

Normalization of the vagina by dilator treatment alone in Complete Androgen Insensitivity Syndrome and Mayer-Rokitansky-Kuster-Hauser Syndrome

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BACKGROUND: Various surgical and non-surgical treatment options are available for women with congenital vaginal agenesis. We report results of vaginal dilation therapy delivered by a multi-disciplinary team as first line treatment for vaginal agenesis. **METHODS:** Twenty-six women were recruited into a prospective observational study: 18 had Mayer-Rokitansky-Kuster-Hauser syndrome (MRKH) and 8 had Complete Androgen Insensitivity Syndrome (CAIS). All women underwent a vaginal dilation programme co-ordinated by a clinical nurse specialist with input from a clinical psychologist. Vaginal length was compared to a normal reference range, and psycho-sexual questionnaires were completed before and after therapy. **RESULTS:** Twenty-one (81%) patients completed the programme. Seventeen of these 21 (81%) were sexually active without any reported difficulties, whereas 4 were on a maintenance regime. In those who completed the programme the mean vaginal length increased from 4.0 to 8.5 cm and 86% achieved a vaginal length within the normal range. Subjective appraisal of vaginal size recorded that the number of women who reported that their vaginal size was ‘more or less normal’ increased from 1 to 12 following treatment. Questionnaire scores for sexual satisfaction and sexual depression improved in the CAIS group but did not alter significantly in the MRKH group. **CONCLUSION:** Non-surgical dilation delivered by a multi-disciplinary team is an effective alternative to vaginal surgery and usually normalizes vaginal length.

Keywords: vaginal dilation; vaginal reconstruction; psychology; MRKH; CAIS

Introduction

Vaginal dilation has been used to treat vaginal agenesis for over 70 years, but outcome data to date has been retrospective with poor definitions of ‘success’. In this study, we have undertaken a prospective assessment of a vaginal dilation programme testing multiple outcomes.

Congenital vaginal agenesis is most commonly seen in women with Mayer-Rokitansky-Kuster-Hauser syndrome (MRKH) and Complete Androgen Insensitivity Syndrome (CAIS). In MRKH, women have functioning ovaries but no uterus and a short vagina or vaginal dimple, resulting from failed embryologic development of the Mullerian duct. The incidence of MRKH has been quoted to be 1 in 5000 female births or 1 in 20 000 hospital admissions (Burel *et al.*, 2006). The cause is currently unknown, but current theories point towards genetic predisposition (Blackless *et al.*, 2000). CAIS has an estimated incidence of between 1 in 13 000–40 000 live births and results from loss of function mutations of the androgen receptor (Quigley *et al.*, 1995). Females with the complete form of androgen insensitivity (CAIS) have a

46XY karyotype, an absent uterus and may also have a short vagina (Minto *et al.*, 2003).

Surgical reconstructive techniques for a small vagina have known drawbacks (Davies *et al.*, 2005). There are risks associated with major surgery and anaesthesia. Irreversible scarring may lead to vaginal stenosis and further dyspareunia or apareunia. Other specific complications may include offensive vaginal discharge (Kwun *et al.*, 2003) and diversion colitis (Syed *et al.*, 2001; Abbasakoor *et al.*, 2004). The newer and more elegant laparoscopic vaginoplasty techniques may be associated with fewer complications (Fedele *et al.*, 2000), although peri-operative ureteric and bladder injury has been reported (D’Argent *et al.*, 2004). Furthermore, there are scanty long-term outcome data and little information on psycho-sexual factors with either the traditional or more modern vaginoplasty options. Most of all, many of the surgical techniques have to be followed by post-operative vaginal dilation to maintain volume. Surgery may be perceived as a quick and uncomplicated solution to vaginal absence, but psychological barriers to sexual intimacy could remain

(Liao *et al.*, 2006). Such barriers could result in emotional avoidance, thereby interfering with the patient's intention to self-manage post-surgical dilation. Poor self-management after surgery could permanently frustrate the patient's aspirations for normalizing the vagina, because effectiveness of future reconstruction could be compromised due to surgical scarring. The argument for developing an effective dilation treatment programme with demonstrable psycho-sexual benefits as a first line approach is thus obvious.

