Gynaecological and Psychosexual Outcomes
of Feminising Genital Surgery

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Thesis submitted to the University of London
for the Degree of Doctor of Medicine
Abstract

Childhood feminising surgery remains standard clinical practice for those born with ambiguous genitalia, such as women with Congenital Adrenal Hyperplasia (CAH). The aims of such an intervention are to promote “normal” female appearance, allow comfortable penetrative intercourse with unimpaired sensation, avoid increased psychological sequelae and prevent urinary difficulties due to anatomical variations. However, these aims remain largely unevaluated. Little is known about the range of normal female genital appearance with few objective measurements in the literature. Scanty long-term data is available regarding sexual function and sensation following childhood feminising surgery. To date there is no evidence to suggest that childhood surgery reduces psychological distress compared with those who did not have operations. Finally, no studies are available assessing urinary outcomes following surgery. These areas are assessed in turn, starting with a study to ascertain normal female appearance of the genital area, and to illustrate the variations of normality. Genital sensation is next considered, with a study of 28 women with CAH who underwent objective sensation testing to the clitoris, where surgery had taken place, and to the upper vagina, where no operations had been performed. This data was compared with 9 normal subjects who had no history of sexual function difficulties or previous operations to the genital area. Clitoral sensation was significantly impaired in those who had undergone surgery, but not vaginal sensation. Sexual function and subjective views regarding surgery were assessed, with 32 women with CAH recruited to complete a detailed questionnaire assessing various aspects of anatomical and psychosexual function. This was then compared with data from 10 normal controls, showing women with a history of surgery had increased sexual function difficulties. Finally, a further study assessed the degree of lower urinary tract symptoms in those who had undergone surgery, and compared this with a normal control group. This showed increased urinary tract symptomatology in the group who had undergone childhood surgery. The results of these studies are discussed and considered in the context of current knowledge of intersex research.

Recommendations for clinical practice and future research are given.
Declaration

The research leading to this thesis was carried out in the Middlesex Centre at the Elizabeth Garrett Anderson Hospital and the Academic Department of Obstetrics and Gynaecology, University College London. All work contained in this thesis is my own. None of the data forms part of any other thesis. All studies were approved by the Joint University and Hospital Ethics Committee, with written consent obtained from all participants prior to their involvement.

Naomi S Crouch
Acknowledgements

I would like to thank and acknowledge the assistance of the following in this research. Sister Maligaye Bikoo for assisting in the practical testing, Dr Lih-Mei Liao for guidance and advice on psychological aspects of the work. Dr Gerard Conway for clinical advice and for guidance as a second supervisor. I would especially like to thank Miss Sarah Creighton during my time as her research fellow. Her cheerfulness and humour, along with patience and advice were invaluable, and never failed during my time as her research fellow.

Above all I would like to thank my husband Adrian, without whose unswerving support and the provision of many meals, this thesis could not have been written.
Publications and Presentations

The following work from this thesis has been published in peer-reviewed journals (appendix 4) or presented to the learned societies:

Genital Sensation Following Feminising Genitoplasty for CAH: A Pilot Study
Crouch NS, Minto CL, Liao LM, Woodhouse CRJ, Creighton SM.
BJUInt 2004. 93:135-138

Female Genital Appearance: "Normality" unfolds
Lloyd J, Crouch NS, Minto CL, Liao LM, Creighton SM
BJOG 2005 May;112(5):643-6

Congenital Adrenal Hyperplasia and Lower Urinary Tract Symptoms
Davies MC, Crouch NS, Woodhouse CRJ, Creighton SM
BJUInt 2005 Jun;95(9):1263-6

Abstract Presentations:
2003 "Genital Sensation following Feminising Genitoplasty for CAH: A Pilot Study"
British Association for Urological Surgeons, Manchester, UK, and at the North American Society for Pediatric and Adolescent Gynecology, Philadelphia, USA.

2004 "Genital Sensation following feminising Genitoplasty: Interim results"
British Congress of Obstetrics and Gynaecology, Glasgow, UK.

