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Sexuality and Fertility in People Born with Classical Bladder Exstrophy

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It should come as no surprise that people who are born with exstrophy wish to be normal. Reconstructive surgery of the basic bladder problems has progressed so much in the last 25 years, that they can expect to have a normally working bladder or at least one that can be managed with intermittent clean self catheterisation. Although it has always been recognised that the penis required reconstruction as well, a good functional result for sexual intercourse was not always achieved. The exstrophy patient now grows up in normal society and has the same sexual and reproductive aspirations as his more normal peers. Their libido is as high as that of other adolescents.[1]

Males Born with Exstrophy

Genital Anatomy

The anatomy of the exstrophy pelvis and penis is obviously abnormal. The details of have been investigated clinically, by cavernosography, computerised tomography (CT) and magnetic resonance imaging (MRI), by experimental models and by dissection.[2]

The visible part of the penis (Fig. 1) is short, not, as might be thought, because most of the penis is buried in the perineum. However, the penis is longer if the divarication of the pubic bones is 3cm or less and it is shorter if the divarication is 4cm or more. In the past, surgical apposition of the pubic bones was said not to lengthen the visible penis. Some evidence suggests that the visible penis is longer if the pelvic ring is closed. Osteotomies performed in infancy may be more effective in producing a normal penis at least in childhood. It is disappointing to find that the Kelly operation, which may give an excellent result for bladder function is not so good at making the penis or abdominal wall look better.[3]

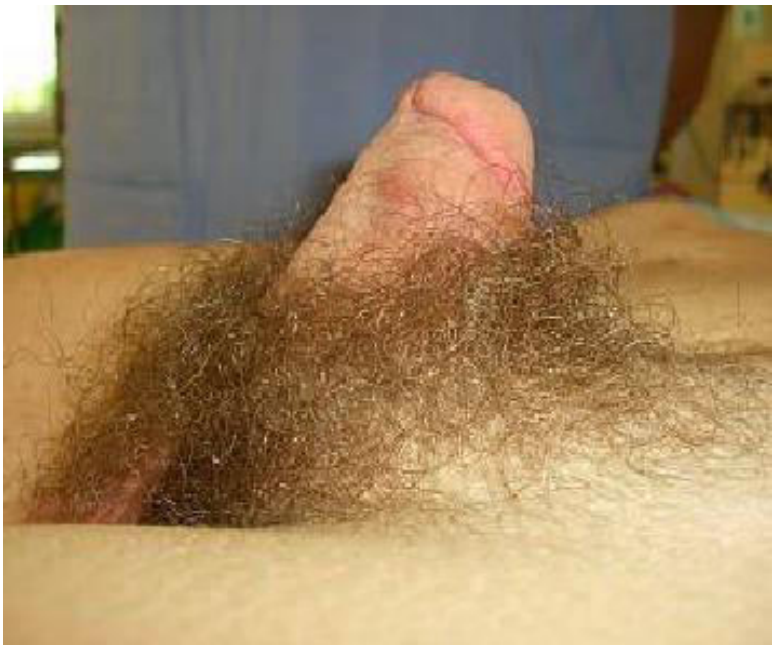

Fig. 1. Clinical photograph of the adult flaccid exstrophy penis

MRI investigation of the normal and the exstrophy penis has established that, whatever the condition of the pelvic ring, the exstrophy penis is short but broad. The total corporeal length is 60% greater in normal men (16.1cm v. 10.1cm in exstrophy). Most of this deficiency is in the anterior or exophytic part of the penis

(12.3cm for normals v. 6.9cm for exstrophy). The posterior penis is much the same length in both (3.9cm v. 3.2cm). The mean corporeal diameter is 1.0cm in normal men and 1.4cm in exstrophy men. The abnormalities may be exaggerated by the recession of the supra pubic area (Fig. 2), absence of the mons pubis and the normal size of the scrotum.

The prostate is present. In the initial dissection in the neonate it is detached from the penile urethra and remains in its normal relationship to the bladder base. In adult men the prostate is of normal weight for age but lies completely behind the urethra. The veru montanum which is normally positioned, is a useful landmark for surgery in later life.