Non-surgical vaginal dilation for vaginal agenesis was first reported by Frank in 1938, who described the use of vaginal moulds of increasing width and length to successfully create a neovagina for five out of six women (Frank, 1938). The single failure was attributed to the patient's 'unco-operative attitude'. Since then several studies have reported success rates varying from 43 to 100% (Wabrek *et al.*, 1971; Ingram, 1981; Rock *et al.*, 1983; Williams *et al.*, 1985). However, all such studies have been retrospective and offer no clear definition of success. Questions have been raised by psycho-sexual workers as to how 'success' should be defined in vaginal reconstruction (Liao *et al.*, 2006). Vaginal capacity for coitus is certainly possible, but it is not known to what extent increased capacity benefits sexual function and experiences, as perceived by patients. Motivation for reconstruction is often based on aspirations for normalcy not just in terms of sex anatomy but also sexual activities and experiences (Minto *et al.*, 2003; Boyle *et al.*, 2005; Liao *et al.*, 2006).

Dilation treatment may take several months, and the regime has been described as 'distasteful' in interview studies with women (Boyle *et al.*, 2005). It has been suggested that compliance and patient satisfaction is generally low (Minto *et al.*, 2003). Given the stigma attached to genital anomalies and the potential drawbacks in approaches to vaginal reconstruction, specialist emotional and psychological support must be planned alongside expert medical care. Within such a broad approach to care provision, barriers to dilation treatment adherence are more likely to be overcome, rendering it viable as an alternative to surgery as first line approach.

Even so, the effectiveness of dilator treatment, like any other intervention, should be thoroughly evaluated, ideally in a prospective study of multiple outcomes. This is the purpose of the current study—the first to report prospectively the short-term results of first line dilation treatment derived from the original Frank technique (Frank, 1938) and delivered by a multi-disciplinary team, for women with vaginal agenesis and without a previous history of vaginal surgery.

Materials and Methods

This study took place at a tertiary referral centre for the management of women with congenital vaginal agenesis. Ethics approval was granted by the joint university and hospital ethics committee. This was a prospective observational study of all women over the age of 18 who were prescribed vaginal dilation treatment for vaginal agenesis between May 2003 and December 2005. Twenty-six women were enrolled in the study, of whom 18 had a diagnosis of MRKH and 8 had CAIS.

A group of normal women were recruited to provide reference values for vaginal length as previously described (Lloyd *et al.*,

2005). These women were a subgroup of healthy volunteers from a previous study, selecting those who were nulliparous and who were matched for age to the study group. Data from 20 women were used, for whom the mean \pm SD age was 26.5 ± 5.2 years and mean \pm SD vaginal length was 9.25 ± 1.56 cm. The range of vaginal length in these women was 7–13 cm and these values were used to define the normal reference range for vaginal size.

Treatment protocol

Noting that a previous study suggesting that compliance and treatment satisfaction in relation to dilation could be low (Minto *et al.*, 2003), the current protocol was developed after careful pilot work. The programme was out-patient based, nurse-co-ordinated and informed by motivational and behavioural psychology (Liao *et al.*, 2006). A vaginal examination was performed by a single observer (S.M.C.) and was followed by a structured interview by a Clinical Nurse Specialist (M.B.) to prepare each patient for treatment. The interview elicited not only the potential benefits of dilation as perceived by the patient but also the potential barriers or obstacles associated with implementing the regime. The individual was then encouraged to solve problem around any identified difficulty. Patients also rated their confidence in being able to carry out the treatment. Where confidence was low, there was opportunity to explore how confidence could be enhanced. Once treatment uptake was agreed, spoken and written instructions on vaginal dilation were given and patients were shown how to apply gentle pressure to vaginal dimple using graduated dilators for 30 min daily and to self-monitor their practice and associated pain/discomfort ratings. Patients attended for up to five follow-up visits at 6–8 weeks apart with the Clinical Nurse Specialist; telephone and email contact was available if required. Emotional and psychological support from the team clinical psychologist was available as needed before, during or after treatment, as were opportunities for education in sexual health and well being. Treatment was deemed completed when a patient was able to insert a size 3 dilator (14 \times 3 cm) completely with no difficulty or if she engaged in coitus with no difficulty. At completion of the treatment, a further vaginal examination was performed.