2005 "Genital Sensation following Feminising Genitoplasty: Final results"
British Association for Urological Surgeons, Glasgow, UK, and at The European Society for Pediatric Urology, Uppsala, Sweden.
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Chapter 1

1.1 Introduction and Background

Intersex conditions may be defined as a co-existence of male and female characteristics in the same individual, with some alteration occurring along the normal pathways for male and female development in utero. This may occur at the chromosomes, the gonads, or genital development. Examples include a female with an XY karyotype or testes, or conversely ovarian tissue or XX chromosomes in a male. Alternatively individuals may be born with the appropriate internal genitalia for their karyotype, but undervirilisation in a male or overvirilisation in a female may lead to the development of ambiguous genitalia.

This thesis will concentrate on the gynaecological and psychosexual outcomes of individuals who have undergone an intervention which has been standard practice for nearly 50 years, yet has rarely been objectively assessed. The individuals concerned all have the condition Congenital Adrenal Hyperplasia (CAH), which is the most commonly occurring intersex condition.

1.1.1 Historical Aspects of Intersex Conditions

Intersex conditions, or hermaphrodites as they were previously termed, have been identified for several thousands of years and have always attracted controversy by their very existence. Throughout the centuries they have represented “difference” and have therefore been regarded either with respect, or more commonly suspicion and hostility. The term hermaphrodite was derived from Ovid’s myth of the joining of the gods Hermes and Aphrodite. Thus in Ancient Greece hermaphrodites were revered and treated with God-like status, or eternity. But by the Middle Ages, intersexuels were scorned, sometimes denounced as witches, and risked being burned at
the stake. The seventeenth century in Britain ushered in a more tolerant attitude with a desire to accommodate and allocate intersex patients to living in a male or female role. The male role clearly carried more social advantage in permitting marriage, the ownership of property and possibility of voting, depending on social class. Allocation of sex was determined by the characteristics an individual possessed. Those of a gentle disposition would be viewed as more feminine, whereas more assertive, strong-willed individuals must clearly be male. This desire for “correct” classification was developed further in the nineteenth century.

The Victorian obsession with the science of taxonomy led to an urgent desire to categorise intersexed individuals to either sex, and chose to use the gonads as revealing the “true sex”\(^2\). Therefore, those who were found to have testes would be (re) assigned male, regardless of the fact they may have been brought up as female, possibly married, and living a female role. Attitudes in the twentieth century have varied, but the mainstay of treatment is still to allocate sex of rearing at or shortly after birth. Many factors go into the decision making process, such as the potential for fertility, and the wishes of parents, but not least is the appearance of the external genitalia. For many intersex conditions there has been a historical preference to choose the female sex, partly based on the long standing assumption that female genitalia can sometimes prove easier to reconstruct than male genital organs\(^3\). Furthermore, there has often seemed to be an understated belief that female sexual function is inherently more straightforward, and perhaps less important, than sexual function for men. As one eminent surgeon stated in 1997 “…it is better to be incompletely female than inadequately male in terms of potential social adjustment.”\(^4\).

The last decade of the twentieth century has seen the management of intersex conditions become increasingly controversial, with heated debate between patients and doctors as to the optimal care and treatment for intersexed individuals. Central to this has been the issue of corrective
feminising genitoplasty surgery performed on individuals with ambiguous genitalia who are to be raised female.

1.1.2 The Optimal Gender Policy and the "John/Joan case"

In 1955, John Money, a psychologist practicing at Johns Hopkins Hospital published a paper addressing the management of intersex patients. His conclusions were that in order for a child to have a stable gender identity, the genitalia should be unambiguous and concordant with sex of rearing. In addition there must be unequivocal reinforcement of the chosen gender by the parents. He also believed that gender identity was not innate and instinctive, but rather reflected the experiences of growing up. Sexuality, he believed, was undifferentiated at birth but became differentiated into male or female as life progressed. A management approach for all children born with ambiguous genitalia was developed, including those females virilised as a result of CAH. Once sex of rearing was assigned, corrective genital surgery was be performed as a baby or small child, so the phenotype closely matched the chosen sex of rearing. Yet the theories surrounding assignment of sex, and the need for early surgery remained unevaluated.

