processes have been postulated to be partly regulated by the time and area dependent death of cells (Wyllie et al, '80).

Although commonly misnamed as the simply growing together of two or more structures, fusion is a distinct basic morphological process that can be categorised in three phases. Starting with the outgrowth of swellings, i.e. mesodermal cores covered by an epithelium (phase 1), these swellings reach each other and show signs of adhesion of their epithelial

linings. In this way an epithelial plate of a double layer of ectoderm/endoderm is formed (phase 2). After apoptosis within this epithelial plate causing disruption of the two epithelial layers including their basement membranes, the process of fusion is completed (phase 3). As a result, the two mesodermal cores of both swellings unite.
During a fusion process, formation of a tubular structure can take place by either primary or secondary luminisation. When the epithelial linings of two swellings have adhered (phase 2 of the fusion process), a lumen may be directly included (Fig. 1A). This is called primary luminisation. Examples of structures formed through this process are the formation of the neural tube, the primary nasal cavity, the eye lens and the ear vesicle (Vermeij-Keers et al, '83).

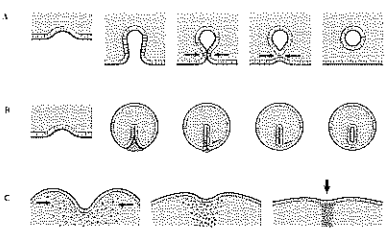

Fig 1A Fusion with primary luminisation in three phases: outgrowth of swellings adhesion of these swellings and apoptosis causing disruption of the formed epithelial plate (arrows). A lumen is directly included in this process.

Fig 1B Fusion with secondary luminisation in three phases: outgrowth of swellings with the formation of a solid epithelial plate, apoptosis causing disruption of this plate (arrows). Within the solid epithelial cord a lumen is formed secondarily by apoptosis.

Fig 1C Merging is the joining of outpocketings as a result of regional variations in growth rates (small arrows). No epithelial plate is formed and at the site of joining, a raphe remains (arrow)

When adhesion of the epithelial linings of two swellings gives rise to a solid epithelial plate consisting of a double layer of ectoderm/endoderm (phase 2 of the fusion process), followed by disconnection of this epithelial plate from the surface by apoptosis (phase 3 of fusion process), a solid epithelial cord results. At a later stage a lumen is formed within this epithelial cord through apoptosis, i.e. secondary luminisation (Fig. 1B). This sequence of events can be observed in the embryogenesis of, for instance, the nasolacrimal duct (Vermeij-Keers et al, '83).
Merging is another basic morphological process involved in embryogenesis and was introduced by Patten ('53). Merging concerns squeezing out of a groove between two outgrowing swellings with neither adhesion of the epithelial linings of these swellings nor formation of an epithelial plate. Therefore, by definition, this process must be distinguished from fusion (fig. 1C).
Taking the above mentioned basic morphological processes into account, human embryogenesis can be partitioned in an early (Crown-Rump Length (CRL) <17 mm) and a late embryonic period (CRL >17 mm) (Vermeij-Keers et al, '96; Nievelstein et al, '98).
The intention of this study is to elucidate the basic morphological processes and sequential steps in the development of the male external genital, in particular the male anterior urethra. Special attention will be paid to the significance of apoptosis in this respect.

Materials and methods

Human embryos and foetuses

From the collections of the departments of Anatomy and Embryology at the Universities of Rotterdam, Leiden and Amsterdam, 80 human serially sectioned embryonic and foetal specimens of indifferent or male sex were reviewed, with an emphasis on embryonic developmental stages. Crown-Rump Length of the specimens ranged from 5 mm to 115 mm and the directions of section were either sagittal, oblique, horizontal or transverse. The staining technique of the specimens was Hematoxylin/Eosin (HE) or Hematoxylin alone. The thickness of section was either 5 µm, 10 µm or 20 µm.

Observations were made on the caudal structures of the embryo: cloacal membrane, genital tubercle, urogenital and labioscrotal swellings or folds, urogenital sinus and urorectal septum. Because these structures are thought to be important in morphogenesis, they were specifically searched for the presence of epithelial plates and apoptotic cells. Whenever possible, findings were checked for consistency in specimens with the same C-RL but a different direction of sectioning.

Mouse embryos

Twenty four serially sectioned mouse embryos of indifferent stages and male sex (CPB-S strain from 10.6 -17.8 days post coitum (p.c.) ; HE- staining, various directions of sectioning) and staged according to Goedbloed ('72) were included, because apoptosis is more easily recognised in freshly fixated tissues.

Moreover, 8 FvB mouse embryos from 10-13 days p.c. were microinjected with biotynilated Annexin V (AnxV-biotin; APOPTEST-BIOTIN, product B500; NeXins Research BV, Hoeven, The Netherlands), which is a specific in vivo apoptosis marker (Van den Eijnde et al, '97) . We performed the experiments and processed the embryos for the detection of apoptotic cells at the whole mount level and in paraffin sections as already described in detail by Van den Eijnde et al. ('97). For whole mount use, five embryos from 11-13 days p.c. were locally injected with AnxV-biotin. The other embryos were injected intracardially.

Results

Human embryos

Early embryonic period (C-RL < 17 mm)

In the 5-7 mm embryos, the cloacal membrane is a distinct structure bordered anterolateral by the horseshoe shaped genital tubercle (Fig. 2). The paired swellings of this genital tubercle have established the second phase of the fusion process, i.e. ectodermal contact in the median plane. The proximal part of the genital tubercle forms a slitlike groove with the cloacal membrane at its bottom. The epithelial plate that is formed by the adhesion of both

swellings, runs from the tip of the genital tubercle to the cloacal membrane (Fig. 2). During rapid proliferation of surface and neural ectoderm, the embryo folds in three directions to form a cylinderlike structure. As a consequence, part of the yolk sac and its diverticulum, the allantois, become incorporated in the embryo. The extra-embryonic mesodermal linings of these two structures fuse to form the urorectal septum. This septum separates two cavities that enter the cloaca in anteroposterior direction with the primitive urogenital sinus or the allantois anteriorly and the anorectal canal posteriorly (previously the yolk sac). In the 5-7 mm embryos this situation has already been established. During the folding process, there is progressive elongation of the genital tubercle and thinning of the cloacal membrane due to apoptosis as visualised in the 9 mm embryo (Fig. 3).

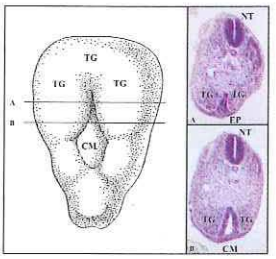

Fig. 2
Schematic representation of the caudal part of a 5-7 mm human embryo in ventral view. The genital tubercle (TG) is a horseshoe shaped swelling with the cloacal membrane (CM) at its bottom (drawing). Cross section micrographs in oblique direction of a human embryo, show the paired swellings of the genital tubercle with a solid epithelial plate (EP) in the median. The continuity with the cloacal membrane is shown in B, NT is neural tube. (adapted from Vermeij-Keers et al. ('96))

At about the 16 mm stage, the genital tubercle has a distinct epithelial plate in the median which is continuous with the future urethral plate of the cloaca and the cloacal membrane. The cloacal membrane is thinner as a result of programmed cell death, but is still intact. The multilayered epithelium of the early stages (Figs. 2 and 3) has changed to a thin membrane of one to four cell layers. The distance from the urorectal septum to the cloacal membrane has decreased in comparison with the 9 mm

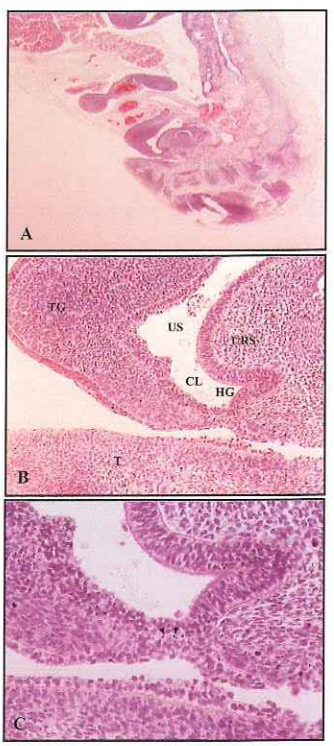

Fig. 3
Sagittal section of a 9 mm human embryo. The genital tubercle has elongated, the primitive urogenital sinus and cloaca can be seen (US and CL in B) with the urorectal septum in between (URS in B). Within the cloacal membrane apoptosis is present (arrows in C).

stage, but the two structures do not meet and no separate urogenital and anal membranes are observed (Fig. 4).

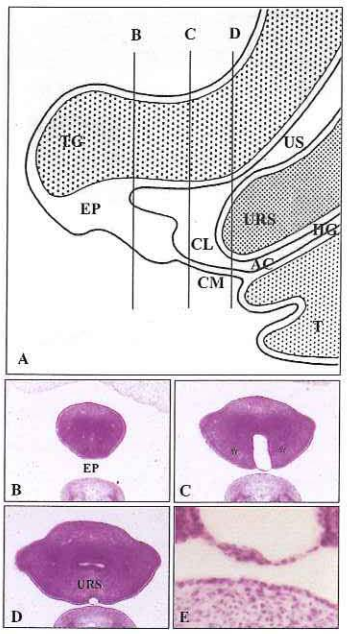

Fig. 4
Schematic representation and frontal sections of a 16 mm human embryo.
A Sagittal diagram of a 16 mm human embryo with indications of frontal crosssections seen in B-D. The urorectal septum does not reach the cloacal membrane.

B Frontal section through the genital tubercle. An epithelial plate is present between both arms of the genital tubercle.

C Frontal section at the level of the cloaca. The cloacal membrane is a thin structure connecting both urogenital swellings (* in micrograph).

D Frontal section through the urorectal septum. The primitive urogenital sinus is separated from the anal opening by the urorectal septum (URS).

E Detail of **C** of the cloacal membrane where apoptotic cells (arrow) are responsible for further thinning and future rupture of the membrane

The cloacal membrane ruptures at approximately 17-18 mm C-RL, in the presence of programmed cell death (Fig. 5). Subsequent to this rupture, two openings become visible: anteriorly lies the urethral groove representing the definitive urogenital sinus (i.e. the primitive urogenital sinus and ventral part of the cloaca) and posteriorly the anal opening (Fig. 6). The part of the cloaca posterior to the urorectal septum becomes component of the amniotic cavity (* in Fig. 6). The floor of the definitive urogenital sinus constitutes the urethral plate which will form the penile urethra. The tip of the urorectal septum transforms into the future perineum in front of the anal opening (Figs. 6-7). Meanwhile, the genital tubercle has further elongated and the urethral groove is recognised as a

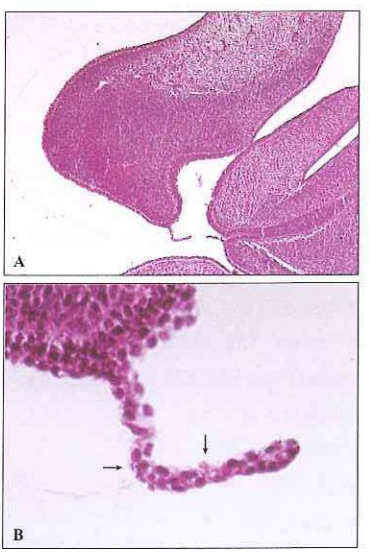

Fig. 5 Sagittal micrograph of an 18 mm human embryo, showing rupture of the cloacal membrane subsequent to apoptotic cell death (arrows in B).

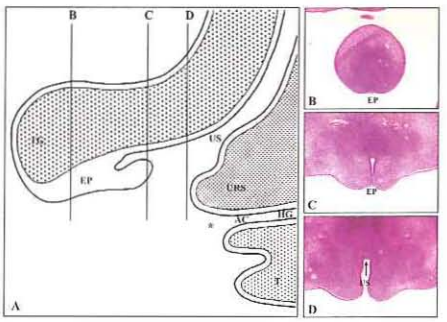

Fig. 6
A Sagittal diagram of an 17-18 mm human embryo after rupture of the cloacal membrane. (* = the part of the cloaca that has been incorporated in the amniotic cavity).
B-D represent sections in the frontal plane.
B Micrograph of a 17-18 mm embryo through the future glans. An epithelial plate is present in the median.
C Micrograph just proximal to the level of the junction between the presumptiveglans and penile shaft. Note the lumen of the definitive urogenital sinus which is visible dorsal from the epithelial plate.
D Section through the definitive urogenital sinus. The floor of this sinus constitutes the urethral plate from which the wall of the penile urethra will be formed (arrow).

slitlike indentation between the urogenital swellings which grow out in a ventral direction. On the lateral sides of the genital tubercle, the labioscrotal swellings have emerged (Fig.7).
The 17-18 mm stage marks the end of the early embryonic period where the external genital system of the embryo still has an indifferent sex. From here on, growth and sex differentiation of this system will take place during the late embryonic period.

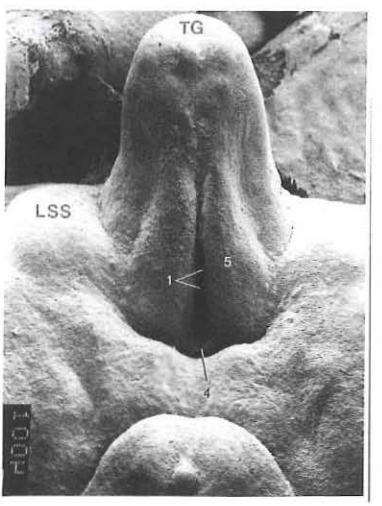

Fig. 7
Scanning electron micrograph of a 17 mm human embryo at the end of the early embryonic period. The genital system is indifferent showing the genital tubercle (TG), opening of the urogenital sinus (1), urogenital swellings (5), labio-scrotal swellings (LSS) and tip of the urorectal septum (4) in ventral view. (from: Hinrichsen V. Humanembryologie. Springer Verlag 1993, printed with permission)

Mouse embryos

Early embryonic period < 13.1 days p.c.

The genital tubercle starts to develop anterior to the cloacal membrane after 10.6 days p.c.. Subsequently, the paired swellings of the tubercle grow out in a ventral direction and form an epithelial plate in the median plane at 11.5 days p.c., which is continuous with the cloacal membrane. The urorectal septum has been incorporated but will never meet the cloacal membrane. Apart from the ad random distributed apoptotic cells, a mass of apoptotic cells is observed in the cloacal membrane, in the endoderm of the tip of the urorectal septum, and in the epithelial plate and

mesodermal cores of the genital tubercle (Figs. 8-9). The cloacal membrane has ruptured dorsally by cell death at 13.1 days p.c. underneath the anal canal. Now, two openings become visible, the urethral groove surrounded by the urogenital swellings and the anal opening. Both openings are separated by the tip of the urorectal septum, which is bilateral continuous with the labioscrotal swellings.

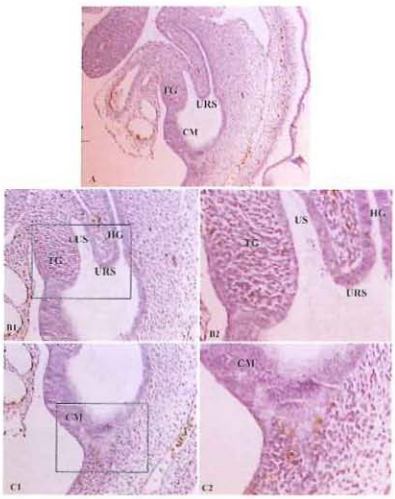

Fig. 8
A Sagittal section of a mouse embryo of 11 days p.c.
B Details of genital tubercle (TG) and urorectal septum (URS, B1), showing apoptosis (brown marked cells, following ANNEXIN V Biotin specific staining (B2).
C Details of cloacal membrane at its dorsal part with overt programmed cell death (brown stained cells).

Fig. 9
A Whole mount photograph of a mouse embryo of 13 days p.c. , in ventral view. Note the presence of apoptosis in the mesodermal cores (arrows) on both sides of the epithelial plate and within this plate in the median plane of the genital tubercle (open arrow).

Human embryos

Late embryonic period (C-RL > 17 mm)

Under the influence of the Y-chromosome, the genital tubercle in male embryos shows a marked anterior growth and differentiation and is now called the phallus with the penile shaft at its base and the glans at its tip. The urethral groove lengthens while the urogenital swellings continue to grow out in a ventromedial direction and start to adhere in the median plane. In this way, the urethral groove is closed off and a double layered epithelial plate is formed between the two urogenital swellings underneath the ventral part of the cloaca. This endodermal plate is in continuity with the earlier formed solid ectodermal plate of the glans. The labioscrotal swellings merge between the base of the phallus and the urorectal septum which, by its position, is now called the perineum. This merging process is both established by posterior outgrowth of the labioscrotal swellings and the rapid anterior outgrowth of the phallus, which "pulls" both labioscrotal swellings between the phallic base and the perineum. In this process of growth and "movement" of the labioscrotal swellings, there is

neither adhesion of these swellings nor formation of an epithelial plate but there is the development of the scrotal raphe in the median plane.
Adhesion of the penile part of the phallus is achieved in proximal as well as distal directions forming the penile urethra. Phase 2 of the fusion process is followed by disruption of the epithelial plates in the glans and the shaft from the surface ectoderm (i.e. phase 3). The line of fusion is marked by the penile raphe which is in continuity with the scrotal raphe. Consequence of phase 3 is that the mesodermal cores of the swellings of the glans and those of the urogenital swellings join on the ventral side of the newly formed urethra. Differentiation of this mesoderm will give rise to the ventral integumental structures of the urethra later during development (for instance the corpus spongiosum and tunica albuginea).
In the 60 mm C-RL embryo, the glandular urethra has been formed as a solid epithelial cord while part of the penile urethra is still in phase 3 of the fusion process (Figs. 1B and 10). Subsequently, an epithelial plug develops in the glandular urethra from the tip of the glans into the urethra of the penile shaft still closing off the lumen. Apoptosis is observed within the plug. It is at this stage in embryogenesis that the prepuce starts to develop as a fold consisting of a core of mesoderm covered by ectoderm (Fig. 10). Within the epithelial plug a lumen is present and so the external urethral ostium has been formed at the 76 mm C-RL stage. During luminisation, apoptotic cells are found in the presumptive urethra. After phase 3 of the fusion process of the penile urethra has finished, the prepuce continues to develop (Fig. 11). When the embryo has reached a length of 115 mm, the prepuce has entirely engulfed the glans

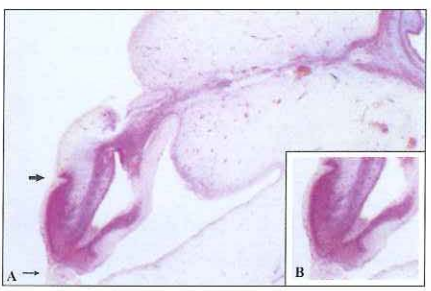

Fig. 10
A Oblique section of a human embryo with a C-RL of 60 mm, with a completed fusion of the glandular urethra (note the epithelial plug, arrow). The fusion-process of the penile urethra (U) is in phase 3. The prepuce starts to develop as a folding from the coronal sulcus (open arrow).
B Detail of the junction between the glans and penile shaft. Note the continuity of the glandular and penile urethra and the epithelial plug.

Fig. 11
Frontal section through the phallus of an 76 mm human embryo. The urethra (U) has been formed entirely, the prepuce (P) covers half of the glans. The epithelial plug in the glandular urethra (arrow) has a small lumen (not shown).

(Fig. 12). The surface ectoderm of the glans and the inner layer of preputial ectoderm are adhered by a cell mass that is continuous with the remnants of the epithelial plug at the tip of the glans.

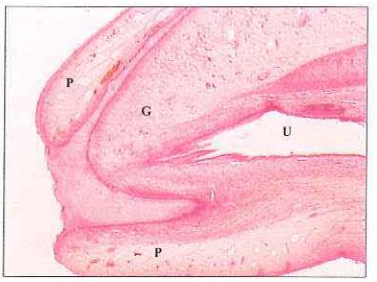

Fig. 12
Close up view of the glans in a 115 mm human embryo in a sagittal section. The prepuce has completely engulfed the glans. (P= prepuce, G= glans, U= urethra)

Mouse embryos

Late embryonic period >13.1 days p.c.

The genital tubercle , i.e. the phallus with the penile shaft at its base and the glans at its tip, grows anteriorly while the urogenital swellings grow in a ventral direction. These swellings adhere and form an epithelial plate continuous with the epithelial plate of the genital tubercle.

The urethral groove will be closed off at 17,2 days p.c.. The epithelial plate in the glandular region starts to disrupt by apoptosis at 14.0 days p.c., forming a solid epithelial cord in the glans which opens between 17.2-17.7 days p.c. by apoptosis and keratinization of the ectoderm (Figs. 1B and 13A). An epithelial plug of the glandular urethra is not observed. The epithelial plate of the penile shaft disappears gradually by programmed cell death starting at 14.1 days p.c. leaving some epithelial pearls in the median (Fig. 13B).

Between the scrotal swellings no epithelial plate is seen. Both swellings are separated by an ectodermal median groove, i.e. the scrotal raphe. The prepuce starts to develop at 15.4 days p.c., grows out and reaches the tip of the glans at 17.2 days p.c.

Within the anal opening an epithelial plug develops closing off the lumen at 14.1 days p.c.. Luminisation of this plug by cell death is observed at 15.2 days p.c..