Outcome variables

Vaginal size

Vaginal length was recorded in centimetres by inserting a cotton bud into the vagina and recording the length from the posterior fourchette to the most distal part of the blind ending vagina. Capacity was recorded by noting the size of the largest dilator that could be fully inserted.

Vaginal perceptions

In order to establish whether the objective anatomical change was associated with changes in self-perceptions, patients were asked to report how they perceived their vagina from the following six statements:

- 1) My vagina is more or less normal.
- 2) I do not know or I am not sure.
- 3) My vagina is tiny or non-existent.
- 4) My vagina is small (short or narrow).
- 5) A sexual partner would notice it is different from other women.
- 6) I would like a bigger vagina (longer or wider).

Psycho-sexual capacities

Standardized sexual function assessments tend to be usable only with individuals already sexually active. Because many patients with vaginal agenesis are not sexually active prior to treatment, psycho-sexual tendencies were assessed instead, using the Multidimensional Sexuality Questionnaire (MSQ). The MSQ is a self-reported questionnaire, responses to which can be based on a current, past or imagined relationship, making it applicable to all our patients. Because the full MSQ is long and comprises 12 subscales each with 5 items (60 items), only 6 of the 12 subscales (30 items) were incorporated into our evaluation: sexual esteem, sexual anxiety, sexual assertiveness, sexual depression, fear of sexual relationships and sexual satisfaction. Individuals rate their level of agreement with each item on a 5-point Likert scale. Improvements along these dimensions are hypothesized to be more salient in our longer term evaluation, which is the topic of a future report.

Patient satisfaction

On completion, patients rated their satisfaction with our service along a number of dimensions on a scale of 1–5 as well as overall satisfaction (1 = not at all satisfied; 5 = extremely satisfied).

Statistical analysis

Differences in vaginal length were assessed using a paired Student's *t*-test. Parameters from the vaginal perception questionnaire were compared before and after dilation using a χ^2 -test, whereas MSQ scores were compared using Wilcoxon Signed Rank tests

Results

Women with MRKH were younger (median age 20 years (range 18–24 years)) compared with those with CAIS (median age 28 years (range 18–42 years) ($P = 0.019$)). They also had a shorter vaginal length at the start of the study compared with women with CAIS (mean 2.6 cm, SD 1.5 compared with a mean of 5.9 cm, SD 2.2 ($P = 0.003$)). Ten (56%) of the MRKH group and 5 (63%) of the CAIS group had attempted intercourse previously. The treatment programme was completed by 21/26 (81%) of the women. All five (26%) of the women who failed to complete the programme came from the subgroup with MRKH. For those who completed the programme, the median (range) time to completion of treatment was 5.2 (4.2–7.3) months and the median (range) frequency of dilations per week was 5 (0.5–9.3). Seventeen of the 21 (81%) had begun to engage in coitus and 4 were on a maintenance regime using the size 3 dilator two to three times per week. Of the 17 women who were sexually active, 11 had MRKH and 6 CAIS, demonstrating no difference in sexual activity between the two diagnostic groups.

Of the 5/26 (19%) women who did not complete the programme, 2 could not achieve a significant increase in vaginal length despite reporting full compliance with the programme and went on to undergo laparoscopic Vecchietti procedure (Ismail *et al.*, 2006). Three women were unable to dilate regularly and opted out of the programme temporarily. Reasons given by these women included: lack of time, lack of privacy, and lack of a partner rendering dilation not urgent. In considering the characteristics of those who failed to complete the treatment programme, we analysed only those with MRKH. Those who failed to complete the course of treatment

had a shorter mean \pm SD vaginal length at the start of treatment compared with those who completed the course 1.6 ± 0.9 versus 2.9 ± 1.6 cm, respectively, ($P = 0.01$) and were less likely to be sexually active than those who completed the course 0/5 versus 10/13 ($P = 0.007$). Age and questionnaire parameters had no association with failure to complete treatment.