In 1966 a situation presented itself which gave an ideal opportunity for Money's theories to be tested. Twin baby boys were due to undergo circumcision procedures for phimosis. The operative technique utilised electrocautery, but a failure in the equipment led to the complete cauterisation and destruction of the penis of the first twin. The operation for the second twin was cancelled, and both babies returned home. Some months later, the case was referred to John Money, who recommended complete gender reassignment for the first twin. The testicles were removed and the scrotum refashioned into labia. From now on, the child would be reared as female, with complete reinforcement of the gender by the parents. A female name was chosen, and the parents advised that the baby should never know the details of the reassignment. After all, as the theory went if the parents complied, the child would be a well adjusted girl, stable in her gender identity. In addition, this would provide the ideal case-control study to confirm...
his theories. Subsequent publications testify to the success of the policy, which became known as the "John/Joan case". Extrapolation into the management of intersex conditions appeared to confirm the appropriateness of early corrective surgery for CAH. This policy became widely adopted, and early feminising surgery was recommended for all children born with ambiguous genitalia. However, little longer-term data existed then, or now, to support such a blanket policy. Milton Diamond, a biologist in Hawaii, was keen to discover the long-term outcomes of the John/Joan case, and found that rather than it being an unqualified success, it was an abject failure. "Joan" had been a desperately unhappy little girl, and had self-reassigned male at the age of 14. By the time of the investigation he was in his early 30's and had undergone reconstructive penile surgery. Subsequently he had married, adopting the children of his partner, but clearly had experienced difficulties in understanding and accepting his past. He committed suicide in 2004. Widespread media publicity from 1997 onwards ensured that clinicians dealing with intersex could not fail to be aware of the outcome of the case.

1.1.3. Disclosure

A significant aspect of the Optimal Gender Policy was the withholding of medical details from the individual concerned. Surgery had been carried out before the development of permanent memory of the child. Therefore there would be no "evidence" of the genital ambiguity. Money believed if consistent reinforcing of the chosen gender role were given this would lead to a firm gender identity. However, implicit in this was the idea that the individual would never know their own medical history, or diagnosis. This effectively took away the opportunity for peer support, or for simply finding out more details about their diagnosis and also understanding the necessity of regular hospital appointments. Medical science changes rapidly, and the genetic basis for many intersex conditions is now known. However, if an individual does not know they have an intersex condition, clearly this information cannot be accessed. Furthermore, the opportunity to take part in research studies is denied, and reliable data about issues such as subsequent sexual function or risks of gonadal cancer is limited, thus...
making it difficult for clinicians to offer accurate information. The policy of non-disclosure of information was widely practiced until relatively recently. This has been challenged in the last decade, and it is now felt inappropriate to withhold medical information from an individual. Patients did, and still do, discover their diagnosis regardless of what is told to them by doctors, and their parents. In these situations, patients may be angry, hurt, upset, and understandably lose trust in their doctors or parents. It is much more appropriate that patients should receive honest and accurate information from their doctors. This will enable them to plan their lives, and be fully involved in treatment options and decisions. Where appropriate, family members may be offered screening and prenatal diagnosis may be carried out for the pregnancies of unaffected female relatives.

It is easy to be critical of this aspect of the Optimal Gender Policy and it is important to consider Money's work in historical context. Money was working in America in the 1950s. At that time, homosexuality was illegal and was classified as a treatable psychiatric illness by the Diagnostic Statistical Manual of disorders (DSM) published by the American Psychiatric Association until 1973, and by the International Classification of Diseases until 1993. America was gripped with the McCarthy communist witch hunts. Patients and doctors were desperate to minimise "difference" for their children and Money's proposals may have seemed the only possible option. The John/Joan case may have failed due to the surgical procedure being carried out at 17 months of age, after increased testosterone levels and surges would have occurred in boys. Androgens are thought to be involved in early brain development, and in behaviour, and this may have contributed to the failure of the sex-reassignment. Recent work assessing individuals born with XY cloacal extrophy and reassigned female following gonadectomy reported a high incidence of dissatisfaction with assigned gender. They argued that the prenatal influence of androgens is a major factor in gender identity, in addition to postnatal and pubertal surges, and that neonatal female reassignment in those with XY cloacal extrophy should be reconsidered. This is in contrast to other work suggesting that early
surgery and gender reassignment is associated with a female gender identity, and rather than ceasing childhood surgery, watchful waiting is more appropriate. Although this does support Money’s original theories regarding the indication for early childhood surgery, the authors acknowledge the importance of androgens in brain development, rather than suggesting children are sexually neutral with non-hormonal postnatal influences being responsible for sexual identity. The John-Joan case may also have suffered from the practice of non-disclosure, which would not have fostered trust in the parent-child relationship.