The shape of the erect penis depends on the initial reconstruction. In the natural state, the erect epispadiac penis has a tight dorsal chordee (Fig. 3). Cavernosogram in these cases shows that the site of the maximum curvature is at the point where the corpora emerge from the perineum.[4]

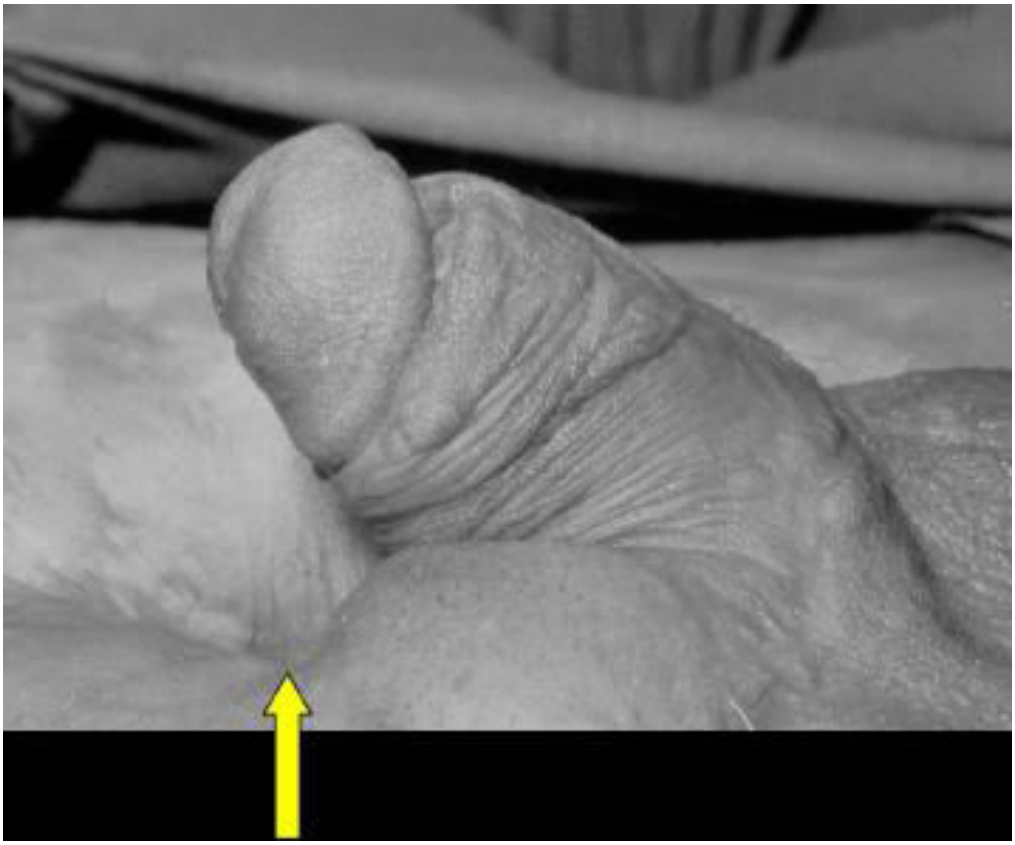

Fig. 2. Clinical photograph of an exstrophy penis illustrating the recession in the mons area (arrowed)