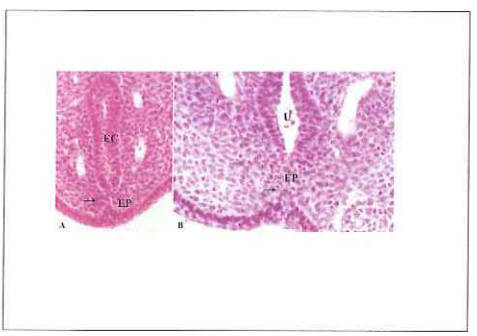

Fig. 13
A Section through the glans of a mouse 14.0 days p.c., showing disruption of the epithelial plate (EP) due to apoptosis (open arrow). In this way the third phase of fusion forms a solid epithelial cord (EC), precluding secondary luminisation.
B Section through the urogenital swellings of a mouse of 14.1 days p.c. with primary luminisation of the penile urethra (U) during disruption of the epithelial plate (EP). Programmed cell death can be observed (open arrow).

Discussion

The development of the male external genital has been a controversy for almost a century (Kluth et al, '88; Glenister, '54; Hunter, '35; Jones, '10; Rowsell and Morgan, '87; Spaulding, '21; Kluth et al, '89; Van der Putte, '86; Kluth et al, '95; Van der Putte and Neeteson, '83; Bellinger, '81; Duckett, '86). When starting with the embryogenesis of the scrotum, Glenister ('54) stated that the entire *perineal* raphe from the anus to the meatus arises from fusion of the urogenital folds and that, as a consequence, the scrotum is formed by fusion. However, our observations showed that: i) the labioscrotal swellings develop bilateral from the urogenital folds or swellings during the early embryonic period, and ii) no epithelial plate is formed between the scrotal swellings and therefore fusion is not evidenced during the late embryonic period. Consequently, the scrotum and its *scrotal* raphe, continuous with the perineal raphe and penile raphe, is formed by merging of the scrotal swellings between the phallus and perineum (Vermeij-Keers et al, '96). The perineal raphe arises from the tip of the urorectal septum.

Concerning the formation of the penile urethra, opinions differ. Glenister ('54) stated that the penile urethra arises by fusion of the primitive urethral groove and the secondary urethral groove, that develops from the urethral plate. Van der Putte ('83) concluded that the male penile urethra is formed by a movement in ventral direction of the urogenital opening relative to the growing perineum and not by fusion of the genital folds. Kluth et al. ('88, '89) described that the urethra is already formed at an early stage from the ventral part of the cloaca and that it arises as a double anlage. They found no signs of fusion or indications of rupture of the urogenital membranes. We suggested that the cloacal membrane is not divided by the urorectal septum to form separate urogenital and anal membranes, as we reported previously (Vermeij-Keers et al, '96, Nievelstein et al, '98). Furthermore, the penile urethra arises from the anterior part of the cloaca through fusion of the urogenital swellings, i.e. primary luminisation. During this fusion process an epithelial plate is formed after adhesion of these urogenital swellings followed by apoptosis and disappearance of that plate leaving the penile raphe on the ventral surface. Fusion of the urogenital swellings results in a continuous mesodermal compartment around the penile urethra. Subsequently, definitive differentiation into the corpus spongiosum and its tunica albuginea takes place.

The formation of the glandular part of the anterior urethra is subject to many theories. Textbooks described the invagination of ectoderm from the tip of the glans during the 4th month as the mechanism of development of this most distal part of the urethra (e.g. Sadler, '95). Glenister ('54) indicated that the proximal part of the glandular urethra is formed by fusion of the urogenital folds and that the distal glandular urethra arises by incorporation

of surface epithelium i.e. ectodermal ingrowth in the 51 mm C-RL embryo. Kluth et al. ('88) stated that the urethra is formed at an early stage without commenting on the formation of the glandular part. In our observations, an epithelial plate in the genital tubercle is formed very early during embryogenesis (C-RL 5-7 mm, human embryos) by outgrowth and adhesion of both swellings of the genital tubercle in the median, i.e. phases 1 and 2 of the fusion process. We found that programmed cell death is responsible for disconnection of this plate from the surface ectoderm later during development thereby forming a solid epithelial cord. Luminisation of this part of the anterior urethra takes place secondarily. In human embryos the formation of an epithelial plug precedes this secondary luminisation. Complete luminisation of the anterior urethra including its orifice and its connection with the penile urethra has been established at 76 mm C-RL of the human foetus.

Because the epithelial plate of the glans is in continuity with the epithelial plate of the urogenital swellings, the formation of the entire anterior urethra is a continuous process. In normal embryogenesis the development of the penile and glandular urethra are thus related.

Timing and nature of morphogenesis of the prepuce are not a matter of much controversy in the literature. Although Hunter ('35) and Glenister ('54) slightly disagree about the onset of development of the prepuce (40 mm and 55 mm , respectively), they both describe the formation of a double layer of ectodermally derived epithelium with mesoderm in between to engulf the entire glans. Their disagreement probably can be explained by the availability of sectioned specimens. We found that the human prepuce first starts to develop at approximately 60 mm C-RL. What is more important in our opinion, is the observation that the formation of the prepuce begins when fusion of the glandular urethra is completed. This finding serves as the basis for a part of the explanation of the external appearance of the penis and its prepuce in the congenital malformation hypospadias (Van der Werff et al., '98).

In conclusion, we feel that basic morphological processes, i.e. luminisation, fusion, merging followed by definitive differentiation, used to describe embryogenesis of structures such as the nose, palate, nasolacrimal duct (Vermeij-Keers, '90), caudal neural tube (Nievelstein et al., '93) and hands (Milaire and Rooze, '83), also apply to the formation of the male anterior urethra. The occurrence of apoptosis plays a very important role in this respect. We feel that the theory presented here not only gives a valid description of the normal development of the male anterior urethra, but can be used to explain the occurrence of congenital malformations in this area as well.

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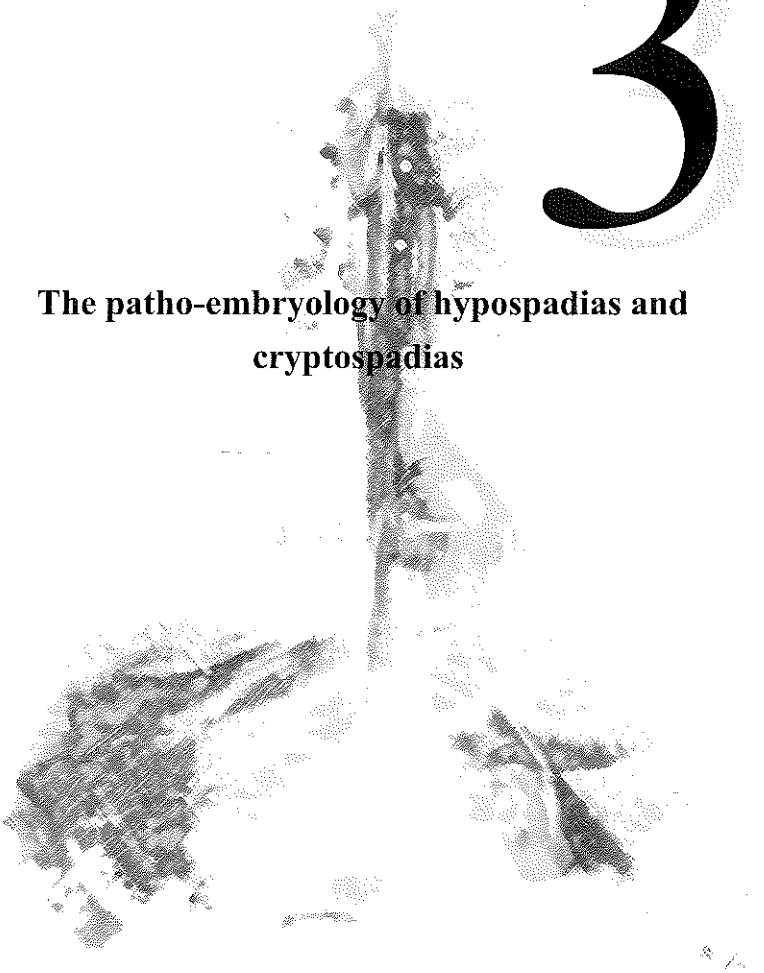
The patho-embryology of hypospadias and cryptospadias



Introduction

Hypospadias represents a major congenital anomaly that is encountered in approximately one in three hundred live male births. Testimony to its difficult treatment are the multitude of operative techniques described in the literature all endowed with their, sometimes high, complication rate [1]. Despite the significance of the problems posed, there seems to be surprisingly little attention for the embryogenesis and pathomorphology of hypospadias and the consequence of this pathology for its treatment [2-5].

Equally remarkable is the lack of observations on the pathomorphology of some infrequent encountered congenital anomalies of the male external genital system that are closely related to hypospadias but differ in certain aspects. The malformations we are referring to can be listed:

* Hypospadias without hypospadias
* Chordee without hypospadias, synonymous with congenital curvature of the penis
* Cryptospadias or cryptohypospadias
* Congenital urethral fistula
* Congenital short urethra

These terms are frequently used for the clinical condition where a penile curvature is associated with a terminal meatus but without giving a precise description of the pathology.

It is the intention of this study to elaborate both on the pathomorphology and the patho-embryology of hypospadias and its related congenital anomalies, based on the normal embryonic development of the male anterior urethra. An attempt will also be made to create order in the nomenclature of these anomalies.

Pathomorphology

Hypospadias

In the sixteenth century, Ambroise Paré [6] already described two forms of hypospadias, namely those with a curvature and those with only an aberrant meatus without curvature. Fascinated by its appearance, Ombrédanne [7] gave a detailed description of hypospadias including a thorough illustration of the association of oblique raphes and the dorsal preputial dog-ears he called "eyes" (fig. 1). Van der Meulen [8] depicted hypospadias having the following external features: meatal dystopia, oblique raphes (with dog-ears) and dorsal hooding of the prepuce as a constant finding as well as the optional occurrence of ventral penile curvature, penoscrotal transposition, scrotal bipartition or penile torsion. No addition to this summary has been made since and everybody seems to agree on the fact that a meatal dystopia is mandatory for hypospadias.

The classic grading of hypospadias uses the position of the urethral orifice at birth and

Figure 1: External appearance of hypospadias showing a dystopic meatus, oblique raphes, curvature and dorsal hooding with dog-ears

comprises perineal, penoscrotal, penile, coronal and (sub) glandular hypospadias. Barcat [9] recognised the need to classify hypospadias after release (or resection) of what he called chordee and differentiated between anterior, middle and posterior hypospadias. In this way he emphasised the relation between curvature of the penis and the severity of hypospadias. Van der Meulen graded hypospadias on the basis of the necessity to perform an orthoplasty. He divided hypospadias into grade I (no penile curvature), grade II A (penile curvature due to skin shortage), grade II B (penile curvature due to chordee) and grade III (penile curvature together with penoscrotal transposition) and as a consequence suggested a one stage repair for grades I and II A and a two stage repair for grade II B and grade III hypospadias [8]. In his thesis he also made an attempt to explain the embryogenesis of oblique raphes and dorsal dog-ears. Adhering to Glenisters' theory, he postulated that a duplication of the edges of the urethral groove following a differentiation disturbance gives rise to an overgrowth of the dorsal prepuce and the appearance of oblique raphes and dog-ears.

The presence of a ventral curvature of the penis is almost constantly referred to as chordee in the literature. First challenged by Smith [10], the general believe was that chordee is caused by fibrosis of the rudimentary corpus spongiosum. Peled [11] later denied the presence of chordee altogether. A daring but excellent study was performed by Avellan [12] who excised the so-called chordee tissue and reviewed its histology. This study showed that the corpus spongiosum from the point of meatal dystopia to the corona is present but that its histology shows poor differentiation with fibrosis and that this tissue fans out to the lateral sides. They confirmed that torsion of the phallus can be part of the hypospadias deformity and that this torsion was associated with a distinct course of the oblique raphes and asymmetrical distribution of the chordee tissue.

Hypospadias without hypospadias

First described by Sievers [13], this condition posed physicians with a problem: a congenital malformation of the penis with an urethral orifice in the normal terminal position but the external characteristics of hypospadias; curvature, oblique raphes, etc. Bergerhof and Gelbke [14] reported the difference between congenital short urethra and hypospadismus sine hypospadia which they described as an anomaly where the distal part of the corpus spongiosum is absent or dysplastic, thereby giving an explanation for the ventral curvature

of the penis. They emphasised that this condition is usually recognised towards adolescence when painful erections prohibit normal copulation.

Chordee without hypospadias or congenital curvature of the penis

This anomaly was first reported by Young [15] and later by Nesbit [16] who didn't give a description of the pathomorphology of this malformation but just called it chordee without hypospadias, congenital short urethra or congenital curvature of the phallus, illustrating the lack of insight of these anomalies. Devine and Horton [17] made an effort to categorise this anomaly by giving a theoretical description of the underlying pathology. They classified chordee without hypospadias as class I when the corpus spongiosum is deficient from the beginning of chordee to the glans. In class II, the urethra is surrounded by normal corpus spongiosum but Buck's and dartos fasciae are abnormal. With class III, only a dysplastic dartos fascia holds the phallus in curvature. Later they added two types to this classification, namely a class IV with an inherent bend in the corpora cavernosa and class V chordee for the congenital short urethra, two malformations which existence they did not mention in their first classification [18]. Their grading system is based on a theoretical deficit of mesodermal derived tissues but they did not show the actual histology of the various deformities. No additional knowledge has been described to this anomaly since, although many case reports on its treatment have been published [19-21].

Cryptospadias

Van der Meulen introduced the term cryptospadias to include the anomalies hypospadias without hypospadias, chordee without hypospadias and congenital urethra fistula [8]. He pointed out the relationship between the anomalous distribution of skin over the surface of the penis and the absence or presence of penile curvature. Apart from the obligatory terminal meatus he described the appearance of a cleft prepuce, oblique raphes without chordee (n=7) and with chordee (n=3) and an intact prepuce, oblique raphes and chordee in another four patients. Dickie [22] and later Avellan [12] followed his description, although Dickie thought the presence of chordee to be mandatory and Avellan added penile torsion as a possible characteristic of this deformity.

Congenital urethral fistula

This is a genuine rare malformation with very few reports from the literature. Its external feature is the presence of a defect in the urethra that is localised. Van der Meulen [8] discerned two types: one type where a urethral fistula occurs with hypospadias and another type where the distal urethra is covered by skin, ending in a terminal meatus. He observed that a congenital fistula can be part of the cryptospadias deformity as well.

Congenital short urethra

McIndoe [23] described this rare condition in two patients: short penis, ventrally curved and bound down. A normal erection was impossible although the urethra emerged from the meatal dimple in the normal way. He found the corpus spongiosum and urethra to be complete but seemingly too short compared with the corpora cavernosa on the dorsal aspect of the penis. Bergerhof [14] confirmed this description of congenital short urethra and added one patient to the literature. Huffstadt [24] presented another case report without describing the extent of the pathology of this malformation. Devine and Horton [17], in their many times quoted article, found no place for this anomaly and called it chordee without hypospadias, thereby equalling the words curvature and chordee. Duckett [25] stated that in two thirds of congenital curvatures, the corpus spongiosum is normal, thereby suggesting that it is abnormal in one third of cases. He did not mention the congenital short urethra as an entity, but he too called it chordee without hypospadias. This review therefore shows several contradictions in the literature on the existence, pathology and nomenclature of the congenital short urethra.

In summary, there is no controversy with respect to the external appearance of hypospadias, where a dystopic meatus is felt to be obligatory. No general agreement, however, seems to exist on the grading of the severity of this deformity. In contrast with this is the jungle of disorders associated with a normal urethral meatus but, may we call it "hypospadiac features". No consensus is at present available: neither for appearance, classification nor even existence.

Normal embryogenesis of the male anterior urethra

The basic processes involved in normal embryogenesis of the male anterior urethra can be categorised as fusion, merging and definitive tissue differentiation [26,27].

Fusion is a distinct process in three phases (fig. 2 A+B): first there is outgrowth of swellings (mesodermal cores covered by ectoderm), followed by opposition and adhesion of the ectodermal linings of these swellings thereby creating a double layer of ectoderm (epithelial plate, phase two). Finally, programmed cell death (apoptosis) causes disconnection of this epithelial plate and completes fusion (third phase). During this disconnection of the epithelial plate, the mesodermal cores from both sides unite between the surface ectoderm and the enclosed structure. With fusion, luminisation of tubular structures can take place in two ways: primary luminisation when a lumen is direct included (fig. 2A) and secondary luminisation when a solid epithelial cord is formed first which later opens to compose a lumen (fig. 2B).

Merging is quite different from fusion and can be described as the joining of swellings that arise through a difference in regional growth rate. With merging, there is no formation of an epithelial plate (fig. 2C).

Definitive differentiation is the capacity of cells derived from the germ layers to form

specialised tissues. Mesodermal cells for instance are capable of forming the integumental structures of the penile body, i.e. corpus spongiosum, cavernous bodies, the tunica albuginea and dermis, whereas ectoderm differentiates into the epidermal structures of the body such as the epidermis and adnexes.

Based on the above-mentioned basic processes, the embryonic period can be divided in an early embryonic period (Crown-Rump Length (C-RL) < 17 mm) and a late embryonic phase [27] (C-RL >17 mm). For clearness, only a summary of the detailed embryogenesis of the male anterior urethra will be given [28].

During the early embryonic period, development of the external genital system is sexually indifferent. In the three dimensional folding process of the embryo, the genital tubercle arises as a horseshoe shaped swelling anterior to the cloacal membrane. Following elongation of the genital tubercle, an epithelial plate will develop between the arms of the genital tubercle, which becomes continuous with the floor of the primitive urogenital sinus, i.e. the future urethral plate. At the end of the early embryonic period, the cloacal membrane has ruptured through apoptosis. As a consequence, the indifferent external genital consists of the genital tubercle with an epithelial plate in its ventral median (the presumptive glans area) and the urethral groove, bordered by the paired urogenital swellings. On the lateral sides of the urogenital swellings, the labioscrotal walls have

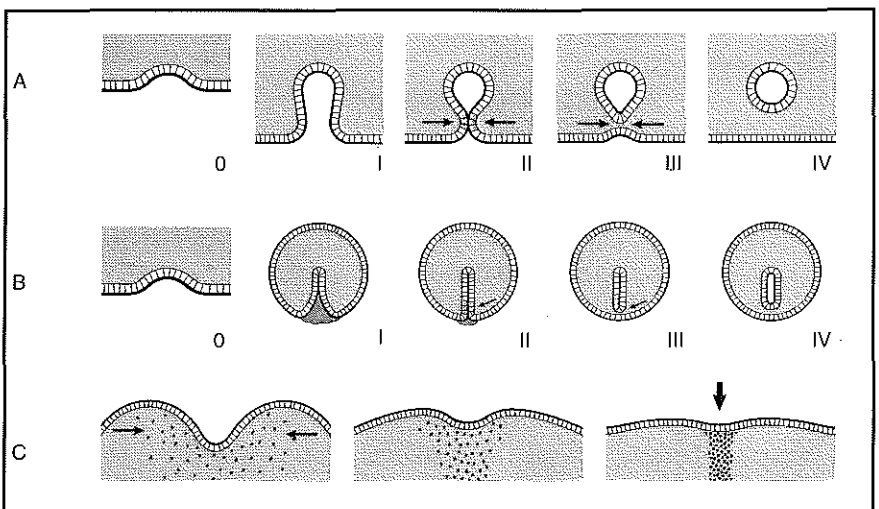


Figure 2
A Fusion with primary luminisation (0= start of outgrowth of swellings, I= phase one, II= phase two, III= phase three of fusion, IV is start of definitive differentiation of mesoderm)
B Fusion with secondary luminisation (0-IV see above)
C Merging of the scrotal swellings

emerged. Thus the genital tubercle has reached the second phase of fusion (outgrowth plus adhesion, fig. 2B, II) whereas the urogenital swellings are still in their first phase (outgrowth and no adherence, fig 2A, I).
The late embryonic period in male is characterised by outgrowth and differentiation of the genital tubercle (now called the phallus), urogenital and labioscrotal swellings. With elongation of the phallus, the urogenital swellings fuse with primary luminisation of the penile urethra (fig 2A, II and III). Fusion in the glans of the phallus is completed by the formation of a solid epithelial cord (fig 2B, III) that forms a lumen later in embryogenesis (secondary luminisation, fig 2B, IV). Both fusion processes are conducted by apoptosis and are continuous in the median. The result of the fusion of the urogenital swellings is that their mesodermal cores unite to encircle the penile urethra (fig. 2A). Subsequent definitive differentiation of this mesoderm gives rise to the integumental layers of the urethra: corpus spongiosum, Bucks' and dartos fasciae i.e. deep and superficial layers of the tunica albuginea. The mesoderm that unites in front of the epithelial plate after fusion of the glans forms a thin layer that covers the glandular urethra (fig.2B). During outgrowth and fusion of the phallus, the labioscrotal swellings arise between the perineum and the phallus. In this way the scrotum is formed through merging, not by fusion because no epithelial plate is formed between the scrotal swellings (fig.2C).
It is only after fusion phase two of the glans and penile body (approximately 60 mm C-RL) that the prepuce starts to develop as a fold consisting of a core of mesoderm covered by ectoderm. In the 115 mm foetus, this prepuce can be seen to entirely engulf the glans.

