Anomalies of the penis and scrotum in adults
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General introduction
Chapter 1

There are many different scrotal and penile anomalies, some common and some rarely encountered. They affect men of all ages and symptoms can vary considerably depending on the particular condition involved. Despite their heterogeneous pathological background, they are all likely to cause psychological distress, sexual dysfunction, and may disrupt sexual life and thereby diminish quality of life. Given this broad variety of “problems”, it is not surprising that a broad variety of “solutions” are also available and used in clinical practice. Some of the anomalies require surgical treatment, while other times a more psychological or counseling approach is put into practice; however, very often it is a multidimensional approach that prevails. Human sexuality is an illustration of bio-psycho-social interaction, and, when problematic, professional help needs to encompass all three of these domains. Depending on the exact nature of the problem and its context, one or more treatment options may be chosen and/or combined. Just as scientists do, clinicians use the principle of Ockham’s razor: Keep it as simple as possible. If a simple, preferably non-invasive intervention suffices, then this should prevail.

In this thesis, four scrotal and penile anomalies are studied: the short penis, the acute erection angle, Peyronie’s disease, and genital lymph edema. Some of these pathologies are so rarely encountered in our daily practice that their treatment is mainly based on the personal experience of the surgeon or of his/her colleagues.

The first aim of this introduction is to provide general information about these four anomalies, including their prevalence, etiology, and treatment. The second aim of this introduction is to describe the two main research questions, a number of sub-questions, and the accompanying outline of this thesis. In the following chapters, each one of the four anomalies will be put into a urological and sexological perspective. In order to arrive at a clear insight into these kinds of urological anomalies and their treatment options, it is important to understand their various anatomical backgrounds. A short review of the embryologic aspects of the male urogenital tract, which form the basis for congenital anomalies, is provided.

EMBRYOLOGY OF THE MALE GENITALS

Early development of the external genitalia is similar in both genders. External genital differentiation for the male sex begins in the seventh week of gestation and is completed by the sixteenth to seventeenth week. It is a complex process involving SRY genetic programming, cell differentiation, hormonal signaling, enzyme activity, and tissue remodeling.

Under the influence of the SRY gene, the bipotential gonad differentiates into a testes ultimately resulting in androgen production. External genital development undergoes two stages that can be distinguished by independent hormone growth prior to testicular development and hormone dependent growth under the influence of androgens. Hormone
independent development occurs between conception and seven to eight weeks' gestation.\textsuperscript{1} This takes place under the influence of a cascade of genes including sonic hedgehog, BMP4, Glia 123, and Wilms Tumor gene.

While the anorectal canal and urogenital sinus are being separated by the urorectal septum, the mesoderm anterior and cranial to the phallic segment of the urogenital sinus expands. This forms the genital tubercle, which will eventually form the phallic segment. In this indifferent stage around the third week of development, mesenchyme cells originating in the region of the primitive streak migrate around the cloacal membrane to form a pair of cloacal folds (or urogenital folds). Cranial to the cloacal membrane, the folds unite to form the genital tubercle, whereas in the caudal part cloacal folds are subdivided into the urethral folds anteriorly and into the anal folds posteriorly (figure 1).\textsuperscript{2,3} The urogenital (cloacal) membrane starts to resolve in the seventh week, forming a urogenital sinus. The formation of the penis starts by elongation of the genital tubercle to form the corpora cavernosa and glans penis. By the tenth week, the urethral folds start to fuse from the urogenital sinus orifice toward the tip of the phallus. At the fourteenth week, the fusion is complete and the penile urethra is formed. The corpus spongiosum results from the differentiation of the mesenchymal masses around the urethra. The glandular urethra

Figure 1. Human urogenital embryology. (A) Sex undifferentiated precursors prior to 7 weeks gestational age. (B) Male development in gestational weeks 7-17.\textsuperscript{3}
develops as a result of canalization of an ectodermal epithelial cord that has grown through the glans. During the third month, the prepuce is formed by growing a fold at the base of the glans. Meanwhile, the genital swellings shift caudally and are recognizable as scrotal swellings. They meet and fuse, resulting in the formation of the scrotum.\textsuperscript{4,5} During this complex developmental process, not only is the basis laid for a large variety of morphological appearances but also for anatomical and/or physiological anomalies. Sometimes the difference between “normal variation” and pathology is hard to discern. Therefore, we will now focus in more detail on the four anomalies, which together form the core of this thesis.