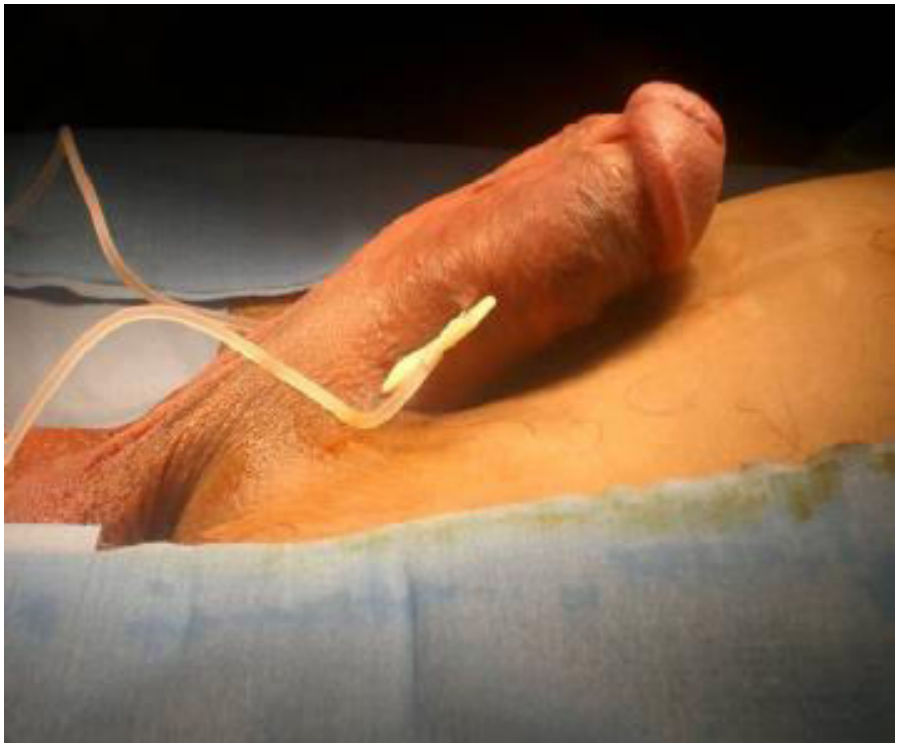

Fig. 3. Clinical photograph to show dorsal chordee in exstrophy

The degree of chordee is variable. In some the angle is such that sexual intercourse is possible either in the conventional position or in one that brings the female introitus in more direct apposition to the penis.

The evidence suggests that the corpora are of equal size at birth but may be damaged at the primary (and revision) reconstructive surgery. Twenty-eight cases of complete or partial penile loss have been reported, 24 after exstrophy closure and 4 after radical penile reconstruction.[5]

Awareness of the erectile problems and appropriate reconstruction in infancy may improve the function in adults. The techniques for children reviewed by Snyder[6] do produce a short but normal penis with a normal angle of erection. Indeed, Perovic *et al* have reported that the penis in infants is similar in length to that of normal boys although slightly different in appearance.[7] Even in adolescents and adults correction of chordee can be successful and will give a little increase in length.

In adult exstrophy patients at present, the pubic area is nearly always recessed from the uncorrected divarication of the pubic bones. The pubic hair lies on either side of the midline. Many exstrophy patients find the appearance distressing and try to hide it from their partner.

It is most important, either in infancy or in adolescence, to rotate hair bearing flaps of skin and fat to cover the mid line defect.

Sexual Function

There is no reason, special to exstrophy, why the erections should not be normal. Even where both corpora are rudimentary, penile tumescence occurs. However, in a comparison with normal men, 11 of 19 (58%) exstrophy patients had erectile dysfunction on the international index of erectile function-15 (IIEF-15), while the incidence in controls was 23%. It is interesting to note that virtually all patients had normal frequency and rigidity of erections. The dysfunction was mainly related to inability to maintain an erection and to penetrate.[1] This suggests that the dysfunction is mainly from non-physical causes.

Exstrophy patients presenting with impotence should be investigated in the same manner as other males. The only difference is that there is no cross circulation between the corpora. Therefore, if intra corporeal prostaglandin is to be used, each corpus will have to be injected individually. Occasional boys appear to have

suffered damage to the erectile nerves during pelvic dissection and report lifelong inadequate or absent erections. They respond to small doses of standard medication such as sildenafil.

Masturbation is virtually universal in all reported series. In a review of the literature from 1974 to 1997 I identified 134 men from eight series. One hundred and one (75%) were able to ejaculate, occasionally producing as much as 5ml. Some patients describe a more or less continuous urethral discharge of semen-like fluid.[8,9,10]

Much the commonest problem, however, is fear of rejection by a partner because of the obvious penile anomalies. Unfortunately, there is no easy solution and much may depend on the environment in which the man lives. In most countries, until fairly recently, marriage preceded sexual intercourse. It was possible to establish a relationship that was based on something more than random sex. The difficulty then was that, if the penile abnormality was not explained before the marriage, there could be a good deal of disappointment afterwards. Nonetheless, where a stable partnership was formed, it seemed to include a satisfactory sexual component. Unfortunately, there are no data to confirm this view from the perspective of the wife.