Analysis based on intention to treat showed that the mean \pm SD vaginal length increased from 3.6 ± 2.3 cm before treatment to 7.0 ± 3.5 cm following dilation therapy ($P < 0.01$) and that 16/26 (62%) women achieved a value in the normal range (Fig. 1). Analysis per protocol showed that for the 21 women who successfully completed the programme, the mean \pm SD vaginal length from 4 ± 2.3 to 8.5 ± 2.4 cm ($P < 0.01$) following dilation therapy and that 16/21 (76%) achieved a value in the normal range. There was no significant association between starting vaginal length or duration of treatment and the increase in vaginal size and no difference between the diagnostic groups.

There was an overall significant change in vaginal perception following dilation therapy (Fig. 2). Improvement was reported for all of the vaginal perception items following dilation therapy, in particular, a significantly higher proportion of women felt that their vagina was 'more or less normal'.

There was a reduction in the MSQ scores for sexual satisfaction and sexual depression following vaginal dilation therapy that only achieved significance in the CAIS group (Table 1). MSQ scores were not related to vaginal length.

Sixteen patients rated the extent of satisfaction with the clinic on the whole. The mean (range) overall satisfaction for these women was 4.82 (4–5). Because the ratings were generally high with little variability—so called ceiling effect—it was not possible to associate service satisfaction with treatment compliance as we had hoped.

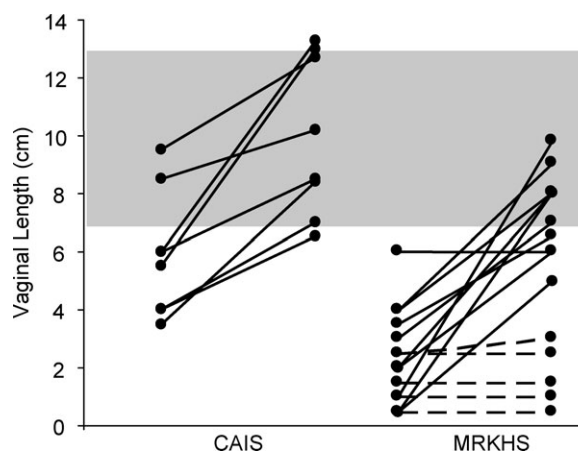


Figure 1: Vaginal length in 26 women with vaginal agenesis before and after dilation therapy as first line treatment. Women who did not complete the treatment programme are shown with dotted lines. The normal reference range (shaded) is derived from 20 control women

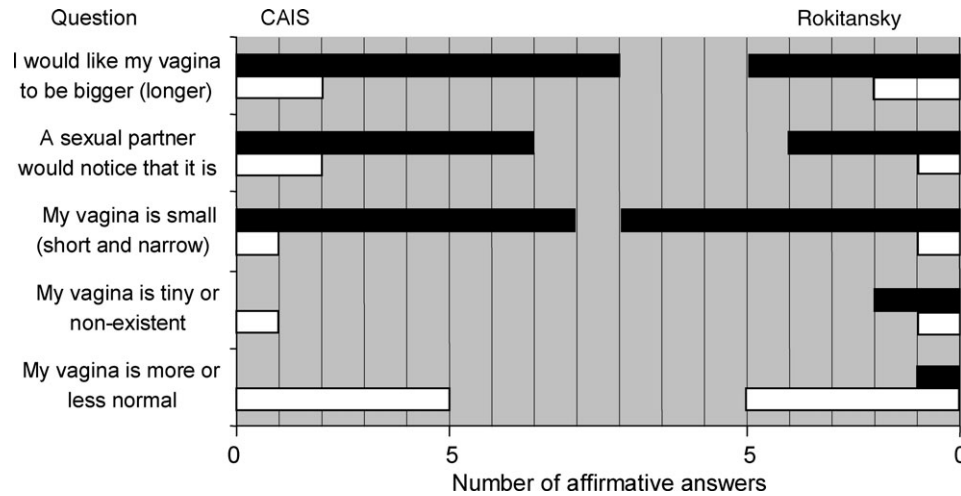


Figure 2: Vaginal perception questionnaire.