1.1.4. Current Attitudes

In contrast to the changes which have occurred with disclosure of medical information, the policy of needing surgical reconstruction of the genital area in infancy, to make the phenotype concordant with the sex of rearing is still the standard and widely adopted management. As the John/Joan case illustrates, long-term outcomes of medical interventions are necessary to assess policy. However, surprisingly little exists in the literature regarding the long-term outcomes of surgery for CAH, and that which does rarely involves the opinions of patients. By the late 1980s and early 1990s patients and parents had started to set up peer support groups to address the needs of intersexed individuals and their families, particularly in those areas where it was felt it had been largely neglected by the medical profession. The Androgen Insensitivity Support Group (AISSG) was the first of its kind, set up in 1988, offering information and support to individuals and family members of those with an intersex condition. This was shortly followed by the formation of the Intersex Society of North America (ISNA). It is striking that both organisations state the ending of secrecy and encouragement of openness as the first aim of the support groups, reflecting the lack of disclosure of diagnosis and information in previous management. The AISSG also states the aim to encourage research into the effects of genital surgery in order to evaluate whether surgery is an “effective treatment”. ISNA goes further by calling for an end to “unnecessary” genital surgery to all intersexed children, stating that “no surgery should be performed unless it is absolutely
necessary for the physical health and comfort of the intersexual child" until
they are old enough to "understand the risks and give informed consent".
Both support groups argue that surgery is an irreversible intervention, and as
such, the individual concerned should be in a position to give informed
consent. Clearly this cannot be the case when surgery is carried out on
children. Such opinions have not been welcomed by the whole of the medical
profession. Some surgeons feel that support groups only consist of
individuals who are unhappy with their previous management, and therefore
are not representative of the majority of intersex patients.  

1.2 Congenital Adrenal Hyperplasia

Congenital Adrenal Hyperplasia is the commonest intersex condition, with an
incidence of 1 in 14,000 worldwide. The name is derived from the relative
hyperplasia in the adrenal gland which arises from the overproduction of
steroids, as shown in figure 1.1.

![Figure 1.1 Appearance of hyperplastic adrenal glands, as seen in Congenital Adrenal Hyperplasia (left), compared with normal appearance of adrenal glands (right)](image)

Affected individuals have an enzyme block in the steroidogenic pathway in
the adrenal gland (see figure 1.2), with over 90% being a deficiency in 21
Hydroxylase, which converts progesterone to deoxycorticosterone, and 17-
hydroxyprogesterone (17-OHP) to deoxycortisol. Other causes of CAH are a
deficiency in 11β-hydroxylase, and 3β-hydroxysteroid dehydrogenase. Both
of these variants are rare, accounting for less than 10% of all CAH cases. The gene for 21-OH CAH is located on chromosome 6 at CYp21, and the inheritance pattern is autosomal recessive. There does not appear to be a correlation between exact genetic mutation and phenotype.

Figure 1.2 Steroidogenic pathway with the most common block at 21-hydroxylase (21-OH) shown, accounting for 95% of individuals with CAH, and which all of the studied subjects have.

The net effect of 21-OH deficiency is a reduction in cortisol synthesis. Due to the absence of a negative feedback loop, ACTH is stimulated leading to an increase in synthesis of precursors. This causes a build up of 17-hydroxyprogesterone leading to excessive production of androgens. In approximately 75% of cases, aldosterone production is also impaired, leading to salt loss. This represents a life-threatening situation, and those children who are salt-losing often become dangerously unwell within a few days of birth. In 1950 Lawson Wilkins et al realised that giving exogenous
corticosterone would suppress the adrenal gland. They cautiously commented that this medical breakthrough “may prove of therapeutic value”.

Those patients with CAH who have a reduction of both cortisol and aldosterone are considered to be “salt wasters”, whilst those who only have difficulties with cortisol production are referred to as “simple-virilisers”. Others, presumably with a less severe form of CAH, are not diagnosed until teenage years or later and are known as having the “late-diagnosis” variety of the condition. This is sometimes, erroneously, referred to as “Late-onset” CAH.

The presence of testosterone and dihydrotestosterone in the fetus leads to the development of the external genitalia in a male. Excessive levels in a female will therefore lead to some degree of virilisation in the fetus, with the upper vagina joining the male type urethra and opening as one channel onto the perineum. Figure 1.3 shows the appearance of virilisation in an affected female baby.