In an interesting series from Switzerland, follow-up was available on 21 male patients born between 1937 and 1968 with a mean age of 50 years at follow-up. Nineteen of 21 males were or had been sexually active and 16 had been married. However, only 56% described their intercourse as satisfactory. The main cause of dissatisfaction was the dorsal chordee (which nowadays would be corrected). Their adolescent sexual activity was similar to that of a survey of Swiss men from a later generation published in 2002.[11] This is probably the longest available follow-up but other groups give very similar figures with about 75% of men co-habiting.[12]

In some countries, including the UK, there has been a substantial change in sexual behaviour amongst the young. Casual sex with multiple partners has become common. Patients with exstrophy, especially those who live in small towns, complain that they are excluded from socialising with their peers because of a fear of discovery of their abnormality. Whatever we might think of the morality of such behaviour, it is a cause of distress to some adolescents with exstrophy. Boys with exstrophy are unlikely to be successful with ‘one night stands’ though patients reported by Ben-Chaim *et al* were said to have random and short-term relationships.[13]

Pressure is then put on the surgeon to make the penis bigger. In my experience, the most important part of management is not to raise false expectations from surgery. Chordee and other erectile deformities can be corrected but there is no surgical means of producing the long, normal penis for which they hope. It is better to use knowledgeable and sympathetic counselling to help the adolescent establish a durable relationship in which normal sex takes place.

There have been several reports of the use of techniques similar to those for female to male gender re-assignment, to piggy-back a reconstructed phallus onto the natural penis of men who consider their penis to be inadequate. In 2001 de Fontaine and colleagues reported the first case of radial artery free flap phalloplasty for a man with exstrophy. The natural penis was incorporated within the new phallus with the glans and urethra emerging close to the base on the dorsum. A single inflatable prosthesis was inserted at a second operation.[14]

This is a surgical tour de force. The patient was reviewed six years after surgery and was said to be having satisfactory sexual intercourse with his wife.

However, in selecting patients for such surgery great care must be taken to ensure that it is not out of proportion to the problem. In de Fontaine’s patient, the indication was ‘severe conjugal problems.... associated with psychological difficulty’. His penis appeared, from the pre-operative photograph, to be of reasonable size for exstrophy. It did not have erogenous sensation. He had been diverted into a ureterosigmoidostomy so it was not necessary to construct a urethra to the end of the new penis.

There have been few further reports of this type of management. Six patients have been reported from France with a mean follow-up of nearly ten years. Five were said to be fully satisfied with the size and appearance of the penis and had cutaneous sensation. Only three had regular intercourse.[15] There can be a surgical complication rate of nearly 50%. It takes a year or more for even cutaneous sensation to return to the new penis and only then can stiffeners be inserted, up to a half of which have to be removed for erosion or infection.[16]

I have found it impossible to determine the true sexual results of this operation. Do the men have true erogenous sensation. Does the enclosed natural phallus retain sexual function. What proportion of men can confirm that their sexual satisfaction (and perhaps that of their partners) is improved.

Fertility

There are no data on the state of the testes at birth in exstrophy. They are presumed to be normal. There may be an increased incidence of undescended testes, being reported in six of 26 neonates (23%). However, the structural integrity of the testes and epididymes suggests that the association is anatomical rather than endocrine in origin.[17]

Similarly, little is known of their seminology except in those who present with infertility. In a literature review in 1998, I was able to find 66 adults who had had semen analyses for a variety of reasons. The results are shown in (Table 1.) Historically, between a third and a half of men who were trying to father a child were successful.

TABLE 1. Results of a literature search for the results of semen analysis in adults born with exstrophy.[12]

Azoospermia	32
Poor	01
Good	14
Paternity	19
Total	**66**

Assuming that they had normal testes at birth, infertility may be caused by infective destruction of the seminiferous tubules or by failure to deliver the sperm to the partner's cervix.

It is known that urinary infections in men with exstrophy are common but no figures on the incidence are available. Patients also report frequent episodes of epididymitis. In a recent series, six of 17 patients were said to have epididymitis which was probably a description of the indurated feeling on palpation. Seven of the 17 had azoospermia but this finding was not correlated with the epididymal findings.[18]

If there is an ejaculate containing reasonable numbers of sperm, patients can be taught a simple form of artificial insemination. Making use of the woman's fertile days, the man collects his ejaculated semen in a 10ml syringe and deposits it in the vaginal vault.