Patho-embryology

Based both on the descriptive pathomorphology from the literature and the normal developmental processes presented, i.e. fusion, merging and definitive differentiation, it is now possible to give an explanation for the pathoembryology and to propose a classification of malformations of the male external genital. This pathoembryology should be considered a continuum with a normal, well differentiated male genital on one side of the spectrum and a strongly curved, perineal hypospadias resembling the female state at the other end.
Disturbances of fusion can arise in any of the three phases of the fusion process, this means in any phase of the embryogenesis and at any place of the fusion line of the phallus. These fusion disturbances are caused by a lack of outgrowth, adhesion and/or apoptosis. When the first phase of fusion is disturbed (i.e. lack of outgrowth of the genital tubercle and urogenital swellings), a very proximal hypospadias results, with a severe curvature, small penis, a perineal or penoscrotal meatus and scrotal bipartition. Following a defective fusion in phase two, there is no adhesion of the urogenital swellings and genital tubercle. The result is a lesser degree of hypoplasticity of the phallus than with a phase one fusion disturbance, a less proximal meatus and a milder curvature. When fusion of the glans alone

is involved, a glandular hypospadias arises (fig. 3). Because the glans has not fused properly, and formation of the prepuce starts at a later stage then phase two of fusion, the prepuce is unable to form a midline frenulum. This deficiency allows for the malpositioning and maldistribution of skin which gives the prepuce its hooded appearance in hypospadias and cryptospadias where there is a dorsal surplus of preputial skin. If the third phase of fusion is established but halted before the mesodermal cores have properly united, a terminal meatus is the result with the definitive differentiation of mesodermal structures being inadequate (pellucid urethra for instance). A curvature due to this differentiation defect occurs as well as maldistribution of penile skin (dorsal hood with dog-ears and oblique raphes). If fusion phase three is completed and the mesodermal cores have united around the urethra, diminished differentiation can still render the ventral aspect of the phallus short in comparison with its dorsal structures. Finally, a localised defective fusion between phase two and three, can give rise to a fistula in the urethra.

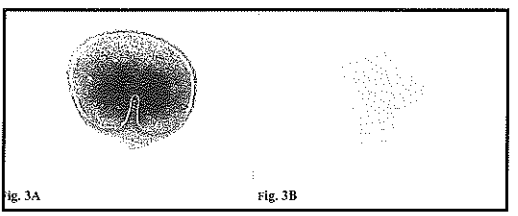


Figure 3
Normal glandular part of the genital tubercle showing epithelial plate in median (fig.3A, human embryo, 16 mm Crown Rump Length (CRL)). Micrograph of presumptive hypospadias, showing divergence of the glans because the second phase of fusion is not established (fig.3B,male human embryo, 20 mm CRL).

A merging deficiency, together with a relative growth retardation of the phallus, causes the labioscrotal swellings to assume a position more cranial then normal. This accounts for scrotal transposition or bipartition, giving the genitalia a more "feminine" appearance. Whether this merging disturbance is secondary to a fusion defect or growth interruption of the phallus or can occur as an entity cannot be assessed with certainty.

Based on this theory, we suggest a classification for congenital malformations of the male external genital. In this classification some older terms have been abandoned such as hypospadias without hypospadias and chordee without hypospadias. In fact we propose to depart from the expression chordee as a general term but instead reserve this phrase for the condition where a penile curvature is caused by a disturbance of differentiation of the mesodermally derived tissues surrounding the urethra, i.e. chordee as a description of poorly differentiated tissue.

Classification and nomenclature

Hypospadias

With this anomaly, a dystopic meatus of the urethra is mandatory. When there is no associated curvature of the penis with an artificial erection test, this malformation is the result of a small and distal fusion defect only. We therefore suggest the name **Class I hypospadias** (fig. 4). When there is a ventral curvature of the penis, this can be caused by a differentiation defect, secondary to the fusion defect. If the curvature is caused by a ventral skin shortage only, we call this **Class II A hypospadias** (fig. 5A). If, however, the curvature is brought about by chordee tissue as well, then this anomaly is classified as **Class II B hypospadias** (fig.5B). All hypospadias can be seen to have oblique raphes and dorsal hooding with dog-ears, being the consequence of the fusion defect. This classification is based on the original grading by Van der Meulen, with the exception that grade III has been incoorporated in class IIB hypospadias

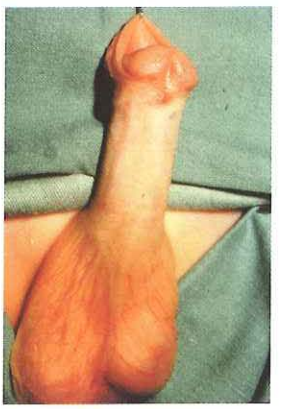


Figure 4
Example of class I hypospadias (dystopia, no curvature, oblique raphes, dorsal hood)

Fig. 5A

Fig. 5B

Figure
5A Class IIA hypospadias (dystopia, curvature, oblique raphes, dorsal hood)
5B Class IIB hypospadias (dystopia, chordee, oblique raphes, dorsal hood)

Cryptospadias

Disfigurement of this type is identified by the presence of a normally placed urethral meatus but with a ventral curvature of the phallus. From an embryogenetical point of view, ectodermal fusion seems complete because there is a terminal meatus. In fact, the mesodermal cores have not properly differentiated in front of the newly formed penile urethra because of a lack of proliferation of this mesoderm during its disconnection from

the surface ectoderm. The subsequent disturbance of definitive differentiation of this mesoderm, causes a malformation in the integument of the urethra. The deficiency of integumental structures can in theory be in all layers (corpus spongiosum, tunica albuginea and skin). The curvature is caused by shortage of skin and integument as well as tethering bands of fibrous tissue penetrating to the lateral side (maldifferentiated corpus spongiosum, i.e. chordee). Oblique raphes with dog-ears and dorsal hooding of the prepuce usually accompany this anomaly, which is, in summary, a differentiation defect (fig. 6).

Fig. 6A

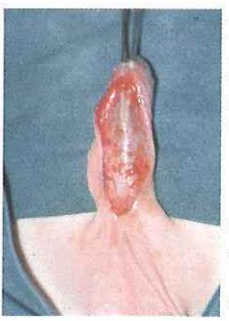


Fig. 6B

Figure 6
A Example of cryptospadias (normal meatus, curvature, oblique raphes with dog ears).
B Cryptospadias intra operatively showing pellucid urethra.

Congenital urethra fistula

This deformity is characterised by an extra opening of the urethra (fig. 7). It can be seen with all other anomalies of the anterior urethra and its embryological basis is a localised fusion defect between phase two and three. It is probably caused by a local disturbance of apoptosis and it can occur on any location of the fusion line.

Figure 7
Example of congenital urethral fistula (localised defect in urethra)

Congenital short urethra

This is a very rare malformation if one reviews the literature. The clinical picture shows a terminal meatus indicating an undisturbed fusion (fig. 8). Furthermore, the integument of the urethra is well differentiated, with all layers being present, but it is short compared to the dorsal structures of the penis. We therefore believe that a relative ventral growth retardation gives rise to this anomaly. Neither oblique raphes nor dorsal hooding are seen with this disfigurement. In summary, the dorsal structures of the penis are relatively long compared to the well differentiated parts of the ventral side. The aetiology of this growth disturbance remains obscure.

Figure 8:
Congenital short urethra (terminal meatus, normal prepuce, strong curvature)

Discussion and conclusions

The rationale for any classification system should be its simplicity, clinical applicability and consequences for treatment. In hypospadias surgery where several hundred operative techniques have been presented in the world literature, time seems right to reach some form of consensus on the pathology involved. This however, requires a common language for all surgeons working in the field of reconstructive hypospadias repairs. By simply classifying hypospadias based on the position of the urethral meatus, other, equally important, factors such as curvature or integumental deficiencies are overlooked. Reconstructive surgery of the hypospadias deformity should be based on the embryological defect involved. We therefore want to suggest a classification based on our embryological observations.

The main disadvantage of a new categorisation is how to deal with older terms. One such phenomenon is the expression chordee. Used in the literature to point out curvature of the penis as well as a name of "scar tissue", we suggest to abandon the general use of this expression. Instead, we emphasise the need to use the word curvature in case of a bending of the penis as a descriptive morphologic term. The explanation for this condition then can be given, based on the underlying anomaly. A differentiation disturbance resulting in only a skin shortage in hypospadias gives rise to a curvature and not to chordee. When disturbance of differentiation gives rise to dysplastic mesodermal tissue, this can be called chordee.

With congenital short urethra, no histological data are available that show the actual pathology. We do not supply these data either but based on our embryological theory we suggest that the main difference between a congenital short urethra and cryptospadias is a relative ventral growth retardation in the first and the underdevelopment of the urethra or penile integument in the latter condition. Congenital short urethra therefore represents an entity of which the precise nature remains obscure. The only true difference between cryptospadias and hypospadias is the apical meatus seen with the first. Both conditions can show a varying degree of curvature and integumental deficiencies.

The consequences of this classification for treatment of the various anomalies are open for discussion. We feel that in the case of a class I hypospadias (no curvature, dystopic meatus), no chordectomy, orthoplasty or rearrangement of skin is necessary. A new distal meatus has to be created together with a glandular urethra. Usually both goals can be reached in a one-stage procedure. With a class IIA hypospadias (dystopic meatus, curvature due to skin shortage, normal urethral plate), redistribution of skin from the prepuce to the ventral side will correct the curvature. Therefore no chordectomy is necessary, the urethral plate does not have to be incised and a one-stage procedure can be advocated for the treatment of this anomaly. When a class IIB hypospadias (dystopic meatus, skin shortage and chordee tissue) has to be straightened, incision of the urethral plate may be necessary together with redistribution of skin. A two-stage repair consisting

of an orthoplasty as a first procedure followed by an urethroplasty then seems to be legitimate.

In conclusion, we strongly feel that there is a need to properly classify disorders of the male anterior urethra on an embryological basis. With the establishment of a proper classification, a start can be made to compare the outcome of treatment of the different congenital anomalies of the anterior urethra.

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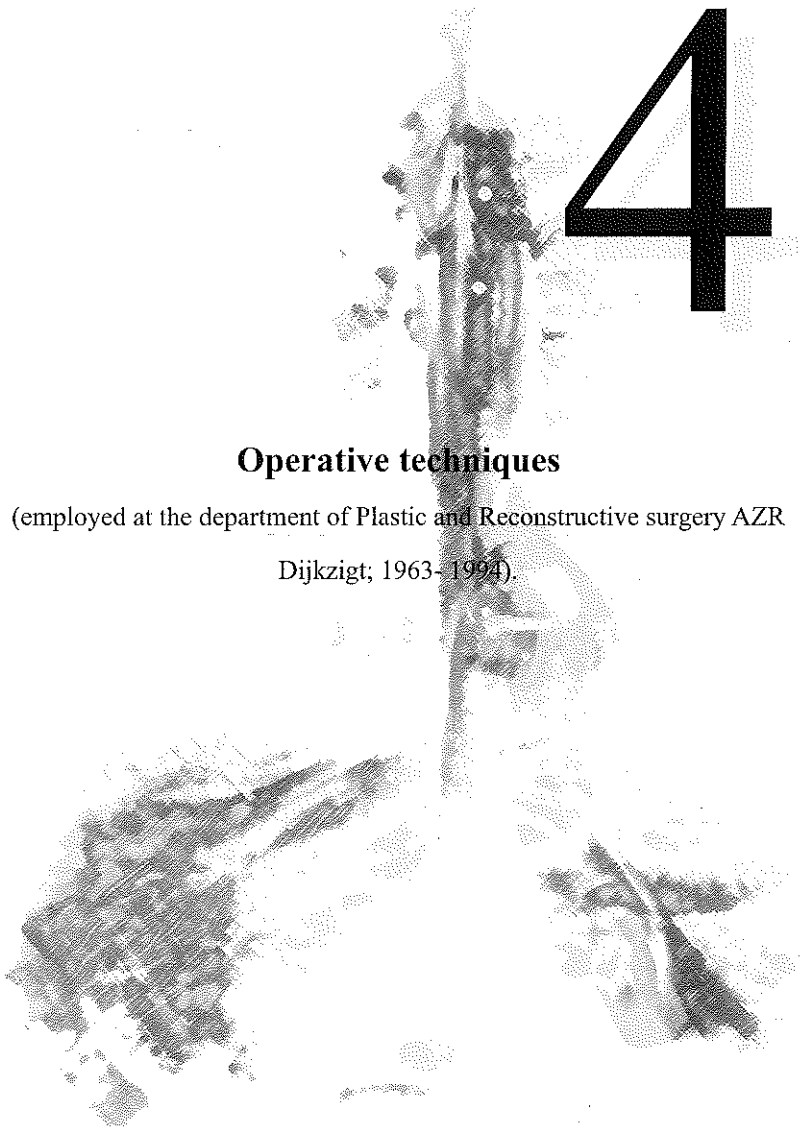
4

Operative techniques

(employed at the department of Plastic and Reconstructive surgery AZR Dijkzigt; 1963- 1994).



History

In the history of Dutch urogenital plastic surgery, the year 1964 is of particular importance. In this year, three theses were written on hypospadias. Heybroek [1] presented a modification of the Ombrédanne technique [2] which was called "The Groningen method of urethra reconstruction in hypospadias." The results of this technique were reviewed retrospectively by Roldaan and Nicolai in 1989 [3]. Van der Meulen [4] published a thesis concerning his operative strategy for hypospadias repair in this same year. During the thirty years that followed he adjusted his principles slightly but never on major topics [5-10]. Validation of this technique has been reported by himself at a later stage, by other authors later describing their own technique [11] as well as by several authors having performed his type of operation [12-16].

The third Dutch surgeon to write about hypospadias in 1964 was Lamaker [17] who described a technique which was a modification of the Dennis Brown repair. No reports about this technique have been published in the literature following his original paper.

During the period 1963 to 1994, the Department of Plastic and Reconstructive Surgery of the University Hospital Rotterdam comprised three hospitals: the Dijkzigt hospital, the Sophia's Children's hospital and the St.Franciscus Gasthuis. All three hospitals were active in the treatment of children or adults with hypospadias. It became a centre for primary and secondary referral of hypospadias patients from all specialities. During this period, the technique used for treatment of hypospadias, was the van der Meulen repair [18]. Avoidance of complications was thought to be achieved by adequate closure of the wound with adequate suturing using intracuticular stitches without superimposing suture lines and adequate protection, positioning and drainage of the wound [8]. The correction of hypospadias with the van der Meulen technique was carried out as a one-stage procedure when straightening of the penis was not needed and as a two-stage repair when an orthoplasty was necessary.

In later years, another plastic surgeon joined the department and started using another technique of hypospadias repair. He advocated the use of a two-stage repair in *all* patients, starting with a Byars orthoplasty, followed by a Denis Browne buried strip urethroplasty [19]

Description of techniques

Van der Meulen Type I Procedure

This method is used for distal hypospadias were no straightening of the penile body or glans is needed. For this reason it is called a urethroplasty [18] (fig. 1).

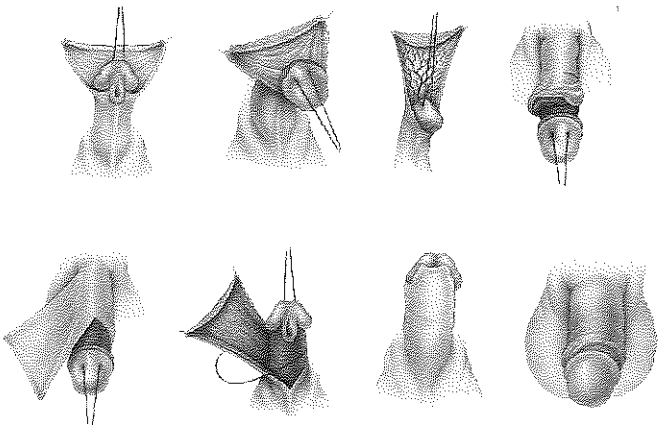


Fig. 1

The technique is based on the formation of a buried strip that is wide enough to form a urethra of sufficient calibre. The buried strip is covered with a well vascularised transposition flap from the dorsal prepuce.

Firstly, a traction suture is passed through the dorsal rim of the glans. Then the urethral strip with two triangular areas on both sides of the fossa navicularis are outlined using a cutting diathermy needle. The inner surface of the dorsal prepuce is dissected from its insertion at the glans through a circumferential incision. This dissection is carried proximal around the shaft of the penis. In this way a minimal curvature, if present, can be released.

Next step is the transsection of the dorsal hood at or somewhat distally to the coronal level. Rotation of the dorsal skin flap to the ventral side follows, using a backcut to facilitate this manoeuvre. Care is taken not to extend the backcut beyond the midline to avoid damage to the dorsal artery. Tubing of the urethral strip is optional but not necessary because epithelium will form during woundhealing.

After meticulous haemostasis, the transposition flap is sutured to *both* sides of the urethral strip. The edge of the V-shaped defect from the dorsal backcut is sutured to the corona. All suturing is done using absorbable, interrupted and subcutaneously placed sutures. *No* transcutaneous sutures are used for the avoidance of fistula formation.

A simple "sandwich dressing" is applied at the end of the operation. One piece of gauze below the upward bent penis and one on top. This bandage is changed after every voiding and makes nursing simple. No circular dressing or urinary diversion are used in this procedure.

Van der Meulen Type II Procedure

This operative technique consists of two stages with a time interval of approximately six months and is used for more severe hypospadias where an orthoplasty is necessary before reconstructing the urethra [18]. For this reason it is called an orthourethro-plasty .

Stage I of type II procedure:
(orthoplasty, fig.2)

A traction suture is placed through the dorsal rim of the glans. Incision of the inner surface of the preputium and glans is made circumferentially by using a diathermy needle. This incision crosses the urethral delta just distal to the dystopic meatus at the level of the corona. The V-shaped incision of the fossa navicularis is opened widely on both sides for sufficient coverage with skin.

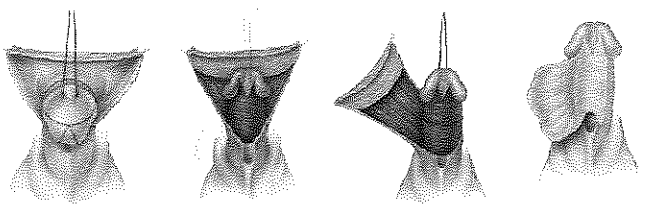


Fig. 2

Straightening of the penis is performed by holding the corpora cavernosa under tension with thumb and index finger and dissecting in a plane between the urethra and the corpora using diathermy. The deep layer of the tunica albuginea should be left untouched. Any damage to this layer should be carefully sutured. Through this dissection, the meatus will drop back to a more proximal position on the penile body. Next, the dorsal hood is dissected proximal in an avascular plane to get a complete mobilisation of the penis. An artificial erection test can be used at this stage of the operation to establish any residual curvature [20].
A transverse backcut is made similar to the type I procedure. This back cut should stop just before the midline for preservation of the flaps vascularity. The flap created in this way is transposed to the ventrolateral side for coverage of the defect between the glans and the dystopic meatus. Suturing is done without tension with subcutaneously placed, absorbable sutures.
With this first operation, straightening of the penis is achieved together with deposition of a sufficient supply of skin on the lateral side of the penis to be used for a future urethroplasty. A simple sandwich dressing is applied and no urinary diversion is used postoperatively.

Stage II of type II procedure:
(urethroplasty, fig.3)

After healing of all wounds (approximately six months) an urethroplasty is performed. A strip of skin of sufficient width on the ventral side between the dystopic meatus and the glans is outlined and incised. The deposited skin on the rightsided lateral aspect is mobilised and brought over to the opposing lateral side for coverage of the urethral strip. Suturing is again done with absorbable, subcutaneous sutures in two planes: one at the junction of the mobilised skin flap and the skin strip and one more lateral. In this way overlying suture lines are avoided thus reducing the risk of fistula formation. The outlined skin strip *can* be tubed, but this is not necessary. In this second operation a wide meatus is created on the cranioventral side of the glans. Urinary diversion with this type of operation depends on natural miction. Drainage incisions on either side of the penis at a safe distance from the neo-urethra or a fenestrated Silastic stent are used to prevent stasis of blood or urine.
No circular dressing is applied but a simple sandwich dressing is utilised instead that is changed after every miction.

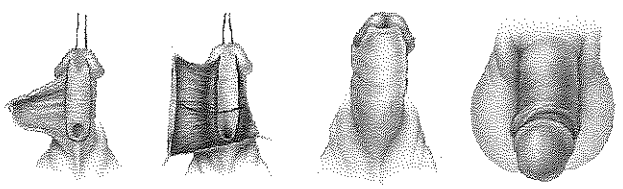


Fig. 3

* The type I operation was performed in the class I and IIA hypospadias, according to the classification mentioned in chapter three. The type II procedure was executed in class IIB hypospadias (chapter three).

Combined Byars / Denis Brown repair

All patients, irrespective of the severity of the hypospadias are operated with the same two-stage procedure [19].

Stage I
(Byars orthoplasty, fig.4)

An incision is made distal to the meatus and continued right around the circumference of the penis just proximal to the glans which is then split ventrally. Chordee tissue is excised, haemostasis is completed and any nicks in the tunica albuginea are repaired with 6/0

catgut. The prepuce is incised dorsal through both layers, opened out and thoroughly freed so that the two resultant flaps can be transposed with ease to the ventral surface. The distal one-third of each flap is then trimmed off and the flaps sutured into the ventral defect. Where they meet each other in the midline they are sutured together, the sutures catching the underlying tunica.

The rest of the wound is then closed dorsal and laterally. A dorsal slit is never needed. Finally, a Fowley catheter is passed via the ectopic meatus into the bladder. The catheter overlying the flaps is then rolled up in a piece of tulle gras and tied down to the area between the meatus and the tip of the glans.