Figure 1.3 Virilisation of a female baby

The discovery of therapeutic cortisol for the treatment of CAH occurred at the same hospital in which John Money later developed the Optimal Gender Policy, and a general management plan evolved between the departments of endocrinology, psychology, and paediatric surgery. Thousands of children’s lives have been saved since this time, thanks to the pioneering work by Wilkins et al. However, the basis for surgical treatment, and the timing of intervention has remained strikingly similar and underevaluated for over 50 years.
1.3 Thesis Structure

This thesis is the result of work carried out in the Middlesex Centre on a group of patients with CAH. It addresses perhaps the most controversial aspect of the current standard care of women with CAH – that of corrective genital surgery. The aims of such an intervention may broadly be considered to:

- promote "normal" female appearance
- allow comfortable penetrative intercourse with unimpaired sensation
- avoid increased psychological and psychosexual difficulties
- prevent lower urinary tract symptoms due to anatomical variations

These four main areas are addressed in a series of studies. The most hotly debated aspect of feminising surgery is the perceived need to operate on the clitoris. The clitoris is a poorly understood organ, and chapter 3 focuses on the history, anatomy, and surgery to this enigmatic structure. The need for "corrective surgery" suggests that the genitalia differ from normal, and that there is such a thing as "normal genitalia". Yet information regarding this is surprisingly sparse, and chapter 4 addresses this gap. Chapter 5 discusses the methodology and results of objective sensation testing to the genital area in the study participants. It is rare for psychological studies of CAH to be carried out in conjunction with clinical research, and chapter 6 details the work in this area and considers the psychological and psychosexual outcomes of women with CAH. This thesis led to the discovery of urinary symptoms experienced by those with CAH, and chapter 7 evaluates difficulties with the lower urinary tract. Chapter 8 discusses all findings, and makes recommendations for future research work, but also offers guidance for the care of children and women with CAH.
Chapter 2

The Clitoris

2.1 Historical Aspects

2.1.1 "Discovery"
The clitoris was first described by Ronaldo Colombus in 1559, an eminent anatomist working in Padua, in Italy. Subsequent accounts suggest he declared it to be "so pretty a thing" and expressed his astonishment that many other anatomists had overlooked it. However, Colombus' claim to discovery was disputed by his fellow anatomist, Gabrielo Fallopia, also working in Padua at the time, who maintained he had discovered the clitoris several years earlier. It is not clear whether the two ever settled their dispute.

2.1.2 Cultural Representations
This "discovery" of a new organ should have ensured the structure and description of the clitoris was routinely and consistently added to anatomical texts. Anatomy as a science is usually seen as fixed and unchanging. Yet interestingly, representations of the clitoris have varied considerably over time. Gray's Anatomy has been published for over 150 years, and is generally seen as an authoritative anatomical text. The first edition of the twentieth century was published in 1901 and shows the clitoris to be a fairly prominent structure. There are labels to the prepuce, glans and body of the clitoris. However, the 1942 edition shows the structure as proportionately smaller, with one label only to the "clitoris". Other cross sections have omitted labels to the clitoris completely.
Figure 2.1 Gray's Anatomy 1901 compared with Gray's Anatomy 1942

This represents a definite shift in what was seen as relevant and important, suggesting the clitoris was of minimal interest or significance. It would be easy to dismiss this as representing 1940s prudery and lack of open acknowledgment of the role of the clitoris in female sexual function. Yet, subsequent texts in the 20th Century also downplay the presence of the clitoral structures. Snell's Anatomy for Medical Students is a standard text, used widely in medical schools. Yet the 1986 edition shows discordance in the labelling of comparative male and female pelvic anatomy. Sagittal diagrams of both are shown, with the penis and male genitalia well labelled. The corresponding female diagram does not display the clitoris anywhere on the cross-section.
In 1981 a group of feminists based in the United States published "A New View of a Woman's Body" with detailed drawings by Suzann Gage, in order to counteract what they saw as a degradation of female anatomy. The information came largely as a result of self-help groups, where non-medically trained women learned about gynaecology. The illustrations were researched using drawings from unspecified European texts, and by examining a volunteer model to assess uterine size and vaginal size and direction. Photographs were also produced after imaging the external genitalia of over a hundred women. Included were cross sectional diagrams of the female pelvis, with detailed labelling to the clitoris.
Figure 2.3 Cross section of female pelvis, reproduced from A New View of a Woman’s Body, published Simon and Schuster 1981, reprinted 1995.