Responses in women with androgen insensitivity (CAIS) on the left and MRKH syndrome on the right before (black bars) and after (open bars) treatment programme (χ^2 -test, overall $P \leq 0.05$)

Discussion

Congenital vaginal agenesis is most commonly seen in women with MRKH and CAIS. In both these conditions, the absent or short vagina may lead to the inability to have penetrative sexual intercourse. Various operative (Ismail and Creighton, 2005) and non-operative techniques (Frank, 1938) of vaginal reconstruction have been developed to allow penetrative sexual activity.

Although dilation without surgery may have fewer risks and appear to be an obvious first line treatment, the treatment can be arduous and unpleasant for some patients. Patients are asked to use their dilator for 30 min each day for an average of 5 months and to endure a degree of discomfort. The regime can have negative meanings for some women (Liao *et al.*, 2006) or it may be experienced as embarrassing or shameful. On the other hand, recognition of emotional problems during this time has the advantage of signalling to the patient the need to come to terms with the diagnosis and to overcome avoidance.

A major difficulty in evaluating the outcomes of dilation (and surgery) lies in defining what comprises a successful outcome. Studies, including this current one, have measured vaginal size before and after treatment. Although 'normal' vaginal size is not an unreasonable goal, it may not lead to normal sexual function and positive sexual experiences.

There is increasing recognition of the value of standardized measures of sexual function dimensions following vaginal reconstruction (Roberts *et al.*, 2001; Brun *et al.*, 2002; Hensle *et al.*, 2006) to enable patients' reports to be compared with general population data.

This study confirmed that vaginal dilation is effective in women with both MRKH and CAIS. However, it is possible the treatment is less successful in those women with the former syndrome. All five women who failed the dilation programme had MRKH. Both groups showed improvement on analysis of the MSQ but the only significant changes seen were in those women with CAIS (Table 1). From this study it is not possible to determine whether there really is a difference between the two diagnostic groups. The number of women sexually active after treatment did not differ between the two groups. However, the numbers of women are small, particularly those with CAIS. Importantly, the second MSQ was administered on completion of the dilator programme and is likely to alter when these women continue or enter into sexual relationships. More meaningful comparison between the groups will be possible at that time and future follow-up studies of this group are ongoing.

This is the first study to demonstrate that in the majority of women with a shortened vagina, vaginal dilation therapy can increase vaginal length to fall within the normal ranges. In recent studies of normal female genitalia, vaginal length

Table 1: MSQ scores before and after vaginal dilation therapy

	CAIS			MRKH		
	Before	After	<i>P</i> -value	Before	After	<i>P</i> -value
Sexual esteem	6 (0–14)	7 (2–12)	0.26	2 (0–12)	4 (1–12)	0.19
Sexual anxiety	9 (3–20)	6 (3–12)	0.07	12.5 (3–20)	7 (4–15)	0.14
Sexual assertiveness	8 (5–13)	7 (4–9)	0.34	8 (2–11)	6 (0–10)	0.35
Sexual depression	11.5 (1–15)	8 (0–11)	0.04	11 (2–17)	5 (0–13)	0.10
Fear of sex	9 (4–13)	8 (4–10)	0.34	9 (6–15)	8 (5–11)	0.13
Sexual satisfaction	2.5 (0–14)	9 (1–14)	0.04	5 (0–14)	6 (0–17)	0.22

Median and range for each domain is shown. The effects of therapy were tested using Wilcoxon Signed Ranks Test.

ranged from 6.5 to 13.0 cm (Weber *et al.*, 1995; Lloyd *et al.*, 2005) in women who do not report any penetrative sexual difficulties. However, vaginal size in non-sexual situations may be a poor predictor of penetrability upon sexual arousal. This makes strong argument for clinicians to emphasize arousal and enjoyment and to reduce the level of preoccupation with size and performance which could, in turn, and inadvertently, raise anxiety thereby compromising sexual responses (Liao *et al.*, 2006).

This is the first prospective study that objectively assesses the multiple outcomes of vaginal dilation for vaginal agenesis and associates anatomical change with psycho-sexual outcomes. We have demonstrated that dilation treatment, when delivered by a specialist multi-disciplinary team, can help the majority of women with vaginal agenesis to avoid surgery and its attendant risks, with the potential to maximize psycho-sexual outcome. Although the commitment from health care professionals may be greater than standard care, the health care costs are likely to be offset by the considerable savings in being able to avoid the costs associated with an initial operation, post-operative care, potential post-operative complications or repeat operations in future. We conclude that dilation delivered in a multi-disciplinary context that is sensitive to patients' perspectives should be a first line treatment for all women with a short or absent vagina.