The management of male factor infertility has been radically changed by the various forms of test-tube insemination. Men with exstrophy can be managed with the same technologies as other infertile men.[19]

Females Born with Exstrophy

Genital Anatomy

The pelvis has the same orientation as in the male. The ovaries and uterus are normal. However, the supports of the uterus are deficient so that even in the nulliparous female the cervix is low and close to the introitus. Although MRI appearances of the pelvis after osteotomy have been reported for boys, there is no report on females. If extrapolation can be made from the male appearances, the pelvic floor remains deficient with lateral deviation of the levator ani. The levator hiatus is twice as wide as in normals.[20,21]

In the perineum it could be said that each orifice is displaced anteriorly. If there is a urethra, it is partly on the lower anterior abdominal wall. The anus is in the position of the normal vaginal introitus. The vagina lies almost horizontally, parallel to the floor when the girl is upright. It is shorter than normal, being seldom more than five or six centimetres in length but of normal calibre. The introitus is narrow, not because of a hymen but from a substantial bulk of tissue which appears to be a continuation of the posterior vaginal wall (Fig. 4). For most girls this tissue will have to be incised or even reconstructed before intercourse is possible. The labia are poorly formed and do not fuse anteriorly to form a fourchette. The clitoris is bifid. The distribution of pubic hair is the same as that seen in males.

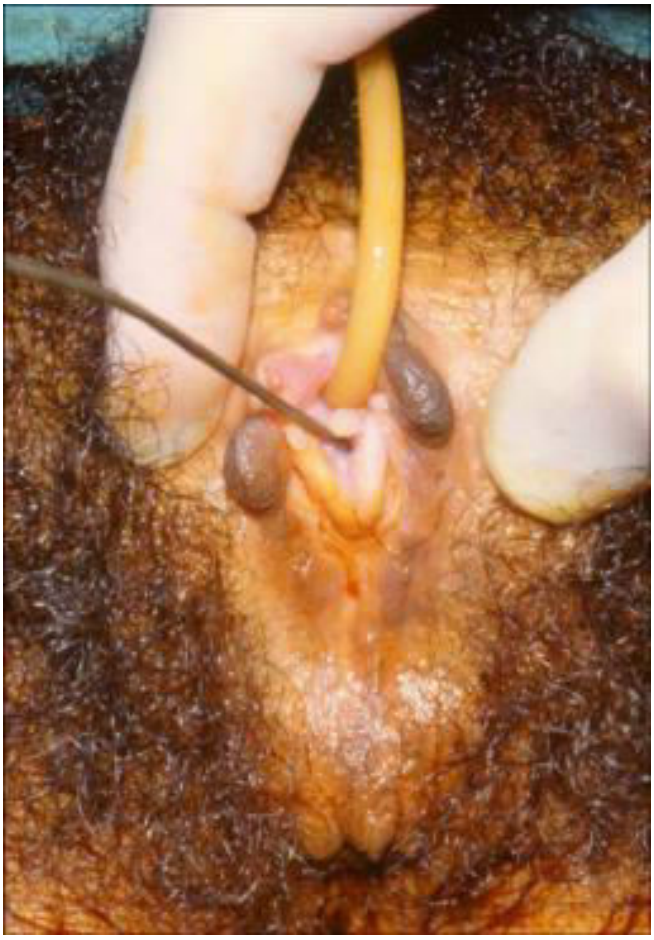

Fig. 4. Clinical photograph of the perineum of a woman born with exstrophy. There is a foley catheter in the urethra and a probe in the introitus. Note the rudimentary labia and the long distance between the introitus and the anus

Reconstruction of the Genitalia

At least 80% of women will require genital reconstruction in puberty or early adult life.[22] The objectives are to open the introitus, to unite the two halves of the clitoris and to fuse the anterior ends of the labia to make a fourchette. It is not easy to move the vagina posteriorly to its usual anatomical position, but labial and pubic reconstruction does disguise the abnormality very well. With complete soft tissue mobilisation of the urogenital complex, especially if done in early childhood, it is possible to achieve a more anatomically correct outcome.[23]

A narrow introitus is an integral part of the exstrophy complex. It can be very hard to identify the opening even in adults and it may be mistaken for a urethra. The vagina above is of normal calibre. To open it, an episiotomy incision is made posteriorly from the introitus until a two to three finger opening has been created. It is usually possible to close the vaginal mucosa to the perineal skin directly (Fig. 5).