THE SMALL PENIS

The mechanism of growth cessation is still not completely clear, and therefore little is known about the cause of a penis that is too small. A small penis can occur as a separate abnormality, or it can be part of a series of anatomical abnormalities, such as bladder extrophy, epispadias, hypospadias, and disorders of sex development (DSD).

There are three anomalies that need further attention and will be discussed here: the micropenis, the small penis, and the webbed penis. Following on this, treatment for a small penis, which has a long history with broad cultural differences, will be briefly presented.

The micropenis

A small penis is not always a micropenis (figure 2). A micropenis refers to a specific disorder that has a specific set of causative factors and a different set of treatment modalities than does the small penis. The true micropenis is the result of a hormonal abnormality occurring after twelve weeks of gestation. There are three main causes for this condition: hypogonadotrophic hypogonadism, hypergonadotrophic hypogonadism (also known as primary hypogonadism), and idiopathic causes (table 1).\textsuperscript{6,7}

![Figure 2. A micropenis](image)
Table 1. Etiology of micropenis

<table>
<thead>
<tr>
<th>Deficient testosterone secretion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> Hypogonadotropic hypogonadism</td>
</tr>
<tr>
<td>1. Isolated, including Kallmann's syndrome</td>
</tr>
<tr>
<td>2. Associated with other pituitary hormone deficiencies (e.g., CHARGE association)</td>
</tr>
<tr>
<td>3. Prader-Willi syndrome</td>
</tr>
<tr>
<td>4. Laurence-Moon syndrome</td>
</tr>
<tr>
<td>5. Bardet-Biedl syndrome</td>
</tr>
<tr>
<td>6. Rud's syndrome</td>
</tr>
<tr>
<td><strong>B</strong> Primary hypogonadism</td>
</tr>
<tr>
<td>1. Anorchia</td>
</tr>
<tr>
<td>2. Klinefelter's syndrome and poly X syndrome</td>
</tr>
<tr>
<td>3. Gonadal dysgenesis (incomplete)</td>
</tr>
<tr>
<td>4. Luteinizing hormone receptor defects (incomplete)</td>
</tr>
<tr>
<td>5. Genetic defects in testosterone steroidogenesis (incomplete)</td>
</tr>
<tr>
<td>6. Noonan's syndrome</td>
</tr>
<tr>
<td>7. Down syndrome</td>
</tr>
<tr>
<td>8. Robinow's syndrome</td>
</tr>
<tr>
<td>9. Bardet-Biedl syndrome</td>
</tr>
<tr>
<td>10. Laurence-Moon syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Defects in testosterone action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> Growth hormone/insulin-like growth factor-I deficiency</td>
</tr>
<tr>
<td><strong>B</strong> Androgen receptor defects (incomplete)</td>
</tr>
<tr>
<td><strong>C</strong> 5α-reductase deficiency (incomplete)</td>
</tr>
<tr>
<td><strong>D</strong> Fetal hydantoin syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Development anomalies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> Aphallia</td>
</tr>
<tr>
<td><strong>B</strong> Cloacal extrophy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Idiopathic causes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>V</strong> Associated with other congenital malformations</td>
</tr>
</tbody>
</table>

In a study by Nelson and colleagues the incidence of a micropenis was reported as 1.5 in 10,000 male children born in the United States of America (USA) between 1997 and 2000.8