All female anatomy was also deliberately presented first, then followed by comparable male sections in order to challenge the tradition of male anatomy being presented initially, as the “normal” state. The clitoris has been shown as a dynamic organ, and illustrations show the clitoris in passive and active forms, emphasising that to date, the only known function of the clitoris is to contribute to sexual pleasure.
2.1.3 History of Clitoral Surgery

Throughout history clitoral surgery has been advocated or promoted for a variety of indications. In 1866 Isaac Baker Brown, a founder member of the London Obstetrical Society advocated clitorectomy for the cure of excessive masturbation, epilepsy and hysteria. Amongst the 48 cases he reported on, there were 5 women who had been referred by their husbands for this new treatment. The main indication had been their intent to take advantage of the new 1857 law permitting wives to commence divorce proceedings. Clearly this was perceived as an inappropriate assertiveness by these women, for which the clitoris was blamed. Baker Brown performed the surgery and noted that all cases returned meek and docile to their husbands. It was not only men that sought his treatment for their wives. One woman referred her 25 year old daughter for clitorectomy as she was “disobedient to her mother’s wishes”. Her disobedience took the form of sending cards to men she liked, and reading. Baker Brown was considered to be a maverick by his peers and his actions were frowned upon by the London Obstetrical Society, partly for advertising for private patients in their journal, and partly through disapproval of his surgery. Eventually he was expelled from the...
society, and travelled to the United States where his recommendations were generally more widely adopted. A medical journal produced in Chicago until 1925 promoted clitoral removal as a general panacea for all ills. Other eminent clinicians continued to advocate clitorectomy for specific indications. Blair Bell in 1917 recommended clitoral excision for those women who were "...not suffering with excessive sexuality, but rather, with the fascination of a bad but pleasant habit, to the detriment of her moral and physical equilibrium" 28. As late as 1936, Holt supported clitorectomy for the treatment of masturbation in girls, in his text Diseases of Infancy and Childhood 29.

2.1.4 Historical view of clitoral function

The role of the clitoris has been poorly understood, although since Victorian times it was generally understood to play a part in sexual function, particularly with orgasm. In 1905 Freud distinguished between clitoral and vaginal orgasm and argued that clitoral stimulation led to an immature version. Therefore, to be truly female, women should adopt a transition to vaginal orgasm, thus down playing the importance of the clitoris. Due to the widespread popularity and dissemination of psychoanalytical ideas in the early 20th century, this view, with the implied lack of importance of the clitoris in sexual function, became commonly accepted. It was not until 1948 that Dickinson suggested that promoting vaginal orgasm whilst decrying clitoral orgasm was inconsistent. Surely, he argued, if orgasm were important, the site of origin was irrelevant. Kinsey's work in the 1950s reversed previously held notions and suggested that the majority of orgasms were generated by clitoral stimulation, therefore restoring the clitoris as important in contributing to sexual pleasure. However, as late as the 1970s some surgeons were still suggesting that the clitoris was not necessary for satisfactory sexual gratification 30, therefore implying that the consideration of subsequent sexual function was irrelevant in clitoral surgery.
2.2 Current Knowledge

2.2.1 Anatomy of the clitoris

Despite having been initially described more than 400 years ago, recent anatomical studies have shown the structure of the clitoris to be considerably larger than previously thought. The external appearance of the clitoris consists of paired corpora of erectile tissue capped by the glans at the distal end. The corpora are covered in tunica, with the glans partially concealed by the clitoral hood, which goes on to form a continuum with the labia minora.