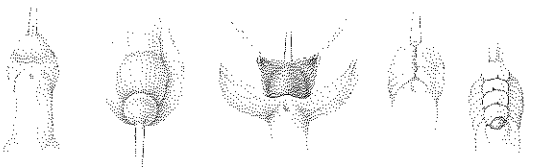


Fig.4

A synthetic foam dressing [21] is applied and left in place for 5 days. The dressing and catheter are then removed, the flaps inspected and, if well healed, the child is discharged.

Stage II

(Denis Brown urethroplasty, fig.5)

After a suitable period has elapsed which allows the scars to soften, the ventral surface of the penis is inspected for irregular skin folds and pits. If these are present, minor excisions may be needed, but if the skin is smooth and supple, the second stage is undertaken.

A perineal urethrostomy is performed and a modified Fowley catheter inserted. The ventral surface of the penis incised to create a skin strip. The surplus skin brought into the cleft glans at the first operation allows the incision to be carried right to the tip of the penis. Next, the skin proximal and lateral to the incision is undermined just superficial to the tunica albuginea and the edges united with three layers of subcuticular 5/0 dexon. Several 6/0 catgut sutures are inserted to ensure good approximation of the skin edges. A double layer of tulle gras is wound around the penis and a synthetic foam dressing is again applied. The dressing is removed on the following day and the patient is discharged.

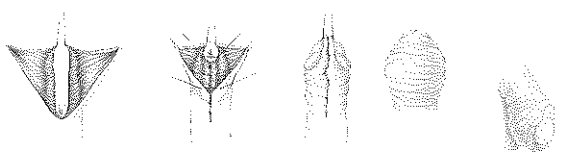


Fig. 5

All drawings were made by Michael Budowick, Munich.
The figures 1-3 are published with permission from Urban & Schwarzenberg [18].

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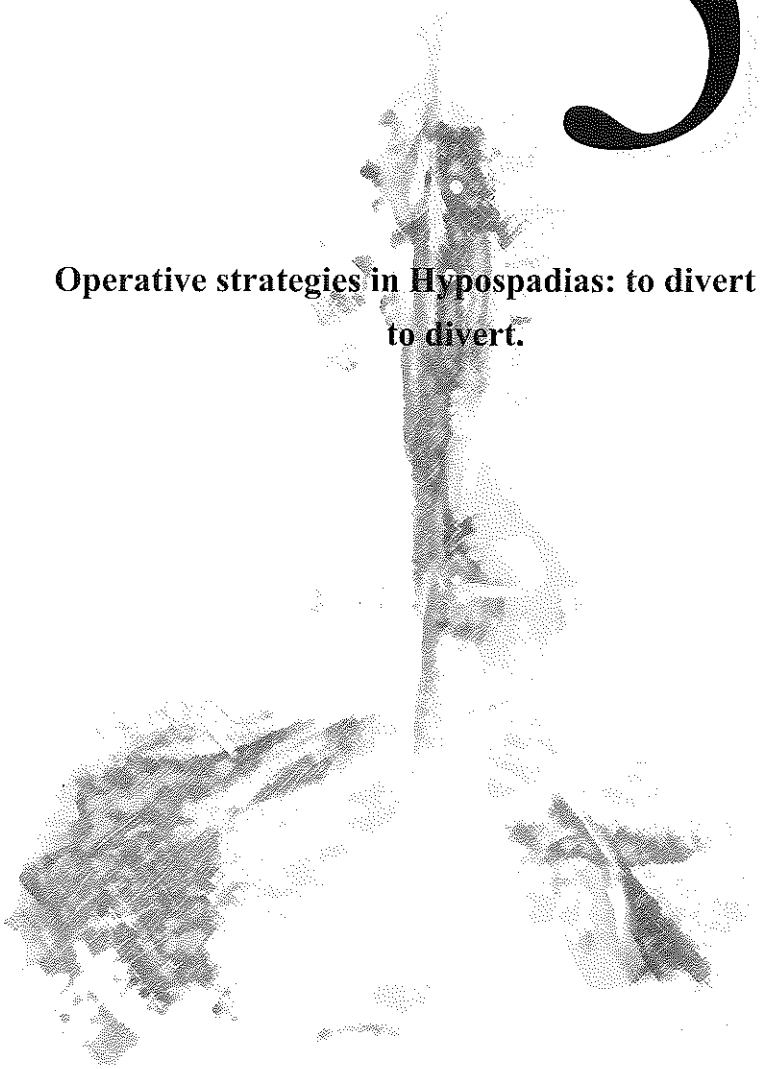
5

Operative strategies in Hypospadias: to divert or not to divert.



Introduction

Despite the multitude of procedures available for the correction of Hypospadias in the nineteen sixties and early seventies, only a few techniques were commonly used [1]. All these techniques shared the (seemingly accepted) consequence of a high complication rate mainly caused by fistulas [1 2 3 4]. Since this rate was felt to be unacceptably high and at that time (1961) no explanation was given in the literature for these dismal results, a study of possible causes was started at the "Dijkzigt Hospital" in Rotterdam. The following factors were found to be responsible: inadequate closure, inadequate suturing, inadequate dressing, inadequate protection and inadequate drainage of the wound [5].
Identification of these factors and the desire to eliminate them, led to the development of two new techniques. One for the correction of Hypospadias without curvature that subsequently did not require straightening of the phallus by release of the dystopic meatus before a neo-urethra was formed (one-stage repair = urethroplasty). Another procedure for Hypospadias with a ventral curvature in which straightening of the corpora cavernosa by release of the dystopic meatus was necessary preliminary to the formation of a new urethra (two-stage repair, orthoplasty + urethroplasty).[6] The principles, on which these techniques for reconstruction of the neo-urethra were based, comprised the following; [6,7]

1. Redistribution of well vascularised skin avoiding tension on and overlap of suture lines.
2. Connection of the wound edges by subcutaneous sutures thereby preventing ingrowth of epithelium along the sutures and possible fistula formation.
3. Protection of the wound by a simple sandwich dressing, eliminating ischaemia induced by constrictive dressings and infection of less vascularised skin by stagnation of blood and urine.
4. Evacuation of blood and urine, initially by placing drainage incisions at a safe distance from the neo-urethra, and in later years by the insertion of a fenestrated, non indwelling Silastic stent in the urethra.

Application of these principles led to a considerable reduction of fistulas [5]. The question to what extent the urinary diversion without indwelling catheters contributed to this success, however, remained. This stimulated the author to compare the results of two different regimes of hypospadias repair, i.e. the combination of the van der Meulen techniques without the use of indwelling catheters and the technique of Byars/ Denis Brown with the use of indwelling diversion, which was used by another surgeon in the department [8]. Moreover, very few authors report about the prospectively controlled use of urinary diversion [9-12] and no rationale is described in the literature for the indication of urinary diversion methods in different degrees of Hypospadias severity.
This article represents the review of a thirty year institutional experience in Hypospadias surgery. During this period, two surgeons both had their own vision on how to treat their

patients with Hypospadias. Emphasis will be put on the complications (fistulas in particular) occurring with these different approaches.

Materials and methods

A study was carried out using data from the files of the department of Plastic and Reconstructive Surgery of the University Hospital Rotterdam. Records of all patients operated between 1963 and 1993 for Hypospadias were examined. This group comprises primarily referred patients (n=472) with varying degrees of Hypospadias (table 1).

Grading of hypospadias	Number of patients	Percentage
Glanular	196	42%
Distal penile	220	47%
Proximal penile	49	10%
Peno-scrotal	7	1%
Total	472	100%

Table 1: Patient population according to severity of disease.

Postoperative complications were graded and scored.

Grade I Minor complications(no re-operation needed)
e.g. small dehiscence, haematoma, urinary retention

Grade II Cosmetic complications (re-operation optional)
e.g. meatal retraction or dystopia, skin surplus, scar contraction or circumcised appearance

Grade III Major complications (re-operation required)
e.g. bleeding, fistula, curvature, meatal or urethral stenosis

All data were stored in and analysed with a spreadsheet database (Reflex ™).

One senior surgeon applied the van der Meulen type I repair for mild hypospadias, which uses a dorsal transposition flap for coverage of a ventrally outlined skin strip for urethral reconstruction [6,7,13]. This is a one stage procedure where no straightening of the penis by release of the dystopic meatus is necessary. With this technique, no urinary diversion is used. For the more severe Hypospadias, the van der Meulen type II repair was used, which is a two stage technique where straightening of the penis by release of the corpora cavernosa and dystopic meatus is necessary with transposition of a dorsal preputial flap to the ventral surface to restore ventral skin shortage as an initial procedure (orthoplasty).

The second stage is an urethroplasty created from the previously deposited skin of the first operation. With this last operation, drainage incisions were made at a safe distance from the junction of the resident -and neo-urethra for drainage of urine. This diversion technique was replaced by employing a fenestrated, non indwelling Silastic stent in the urethra in later years [6,7]. *(The type I operation was performed in the class I and IIA hypospadias, according to the classification mentioned in chapter three. The type II procedure was executed in class IIB hypospadias (chapter three).*

Another senior surgeon practised a two stage technique with all hypospadias. A Byars orthoplasty (with the application of an indwelling Fowley catheter), utilising split dorsal preputial flaps for coverage of the ventral skin defect, was followed by a Denis Browne urethroplasty (buried skin strip sutured with dexon and covered with bilateral advanced penile skin closed in the median over the neo-urethra) with the appliance of a perineal urethrostomy [8]. The operative techniques and diversion methods are summarised in table 2. The urinary diversion methods were correlated with the number of postoperative complications. Because this study (based on patient record data) does not include a follow up of patient satisfaction, grade II i.e. cosmetic complications could not be scored.

Operative technique	**Diversion method**
van der Meulen type I (urethroplasty)	no diversion
van der Meulen type II (ortho/urethroplasty)	drainage incisions/ non indwelling fenestrated stent
Byars orthoplasty	indwelling Foley catheter
Denis Brown urethroplasty	perineal urethrostomy

Table 2: Urinary diversion methods used with different operation techniques.

Results

Between 1963 and 1993, four hundred and seventy-two primary referred patients were operated using the aforementioned techniques. The degree of initial disease ranged from mild (glanular) to severe (peno-scrotal) (table 1). Intra-operatively, the initial grading of the disease was again established on the basis of an artificial erection test.

		vd Meulen I (n=320)	vd Meulen II (n=56)	Byars/Denis Brown (n=87)
Minor compl.	Dehiscence (small)	1%	-	1%
(Grade I)	Hematoma	2%	-	2%
	Urinary retention	<1%	-	3%
Major compl.	Bleeding	-	3%	1%
(Grade III)	Fistula	<1%	5%	20%
	Meatal stenosis	<1%	3%	10%

Table 3: Complication rates following different procedures of Hypospadias repair.

The complication rates related with the operative technique used, are listed in table 3. Postoperative complications were classified as Grade I (minor) or Grade III (major or functional) complications. Minor complications are distinguished from major complications by the fact that an accessory operation is imperative in the latter and unnecessary in the first. Because of the relative importance of postoperative fistula formation, a differentiation of the fistula rate for increasing severity of disease was made (table 4).

	vd Meulen I		vd Meulen II		Byars/Denis Browne	
	# patients	Fistula	# patients	Fistula	# patients	Fistula
Glandular	162	-	-	-	34	18%
Distal penile	153	<1%	16	6%	44	20%
Proximal penile	5	-	34	6%	9	22%
Peno-scrotal	-	-	6	-	-	-
Total	320	<1%	56	5%	87	20%

Table 4: Fistula rate in relation to severity of disease and operation technique.

Three hundred and twenty urethroplasties of the van der Meulen type I were performed using no diversion postoperatively. In this group of patients, 1 fistula developed which needed surgical correction (<1 %). Two patients (<1 %) suffered from urinary retention which was treated with a suprapubic catheter , one patient with a meatal stenosis needed a meatotomy whereas nine other minor complications occurred .
In the group of patients undergoing a van der Meulen type II repair, fifty-six urethroplasties were performed, having either drainage incisions at the penile base or a fenestrated non indwelling Silastic stent for two days as the methods of urinary diversion. The complications in this group were: three fistulas (5%), postoperative bleeding twice (3%) and two meatal stenoses (3%). No urinary retention was encountered with these patients.
Under the regime of the combined Byars / Denis Browne two stage repair, twenty percent fistula occurred, whereas three patients (3%) suffered from urinary retention despite having either a Fowley catheter or a perineal urethrostomy as the means of diversion. This group of patients developed other complications to a total of 14 %. Noteworthy is the high incidence of meatal stenosis following the Denis Browne urethroplasty (10%).

Discussion

Although there seems to be a consensus on the use of indwelling catheters, the effects of urinary diversion in hypospadias surgery are still not well known. Few reports are available with particular emphasis on this subject. Most authors present the results of their Hypospadias repair without mentioning the means of urinary diversion. Wehnert and Schubert [14] reported on the effects of suprapubic catheters, transurethral catheters and perineal urethrostomies after Denis Browne repairs and their complication rate varied between 14,6 % and 40 %. Cromie and Bellinger [9] presented the results of a questionnaire sent to American paediatric urologists concerning the use of dressings and catheters after hypospadias repair. The limitation of this study is that it only presented the opinion of the involved surgeons without showing any data concerning the operative technique or the complication rate of these procedures. Furthermore, no rationale for their opinion was given. In an attempt to diversify the need for urinary diversion with different grades of Hypospadia, Oesterling et al [15] put forward yet another questionnaire among American and Canadian paediatric urologists. A precise description was given on which method of diversion should be used with different types of Hypospadias. Again, however, no complication rates were specified, there was no description of the operative techniques used by the interviewed surgeons and no rationale for any choice was stated. Snow et al [11] advocated the use of an indwelling Silastic urethral stent on an outpatient basis for all procedures except MAGPI repairs. The number of patients in this study however, was relatively small, no follow up time was given and the complication rate was 20%. Mc Cormack et al [10] displayed the results of a randomised trial with one operative technique (Mathieu repair) using either no stent and no diversion or the combination of a no. 8F silicone stent with a perineal urethrostomy. The complication rate in the first group was much lower but still considerable (42% versus 82%). Finally, Grobbelaar et al presented a study on the influence of postoperative care on surgical complications [16]. They thoroughly described the effect of what they call "patient factors" on the occurrence of fistula. These factors include blocking of catheters, urinary obstruction, straining, dressings etc. Their conclusion is that identification of a patient factor highlighted the importance of postoperative care. They gave an excellent summary of the trends in urinary diversion during the last three decades, but failed to give a report on what methods of diversion have been used in their own patients.

All these reports do not answer the seemingly futile and outdated question: is there a need for urinary diversion in Hypospadia surgery and if so, what form of diversion is preferred and for how long should it be used ? The rationale for using urinary diversion should be: the enhancement of patient comfort and avoidance of complications.

Comfort relies on the freedom of motion, the absence of pain and the presence of adequate diversion of urine, which involves absence of bladder spasms and forceful, jetlike miction

alongside an urethral catheter. Since these conditions can not be guaranteed by either a transurethral catheter or a suprapubic cystostomy [16], patient comfort is frequently found to be an illusion, while fistula formation and infection are not necessarily prevented by these diversion methods and may even by caused by them.
Natural micturition has never been considered a serious alternative for obvious reasons (anxiety, etc.) except in very distal hypospadias [10,12]. Unrestricted passage of urine by natural miction can be achieved however if no circular dressing is applied and if drainage incisions or a fenestrated stent are used when the length of the neo-urethra or the specific type of urethroplasty such as a tunnelling procedure requires this. Absence of a dressing and the use of a stent will even be beneficial for woundhealing since stasis of urine and blood is avoided and possible sources of wound infection are eliminated. Testimony to this is the fact that in our population treated without an indwelling catheter diversion, 98 % of the patients did not have any postoperative complication related to urinary diversion.
The outcome of hypospadias surgery depends on a multitude of factors. The operative technique is a determinant factor but closely related are the use of postoperative dressings, urinary diversion and the aftercare. The effect of one single parameter on the outcome of treatment is difficult to evaluate. Only prospective randomised long-term studies with an emphasis on one factor would provide the necessary information. Such studies have as yet not been performed and are methodologically difficult to carry out. This, however should be considered when papers advocate the use of any means of urinary diversion or postoperative dressing.
This study presents the difference between two operative techniques of hypospadias surgery together with their urinary diversion methods and the outcome concerning related complications. It is in essence a prospective non randomised study because both methods have been advocated from the beginning by their respective surgeons. *It clearly shows that in a population operated for hypospadias with varying degrees of deformity, the absence of indwelling postoperative urinary diversion does not cause a high complication rate and may even be associated with fewer complications. Inversely, the application of a technique that uses indwelling urinary diversion in a similar group of patients does not exclude a high complication rate. If a reliable technique of urethroplasty is used, the use of an indwelling catheter diversion appears to be of no beneficial effect to the outcome of hypospadia surgery. Certainly the use of an indwelling catheter diversion does not give guarantees for a low complication rate.*

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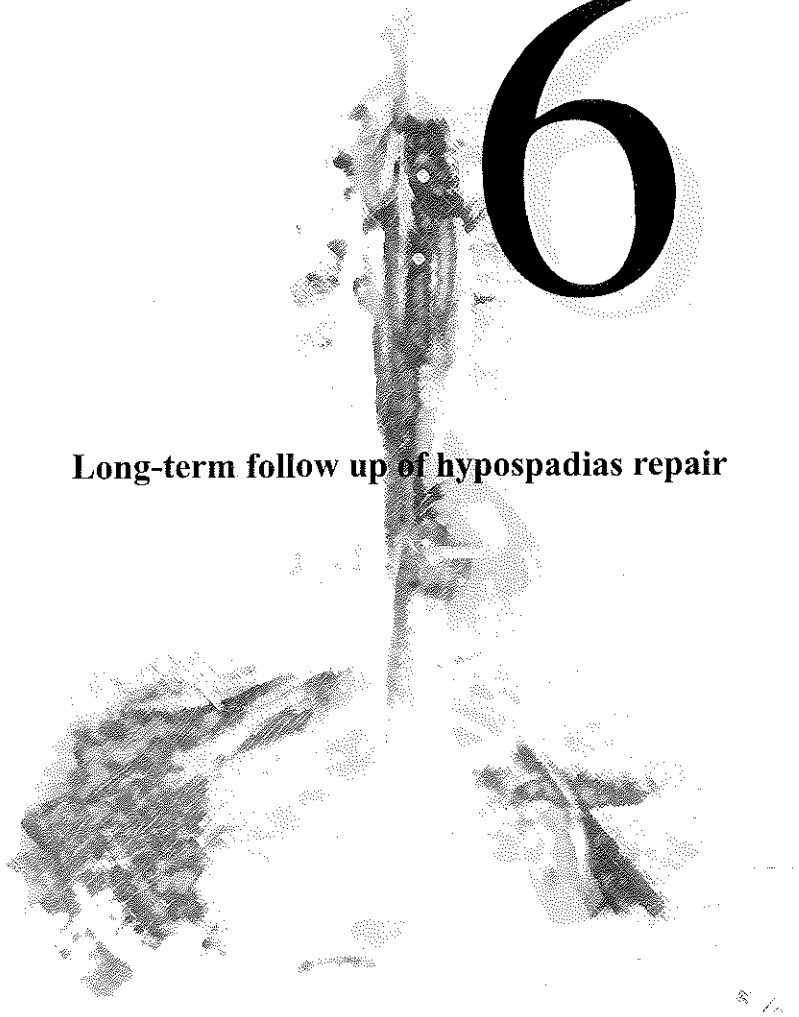
Long-term follow up of hypospadias repair



Introduction

Essential in the evaluation of operative techniques for congenital malformations is their long-term follow up. New techniques with seemingly obvious advantages (one stage repairs for instance) should have their final judgement when patients reach their twenties. Just as in cleft lip and palate surgery, where patients are followed up to and, if necessary, are treated beyond adolescence, the hypospadiac patient deserves a similar attention because it is only towards adulthood when the full range of functions of the male external genital becomes apparent (micturition, copulation, ejaculation, etc.). For a professional guidance of growing up patients, data on the long-term results of hypospadias repairs therefore should be available. These data comprise information on scar formation and maturation, the evolution of micturition after hypospadias repair, occurrence of infertility, psychological maturation of the patient and possible upper urinary tract influences. In summary, the surgeon must be aware of his patients' satisfaction and the adolescent patient should be given the opportunity to discuss his wishes. This obviously applies for somatic as well as psychological problems.
The techniques of Ombredanne and Denis Browne in particular have been used and evaluated by a number of surgeons [1-6]. Other techniques that were reviewed at long-term follow up are those by Nové-Josserand, Broadbent, Mustarde, Culp, Duplay, Edmunds, Mathieu and Harris [3,6,7,8,9]. The last two repairs are the only one stage techniques that have been evaluated at long-term. The van der Meulen repair has been used and reported by several authors, but there is no report of a follow up longer then a few years.[10-20]
We would like to present data on the long-term follow up of patients operated for hypospadias either by the van der Meulen technique or that of Byars/Denis Browne. [21]

Materials and methods

The files of all patients operated for congenital urogenital malformations from a thirty year period (1963-1993), were collected and reviewed. A Hypospadias Assessment Chart was designed to score all relevant data: demographic information (name, address, etc.), referral status (primary vs. secondary, speciality of referral), diagnosis (hypospadia, epispadia, cryptospadia or congenital short urethra), associated congenital malformations and details concerning treatment (time and type of operation, operative surgeon, peri operative measures and postoperative complications). All data were saved in a computer database for further analysis. A letter explaining the purpose and extent of the follow-up study together with an invitation for a hospital visit was sent to all hypospadias patients at their latest known address. When a patient had moved, two attempts were made to get hold of the current address through the City Council. When this was not successful, no further steps were undertaken. The men that did not respond, were contacted by phone to persuade

them to cooperate. No attempt was made to send the non attendees a questionnaire since it was felt mandatory to perform a physical examination on all patients.
The operations performed were the van der Meulen type I repair, which uses a dorsal transposition flap for coverage of a ventral outlined strip for urethral reconstruction. This is a one stage procedure for mild Hypospadias where no straightening of the penis by release of the dystopic meatus is necessary. For the more severe Hypospadias, the van der Meulen type II repair was used. This is a two stage technique where straightening of the penis by release of the corpora cavernosa and dystopic meatus is necessary with transposition of a dorsal preputial flap to the ventral surface as an initial procedure (orthoplasty). The second stage is an urethroplasty created from the previously deposited skin of the first operation [14]. *(The type I operation was performed in the class I and IIA hypospadias, according to the classification mentioned in chapter three. The type II procedure was executed in class IIB hypospadias (chapter three).* The alternative procedure was a combination of a Byars orthoplasty, applying two dorsal preputial flaps for coverage of the ventral skin defect, followed by a Denis Browne urethroplasty as a two staged procedure (buried skin strip sutured with Dexon and covered with bilateral advanced penile skin closed in the median over the neo-urethra).[21]
At the time of the follow up visit, a questionnaire was used to assess the patients social status, religion and physical well being. Specific attention was paid to miction (spraying, quality of urinary stream, painful miction, hesitation, straining and dribbling), the occurrence of urinary tract infections and psychosexual function and development. Furthermore, patients were asked to perform a flowmetry study on a rotating disk flowmeter. A physical examination by an independent assessor (the first author of this paper) always followed the interrogation with special attention for residual curvature (no erection test was performed), penile torsion, skin surplus, stenosis of the urethral meatus, quality of scars, urethral hair growth and fistula.
Penile torsion was measured with the patient in the supine position, the penis reflected on the abdominal wall. Torsion was then established with a goniometer, measuring the angle between the meatal slit and the sagittal plane. When torsion was present, this was checked with the patient in a standing position from an inferior view. The patient was offered the opportunity to present his problems and possible future surgery was discussed. All questionnaires and physical examination were processed by the first author, as an independent observer, not the surgeon.
The results of the psychosexual interrogation and uroflowmetry were analysed and published previously.[22-23] Because referral status obviously determines the final outcome of hypospadias surgery, the secondary referred patients from this population will be reviewed elsewhere. [24]
For primarily referred mature patients, the correlation of the data found at retrospective analysis of the patients records and the results from the follow-up visit will be presented.