To make an accurate diagnosis, the stretched penis length (SPL) should be measured.9 This length is measured by stretching the flaccid penis to its maximum length and to measure from the pubis to the tip of the stretched penis. Micropenis is defined as SPL 2.5 standard deviations less than the mean for a group without penile anomalies (table 2).10 The micropenis can be associated with cryptorchidism and small-volume testicles, as well as a hypoplastic scrotum, most likely due to the same causative factors that are responsible for the micropenis.6
The work up of the patient with a micropenis should be directed towards early diagnosis and therapy. Micropenis should be diagnosed in the neonatal period and differentiated from associated deformities and syndromes. Therefore, the patient should be referred to a (pediatric) endocrinologist. Endocrinologic assessment helps to determine at what level the cause of the micropenis is to be found, in terms of the hypothalamic-pituitary-testicular axis. Measurement of serum gonadotropins, testosterone, DHT, and precursors of testosterone are often helpful in evaluating the etiology. Sometimes genetic testing may be necessary to identify genetic sex and to rule out gonadal dysgenesis with a Y chromosome cell line. The most important concern is whether the child will have sufficient penile growth to allow sexual function as an adult.\textsuperscript{11,12}

### Table 2. Normal Stretched Penis Length (SPL)\textsuperscript{10}

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean ± SD</th>
<th>Mean – 2.5 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn, 60-week gestation</td>
<td>2.5 ± 0.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Newborn, 34-week gestation</td>
<td>3.0 ± 0.4</td>
<td>2.0</td>
</tr>
<tr>
<td>0-5 months</td>
<td>3.9 ± 0.8</td>
<td>1.9</td>
</tr>
<tr>
<td>6-12 months</td>
<td>4.3 ± 0.8</td>
<td>2.3</td>
</tr>
<tr>
<td>1-2 years</td>
<td>4.7 ± 0.8</td>
<td>2.6</td>
</tr>
<tr>
<td>2-3 years</td>
<td>5.1 ± 0.9</td>
<td>2.9</td>
</tr>
<tr>
<td>3-4 years</td>
<td>5.5 ± 0.9</td>
<td>3.3</td>
</tr>
<tr>
<td>4-5 years</td>
<td>5.7 ± 0.9</td>
<td>3.5</td>
</tr>
<tr>
<td>5-6 years</td>
<td>6.0 ± 0.9</td>
<td>3.8</td>
</tr>
<tr>
<td>6-7 years</td>
<td>6.1 ± 0.9</td>
<td>3.9</td>
</tr>
<tr>
<td>7-8 years</td>
<td>6.2 ± 1.0</td>
<td>3.7</td>
</tr>
<tr>
<td>8-9 years</td>
<td>6.3 ± 1.0</td>
<td>3.8</td>
</tr>
<tr>
<td>9-10 years</td>
<td>6.3 ± 1.0</td>
<td>3.8</td>
</tr>
<tr>
<td>10-11 years</td>
<td>6.4 ± 1.1</td>
<td>3.7</td>
</tr>
<tr>
<td>adult</td>
<td>13.3 ± 1.6</td>
<td>9.3</td>
</tr>
</tbody>
</table>

In the management of patients with micropenis, an assessment should be made as to the ability of the penis to respond to testosterone application. If the penis does not increase in length, there is probably an androgen resistance and therefore failure to virilize at puberty.

Is it important that the treatment with testosterone starts in early infancy? There is a natural decrease in androgen receptors during the early adulthood period and early
application of testosterone allows for penile androgen receptor concentration to increase.\textsuperscript{12} In patients who do not respond to testosterone, application of 5-\(\alpha\) dihydrotestosterone gel might be an alternative.\textsuperscript{13} If the micropenis does not show sufficient growth despite endocrine treatment, surgical treatment can offer an alternative. Different penile reconstructions are described, of which the radial forearm flap remains the most popular.\textsuperscript{14} Cosmetic and functional results are acceptable; the complication rate, however, is very high.\textsuperscript{6} A large study by Monstrey and colleagues showed a flap revision rate of 12\%.\textsuperscript{15}