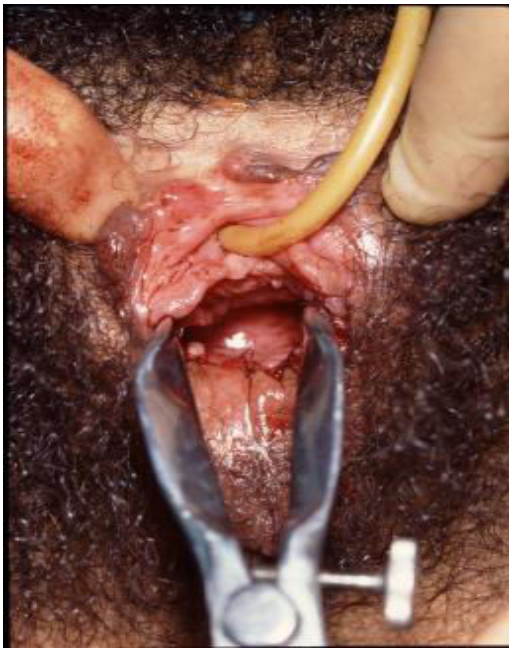

Fig. 5. Clinical photograph of the same patient as in Fig. 4. The introitus has been opened and a speculum demonstrates the normal vagina above

Cervellione and colleagues describe a longitudinal incision of the vagina alone and laying in of a perineal flap. This is their operation of choice but they do not give any reason. The results in all but one of their 29 cases were good, regardless of the technique that was used, but they do not mention if any were having intercourse.[24] My own experience has been that without some form of introitoplasty very few are able to have intercourse, but post operatively all are physically able have penetration (though not all do so).

The two halves of the clitoris (assuming that they can be identified), and the anterior ends of the labia are united to make a fourchette. The labia are short in anterior/posterior aspect and usually need to re-aligned to make them lie alongside the introitus.[24]

The greatest difficulty is with the clitoris. It is bifid at birth. It is possible to unite the two halves in infancy. A good cosmetic result has been reported in all of 9 children in one series but the longest follow-up was a year. No data are available on the functional outcomes.[25]

I am worried about the idea of doing genital surgery on children. Although parents may be pleased with a better appearance and there may be an improvement in self-esteem, the surgery is not necessary at that time. Work in my unit on adults with congenital adrenal hyperplasia who had a clitoral surgery in childhood has shown a considerable reduction in erogenous sensation and loss of orgasmic ability.[26] Although with very small numbers, one of eight adult women with exstrophy undergoing cliteroplasty had the same result.[27] In a series on of 26 children with exstrophy who underwent clitoral reconstruction, three suffered partial clitoral atrophy.[28] As the authors recommended ‘second-look’ surgery at puberty, there seems little point in doing the operation in childhood when children cannot give informed consent. I believe that non-essential genital surgery, in both sexes, should be left until the patient is old enough to understand the implications and potential complications.

Procedentia Repair

The defective pelvic floor, open pelvic ring and poor uterine supports make prolapse common. In a postal survey to which 34 women responded, vaginal and uterine prolapse was reported by 29%, occurring at a mean age of 16 years. Seven of my patients have had a total procedentia, one of whom had never had intercourse or a pregnancy.[29] It may be found in up to 50% of patients after pregnancy.

Reconstructions that create near normal anatomy may reduce the incidence of this complication. None of nine patients who have had the Kelly operation have prolapse (compared to two of three in the same series who had a different reconstruction) though some of the patients were barely into puberty.[30]

Several techniques have been reported for the repair of this difficult condition. Hohenfellner advocates fixation of the uterus to the anterior abdominal wall in childhood. This is said to prevent prolapse but still allow normal pregnancy.[31] Two women were able to have normal pregnancies without prolapse, while one of two women who did not have a fixation had 'slight prolapse' after delivery. All deliveries were by Caesarean section. This 'prophylactic surgery' may well be helpful. However, once prolapse has occurred, I have not found an anterior fixation to be an effective repair.

Although hysterectomy or partial hysterectomy has been advocated in occasional patients,[22] in the present author's view the uterus should not be removed as it is the only solid organ in the pelvis that has any hope of filling the large defect in the pelvic floor.