Results

Of the 473 patients primarily operated for hypospadias, 140 subjects eventually attended the follow-up visit and were examined, which means an attendance score of 30 %. Comparison of referral status and severity of disease revealed that the initial population of treatment correlated well with the responding follow-up group (table 1).

		Treatment group	Follow-up group
Referral status	Primary	473 (83%)	140 (77%)
	Secondary	94 (17%)	43 (23%)
	Total	567 (100%)	183 (100%)
Grading of hypospadias	Glandular	211 (37%)	49 (27%)
	Distal penile	261 (46%)	100 (55%)
	Proximal penile	76 (13%)	26 (14%)
	Peno-scrotal	15 (3%)	6 (3%)
	Unknown	4 (1%)	2 (1%)

Table 1. Referral status and grading of hypospadias of the study group in comparison with the treatment group.

Follow-up time ranged from three to twenty-eight years with a mean follow-up of fifteen years. The age of first operation for the primarily referred patients ranged from 3 months to 24 years with an average of five years (median age 3,5 years). The primarily referred patients were operated either according to the one stage procedure by van der Meulen (87 patients), the two stage technique by van der Meulen (17 patients), the two stage Byars/ Denis Brown repair (33 patients) or miscellaneous operations (3 patients, who will not be discussed). The results at follow-up can be listed according to the operative technique used: (tables 2 and 3)

	Van der Meulen type I (n=87)	Van der Meulen type II (n=17)	Byars/Denis Browne (n=33)
Spraying	7 (8%)	2 (12%)	4 (12%)
Stream deviation	28 (32%)	3 (18%)	7 (21%)
Urinary tract infection	1 (1%)	1 (6%)	1 (3%)
Painful miction	0	1 (6%)	0
Dribbling	14 (16%)	4 (24%)	10 (30%)
Hesitation	4 (5%)	1 (6%)	3 (9%)
Straining	0	0	0

Table 2 Results from questionnaire of patients at follow-up, using three different operative techniques.

Van der Meulen type I repair

Spraying was reported by seven out of eighty-seven patients (8%). At physical examination, none of these patients had major irregularities of the urethral meatus, two had a surplus of skin that was on the lateral side of the glans and two patients had a minor

	vd Meulen type I (n=87)	vd Meulen type II (n=17)	Byars/Denis Browne (n=33)
Residual curvature	2 (2%)	1 (6%)	3 (9%)
Skin surplus	20 (23%)	4 (23%)	7 (21%)
Fistula	0	0	0
Meatal stenosis	1 (1%)	0	1 (3%)
Penile torsion			
< 10 degrees	34 (39%)	4 (23%)	13 (39%)
> 10 degrees	2 (2%)	0	1 (3%)

Table 3 Results of physical examination at follow-up of three techniques

torsion of the penis (less then 10 degrees). No explanation could be found for spraying in these patients. A deviation of the urinary stream was mentioned by 28 patients (32%), sixteen of which had a mild torsion of the penis (less than 10 degrees) without further abnormalities at examination. One patient touched on recurrent urinary tract infection in the past, without being able to recollect the incidence and at examination, no meatal stenosis or other abnormalities could be found. Bothersome postmictional dribbling was brought about by fourteen patients (16%), without physical abnormalities being present. Intermittent hesitation was mentioned by four patients without clinical relevance nor causative physical abnormalities. Straining at miction was not encountered.
At physical examination, minor residual curvature was found with two patients (2%), a small lateral skin surplus was encountered in twenty patients (23%), one patient had a relatively narrow meatus and torsion of the penis was seen with 36 patients. Of the patients having a torsion, only two had a leftsided turning of more than ten degrees (15 and 20 degrees respectively). None of these patients had a problem with miction other than a mild deviation of the urinary stream. All patients could perform their miction in the standing position. Finally, no fistula were encountered during the physical check-ups.

Van der Meulen type II repair

Two out of seventeen patients complained of spraying (12%), where no substrate could be found at physical examination. A deviated miction was cited by three patients (18%) without any abnormality being present (no torsion, curvature or stenosis). One patient reported four urinary tract infections in a period of twenty years. No abnormalities were found accounting for this fact. One patient suffered from occasional painful miction and copulation. On physical examination, hair growth could be observed in the urethra. Previous electrolysis had not been successful and this patient did not want any further treatment. Dribbling was mentioned by four patients (24%), where no physical substrate could be found. Straining at miction was not seen and one patient revealed intermittent hesitation without clinical consequence.

At physical examination, one patient had a minor curvature without clinical significance, four patients had a lateral skin redundancy without a wish for further surgery and four had mild torsion of the penis (less then ten degrees). Neither meatal stenosis nor fistula were found at follow up.

Byars / Denis Brown repair

Four of the thirty three patients seen at follow up, complained of spraying (12%), one of whom showed to have a relative meatal stenosis and a mild penile torsion (less than ten degrees). This patient decided not to have any further surgery. Deviation of the urinary stream was brought about by seven patients (21%) of which six were found to have a mild torsion one of which was associated with a meatal stenosis (the same patient with spraying and torsion mentioned previously). One patient complaining of stream deviation, showed to have a torsion of sixty degrees to the left. This person, however, judged the quality of his urinary stream as sufficient. No deformities were found in the one patient complaining of recurrent urinary tract infections (four bladder infections in fourteen years follow up). Ten patients complained about postmictional dribbling (30%) none of which had abnormalities accounting for this fact. Hesitation of the urinary stream was reported by three patients without clinical importance and straining at miction was not encountered. At physical examination, no fistula were found, three patients had a minimal residual curvature (9%) and seven patients had redundant skin (21%) without a wish to trim this surplus.
Data on the psychosexual adjustment of patients, cosmetic appearance and the desire to have further surgery were presented in a previously published study [22].

Discussion

Because proper information to parents and patients concerning long-term outcome after hypospadias repair is imperative, data on this matter should be available. Today's adult results are the consequence of yesterdays operations and today's infancy techniques subsequently will give tomorrow's aftermath's.
Possible long-term troubles following hypospadias repair can be summarised as problems of function or of appearance. Functional bothers can be divided between those of miction, copulation and of upper urinary tract problems. For miction, the quality, quantity and course of the urinary stream are important factors. Spraying may occur as well as deflection of the stream, dribbling or hesitation. Sommerlad reported an extensive follow up of the Denis Browne and Ombredanne operations and found that more then two thirds of his patients complained of spraying [5]. Kumar and Harris [9] presented the results of the Harris one stage technique and documented a forty percent spraying rate, which is in agreement with the study by Aho et al. [8] reporting 39% of patients operated by Denis Browne, Mathieu or Ombredanne repairs suffering from sprinkling. In our series, spraying

was encountered in 8-12 % of patients. It therefore seems justified to warn patients and parents of future spraying. Whether or not this is the result of the hypospadias repair or from the circumcising effect, remains an unsolved question.

Deviation of the urinary stream can be another bothersome sequel of hypospadias repair. Data on the occurrence of deflection of the urinary flow reveal that at long-term follow-up, more than half the men operated by the Denis Browne or Ombrédanne techniques complained of this annoyance [5]. We report deviation rates ranging from 18% to 32%, whereas Aho et al. [8] found deviated miction in only 17% of patients.

Pompino et al. [1] presented a long term review of Denis Browne and Ombrédanne's repairs. They did not supply information on spraying and stream deflection, but reported postmictional dribbling in approximately 10% of their patients, whereas Sommerlad described dribbling in close to 40% of his patients [5]. We found that between 16% (van der Meulen type I) and 33% (Byars/Denis Brown) of our patients complained of trickling.

Discussing the relevance of these figures (spraying, deviation and dribbling), we must realise their normative values in every day life. No data are available on the number of men in the normal population that have troubles with spraying during miction. It could well be that a substantial amount of, for instance, circumcised men feel that they have a sprinkled miction. The normal urethral meatus is slitlike and (in uncircumcised men) covered by the preputium. When miction starts, fluid is accumulated between the preputial skin and the glans and by pressure exerted from the bladder, urine is forced out of the prepuce to produce a regular stream forward and downward. When the prepuce is not covering the glans, there is no smoothing out of the stream and therefore the shape of this stream can potentially be influenced by any irregularity in the orifice of the urethra. Leuthardt and Morger [4] found that deflection of the urinary stream is not correlated to the site of the meatus of the urethra in the glans. We believe that the force exerted at miction in this respect has a far more substantial influence.

Although bothersome, we think that some degree of postmictional dribbling is inevitable in the patient operated for hypospadias. The smooth muscle fibres in the adventitia of the normal urethra and the elasticity of the corpus spongiosum cause a collapse of the urethra at the end of miction. Since the hypospadias deformity is characterised by an abnormal or deficient development of the corpus spongiosum distal to the meatus, the neo urethra is not supported by this structure and therefore collapse can be difficult or impossible. This may explain the occurrence of postmictional dribbling which, however, can be observed in the normal population too [25]. Since no normative data are at hand, conclusions can not be drawn with certainty.

Another physical finding where no normative values are obtainable is the presence of penile torsion. Although Avellan [26] pointed out that torsion of the glans can be visualised in hypospadias patients and that asymmetry in the distribution of the maldeveloped corpus spongiosum is probably the causative factor, no other reports on this subject are available. Three patients in our series showed to have significant torsion but from the patients

records no data could be found on the pre operative existence of this torsion. Therefore it remains unclear whether the operations have caused , worsened or diminished it. Moreover, the actual measurement of torsion is not easy to perform. To get a good quantification of penile body torsion, an erection test is necessary.
Apart from psychological aspects, problems of copulation can be caused by pain, residual curvature of the phallus at erection or insufficient penile length. Tethering ventral skin shortage with micro trauma to the skin, infection or callus formation with urethral hair growth or fragile scars, can all be a cause for pain. Residual curvature too can originate from skin shortage as well as insufficient release of tethering bands. Insufficient penile length is a condition that principally is not the consequence of surgery but of under development. Therefore the prevention of copulation problems should be directed towards proper wound healing, sufficient straightening of the penile body, avoid potentially hair-bearing skin for reconstruction and alleviation of skin shortage on the ventral side. Finally, psychosexual adjustment seems to depend on the severity of initial disease, age of completion of repair and not on the operative technique [22].
Surprisingly, no patient of the follow-up group had sought doctors' advise on his own initiative. Most of them however, were more than happy to discuss their problems. On this occasion, it was found that many problems could be solved by supplying proper information.
This paper gives long-term results of two strategies of hypospadias repair from one Plastic Surgery unit. The period in which patients were treated lies between an era of many complications following hypospadias repair (i.e. before 1960) and the development of more modern and extensive techniques. Of the latter group, no long-term adult results are available yet and we hope to see the beneficial effects on sexual function and micturition of the so-called glans closing techniques in the future.
In conclusion we can state that hypospadias patients at long-term follow-up may show signs of spraying, postmictional dribbling, deviation of the urinary stream, skin surplus and mild penile torsion. Whether or not this is normal or aberrant remains unclear because of a lack of normative values in the literature. It seems clear however that both providing proper information and follow-up through adolescence may avoid many problems and therefore must be strongly advocated.

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Urodynamic evaluation of hypospadias repair

Introduction

Reconstruction of the distal urethra in hypospadias patients needs to be evaluated beyond adolescence [1]. Several strategies can be followed in this assessment. A consequent patient follow up should be completed with one or more objective parameters.
Miction and ejaculation are the two main functions of the newly formed urethra, the latter being difficult to measure qualitatively. Miction can be visualized either qualitatively (e.g. miction cystourethrogram or intravenous urethrography) or quantitatively (uroflowmetry or cystometry). Uroflowmetry is a widely accepted technique for screening of voiding function [2]. It is easy to perform, non invasive, reliable and relatively cheap. The purpose of this study is to establish the voiding function of a population operated for hypospadias. It is part of a larger study concerning the longterm follow up of patients from our department of Plastic and Reconstructive surgery, reflecting thirty years of experience with hypospadias surgery.

Material and methods

From the files of the department of Plastic and Reconstructive Surgery a cross sectional group of patients was selected which was operated for hypospadias in the past. Both primary and secondary referred patients were included in this study. Records of 175 patients operated for hypospadias were reviewed. Severity of the initial hypospadias was established from Grade I to Grade IV (table I) together with the number of operations, operation technique, number and nature of complications.

Grading	Number of patients
Grade I	52 (30%)
Grade II	99 (57%)
Grade III	17 (10%)
Grade IV	3 (2%)
Unknown	4 (2%)
Total	175

Table 1 Grading of hypospadias

The age of first operation of the studied group varied between one year and 55 years of age. All primary referred patients had their first operation before the age of six. With the secondary referred patients, this depended on the age at the time of referral. Because the group under study was a cross section through a population operated for hypospadias, length of follow up varied concordantly. No urethral dilatations were performed in this group of patients.
The operative procedures followed were either the Van der Meulen repair [3], which uses a dorsal transposition flap for coverage of the ventral surface and reconstruction of the

urethra. This operation is performed either as a type I procedure (one stage repair) or as a type II procedure (two stage repair), depending on severity of the hypospadias (table II). The alternative procedure was a combined Byars / Dennis Brown repair , which was always a two stage repair (Tolhurst [4]).

Operation technique	Number of patients	Mean number of patients
Van der Meulen (type I or II)	113	1,5
Byars/Denis Browne	56	2,4
Miscellaneous	6	1,7
Total	175	

Table 2 Operation methods

All patients were seen for an interview, a physical examination and an uroflowmetry. Suspicion of obstruction following uroflowmetry, was never associated with clinical obvious obstruction therefore no other urodynamic parameters were obtained. The age of the studied population varied between 3,3 and 66 years. All patients had had their last operation more then one year previously and were toilet trained. Uroflowmetry was performed by using a rotating disk uroflowmeter. Measurements taken were delay time, voiding time, flow time, time to maximum flow, maximum flow rate (Qmax), average flow rate and voided volume (Vcomp). For evaluation, Qmax and Vcomp were taken into consideration only and were plotted in age related nomograms [5] in four age groups (<8 years, 9-14 years, 15-21 years and >21 years). All uroflowmetry charts were reviewed by the two senior authors independent from the patients' records. Finally ,the review of the uroflowmetry was combined with the patients' records and medical history.

Results

Of the 175 patients interviewed, 27 patients complained of intermittent spraying (15%), painfull miction was marked in one case and 3 patients made notice of recurrent lower urinary tract infections (UTI). Physical examination didn't reveal any patients with a meatal stenosis. In some patients spraying could be contributed to skin irregularities at the meatus, although this was not a consistent finding.
Flowmetry data (Qmax and Vcomp) were plotted in age related nomograms [5] according to four different groups (fig 1 A-D). Because no difference could be established according to the operation technique, all patients were combined. In the age group less then 8 years, a relative large number of patients has low maximum flow rates (< P5, n=10 ; 37%). In the age group 9 - 14 years, this number was relatively smaller but still substantial (n=7 ; 38 %). The interpretation of these data in the group between 15 and 21 years is somewhat difficult because no normal values for Qmax with a high Vcomp are known from the

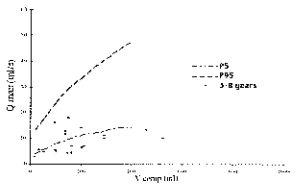

Fig 1A Age group 3-8 years flowmetry in nomograms

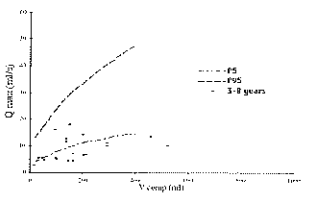

Fig 1B Age group 9-14 years flowmetry in nomograms

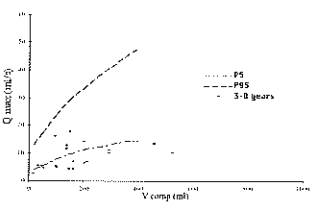

Fig 1C Age group 15-21 years flowmetry in nomograms

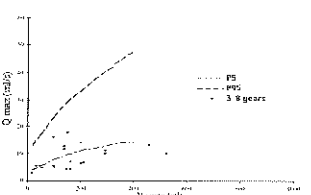

Fig 1D Age group >21years flowmetry in nomograms

literature. Estimating beyond these normal values, shows a maximum of six patients with values below P5 (15%). The large group of patients older then 21 years comprises ten patients with a low Qmax (11%).
Review of the uroflowmetry charts showed 108 patients with a normal profile, 20 patients with a mild suspicion for obstruction, 14 patients with a suspicion for obstruction and two patients with probable bladder dysfunction. The flow data of 31 patients were not conclusive, but not obstructive (table III).
Combination of the flow data with the interview, showed that no patient with an abnormal flow pattern complained of straining, voiding pain, hesitation or recurrent lower UTI. Patients with lower then normal flow rates did not differ according to the initial severity of hypospadias, operation technique or urinary diversion technique.
The three patients making notice of recurrent UTI, had a normal Qmax/Vcomp with normal flowpatterns. One patient complained of voiding pain but in retrospection this was not severe and of intermittent character. He did not have a meatal stenosis nor did his flowmetry charts show any abnormalities.

Interpretation	Number of patients
Normal	108
Borderline	20
Obstruction	14
Bladder dysfunction	2
Non conclusive	31
Total	175

Table 3 Interpretation of uroflowmetry

Discussion

Hypospadias is a congenital anomaly for which many operations have been advocated [6]. Numerous are the techniques with their subsequent modifications which have passed the literature. Fewer are the reports concerning longterm follow up of these techniques. Functional results of some techniques using uroflowmetry were described by even less authors. Kumar and Harris[7] present a group of 21 patients operated by the Harris technique with an age distribution at follow up of 13 - 25 years (table IV). This group shows only one patient (5%) with low maximum flow rate, but a large number of patients (40%) with intermittent spraying. Svensson et al[8] report on 33 patients (15-34 years) after a Dennis Browne technique. Spraying was frequent in this series as well (39%) with 15 % of the patients having a low Qmax. Jayanthi et al [9] describe two distinct age groups (3-7 years and 8-14 years) operated by either a vascularised or tubed preputial island flap. Their flow data, however, are inconsistent with their illustrations, so no conclusions can be drawn.

Festge et al [10] also report on two age groups (3-7 years and 8-13 years). In the first group, 52 % of patients have lower than normal maximum flow rates, where in the older age group this ratio is 27 % (overall average 40 %). Garibay et al [11] report on 32 patients operated with various techniques. Their series consists of relatively young children (3,6-8,6 years) and shows 20 % of patients with subnormal maximum flow rates, mostly after a tubularized preputial island flap. MacMillan et al [12] have the most differentiated study with three separate age groups, 3-7 years, 8-14 years and 15-21 years. Only two patients have low flow rates in the youngest group (5 % of total). This population, however, consists entirely of patients operated on by the MAGPI technique and ,therefore, all have relatively low grade hypospadias.