In the patient with a micropenis, psychological counseling should be an integral part of management. It is important to minimize stigmatization and achieve greater self-acceptance as well as social acceptance of their condition.\textsuperscript{16}

**The small penis**

According to the American sexologist Barry McCarthy, two out of three men believe that their penis is too small.\textsuperscript{17} He attributes the worries they have about the length of their penis to various factors. First, little boys see their father’s penis for the first time at a “sensitive” age. Second, in a locker room, men usually see other men from the front. Apparently, the other man’s penis is larger, because a man can only see his own penis from above. From above, one has an effect that artists refer to as “fore-shortening.” The penis looks smaller than it really is. Third, there are considerable differences in the lengths of flaccid penises, while in erection there is not much difference. Fourth, men generally do not know all that much about the subject, because they do not like to talk openly about such intimate matters. To these factors a new factor can be added, which stems from the context of the Internet. The Worldwide Web has made pornography available to everybody, and young adult men especially see a lot of penises in action. These penises, however, usually belong to porn stars, who are selected for mega-sized penises. Like young women seeking “designer vulvas,” young adult men think their penis should match the size of a porn star’s penis.

The size of penises has a long history as a topic of scientific research and debate. In 1899, the German physician Loeb performed a study on fifty men aged between 18 and 35 years.\textsuperscript{18} The length of the visible part of the flaccid penis varied from 8 to 11 centimeters (average 9.4 cm) and the circumference from 8 to 10.5 cm. The Kinsey Report showed that only one quarter of men had an average-sized penis.\textsuperscript{19} However, extremes were fairly rare. Five percent of the men had an erection of less than 9 cm, and one percent was very well endowed with an erection of longer than 20 cm.

Doctor Jacobus X was the pseudonym of the surgeon in the French army who spent many years of his life examining and measuring hundreds of male and female genital organs from all corners of the world.\textsuperscript{20} Africans had the longest penises: flaccid 12.5 to 15 cm, in erection 19 to 20 cm. According to this surgeon, the size of the penis was always closely linked to the size of the vagina of each particular race. “Hindu women whose men
have a short and thin penis, will have trouble with the average European,” wrote the army
doctor. “The enormous penis of the African Negro would, in their view, be an instrument of
torture.” Jacobs seems to be saying that Mother Nature has made sure that members of
the same race seek each other out. The mixing of races would be unnatural. Nowadays,
this notion is frowned upon, but in the 1930s such ideas were not uncommon. In 2007,
Wylie and Eardley also reviewed measurements of penile sizes in different races (table
3).21

The webbed penis
A special form of small penis is the “webbed” penis (figure 3). It is in fact not small, but it
does seem so, because the penis and the skin of the scrotum are joined together forming
a so-called “web.” This may lead to problems with condom usage, because not only are
standard diameters used but condoms also have the same diameter at the base as on
the top. This may lead to a Procrustes dilemma: A condom that is too tight will lead to
complaints, ranging from “it doesn’t feel comfortable” to “it is strangling me.” In contrast,
a condom that is too loose may slip off accidentally. In this light, the study of a Dutch
sexologist is of interest.22 Janssen performed a study on the circumference of the penis in
erection and showed that, measured around the base, the average circumference of the
Dutch penis in full erection was about 121 millimeters, with a range from 90 to 161 mm.
In addition, in a quarter of the study subjects, the circumference of the penis in erection
was less than 110 mm, in three quarters less than 130 mm, and in ninety percent less
than 140 mm. The conclusion was that good instructions about condoms should always
contain information about the circumference of the penis in relation to various sizes of
condom.