The most successful procedure is the gortex wrap. The sacral promontory is exposed. A strip of gortex is sutured or screwed to the periosteum. The end is passed around the cervix through the base of the broad ligament and brought back to the sacrum. This procedure has been successful in all cases with follow-up to a maximum of six years.[32]

Female Sexual Function

Even in normal women, sexual function has been little studied. An objective measure of successful female sexual function, equivalent to erection or ejaculation, is difficult to define. Most series are confined to expressions of the patients' global satisfaction. The results of vaginal reconstruction in exstrophy appear to be satisfactory in the sense that most patients do not request further cosmetic surgery and most engage in sexual intercourse.

There is no large or scientific survey of their sexuality. Three series with reasonable numbers cover 43 patients, but they represent only about 20% of the women recorded in the relevant Institutions data bases.[33,34,35] Thirty-four (79%) had regular intercourse and ten of them had dyspareunia (29% of those having regular intercourse). No other general information is available from these three series. Individually, it would appear that libido is normal; the age of sexual debut is 19.9 years; 13 of 22 (59%) who were specifically asked had regular orgasms.

Unfortunately, we do not know if this reflects the normal spectrum of female sexual experience. In Castagnetti's norm related study on males with exstrophy, 23% of the control group had sexual dysfunction on the IIEF-15 questionnaire. This compared to 58% of men with exstrophy. However, even this had a statistical significance of only $p = 0.02$. A similar study is needed for women.

Fertility

Although there has been no formal study, it seems likely that females with exstrophy have normal fertility unless surgery has caused tubal obstruction or some other genital complication.

Pregnancy and Delivery

With modern obstetric care, pregnancy and delivery should be uncomplicated except for the risk of prolapse, at least as far as the exstrophy is concerned. In a combined series of patients 43 pregnancies in 28 women were identified. Four ended in spontaneous and four in therapeutic abortion. There were 34 live births and one intra uterine death of twins.[22,36] There is a high incidence of breech presentation at 57% compared to 4% in normal women.[37]

The incidence of prolapse is high and presumably is increased by pregnancy and vaginal delivery. Women must be advised of the risk, but as it occurs even in nulliparous women with exstrophy, it does not seem to be a reason, on its own, to avoid pregnancy.

Perhaps a greater problem is the complexity of the urinary tract reconstruction. Pregnant women who were born with exstrophy should be under the joint care of a urologist and an obstetrician. A decision about the mode of delivery depends on the bladder drainage and control mechanism, the nature of the reservoir and, with an intestinal reservoir, the anatomy of its blood supply. The worst outcome is with an emergency caesarean. Most centres, including my own, recommend an elective caesarean.[38]

Inheritance

The aetiology of the exstrophy complex is unresolved. Classical exstrophy is a rare condition. The incidence is about 1:25,000 to 1:30,000 live births and about 1:10,000 still births. Several non-genetic factors may increase the risk for any pregnancy including maternal age over 30 and maternal smoking.[39,40]

Epidemiological surveys of the families of individuals with any of the spectrum of exstrophy/epispadias anomalies show one or two families with more than one affected member and an increased risk of affected offspring from people who themselves have exstrophy.

At Great Ormond Street, no cases of exstrophy were found in 162 siblings of 102 exstrophy children, though there was a slightly increased incidence of relatives with neural tube defects. The Baltimore survey found that 200 families with an affected child had 259 unaffected children between them.[41] A European survey with data on 199 families similarly showed no affected siblings.[42] However, both of these latter surveys identified families with remoter relatives affected.

A very detailed analysis of 56 pairs of twins drawn from the literature strongly suggests that there is some genetic element in the aetiology. Monozygotic twins were found to be 5.6 times more likely to be concordant for exstrophy than dizygotic twins.[43] This means that if one of a monozygotic pair has exstrophy, the risk that other twin also has it is 4500 times greater than the risk in the normal population. For dizygotic twins the second twin risk is 600 times that of the normal population.

If the concordance rates for the two types of twin were the same, it would suggest an environmental cause. The fact that the concordance rate in monozygotic twins is not 100% can be explained by somatic events occurring after the splitting of the two embryos or by environmental factors.[44] No gene locus has been identified, but some candidates are under investigation.[45]

For couples who have had a baby with exstrophy, it is reassuring to know that the risk of them having another is very much less than 1%.[46]

A postal survey gave a 1:70 risk of an exstrophy patient being the parent of an exstrophy baby.[47]

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