Author	Number of patients	Age group (yr)	Spraying (%)	Low
Kumar and Harris	21	13-25	40	5
Svensson	33	15-34	39	15
Jayanthi	80	3-7, 8-14	no data	31
Festge	54	5-16	40	40
Garibay	32	0.6-8,6	no data	20
MacMillan	44	2-15	unclear	5
van der Werff	175	4,3-66	15	17

Table IV Review of literature on low flowrates in uroflowmetry for hypospadias patients

Our series consists of a large number of patients (n=175) operated on according to two techniques. It is a long term follow up study of patients with initial moderate to severe hypospadias, a fact which is unfortunately only mentioned in the reports by Svennson et al [8] (mild to severe hypospadias) and McMillan et al [12] (all anterior hypospadias) .
Spraying was observed infrequently, low maximum flow rates were mostly seen in the younger age group (3-7 years, 37%), but not with increasing age. This tendency for a higher number of low flow rates with younger patients is consistent in all reports differentiating for age. A possible explanation could be that at short-term follow-up the newly constructed urethra is relatively small in diameter and semi-rigid. After several years of miction pressure and wound healing this urethra could have turned more elastic and wider. These conclusions, however, can only be drawn from a prospective study with consecutive uroflowmetry in the same patient. Such a report is still lacking in the literature unfortunately

Conclusions

No differences concerning flowmetry data could be established between patients operated on by the Van der Meulen technique and the combined Byars/Dennis Browne technique. Uroflowmetry in this report as well as in other series suggests a larger number of restricted flow data at a relative younger age. Further studies are necessary to disclose this consistent finding. The clinical relevance of low flow rates remains another unsolved problem because all reports find a strong discrepancy between low flow rates and patients' complaints or abnormal physical signs.
Evaluation of hypospadias surgery should include uroflowmetry at consecutive intervals postoperatively throughout adolescence. Only in this way an objective comparison can be made between various operation techniques.

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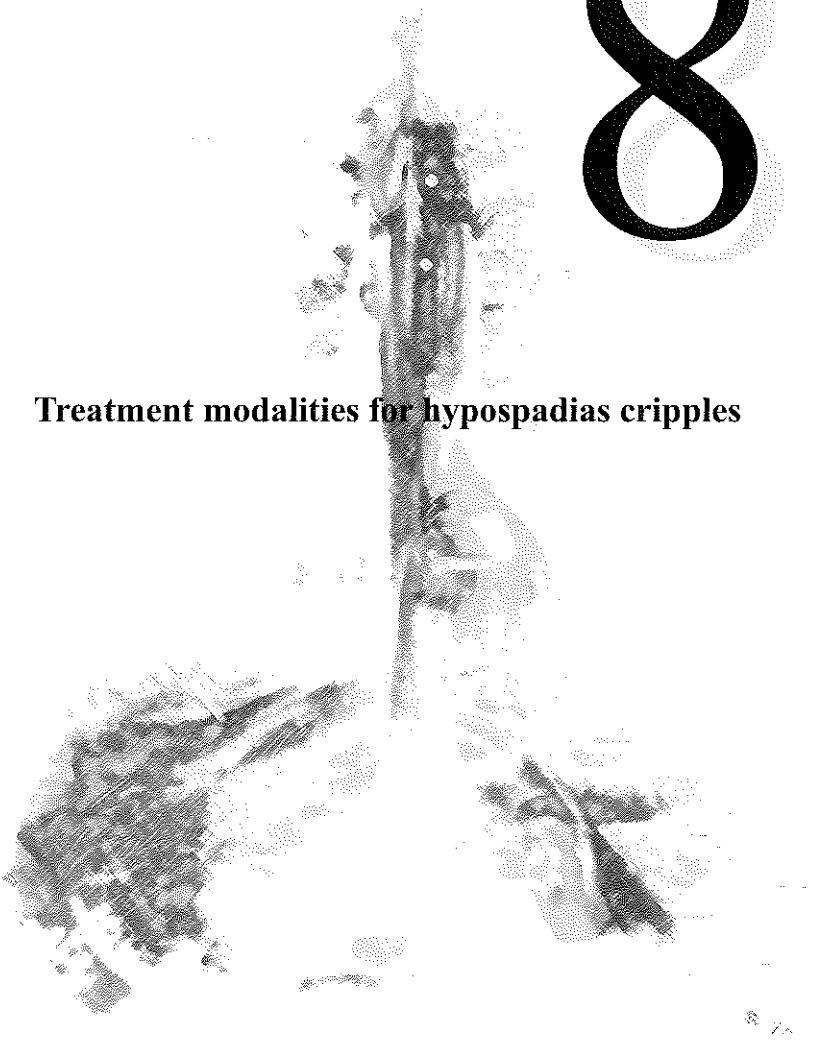

Treatment modalities for hypospadias cripples

Introduction

Despite the multitude of approximately three hundred original or modified techniques described in the literature for the management of hypospadias, the use of meticulous technique, delicate tissue handling and advanced postoperative care, a category of patients called "hypospadias cripples" still exists [1-3]. They are the boys or men that have been operated several times without the desired result and, more important, who still have major functional problems. In general, complications following hypospadias surgery can be graded according to the need for an additional operation: [4]

Grade I Minor complications (no re-operation needed)
e.g. small dehiscence, haematoma, urinary retention
Grade II Cosmetic complications (re-operation optional)
e.g. meatal retraction or dystopia, skin surplus, scar contraction or circumcised appearance
Grade III Major or functional complications (re-operation required)
e.g. bleeding, fistula, curvature, meatal or urethral stenosis

With hypospadias cripples, the Grade III complications can be confined to the urethra in the case of stenosis, stricture or hair growth. The penile skin can be another source of problems when there is either a severe shortage following rigorous previous surgery, it shows fistula or has a residual contracture giving rise to a penile curvature. Whatever the problems posed, a thorough assessment is mandatory in all cases as was already mentioned by Hinderer [5]. The factors to be assessed can be summarised: amount, position and quality of scars, laxity of penile skin, presence or absence of preputial skin, site, shape and position of the urethral meatus, persistent curvature (artificial erection test), fistula and urethral irregularities. Some of these elements can only be judged intra-operatively and the definitive strategy for treatment must therefore be postponed until a full assessment has been made.
The treatment of hypospadias cripples has had attention in the literature because primary repairs give rise to a sufficient number of complications. The majority of papers on hypospadias complications are dealing with the management of fistulas, which, although quite common in the urological literature, do not pose the only problem to be solved in hypospadias cripples [5-11]. Residual curvature, meatal stenosis and dystopia are equally important but often more difficult to treat.
We present the technical considerations in the treatment of hypospadias cripples over a thirty year period on ninety-four patients and show long-term functional results of forty-three patients.

Material and methods

Over a thirty year period (1963-1993), ninety-four patients were referred to our unit for secondary surgery after hypospadias repair. At the time of operation a full assessment was made. The phallus was checked for the presence of curvature (artificial erection test used when necessary), fistulas, the extent and quality of scar tissue and the urethra was examined for irregularities and hairgrowth. Following this assessment, the possible donorsites for solving the problems were established: residual preputial skin, laxity of penile skin or local skin surplus.
The principles of treatment irrespective of the technique used, were the redistribution of well-vascularised skin, avoiding tension on and superposition of suture lines, application of a simple and non constricting dressing, subcutaneous sutures and delicate tissue handling. As a rule, no indwelling catheter diversion was used. The variety of techniques used for reconstruction are outlined:

Circumferential advancement of penile skin (fig. 1).
This technique relies on the laxity of skin that is characteristic for the penile body. Scar tissue from previous operations or severe skin shortage with a residual curvature can render this technique impossible. When, however, the skin can be sufficiently stretched after complete mobilisation of the penile body, it can be used to cover corrected fistulas, a straightened penis after correction of a mild curvature or a meatus that has been brought more distally. The main advantages of this technique are the inconspicuous subglandular scar and the avoidance of overlapping suture lines.

Figure 1: Circumferential advancement of penile skin with closure of a fistula. (fig.1A-C)

Dorsal transposition flap of preputial skin (fig. 2).
When residual preputial skin has survived previous surgery, this can be transposed to the ventral side of the phallus using a dorsal backcut. In this way, well vascularised skin can be used to cover excised fistulas, a newly formed urethra or skin defects that arise after

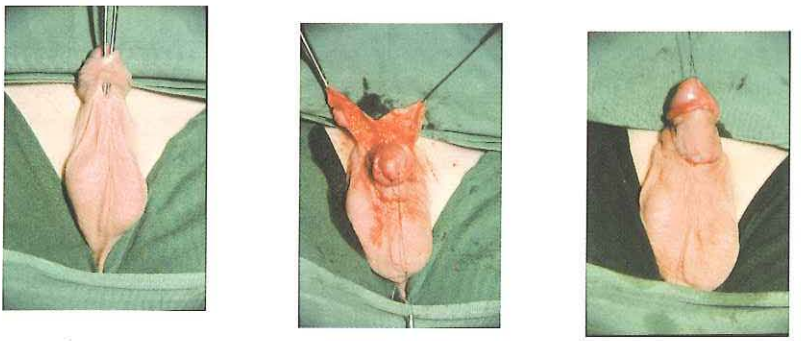

Figure 2: To cover the closure of a large fistula, a dorsal skin flap was trans-posed to the ventral surface.

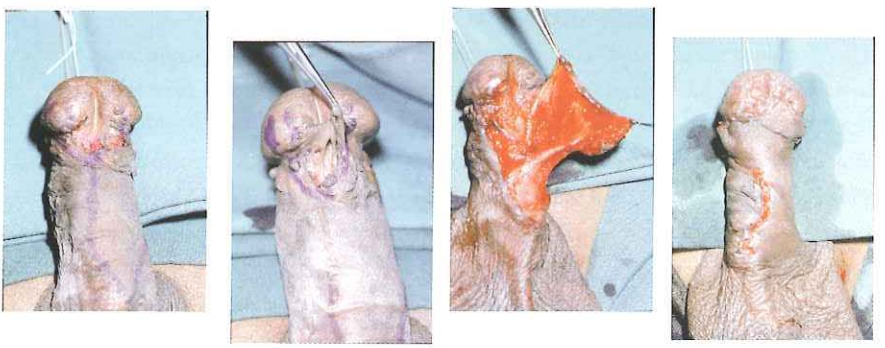

Figure 3: An overt meatal dystopia with bad scarring was treated with excision of scars and development of a distally based penile skin flap together with closure of the glans.

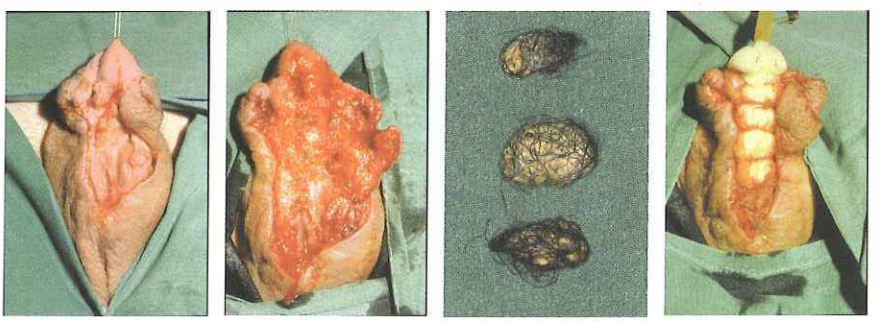

Figure 4: After resection of a badly scarred urethra of hair bearing skin, a full thickness skin graft was necessary to create a new urethral strip for future reconstruction .

release of curvature. It is possible to "bank" this skin on the lateral side of the phallus first for later use in a second stage reconstruction of a new urethra similar to the principles advocated by the two stage Van der Meulen technique for primary hypospadias [12-15].

Distally based transposition flap of penile skin (fig. 3)
This distally based flap can only be used if local penile skin is sufficiently ample and unscarred. Its random pattern vascular supply is usually adequate for the skin to be transposed and cover a neo-urethra or corrected fistulas. In essence, it resembles an uneven Z-plasty.

Full thickness skin graft (fig. 4)
When a staged procedure was required and no skin was at hand to build and cover a new urethra in one stage, the ventral side of the penis was grafted after resection of all scar tissue and total straightening of the corpora cavernosa. In a second stage, the remaining available skin of the penile body was used to cover a skin strip for urethral reconstruction.

When necessary, a combination of techniques was used, sometimes in staged repairs. The abovementioned procedures should therefore be seen as an armentarium or strategy to solve the multitude of problems seen with hypospadias cripples.
The hospital charts of all patients were reviewed and data were scored on a Hypospadias Assessment Chart (fig. 5). A letter explaining the purpose and extent of the follow up study

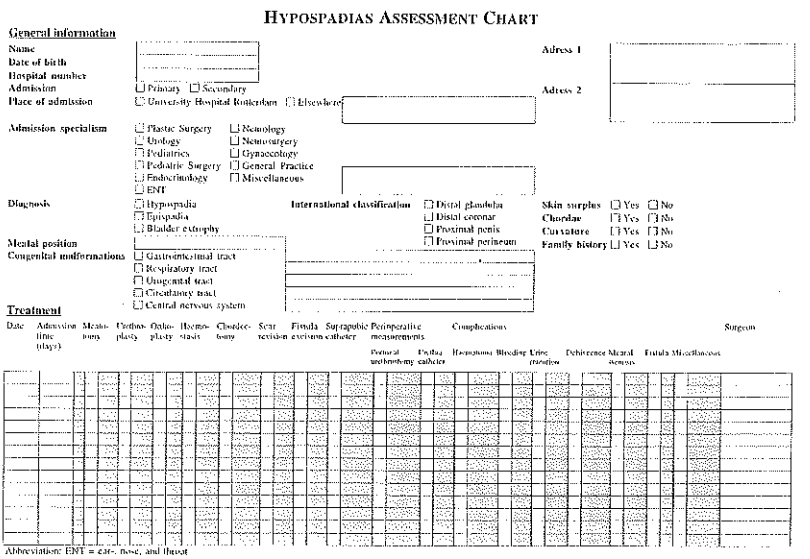

Figure 5: **The Hypospadias Assessment Chart used for evaluation of data.**

together with an invitation for a hospital visit was sent to all patients at their latest known address. When a patient had moved, two attempts were made to get hold of the current address through the City Council. When this was not successful, no further steps were undertaken. The boys or men that did not respond, were contacted by telephone to persuade them to cooperate. No attempt was made to send the non-responders a questionnaire since it was felt mandatory to perform a physical examination on all patients. In this way, short-term and long-term complications could be established in a population of hypospadias cripples.

Results

Population study

Ninety-four patients that had undergone previous surgery for hypospadias in other hospitals were referred to our unit over a thirty year period. The functional problems they carried with them on first presentation are summarised in table 1.

	Number of patients (n= 94)	**Percentage**
Meatal dystopia	82	87 %
Curvature	43	46 %
Meatal stenosis	19	20 %
Fistulas	5	5 %

Table 1: Presentation of functional problems of 94 hypospadias cripples at first visit.

Eighty-two patients had a major meatal dystopia (87%), forty-three patients (46%) had residual curvature at presentation, nine-teen patients (20%) showed meatal stenosis whereas five individuals (5%) had one or more fistulas. Neither the preceding number or nature of operative procedures in other hospitals nor the severity of the initial hypospadias could be traced with certainty for all patients, therefore no data are given.
Between one and nine operations were necessary to achieve a good result (mean and median number of two sessions, figure 6). When a residual curvature was present together with a meatal dystopia, straightening of the penile body was performed first. Whenever possible, a urethroplasty was conducted at the same time but a liberal approach to staged repairs was advocated.

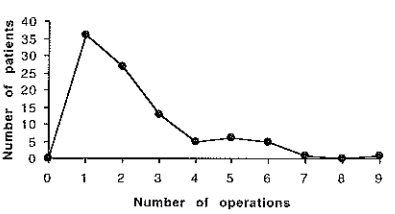

Figure 6: Number of operations to achieve a good result in 94 hypospadias cripples (mean and median number of two operations).

As can be expected in a population of such negative selection, post-operative complications occurred in a higher frequency then normal (table 2). With respect to Grade III complications, nine patients developed a total of eleven fistulas following their surgery, one of which was a primary fistula correction. All fistulas could be managed without great difficulty using one of the aforementioned techniques. Meatal stenosis due to tight scarring was encountered in six subjects.

		Number of patients (n=94)	Percentage
Grade I	Urinary retention	2	2%
	Small dehiscence	5	5%
Grade III	Fistula	11	12%
	Meatal stenosis	6	6%
	Residual curvature	1	1%

Table 2: Postoperative complications in a group of 94 hypospadias cripples

The treatment of these stenoses consisted of a meatotomy. Residual curvature following an orthoplasty had to be released once before a urethroplasty could be carried out. Grade I complications were seen in seven patients. Two boys had a postoperative urinary retention that didn't need an extra operation. A small dehiscence or marginal skin circulation was seen five times as can be visualised in figure 7. These complications had no consequences for the long-term outcome. Thus a total of seven (i.e. 7%) Grade I and eighteen (i.e. 19%) Grade III complications occurred in this patient population, summing up to a total complication rate of twenty-six percent. Because patient satisfaction seriously influences the scoring of Grade II complications, details are given in the follow-up study.
In summary, all patients could be treated to have a satisfactory result in the end whatever the initial problems.

Figure 7: A small dehiscence postoperatively was treated conservatively with a final good result

Follow- up study

Forty-three patients responded to our request for a long term follow up visit to assess the functional result, finishing a questionnaire, a physical examination and uroflowmetry (average follow up time of 12 years, range 2 -25 years; mean age at follow up 22 years, range 9-65 years).

By means of the questionnaire, five patients complained of intermittent spraying at micturition. Two of them showed irregularities of the external meatus, but both didn't want any further surgery. The other three didn't have any physical signs explaining their spraying. Postmictional dribbling was mentioned by six subjects, where physical examination revealed no abnormalities accounting for this annoyance. Seven men reported a deflected urinary stream, where two patients had a physical reason for this. One patient had developed a residual curvature over a period of sixteen years and another patient showed up at the follow-up study stating that he was still waiting for his second operation. He had been operated sixteen times in another hospital before he was referred to our unit. Following an orthoplasty by us, he had been postponing surgery for almost twenty years, despite several attempts from our side to persuade him. At long-term follow-up, he presented with a scrotal meatus with badly scarred penile skin from the previous operations. Needless to say he was again scheduled for a staged repair, but refrained from further surgery after we had brought his meatus to the midpenile level. No patient complained of hesitation at micturition and two patients reported recurrent urinary tract infection. One of them had overgrown juvenile periods of cystitis without specific treatment and one patient had polycystic kidney disease (table 3).

Functional complaint	Number of patients (n= 43)
Spraying	5 (11%)
Painful miction	0
Dribbling	6 (14%)
Hesitation	0
Straining	0
Stream deviation	7 (16%)
Urinary tract infection	2 (5%)

Table 3: Results from questionnaire at long-term follow up of 43 patients

Upon physical examination, four patients had a residual curvature, three of which were mild without causing functional problems. As already mentioned, one man had gradually developed a curvature during the sixteen years following his last operation. One patient presented with a fistula that had occurred after he had undergone refinement surgery of his glans in another hospital after finishing his treatment with us. He persisted in his wish to have treatment of this fistula in the other institute. A surplus of skin was seen with five patients, without causing functional problems. None of these men had the desire for another operation. No patients evidenced a meatal stenosis. Finally, torsion was objecti-

vated in thirteen patients, but only six men had a torsion of the glans of more then ten degrees. The direction of torsion in these six subjects was evenly distributed to the left and right. A relation between torsion and functional problems could not be excluded in the one patient with a residual curvature and spraying already described. No further patients showed functional problems (table 4).

	Number of patients (n= 43)
Residual curvature	4 (9%)
Fistula	1 (2%)
Skin surplus	5 (11%)
Meatal stenosis	0
Penile torsion	
< 10 degrees	7 (16%)
> 10 degrees	6 (14%)

Table 4. Findings of physical examination at long term follow up of 43 patients.

On the whole, patients seemed to be happy to discuss there well-being after so many years of treatment. Some of them regretted not having had an appointment for an outpatient visit earlier. Answering their questions frequently reassured them and only one patient choose to have further surgery for reasons already pointed out.
In summary, at long-term follow up only one patient developed a major problem consisting of a residual curvature. All other initial problems had been treated successfully. Although sometimes bothersome, the functional problems encountered (spraying, stream deflection, dribbling or recurrent urinary tract infections) where either temporary, derived from other sources or mild in character.

Discussion

The attention for secondary procedures in hypospadias surgery focuses mainly on the treatment of urethrocutaneous fistulas [8, 16-24]. Few reports deal with the treatment of true hypospadias cripples. This seems rather strange because hypospadias surgery is still endowed with a complication rate that even in this era can be quite high especially for proximal cases.
Both Hinderer [5] and Devine [6] clearly showed that fistulas pose only part of the problems encountered with hypospadias cripples. Similar to our observations, they found a high frequency of residual penile curvature, meatal dystopia and stenosis. For this reason, treatment of this "unlucky" group of patients is a challenge for the reconstructive genital surgeon. The goals to be achieved are similar to primary repairs: a straight penis with a normal shaped terminal meatus of sufficient calibre. The prognosis, however, is worsened by the frequent absence of preputial skin, the amount and place of scar tissue and with increasing age of the patient, complications due to postoperative erections can be expected. These three factors all influence the final physical and psychological outcome at long term.