Figure 3. The webbed penis
Table 3. A summary of reports of measurements of penile size

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Mean or range age, years</th>
<th>Population</th>
<th>Study</th>
<th>N</th>
<th>Mean or range age, years</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>[20]</td>
<td>184</td>
<td>-</td>
<td>Heterosexual 60%</td>
</tr>
<tr>
<td>[16]</td>
<td>813</td>
<td>30.8</td>
<td>All homosexual</td>
<td>[21]</td>
<td>200</td>
<td>20-22</td>
<td>Turkish men</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3417</td>
<td>30.5</td>
<td>All heterosexual</td>
<td></td>
<td>104</td>
<td>54</td>
<td>British men</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[18]</td>
<td>3300</td>
<td>17-19</td>
<td>Italian men</td>
<td></td>
<td>123</td>
<td>21.7</td>
<td>Korean men</td>
</tr>
<tr>
<td>[17]</td>
<td>124</td>
<td>59</td>
<td>Before RP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>63</td>
<td>59</td>
<td>After RP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Raccid'</th>
<th>Erect'</th>
</tr>
</thead>
<tbody>
<tr>
<td>length</td>
<td>length</td>
</tr>
<tr>
<td>stretched length</td>
<td>circumference</td>
</tr>
<tr>
<td>suprapubic fat depth</td>
<td></td>
</tr>
</tbody>
</table>

*mean values, in cm, unless stated otherwise. RP, radical prostatectomy.
The malformation can be congenital or acquired. The acquired webbed penis is mainly iatrogenic, caused by the removal of too much skin on the ventral side during circumcision.

The etiology of the congenital webbed penis is unknown. Some authors suggest that a webbed penis is secondary to aberrant preputial development, where there is insufficient ventral skin coverage of the penis and, as an alternative, the penis is covered by adjacent scrotal tissue. A webbed penis can be associated with other malformations such as hypospadias, chordee, and micropenis.

In terms of surgical treatment of a webbed penis, it is usually sufficient to incise the skin in a transverse direction and stitch the wounds longitudinally. In patients with associated chordee and/or hypospadias, more extensive urethral reconstruction might be necessary.

A short history of penis enlargement

Throughout the centuries, men have been trying to make their penis longer. The most primitive way is by hanging a weight at the tip of the penis, such as stones. This may work, but also causes pain. In addition, there is the Polynesian stretching method using a moveable heavy pipe, or the Arabic “jelq” treatment (also known as “milking”). In the USA, one can buy equipment that performs massages according to the “jelq” method. The manufacturer claims that within twenty weeks, one can achieve an increase of two and a half centimeters in length. One can read all about it in a booklet by the American Gary Griffin.

According to Jolan Chang, writer of the book *The Tao of Love and Sex*, the answer lies particularly in practising. Taoists believe that every part of the body can be trained and developed. The Tao method does not use artificial means or aids.

In the summer of 1993, the readers of the *Gaykrant*, a Dutch magazine for homosexuals, were surprised to read that in South Africa more than one hundred penile lengthening operations had been performed. When asked, the plastic surgeon from Johannesburg commented: “A month after the operation, the patients could resume their normal sex life. It leaves a scar that goes down as far as the scrotum. The patient receives an unbelievable amount of benefit, at such little inconvenience.” In the same article, it was said that it would not be long before the operation would be introduced in Western Europe. In August 1994, it was all set. A Dutch urologist, named Pieter Dik, told a national newspaper that he had ventured to perform the operation. This news coverage caused great upheaval. The hospital director, an influential professor of Andrology, a famous cosmetic surgeon, board members of the Dutch Society of Urologists, a health ethicist, and the chief editor of the *Gaykrant*, were all to have their say in various newspapers. Unfortunately, not only the urologist in question but all those who had commented did not seem to have done enough research in the scientific literature. The procedure was nothing more than a variation of a surgical procedure that has been known for many years in pediatric urology.
The essence of the surgical intervention is that the ligament which fixes the penis to the front of the pubic bone, the suspensory ligament, is cut. In this way, the “hanging” part of the penis becomes longer; it is optionally lengthened. At the same time, the surgeon cuts the skin in such a way that it can also slide towards the penis and performs a so-called V-Y plasty (figure 4). In other words, the incision has the form of a V, but after it has been sutured it forms a Y-shaped scar.