References

- Abbasakoor F, Mahon C, Boulos PB. Diversion colitis in sigmoid neovagina. *Colorectal Dis* 2004;**6**:290–291.
- Blackless M, Charuvastra A, Derryck A *et al.* How sexually dimorphic are we? Review and synthesis. *Am J Human Biol* 2000;**12**:151–166.
- Boyle ME, Smith S, Liao LM. Adult genital surgery for intersex: a solution to what problem? *J Health Psychol* 2005;**10**:573–584.
- Brun JL, Belleanne G, Grafeille N *et al.* Long-term results after neovagina creation in Mayer-Rokitanski-Kuster-Hauser syndrome by Vecchietti's operation. *Eur J Obstet Gynecol Reprod Biol* 2002;**103**:168–172.
- Burel A, Mouchel T, Odent S *et al.* Role of HOXA7 to HOXA13 and PBX1 genes in various forms of MRKH syndrome (congenital absence of uterus and vagina). *J Negat Results Biomed* 2006;**5**:4.
- D'Argent D, Marchiole P, Giannessi A *et al.* Laparoscopic Davydov or laparoscopic transposition of the peritoneal colpocliesis described by Davydov for the treatment of congenital vaginal agenesis: the technique and it's evolution. *Gynecol Obstet Fertil* 2004;**32**:1023–1030.
- Davies MC, Creighton SM, Woodhouse CR. The pitfalls of vaginal construction. *BJU Int* 2005;**95**:1293–1298.
- Fedele L, Bianchi S, Zanconato G *et al.* Laparoscopic creation of a neovagina in patients with Rokitansky syndrome: analysis of 52 cases. *Fertil Steril* 2001;**74**:384–389.
- Frank RT. The formation of artificial vagina without operation. *Am J Obstet Gynecol* 1938;**35**:1053–1055.
- Hensle TW, Shabsigh A, Shabsigh R *et al.* Sexual function following bowel vaginoplasty. *J Urol* 2006;**175**:2283–2286.
- Ingram JM. The bicycle seat stool in the treatment of vaginal agenesis and stenosis: a preliminary report. *Am J Obstet Gynecol* 1981;**140**:867–873.
- Ismail IS, Creighton SM. Surgery for intersex. *Rev Gynaecol Pract* 2005;**5**:57–64.
- Ismail IS, Cutner AS, Creighton SM. Laparoscopic vaginoplasty: alternative techniques in vaginal reconstruction. *BJOG* 2006;**113**:340–343.
- Kwun KS, Hoon PJ, Cheol LK. Long-term results in patients after rectosigmoid vaginoplasty. *Plast Reconstr Surg* 2003;**112**:143–151.
- Liao L, Doyle J, Crouch NS *et al.* Dilation as treatment for vaginal agenesis and hypoplasia: a pilot exploration of benefits and barriers as perceived by patients. *J Obstet Gynaecol* 2006;**26**:144–148.
- Lloyd J, Crouch NS, Minto CL *et al.* Female genital appearance: "normality" unfolds. *BJOG* 2005;**112**:643–646.
- Minto CL, Liao KL, Conway GS *et al.* Sexual function in women with complete androgen insensitivity syndrome. *Fertil Steril* 2003;**80**:157–164.
- Quigley CA, De Bellis A, Marschke KB *et al.* Androgen receptor defects: historical, clinical, and molecular perspectives. *Endocr Rev* 1995;**16**:271–321.
- Roberts CP, Haber MJ, Rock JA. Vaginal creation for mullerian agenesis. *Am J Obstet Gynecol* 2001;**185**:1349–1352.
- Rock JA, Reeves LA, Retto H *et al.* Success following vaginal creation for Mullerian agenesis. *Fertil Steril* 1983;**39**:809–813.
- Syed HA, Malone PS, Hitchcock RJ. Diversion colitis in children with colovaginoplasty. *BJU Int* 2001;**87**:857–860.