In the literature on hypospadias repair, very few reports deal with the subject of hypospadias cripples. Hinderer [5] presented an elaborate study on the secondary repair of hypospadias failures in forty-three patients. He advocated the use of his tunnelling technique both for primary repairs and hypospadias cripples. Following his treatment for secondary cripples, a Grade III complication rate of twenty-eight percent occurred (26% fistulas and 2% diverticula) whereas an additional two percent Grade I complications were found. He showed no results at long-term follow up. Devine et al described seventy patients with failed primary repairs and severe complications [6]. They used a very wide variety of techniques (more then thirty) to solve individual problems. They advocated the use of staged techniques in this group of patients. The complications they encountered were fistula, strictures, residual curvature, meatal retraction, skin necrosis and urethral diverticulum without giving any numbers or percentages of these complications. They presented an excellent and thorough survey of the problems seen in primary repair of hypospadias and suggestions to avoid these. Kröpfl et al recently demonstrated the short and midterm results of treatment of forty "complicated hypospadias recurrences" [9]. They used miscellaneous techniques for reconstruction of their patients. Fistulas were more often seen in the repairs utilising random pattern flaps (forty percent fistulas) compared to island flaps (fourteen percent fistulas). They emphasised the importance of avoiding pressure necrosis caused by a circular dressing and they pointed out the high frequency of bladder spasms encountered with the use of suprapubic cystostomy in children. Kon and Sagi described the principles of the Van der Meulen dorsal transposition flap in the treatment of hypospadias cripples without a residual curvature [11]. None of their patients needed more then one operation to achieve a good result. Finally, Elder and Duckett gave an anecdotal survey of their experience with secondary surgery for hypospadias without elaborating on their complications or long-term results [10].

The psychosocial and psychosexual adjustment of patients operated secondarily for hypospadias in our unit, were published previously [25]. The present study shows the long-term results of an institutional approach to hypospadias cripples and focuses on the physical outcome. It seems clear that both the number of operations needed to achieve a good result and the complication rate are higher then in primary repairs. The functional problems seen at long-term follow up (spraying, deviation of urinary stream, penile torsion, dribbling and hesitation) are somewhat more difficult to understand. No direct relationship is shown between the existence of any these functional bothers and physical abnormalities. Moreover, normative data from the general population are missing to make a comparison. This makes judgement of the present study somewhat difficult because, to our knowledge, no reports have been published on the long-term results of hypospadias cripples. From our own studies, we learned that with primary repair of hypospadias, a similar discrepancy between functional problems and the lack of physical abnormalities existed [4].

We therefore conclude that hypospadias cripples can be treated with relative simples

operative techniques, provided that an extensive assessment of the involved pathology is made and that a liberal approach to staged repairs is followed. The elements of treatment should comprise meticulous tissue handling, the use of well-vascularised flaps, avoidance of superposition of suture lines and the use of a non-constrictive dressing. These conclusions find support in the sparse literature found on this subject.-

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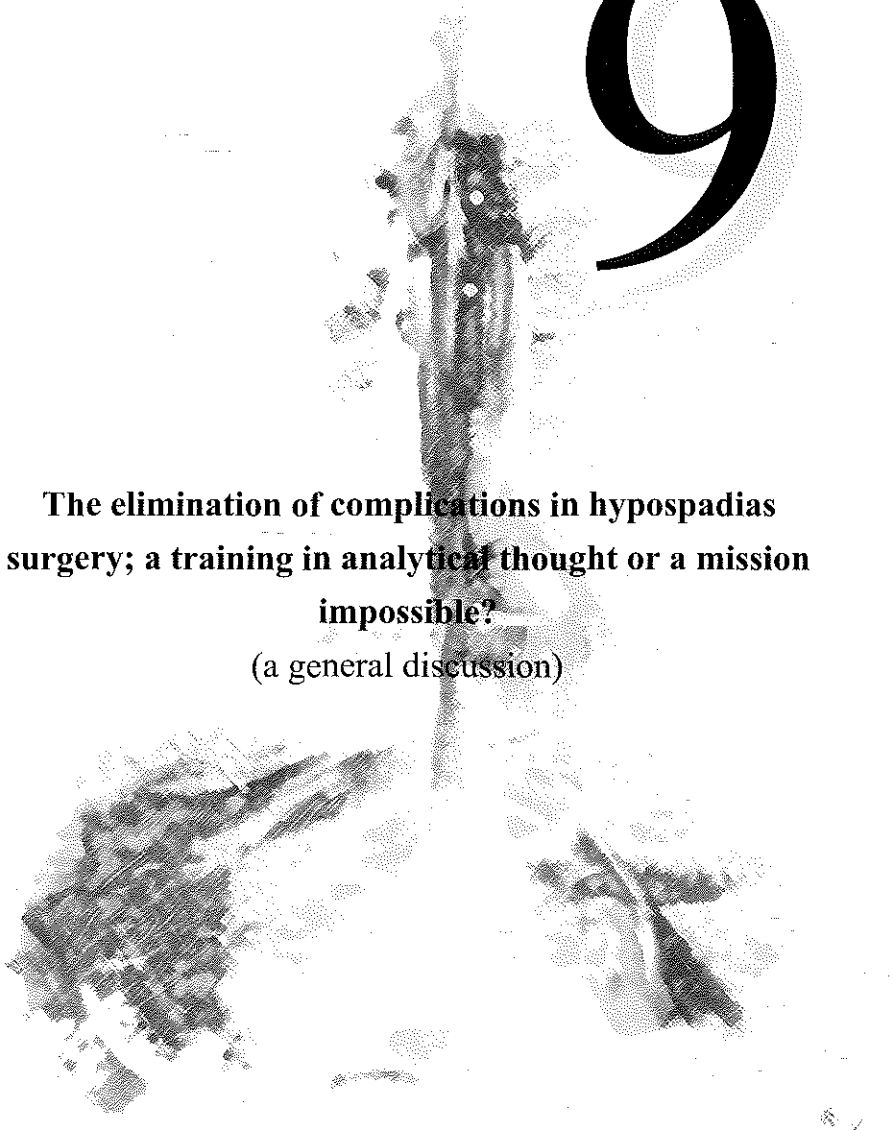

The elimination of complications in hypospadias surgery; a training in analytical thought or a mission impossible?

(a general discussion)

General discussion

After 200 years of hypospadias surgery starting with Dieffenbach [12]and the successive promotion of several hundred techniques, there is still no consensus on the best treatment for this anomaly, nor will there be in the next 200 years if the evaluation of many of these techniques continues to be opinion based instead of fact based.
In a recent discussion [3, 13] on the merits of a one stage versus a two stages correction of hypospadias, one of the opponents [3] referred to the methods of repair that were advocated by the first author of this article as being functionally and aesthetically crude. Ironically the other opponent once wrote that the results of the same procedure were dramatic; no fistulas!
Sufficient reason to discuss the motives that led the first author to develop the two procedures which were introduced in 1967 and present the results that were obtained in a series of 376 patients (chapter five). These motives were inspired by the results of a thesis that was written with the intention to identify the causes of the many complications of hypospadias surgery that were observed in those days and, if possible, eliminate some of these [28].

Complications

Deficient erection of the penile body

Half a century ago all hypospadias patients were considered to have chordee and therefore in need of an orthoplasty before the construction of an urethra (urethroplasty) could be considered. Smith and Blackfield [39]were the first to challenge this concept and Smith [40] later reported having found this strand (chordee) in only 3 of his 73 patients.
Then why the curvature observed so often in patients without chordee? Van der Meulen [28-31] attributed this phenomenon to the ever present shortage of skin on the ventral side of the penis and explained this deficiency as a discrepancy between abnormal growth of the urethral plate and a normal growth of the adjoining skin which continues to augment, while development of the urethra is retarded. Prevented however from growing in a longitudinal direction, the skin will expand in a transverse direction and form a fold at each side of the urethra. This folding will produce a shortage of skin on the ventral side of

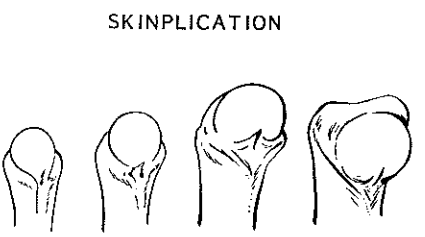

Figure 1: Advancing plication of skin during

the penis, a surplus on the dorsal side and two raphes on the lateral aspect, each ending in a dog ear as visualised in figure 1 (Ombredanne's eyes). The fact that a curvature can be produced by shortage of skin was six years later also recognised by King [26].
Inevitably this explanation had important consequences for many patients with hypospadias. Not only because it allowed for immediate urethral reconstruction following correction of curvature by release of the tight skin, but also because results of treatment for this type of hypospadias dramatically improved [9,14,16,18,23,32,33,45,47].
Today the pendulum has swung even wider to the other extreme. Some surgeons [21,22] have started to question the role of the urethral plate as a tethering structure, blaming chordee on corporal disproportion and advocating dorsal corporoplasty. Peled et al [37] even denied the existence of chordee.
Our experience with hypospadias cripples [34] has shown that severe curvature may be observed in adults if chordee is not adequately corrected and that straightening of the corpora by dissection is the treatment of choice. It has also convinced us that a clear distinction should be made between patients without or with chordee in view of the implications release of chordee has for the treatment of hypospadias. We feel that when a patient has no curvature (class I hypospadias) or has a curvature due to a ventral skin shortage (class IIA hypospadias), his penis is straight or becomes straight following release of tethering skin or fascia. In these cases a urethroplasty can always be performed without retropositioning of the dystopic meatus. This is a class I or IIA hypospadias and the majority belongs to this group (320 patients in our series, chapter five). In all other patients the urethroplasty should be preceded by an orthoplasty because the curvature is caused by chordee. This category forms class IIB hypospadias (56 patients in our series).
Deficient erection of the penile body may be due to inadequate dissection of the corpora cavernosa or to inadequate reconstruction of the corporal defect following the dissection.
Inadequate dissection of the corpora occurs when not all tethering strands over the corporal surface are removed or separated in the class IIB category. This step involves retropositioning of the urethra. The quality of correction should be checked using the artificial erection test.
Inadequate reconstruction of the corporal defect results from a shortage of skin, a mid-line ventral scar or a short urethra. A full thickness graft as advocated by Devine and Horton [10] and more recently by Bracka [4] would seem to be the solution. In untrained hands however, rates of graft failure may be unacceptably high and the question of subsequent growth of the graft itself or in the scarred recipient site has not been answered.

Deficiencies in dimension of the neo-urethra

These problems may be due to inadequate vascularisation, connection, composition or delineation of the urethral strip.
Inadequate vascularisation may occur when the viability of a skin flap or graft is compromised by poorly performed dissection, by compression of a flap tunnelled through

the glans, by pressure exerted by a catheter combined with a constrictive dressing or by failure of graft take.
Inadequate connection is seen when the anastomoses are made in a circular fashion.
Inadequate composition is produced by a combination of scarring and laxity.
Normally the urethra is an adaptable structure which increases its width with passage of urine and its length during erection of the penis. Following an ortho-urethroplasty however, the neo-urethra contains a minimum of one longitudinal plus two circumferential scars: commonly one at each end. In addition to this it is made of skin, and not surrounded by a corpus spongiosum. The absence of this corpus spongiosum may permit excessive widening of the neo-urethra whereas scarring promotes narrowing and shortening [7]. All these factors combine to produce the irregularities of the neo-urethra so well demonstrated by Townsend [46].
Inadequate delineation may be observed when the neo-urethra is made too short or too narrow, too wide or too long. Inevitably the construction of a non adaptable structure in an adaptable organ, is not always based on accurate judgement creating a problem.
In addition to this, the development of urethral abnormalities may be an ongoing process. The dynamics of scar tissue can not be controlled and are not predictable. There is no guarantee that longitudinal scars will increase in length to match growth [7].

Deficient protection of the neo-urethra

Fistulas are the most common complications of hypospadias surgery. This problem may be due to inadequate closure, positioning, suturing, dressing and drainage of the wound.
Inadequate closure occurs when the flaps used to cover the neo-urethra are too small, thin or too scarred. In each instance devascularisation may result, causing wound healing problems and fistulae.
Inadequate positioning exists with super imposition of suture lines. Urine flow tends to take the path of least resistance and the part of the wound most at risk is near or at the proximal junction area where the impact of the flow is first felt. Super imposition of one suture line over another will decrease the resistance to flow and enhance fistula formation.
Inadequate suturing results when the subcutaneous tissues remain separated.
Approximation of these tissues in one or two layers is essential and sufficient.
Transcutaneous suturing facilitates the epithelialisation of suture tracks and the formation of fistulas. In addition to this it requires the removal of sutures which can be quit traumatic in a young child.
Inadequate dressing may cause constriction. Compressive gauze dressings can apply a pressure which is far too high (greater than 150 cm water pressure), consequently they may prevent free flow of urine, cause strangulation and predispose to the formation of fistulae. Furthermore, the dressing does not protect against infection which is usually secondary to haematoma and tissue necrosis, both being worsened by a bad dressing.

Inadequate drainage of the wound is produced when evacuation of blood is impeded. A constrictive dressing may be the cause. More important however is the stagnation of urine. In an urethroplasty with its short neo-urethra there is no need for urinary diversion. Contrary to this it is required following an ortho-urethroplasty. Unfortunately diversion by catheter may be associated with blockage, bladder infections and spasms due to irritation. Tenesmi will lead to leakage around the catheter. Sometimes even to jetlike evacuation of urine through the wound.

Deficient position, dimension and configuration of the neo-meatus

Discrimination between terminalisation and ventralisation procedures does not make sense. Terminalisation of the meatus can be achieved by glans tunnelling, glans onlay and glans inlay procedures (figs. 2-4). Each of the three techniques has its specific advantages

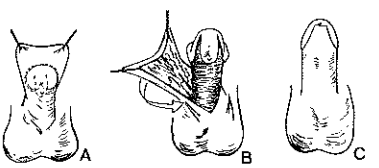

Fig.2 Ortho-urethroplasty

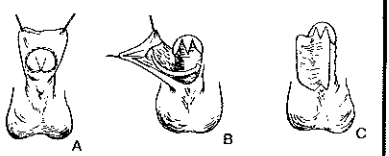

Fig.3 Orthoplasty

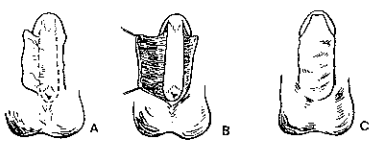

Fig.4 Urethroplasty

and disadvantages affecting size, site and shape of the meatus.

Deficiencies in size may involve constriction or dilatation, narrowing being due to stenosis and widening to skin relaxation.

Deficiencies in site may involve protrusion or retrusion; protrusion being due to excess of urethral lining and retrusion to scar contraction pulling on the meatal rim.

Deficiencies in shape may involve distraction and distortion. Distraction being due to scar contraction and distortion to skin irregularities. These deficiencies seem to be the cause of spraying. They form the price a boy sometimes pays for his neo-urethra and explain the lack of correlation between spraying and site of the meatus which was observed by Sommerlad [41].

Elimination of complications

Following identification of the many causes that were responsible for complications in hypospadias surgery, attempts were made to eliminate these causes as much as possible. For this purpose the following procedures were used.

Type I operation (urethroplasty as a one stage procedure for class I and IIA hypospadias): A skin strip is formed that is wide enough to create an urethra of sufficient calibre. This strip covered with a well vascularised transposition flap. This flap is raised on the dorsal side and rotated to the ventral side using a backcut. It is fixed to the glans on both sides of the strip with subcutaneous sutures, providing adequate protection and producing a terminal meatus. A simple sandwich dressing is applied avoiding circular compression and urinary diversion is omitted.

Type II operation (ortho-urethroplasty as a two-stage procedure for class IIB hypospadias) In stage I, an adequate release of the tethering strands is performed first. A well vascularised flap is raised on the dorsal side and rotated to the ventral side using a backcut. The inner lining of the prepuce is used to resurface the defect incorporating the original meatus by v-shaped interdigitation, to provide the split glans with a lining and to bank the remaining excess of skin on the lateral aspect of the penis. In stage II, inspection is first performed which allows for secondary correction when the penis is not sufficiently straight, a dystopic meatus is too narrow, a urethral lining too short long or irregular (due to scar contracture or fold formation). Elimination of deficiencies related to penile erection or urethral dimension is thus enhanced. Following inspection and, if necessary, correction a urethral strip consisting of soft and pliable skin is outlined and covered by the remaining "banked" skin from the transposition flap. Tubing of this skin is not indicated. Folding of the skin edges is achieved by accurate fixation of the rotation flap and approximation of subcutaneous tissues over the neo urethra and its glanular part. Problems due to tension or superposition of suturelines can thus be avoided with the creation of a terminal meatus. Direct closure of the glanular defect over the urethra was rejected until recent years because of the possible tension on the suturelines. This problem was solved by a modification of the splitting procedure in the first stage. After the sagittal incision has been made and a midline cleft produced, its walls are raised by means of a lamellar incision on each side (fig. 5). The wide space thus

Figure 5: Incision lines for the "louvre door " widening of the glans.
Figure 6: Longterm result of the "louvre door" repair.

created is filled with the inlay, permitting easy closure of the glans over the neo urethra in stage II (fig.6 showing the long-term result).

Remaining problems of function
Stringent application of these principles led to a considerable reduction of the fistula rate. In our series of 376 patients only four fistulas occurred; one in the type I procedure and three in the type II operation. A suprapubic cystostomy (although not trouble free itself) is only needed if these measures fail for some reason. Only one patient proved to have a persistent curvature of clinical significance at long-term follow up. Complications such as straining due to stenosis and fold formation in the neo-urethra could thus be avoided in our series. Constriction did not occur in our onlay procedure. Dilatation was however frequently observed.
Protrusion sometimes occurred following the type II technique and was corrected by reduction of the excess skin in the second stage prior to the urethroplasty. Retrusion was observed in both the type I and type II operation.

Remaining problems of appearance:
Long-term results [22,27,41] have shown that a significant number of patients (20%-44%) is somewhat disappointed with their penile appearance. In our patients 25% shared this feeling which is significantly more than the 12% of a control group of normal boys studied by Mureau [36]. Analysis of these studies shows that the majority of complaints is related to a circumcised appearance, a small penile size, scarring or local skin surplus (dog ears, asymmetrical distribution). The first two abnormalities can not be avoided. The third and fourth can be minimised. This leaves the appearance of the meato-glandular complex as a possible source of discontent and a subject for debate. A minority of 6,5 % out of 186 patients examined by Mureau appeared to be unhappy with meatal position or glandular shape (5,6% in a group of 72 adults and 7,0% in a group of 114 adolescents). Sommerlad [41] reported similar findings conforming our conviction that few patients are concerned about this abnormality.

Conclusions

The thesis that was written to identify the causes of complications in hypospadias surgery and to eliminate these if possible fostered two conclusions [28]:
1. A curvature of the penis (hooded appearance) can be caused by a shortage of skin cover.
2. Fistulas can be caused by deficient coverage, positioning, suturing, dressing or drainage.
The first conclusion led to a dramatic reduction of the number of patients that needed an ortho-urethroplasty (less then 20%) by the elimination of an orthoplasty, redistribution of skin by means of a rotation flap in all patients with a curvature but without chordee.
The second conclusion led to an equally dramatic reduction of fistulas by:

a. the rotation in one or two stages of well vascularised dorsal skin, using a backcut
b. the omission of transcutaneous sutures and a dressing
c. the diversion of urine through drainage incisions or fenestrated stents
Application of these concepts in combination with techniques that long ago have proven their worth in the prevention of persistent chordee or stenosis made it possible to eliminate functional complications in the vast majority of patients. Ironically, functional results seem to have become less important in recent decades. The emphasis today is on aesthetic results. This, however, raises a number of new questions:
What is the definition of a good result: an optimal functional result, an optimal cosmetic result or the combination of both?
What are the criteria that should be fulfilled to achieve this goal: an optimal functional result
(no chordee, no fistulas, no stenosis, no spraying) or an optimal cosmetic result with a normal meatus (no skin excess, no stitch marks, minimal scarring).
What are the priorities that should be agreed upon while knowing that it may be impossible to fulfil all these criteria with one procedure in one stage because the need for efficiency may
interfere with the desire for effectiveness and the sense of cosmetic perfection with the sense of functional perfection. More specifically is it justified to use two stages for the correction of class I and IIA hypospadias, for class IIB hypospadias or for both?
Type I operation: (class I and IIA hypospadias)
Is it justified to use two stages for the treatment of this anomaly [5] which encompasses more then 80% of all hypospadias patients if excellent results can be obtained in one stage (< 1% fistulas, no stenosis) and minor complications such as meatal widening and retrusion, can easily be corrected at a later stage, if the patient happens to be dissatisfied with these deficiencies? We leave the answer to the reader.
Type II operation: (class IIB hypospadias)
Is it justified to use two-stages if a one stage repair is commonly advocated [1,2,6,15,19,20,24,42,43], reflecting a growing demand to simplify management [11]?
Rotation of the penile dorsum using a backcut and including the inner lining of the prepuce was seriously considered to be a logical option for a one stage ortho-urethroplasty. This principle, published by Asopa in 1970, was however rejected because it was felt to be one bridge too far. So were the island flaps used by the first author in the early seventies and the double faced island flap (Asopa 1984, Duckett 1986, van der Meulen 1986). Instead a two stage ortho-urethroplasty was developed. This view proved to be correct. The complication rate of a one stage ortho-urethroplasty is persistently high. On average fistulas or stenoses are observed in 35% of patients [27] and long-term results are not yet available. The operation is more difficult, the margins for error are small, the failures that occur are less easy to correct and the learning curve is longer because the technique is not sufficient straightforward to be undertaken by the average surgeon (Dewan et al [11]

reported 75% fistulas in the first year of their study). Thatte [44] said it in a different but clear way: ..." The rate of complications in one-stage hypospadias repair in average hands in my clinical environment is frightfully high. Also a major breakdown in a one-stage hypospadias operation is extremely difficult to unravel and mend. The task of carrying a tubed axial pattern flap, tagged on to a random pattern flap, through a 90 degree turn and of anastomosing it with success to a hole situated in an area of embryological bankruptcy, surrounded by a fresh raw area made to release chordee, is a surgical exercise flying in the face of all rules of healing and subsequent normal growth as I know them. I am aware that some centres in the USA have high rates of immediate success with this procedure. But let us wait; like the crazes for the hula hoop and the holy men from India, this too may pass away...."