In most cases, however, an even older medical treatment may be successful: a good conversation between patient and physician about worries and facts. After listening and respecting the worries of the patient, this order is of eminent importance, the following facts can be discussed:

- The smaller the penis, the larger it becomes, proportionally, when erect
- Only friction in the outer part of the vagina is important during coitus
- The vagina can adapt itself to accommodate any size of penis
- Thickness is more important than length
- It is not a question of what he has, but how he uses it.

By keeping these general considerations in mind, the majority of men will be able to overcome most worries they may have about the length of their penis. And, as so often even nowadays, these recommendations are not new. In the seventeenth century, Reinier de Graaf (1641-1673) already wrote about the function of the vagina in the following way.\textsuperscript{28}
Its function is simply to constrict, when necessary, the part it embraces, particularly at the time of coitus. The woman’s vagina in fact is so cleverly constructed that it will accommodate itself to each and every penis; it will go out to meet a short one, retire before a long one, dilate for a fat one, and constrict for a thin one. Nature has taken account of every variety of penis and so there is no need to seek a scabbard the same size as your knife.

In this thesis our experience in the management of men complaining of a small penis is described, including the associated emotional stress and physiological complaint that this “illness perception” can bring. In so doing, we will emphasize patient selection, outcome evaluation, and surgical techniques applied for penile enlargement.

THE ACUTE ERECTION ANGLE*

When the angle between the penis and the abdominal wall is too small, penetration may become difficult, if not impossible. In cases such as this the diagnosis of “acute erection angle” is applied. This problem is mostly caused by too much tension on the penile suspensory ligaments (PSL). It is this tension that determines the angle of elevation of the erect penis. Although many erect penises point upwards, most commonly at an angle of between 30° and 95° down from vertical, it is also common and normal for the erect penis to point horizontally forwards or even vertically downwards. This variation in penile erection angle, along with the role of the PSL, has already been described by Kinsey and colleagues.19

In addition to excessive tension on the PSL, another cause of an acute erection angle can be a severe dorsal curvature at the peno-pubic level.29

An acute erection angle can be treated by (partial) release of the suspensory ligament proper. A small suprapubic incision is made until the space between the penile base and the ligament area is reached. Because an acute erection angle is caused by shortness of the suspensory ligament proper, its partial release will decrease the erectile angle down from vertical. If partial release is not sufficient, checked by artificial saline erection, a complete transection may be done. An acute erection angle can also be treated by ventral corporoplasty according to Nesbit.29,30 During this operation ellipses are excised

* During our search of the literature, we found only very limited information about erection angles and the problem with regard to this angle. Because the term hyper-erection, as introduced by Daniel Yachia,29 suggests a cause-effect relationship with the intensity of sexual arousal, we decided it would be more appropriate to use the term “acute erection angle”.
from Buck’s fascia and the tunica albuginea at a point exactly opposite the site of greatest concavity. After this, the defects are closed again with interrupted sutures to straighten the deformity.\(^{31}\)

In chapter 4, the clinical history and subsequent treatment of two men, who have had sexual problems due to their acute erection angle, are described in more detail.

**PEYRONIE’S DISEASE**

De la Peyronie (1693-1747) described an ailment in which the penis was curved or angulated in erection owing to the development of a dense fibrous plaque in the wall of one of the cavernous bodies.\(^{32}\) On the affected site, there is no elasticity, and the penis becomes curved dorsally and/or laterally (figure 5). The main symptoms are pain, penile shortening, along with difficult and painful vaginal intromission. Although the personal physician of the French King Louis XV gave his name to this penile anomaly, he was not the first to describe this phenomenon. Other investigators throughout history have reported on this abnormality, going as far back as Theodoric of Bologna in 1265.\(^{33}\)

![Figure 5. Peyronie’s disease; a severe curvature to the left (home-made picture taken from above)](image)

Peyronie’s disease is mainly encountered in men aged between fifty and sixty. The exact prevalence is unknown, due to the fact that many patients do not seek help.

A curved penis can also be the result of congenital asymmetry of the cavernous bodies, in which case the penis will nearly always be curved ventrally and/or laterally. The prevalence of this congenital asymmetry is estimated to be about six to eight per thousand male births. The pathogenesis of congenital penile curvature is unknown.\(^{34}\)

Until now the only treatment to correct penile curvature was surgery. If the curvature of the penis is stable one year after Peyronie’s disease has presented, and there are difficulties with intercourse, and there is no pain when the penis is flaccid, there is an indication for surgical correction. There are two techniques available: (a) the fibrous
tissue is removed or incised and the defect is covered with a graft; and (b) nothing is
done to the fibrous tissue, but the operation is performed on the healthy side of the penis
where, with excisions of oval parts out of the tunica albuginea, the penis is pulled straight.
A major disadvantage is that the penis becomes shorter, but a considerable advantage is
that there is very little risk of rigidity decrease after the operation. This does not apply to
the former technique, in which the fibrous tissue is removed or incised.

Another fibromatosis is Dupuytren’s disease. This involves the palmar fascias in the
hand, resulting in progressive contracture of one or more fingers. Dupuytren’s disease
is thought to be the most common hereditary connective tissue disorder in Caucasians. In
1928 an association between Dupuytren’s disease and Peyronie’s disease was reported
by Abernathy. According to several studies, there is a three to fifteen percent chance
that a man with Dupuytren’s disease will have Peyronie’s disease.

Chapter 6 describes the coexistence of Dupuytren’s disease in a consecutive series of
patients with Peyronie’s disease, along with their clinical characteristics, as presenting at
our outpatient urological clinic.

**GENITAL LYMPH EDEMA**

Another anomaly discussed in this thesis is genital lymph edema (figure 6). Acquired
(secondary) causes of lymph edema may be classified as: 1) neoplastic, 2) infectious, 3)
granulomatous, 4) reactive, 5) disorders of fluid balance, and 6) idiopathic. If the cause
is due to neoplasm, the inguinal and/or pelvic nodes are involved with metastatic cancer,
most commonly with its origin in the prostate, penis, bladder, or lymphoma. Infections
may be parasitic or bacterial. Worldwide, filariasis is the most common cause of genital
edema, caused by the worms Wuchereria bancrofti, Brugia malayi, and Brugia timori.
These worms occupy the lymphatic system, including the lymph nodes, and in chronic
cases these worms lead to the disease elephantiasis. An estimated 120 million people
in tropical and subtropical areas of the world are infected with lymphatic filariasis; of
these, almost 25 million men have genital edema. Other causes of infectious genital
lymph edema include the following microorganisms and diseases: streptococcus,
lymphogranuloma venerium, tuberculosis, syphilis, chancroid, and leprosy. Genital
edema rarely occurs due to hidradenitis suppurativa. Granulomatous diseases that
may be associated with genital lymph edema include sarcoidosis, rheumatoid arthritis,
and Crohn’s disease. Reactive causes include trauma, venous thrombosis, radiation
therapy, and angioneurotic edema. Angioneurotic scrotal edema occurs most commonly
in 4- to 6-year-old boys. It is sudden in onset, may be unilateral or bilateral, is non-tender,
and extends onto the perineum and anterior abdominal wall. It does not require treatment
and resolves in two to four days. Disorders of fluid balance including cardiac and renal
failure, fluid overload, and hypoproteinemia may also cause genital edema. If the cause
is not clear, the condition is referred to as primary (or congenital) chronic lymph edema.
In such a case the lymph vessels have intrinsic abnormalities; aplasia, hypoplasia, and hyperplasia have been mentioned in the literature.\textsuperscript{45} 