If all adverse factors could be eliminated or controlled then a one-stage ortho-urethroplasty would be acceptable. However, a technique with a high complication rate also becomes a multi-stage procedure in a significant number of cases. Consequently it is not certain that the average one-stage procedure over the years will take less time than the average two-stage procedure. In the study of Dewan et al of 93 boys, 49.2% required further operation [11]. The two-staged ortho-urethroplasty that we used (figs. 3 and 4) is also a multi-stage procedure in a significant number of cases. On average more than 2 operations were needed before patient, parent and surgeon were satisfied. In some patients urethral reconstruction was postponed, because of skin contractures or irregularities that had to be corrected first or performed in stages, because lack of sufficient skin made this imperative. However, a majority of all patients (86%) feels that the number of operations is not very important provided that treatment is completed by schoolage [4].

If we want to improve on what has been proved, a training in analytical thought has to be pursued [17]. All the rest is a waste of paper, causing elimination of complications to remain a mission impossible [44].

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Summary

The aims of this study were the investigation of the normal embryogenesis of the male anterior urethra, the composition of a classification for the hypospadias deformity and related anomalies as well as the evaluation of an institutional experience in the treatment of hypospadias. The major findings from this study will be summarised.

Normal and abnormal embryogenesis of the male anterior urethra

(chapter two and three)

From our studies it seems very likely that the entire anterior urethra in male subjects is formed through a fusionprocess in distinct phases. This fusion is associated by programmed cell death, i.e. apoptosis. The scrotum is formed through merging which is quite different from fusion. In normal embryogenesis two ways of forming the urethral lumen could be distinguished; primary luminisation for the penile urethra with direct formation of a tube at fusion of the urogenital swellings and secondary luminisation of the glandular urethra after fusion of the genital tubercle. Furthermore, we revealed that the prepuce starts to grow as a fold only after completion of the fusion process of the urethra. Our conclusions are based on macroscopic and microscopic observations of human and mouse embryos of different gestational age, direction of sectioning and fixation and staining techniques.

Study of the normal development of the male anterior urethra helped us to identify the similarities and differences of hypospadias and its related anomalies. These findings enabled us to give a classification for the hypospadias deformity as well as a nomenclature for hypospadias and related malformations.

A class I hypospadias is characterised by a meatal dystopia, hooded appearance of the prepuce, oblique raphes with dog-ears and **no** associated curvature. This malformation is the result of a fusion defect of the distal part of the urethra. A class IIA hypospadias shows the same characteristics as a class I hypospadias but **with** a curvature. This bending is caused by a shortage of skin that developed during embryogenesis. The patho-embryology of this anomaly is a fusion defect together with a maldistribution of skin on the ventral side. A class IIB hypospadias is more severe then a class IIA hypospadias because the curvature is caused not only by skin shortage but chordee tissue as well. This chordee tissue arises because mesoderm from the urogenital swellings does not unite and subsequently does not differentiate properly when fusion of the swellings is defective. This anomaly is caused both by a fusion defect and a disturbance of definitive differentiation. Cryptospadias is defined as an anomaly where a terminal meatus of the urethra is present in association with all the possible characteristics of a hypospadias (penile curvature,

dorsal hood, oblique raphes and dog-ears). The integument of the distal part of the urethra is frequently poorly differentiated with a so-called pellucid urethra. Cryptospadias is the result of inappropiate definitive differentiation caused by a shortage of proliferation of mesoderm from the urogenital swellings. A congenital short urethra has a terminal meatus, a curvature of the penis without the associated external features of hypospadias or cryptospadias. The integument of the urethra is well differentiated but is short relative to the dorsal structures of the penis, causing the curvature. The precise patho-embryology remains obscure, but a relative growth disturbance of the ventral structures of the phallus seems to be a reasonable explanation. A congenital urethral fistula is a localised defect in the anterior urethra. It can be associated with a cryptospadias or hypospadias but can occur as an entity, the patho-embryology being a localised fusion defect.

Long-term follow-up of hypospadias repair

(chapter four to eight)

In chapter four the techniques used in our department in a period of approximately thirty years are discussed. Two surgeons were responsible for treating hypospadias patients both with their own regime of procedure and postoperative care. One surgeon used the one-stage van der Meulen repair for class I and IIA hypospadias (urethroplasty). With this procedure, no urinary diversion and a simple sandwich dressing was used postoperatively. For the class IIB hypospadias he used the two stage van der Meulen technique (ortho-urethroplasty). Following this repair, a sandwich dressing was used together with drainage incisions at the penile base or a fenestrated Silastic stent for urinary diversion. The other surgeon always conducted a two stage repair, using a Byars orthoplasty and a Denis Browne urethroplasty. With the orthoplasty, he used a transurethral catheter for urinary diversion and a tie-over dressing. The Denis Browne procedure was accompanied by a perineal urethrostomy and a circular foam dressing.
These different regimes of hypospadias repair were performed in a prospective but not randomised way allowing us to evaluate the short-term and long-term results. Chapter five deals with the immediate and mid-term postoperative complications of our patients. A grading system of severity of complications is given. Grade I complications are minor and do not need an extra operation (small dehiscence, haematoma, urinary retention), grade II complication are problems of appearance where an extra operation is optional and to be discussed with the patient or parents (meatal retraction, skin surplus, scar contraction, circumcised appearance). Finally grade III (major) complications necessitate an extra procedure (bleeding, fistula, curvature, stenosis). This study showed us that postoperative complications are *not* prevented or diminished by the use of indwelling catheters (Byars/ Denis Browne repairs) because the complication rate is high (31 % grade III complications). On the other hand, a low complication rate was achieved without the use of indwelling diversion and circular dressings (van der Meulen type I: < 2% grade III

complications, van der Meulen type II: 11% grade III complications).
This study stresses the multifactorial nature of hypospadias repairs, because the operative technique is at least as important as the diversion method or the dressing.
Chapter six is about long-term results in the two patient groups already mentioned. Through a questionnaire and a physical examination, the long-term outcome of one hundred and eighty three patients could be established. From the questionnaire it became obvious that spraying, deviation of the stream at miction and dribbling were frequently encountered. The results of the physical examination however showed no consistent deformities to explain these functional problems. Furthermore, a flowmetry study was performed in this group of patients which showed low flow-patterns in some patients without functional bothers.
All these data are of relative value because no normative data are at hand from the normal population and no consistent correlation could be found between findings from the questionnaire, the physical examination and the uroflowmetry.
Finally, in chapter eight the results of treatment from a group of approximately hundred patients referred secondarily (hypospadias cripples) are discussed. This study showed that patients were referred following several operations without the desired result and with remaining functional problems (meatal dystopia, curvature, stenosis and fistulae). A liberal approach to multi staged repairs if necessary was advocated in this group of patients with relatively simple techniques (circumferential advancement of penile skin, dorsal transposition flap with a back cut, distally based ventral skin flap or full thickness skin grafts). With these techniques, satisfactory results could be obtained although a slightly higher complication rate compared to primary repairs (19 % grade III complications) was encountered. At long-term follow up of these patients (n=43) similar subjective complaints as with primary repairs (spraying, dribbling and stream deviation) were mentioned, again without a physical anomaly explaining these problems. It became clear that residual curvature in particular can be an annoying complication sometimes occurring only years following surgery. It is therefore very important to perform a thorough assessment of these patients before making plans for treatment.

The assessment of hypospadias
(chapter nine)

The last chapter of this thesis gives an evaluation of the philosophy of hypospadias repair and the elimination of complications. It is based on the observations and the analysis made in the early nineteen sixties by van der Meulen (1985). All factors possibly responsible for complications in hypospadias surgery are scrutinised. Complications are differentiated between problems of function and of appearance, giving a detailed analysis for avoiding them. We concluded that functional problems following hypospadias repair can be minimised using the appropriate measures (safe and simple operating technique, no

circular dressings and no indwelling urinary diversion). Problems of appearance, however, seem to dominate the discussion in hypospadias surgery in recent years. A study by Mureau (1995) of our patients has thought us that problems of genital appraisal are twice as high in boys operated for hypospadias compared with a control group of normal boys. The majority of their complaints is related to a circumcised appearance, a small penile size, scarring or a local skin surplus. Only a minority of our patients was unhappy with the meatal position or shape of the glans. This leaves us with the question which functional price we have to pay for perfection of the cosmetic results in hypospadias repair. No data from the literature can be found to answer this question directly.

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Samenvatting

De uitgangspunten voor dit proefschrift waren het bestuderen van de normale ontwikkeling van het mannelijk genitaal, het creëren van een classificatie voor hypospadie en gerelateerde afwijkingen alsmede de evaluatie van de lange termijn resultaten van de behandeling van hypospadie binnen een plastisch chirurgische afdeling. De belangrijkste resultaten zullen hier worden samengevat.

Normale en abnormale ontwikkeling van de mannelijke urethra
(hoofdstuk twee en drie)

Uit onze studie lijkt het zeer aannemelijk dat de gehele mannelijke urethra ontstaat door een fusieproces bestaande uit circumscripte fasen. Dit fusieproces vindt plaats in de aanwezigheid van apoptosis, ook wel geprogrammeerde celdood genoemd. Het scrotum wordt gevormd door merging, een geheel ander proces dan fusie. Het lumen van de urethra wordt in de normale embryogenese op twee verschillende manieren gevormd. Primaire luminisatie treedt op in de urethra van de penisschacht door fusie van de urogenitale zwellingen met gelijktijdige formatie van een buisvormige structuur. De glandulaire urethra secundaire ontstaat door luminisatie van een epitheliale streng na fusie van de beide helften van het tuberculum genitale. De ontwikkeling van het preputium begint pas op het moment dat de fusie van de gehele ventrale zijde van de phallus is voltooid. Deze bevindingen werden gedaan door macroscopische -en microscopische bestudering van humane en muizenembryo's van verschillende leeftijden, snijrichtingen, fixaties en kleuringstechnieken.
Het onderzoeken van de normale ontwikkeling van de mannelijke urethra stelde ons in staat de overeenkomsten en verschillen tussen hypospadie en daaraan gerelateerde congenitale afwijkingen te herkennen. Deze bevindingen werden gebruikt als basis voor een classificatie van hypospadie alsmede voor de nomenclatuur van hypospadie en aanverwante malformaties.
Een klasse I hypospadie wordt gekenmerkt door een dystopie van de meatus urethrae, een surplus aan voorhuid, oblique raphes met dog-ears **zonder** kromstand van de penis. Deze afwijking ontstaat door een fusiedefect van het distale deel van de urethra. Een klasse IIA hypospadie heeft dezelfde uiterlijke kenmerken als een klasse I maar heeft **wel** een kromstand. Deze curvatuur is het gevolg van een

huidtekort aan de ventrale zijde dat tijdens de embryogenese is ontstaan. De patho-embryologie van deze afwijking ligt in een fusie defect tezamen met een onjuiste huidverdeling aan de ventrale zijde. Een klasse IIB hypospadie is ernstiger dan een klasse IIA omdat de kromstand niet alleen door een huidtekort maar tevens door chorda weefsel wordt veroorzaakt. Dit chorda weefsel ontstaat omdat het mesoderm van de urogenitale zwellingen niet samenkomt ten gevolg van het fusiedefect en derhalve geen goede definitieve differentiatie vertoont. Deze afwijking wordt dus veroorzaakt door zowel een fusiedefect als een definitieve differentiatie stoornis.
Cryptospadie wordt gekenmerkt door een normale terminale meatus urethrae in combinatie met alle mogelijke andere uitingsvormen van hypospadie (kromstand, preputium surplus, oblique raphes en dog-ears). De bedekking van het distale deel van de urethra is vaak matig gedifferentieerd met een doorschijnende urethra. Cryptospadias ontstaat door een stoornis in de definitieve differentiatie ten gevolg van een tekort aan proliferatie van het mesoderm van de urogenitale zwellingen.
Een congenitaal korte urethra vertoont een terminale meatus, een kromstand van de penis zonder de uiterlijke kenmerken van een hypospadie of cryptospadie. Het omhulsel van de urethra is goed gedifferentieerd maar lijkt te kort in vergelijking met de dorsale structuren van de phallus. Omtrent de exacte patho-embryologie van deze afwijking tasten wij nog in het duister maar een relatieve groei achterstand van de ventrale structuren van de phallus lijkt een plausibele verklaring.
Een congenitale urethra fistel ten slotte is een gelokaliseerd defect in de urethra. Een dergelijke fistel kan in combinatie met zowel een hypospadie als een cryptospadie voorkomen maar wordt ook als solitaire afwijking gezien. De patho-embryologie van deze afwijking is een gelokaliseerd fusiedefect.

Lange termijn follow-up van hypospadie behandeling
(hoofdstuk vier tot en met acht)

De technieken welke in ons instituut gedurende dertig jaar werden gebruikt voor de behandeling van hypospadie, worden besproken in hoofdstuk vier. Twee plastisch chirurgen waren verantwoordelijk voor deze behandeling en beiden gebruikten zij hun eigen (verschillende) operatietechniek alsmede postoperatieve maatregelen. Een van de chirurgen gebruikte de one-stage techniek volgens Van der Meulen voor klasse I en IIA hypospadie (urethroplastiek). Bij deze procedure werd geen urine afleiding gebruikt en een simpel verband bestaande uit twee gazen. Voor de klasse IIB hypospadie gebruikte hij de Van der Meulen two-stage techniek (ortho-urethroplastiek). Bij de tweede fase van deze operatie (urethra reconstructie) werden hetzelfde eenvoudige verband gecombineerd met drainage incisies aan de basis van de penis of met een Silastic stent gelegen in de neo-urethra maar niet in de blaas. De andere chirurg maakte altijd gebruik van een two-stage techniek; een Byars orthoplastiek gevolgd door een Denis Browne urethroplastiek. Bij de

orthoplastiek werd een catheter a démeure achtergelaten in combinatie met een tie-over verband. De urine werd bij de Denis Browne urethroplastiek afgeleid met behulp van een perineale urethrostomie. Tevens werd na deze operatie een circulair Silastic foam verband aangelegd.

Deze beide behandelingsstrategieën werden door de respectievelijke chirurgen prospectief maar niet gerandomiseerd uitgeoefend waardoor een evaluatie van korte en lange termijn resultaten mogelijk was. Hoofdstuk vijf behandelt de postoperatieve en korte termijn complicaties van onze patiënten. De complicaties werden in graderingen ondergebracht; graad I complicaties zijn mild van karakter en behoeven geen extra operatie (geringe dehiscentie, hematoom, urine retentie), graad II complicaties zijn problemen van het uiterlijk aspect van de penis waarbij een extra operatie facultatief is en besproken dient te worden met de patiënt (retractie van de meatus, huid surplus, litteken contractie, besneden aspect). Graad III (ernstige) complicaties maken een additionele ingreep noodzakelijk (nabloeding, urethrocutane fistel, kromstand, stenose van de meatus). Deze studie laat zien dat postoperatieve complicaties niet worden voorkomen of verminderd door het gebruik van een verblijfscatheter (Byars/Denis Browne techniek) omdat het complicatie getal hoog is (31% graad III complicaties). Anderzijds werd een laag complicatie getal bereikt zonder het gebruik van urine afleidingen of circulaire verbanden (Van der Meulen type I: <2 % graad III complicaties, Van der Meulen type II: 11% graad III complicaties).

Deze studie benadrukt het multifactoriele karakter van de hypospadie behandeling omdat de gebruikte operatieve techniek minstens zo belangrijk blijkt te zijn als de postoperatieve maatregelen.

Hoofdstuk zes geeft de lange termijn resultaten weer in de hierboven reeds vermelde groepen. Middels een vragenlijst en een lichamelijk onderzoek konden de lange termijn resultaten bij honderddrieentachtig patiënten behandeld voor een hypospadie worden vastgesteld. De resultaten van de vragenlijsten lieten zien dat sproeien, een afwijkende straal en nadruppelen bij het plassen vaak werden gemeld. Het lichamelijk onderzoek leverde echter geen duidelijke oorzaken voor deze klachten op. Bovendien werd een uroflowmetrie studie verricht bij deze patiënten waarbij lage pickflows optraden zonder klinische klachten (hoofdstuk zeven.

Al deze gegevens zijn van relatieve betekenis omdat geen waarden vanuit de normale populatie bekend zijn en er geen consistente correlatie kon worden gevonden tussen anamnestische klachten, lichamelijk onderzoek en uroflowmetrie.

De resultaten ven de behandeling van een groep van circa honderd hypospadie cripples worden weergegeven in hoofdstuk acht. Deze patiënten werden verwezen na diverse malen te zijn geopereerd voor hypospadie zonder het gewenste resultaat en met resterende functionele (graad III) klachten (dystopie van de meatus, kromstand, meatus stenose of fistels). Voor de behandeling van deze problemen werd gebruik gemaakt van relatief eenvoudige operatie technieken, waar nodig in meerdere stappen uitgevoerd (circulaire advancement van penisschacht huid, dorsale transpositielap met een backcut, distaal

gesteelde lap van ventrale huid of een huidtransplantaat van volledige dikte). Met deze technieken kon bij alle patiënten een bevredigend resultaat worden bereikt, hoewel het complicatie percentage iets hoger lag dan bij een primair herstel (19% graad III complicaties). De lange termijn resultaten van deze behandeling (n=43) gaven dezelfde functionele klachten te zien als bij primair geopereerde patiënten (sproeien, nadruppelen en straaldeviatie), wederom zonder dat daar een duidelijke en consistente verklaring voor kon worden gevonden bij lichamelijk onderzoek. Met name werd bij een patiënt duidelijk dat recidivering van kromstand een vervelend probleem kan opleveren, zelfs nog jaren na operatie. Mede hierom is een uitgebreide pre-operatieve evaluatie van essentieel belang bij hypospadie cripples.

De vaststelling van hypospadie

(hoofdstuk negen)

Het laatste hoofdstuk van dit proefschrift is een weergave van alsmede een discussie over de filosofie achter de behandeling van hypospadie en het voorkomen van complicaties. Als basis voor dit chapiter werden de observaties en analyses gebruikt uit de vroege jaren zestig van Van der Meulen (1985). Alle mogelijke factoren met consequenties voor het ontstaan van complicaties worden hier onder de loep genomen. Complicaties worden onderverdeeld in problemen gerelateerd aan functie of uiterlijk, met een gedetailleerde analyse ter preventie. In conclusie kan worden gesteld dat functionele problemen kunnen worden vermeden door de juiste voorzorgsmaatregelen te nemen (veilige en simpele operatietechniek, geen circulaire verbanden en geen verblijfscatheters). Problemen van esthetische aard lijken de laatste jaren de discussie omtrent hypospadie correcties echter te domineren. Een studie welke door Mureau (1995) werd verricht bij onze patientenpopulatie, heeft ons geleerd dat het aantal problemen gerelateerd aan genitale acceptatie twee maal zo groot is bij jongens geopereerd voor hypospadie in vergelijking met een controlegroep. De meerderheid van hun klachten is gerelateerd aan het besneden aspect en het geringe formaat van de penis, littekenvorming of een lokaal huidsurplus. Slechts een minderheid van onze patiënten was ontevreden over de positie van de meatus en/of de vorm van de glans. De vraag welke functionele prijs wij moeten betalen voor een perfect cosmetisch resultaat blijft hiermee onbeantwoord. In de literatuur worden hiervoor ook geen gegevens aangedragen.

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Dankwoord

Met aan zekerheid grenzende waarschijnlijkheid wordt dit het meest gelezen stuk uit het proefschrift. Dit feit alleen al maakt wetenschap en de verslaglegging hiervan tot een elitaire aangelegenheid. Als men zich ook nog realiseert dat een promovendus naarmate het proefschrift vordert meer en meer de (vaak) duistere eenzaamheid opzoekt, kan men de wetenschap zelfs als a-sociale bezigheid kenschetsen. In het geval van dit proefschrift zijn een groot aantal mensen van cruciaal belang geweest en dus mede schuldig. Een beperkt aantal van hen wil ik graag apart vermelden.

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Curriculum vitae

J.F.A. van der Werff, was born on January 9, 1961 in Rotterdam, The Netherlands. In 1979 he graduated at the St. Franciscus College in Rotterdam. After attending the Erasmus University Medical School he obtained his artsdiploma in 1988. During his medical study he started an interest in hypospadias surgery and conducted research with Mr. D.E. Tolhurst on the flowmetry of boys operated for hypospadias. Following his graduation, he became an honorary research assistant at the Department of Plastic and Reconstructive Surgery of the University Hospital in Rotterdam (head: Prof.Dr. J.C.van der Meulen). Postoperative monitoring in microvascular surgery using Laser Doppler Flowmetry was his main topic. The research for this Ph.D. thesis was commenced in 1990 at the same institution. Finishing his basic surgical training in the Zuiderziekenhuis in Rotterdam (head: Dr.K.Brouwer), he specialised in plastic surgery in the University Hospital Rotterdam (head: Prof.Dr. S.E.R. Hovius). Currently he is working as a staff surgeon at the Department of Surgery, subdivision Plastic Surgery, in the University Hospital Groningen.

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