The treatment for genital lymph edema is mostly conservative, particularly if the primary disease is self-limited and there is no permanent damage to the skin, lymphatic vessels, and subcutaneous tissue. Different pharmaceutical options in the treatment for lymphatic filariasis are described, but treatment with diethylcarbamazine (DEC), ivermectin, doxycycline, and/or albendazole is the most commonly used.\textsuperscript{46-49} Chronic edema of the external genitalia generally results in permanent pathological changes. The most effective therapy is surgical, and, when applied in properly selected patients, functional and cosmetic results are excellent. These patients may be rehabilitated so as to enjoy a normal sex life.

In this thesis the clinical history and surgical treatment of six patients with genital lymph edema are discussed.
RESEARCH QUESTIONS AND OUTLINE OF THIS THESIS

In contrast to only a few decades ago, nowadays the penile abnormalities sketched above are considered important as a medical topic. This is not only because they occur more frequently but also because of the combination and interaction of medical technological progression and cultural changes. As always, progress in medical treatment options goes hand in hand with the gradual elimination of taboos on the subject and diminished tolerance of “negative exceptions” or anomalies. With increasing awareness among the general public and reasonable to good results obtained with “repair” in selected cases, some surgical treatments of penile abnormalities have become established procedures in relatively little time. This high level of acceleration may also have some disadvantages; particularly in healthcare, hypes need to be prevented. For urologists, of course, it is important to remain in touch with innovative techniques both in the domain of human sexuality as well as in its problems. Given the primary medical ethical amendment, however, of doing no harm (primum non nocere), it is also important to take note of the limitations of these medical technical developments and of his/her profession. There will always be patients with penile abnormalities who are “surgically incurable,” or who are better off visiting a sexologist or psychotherapist. In all cases iatrogenic damage, big or small, emotional or financial, must be prevented. It was the awareness of this delicate balance that brought us to our first overarching research question:

1. **Is surgery a good, preferably the best, treatment option in case of penile or scrotal deformity?**

This main question was then differentiated into three sub-questions that refer to three morphological qualities and accompanying diagnoses:

1.1 **size:** the small penis
1.2 **angle:** acute erection angle
1.3 **expansion:** genital lymph edema.

These research questions will be answered, respectively, in:

- **Chapter 2** 18-Year experience in the management of men with a complaint of a small penis.
- **Chapter 3** Penile enlargement: from medication to surgery.
- **Chapter 4** Surgery for an “acute erection angle,” when counseling fails.
- **Chapter 7** Chronic genital lymph edema: perineal skin flap plus graft reconstruction after excision.
The second main research question revealed itself along the way. While doing literature research, and based on clinical impressions, an association between Peyronie’s and Dupuytren’s disease became perceptible. The second research question is:

2. Is there a common pathway to Peyronie’s and Dupuytren’s disease?

This question is answered in:

Chapter 6  The association between Peyronie’s and Dupuytren’s disease.

Given the interrelatedness of discussing genital anomalies along with cultural perspectives, a separate chapter was written on myths and facts about the penis. Because it has not been submitted to a scientific journal, it was decided to add this chapter (5) as a “short intermezzo”.

In science, it is not only important to describe the thing one does but also what one does not do. While in some patients erectile ability does not change as a result of deformity, the abnormal shape of the penis may cause severe functional sexual difficulties for the patient or couple. In some cases the shape of the penis may cause severe discomfort or even pain for the partner. The sexual dysfunction can become a psychosexual dysfunction, which may then lead to erectile dysfunction. In order to prevent confusion on a conceptual level, in this thesis we consciously did not discuss the erectile dysfunction that is sometimes associated with the described anomalies.
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General introduction


32. La Peyronie FG. Sur quelques obstacles qui s’opposent à l’éjaculation naturelle de la semence. Memoires Académie Royale Chirurgie 1743;1:337-42.