![Clitoral glans, hood and labia minora.](image)

The external clitoral body measures between 2 to 4 cm in length, and divides into two crura just under the pubic arch. Internally these extend laterally and inferiorly, running along the inferior pubic rami, with the crura extending for up to 9cm. Inferiorly, at the point of the bifurcation two suspensory ligaments extend up to join the mons pubis. There is a deeper ligament complex which extends from the symphysis pubis to join the body and bulbs of the clitoris (previously known as vestibular bulbs). These ligaments were found to be considerably larger than previously documented, and differed in shape, extent and orientation than any analogous structures in the penis. In addition, they differed from clitoral structures described in current anatomical literature.
2.2.2 Neurology of the clitoris

The main fibres supplying the clitoris are derived from the pelvic, pudendal and hypogastric nerves, with a clitoral nerve branching from the pudendal nerve bilaterally. These run each side along the inner and superior aspect of the crura, along the inferior pubic rami. The two nerves join together at the corporal bodies and run as the paired dorsal clitoral nerves in the neurovascular bundle along the dorsal aspect of the clitoris. The cavernosa nerve supplies the erectile bodies and branches off the vaginal neuronal plexus. This runs from behind the bifurcation of the crura into the corpora, and intercommunicates with the dorsal nerve.

The path of the clitoral nerve

Large myelinated fibres run in the dorsal columns of the spinal cord and provide sensation for light pressure and vibration. In addition, small...
unmyelinated fibres are carried in the spinothalamic tracts which provide sensation for temperature and pain. One study injected labelled cells into the rat clitoris to identify central nervous system cells involved in the efferent control of the clitoris. This showed the major input to be centred around preganglionic parasympathetic neurones in L5 to S1, suggesting that spinal control of the clitoris is largely modulated by the lower lumbosacral cord. To a lesser extent preganglionic sympathetic nerves from T13 to L2 were identified, but interestingly not the parasympathetic nerves. This is in contrast to penile nerves studies where the parasympathetic nerves are involved, suggesting neurologically the clitoris is not a complete homologue of the penis. A few labelled cells were found in T10 to T12, L3 to L4, and S2 to S4.

In the brain, cells were identified in the nucleus paragigantocellularis, raphe pallidus, raphe magnus, Barrington’s nucleus, ventrolateral central grey, hypothalamus and medial pre-optic region. Some of these areas are already known to be involved in mediating micturition and it is possible these cells are also involved in sexual reflexes.

Recent work has assessed the nerve distribution of the paired dorsal clitoris nerves, and has shown fibres fanning out around the glans. In addition, nerves were shown to perforate the tunica of the corporal bodies, extending laterally in a manner which was previously undocumented.
Figure 2.7 Clitoral body and glans from the front (above) and behind (below), showing corpora in yellow, tunica in blue, glans in green, and nerve fibres in red. Reproduced from Baskin et al. Anatomical Studies of the Human Clitoris. J. Urol. 1999.

This led the authors to conclude that the current surgical practice of separating the dorsal neurovascular bundle from the tunica, and lifting the tunica from the corporal bodies would cause considerable neuronal disruption. They suggested alternative surgical techniques when removing corporal tissue in order to minimise disturbance of the nerves.

2.2.3 Vascular structure of the clitoris

The clitoris is a dynamic organ which becomes engorged with blood when aroused. Branches of the internal pudendal artery give rise to a left and right clitoral artery. These run on the inner aspect of each crus before meeting at the pubic arch and running parallel along the dorsal aspect of the corpora to the glans, flanking the clitoral nerve. Cavernosa vessels also supply the corporal tissue. Venous drainage is via the single clitoral vein which runs along the dorsal aspect of the clitoris with the clitoral nerve and arteries. The clitoral vein communicates with the veins of the bulbs of the clitoris, and ultimately drains to the internal pudendal vein.
2.2.4 Physiology and function of the clitoris

The clitoris has no other known function except for the mediation of sexual pleasure, although the mechanisms of initiation and feedback are poorly understood. It is important for sexual sensation and contributes significantly to orgasm. During arousal the cavernosa fill with blood, and venous valves close, preventing drainage and facilitating erection. The exact mode of this is not well understood. There are few physiological studies on the human clitoris, the majority of work having been confined to penile studies and male sexual function. During arousal nitric oxide (NO) released from postganglionic parasympathetic nerves is known to relax penile vascular and cavernosal smooth muscle to facilitate erection, and has been demonstrated in animal and human studies. In the clitoris neuronal nitric oxide synthase (nNOS) which synthesises NO from L-arginine has been shown to be present within the neuronal axons. Although animal studies have shown that NO was responsible for autonomic mediated relaxation in the clitoris, it was not until recently that this was demonstrated in the human clitoris, suggesting that the mechanism for male and female erection is similar. Further animal studies have shown that the clitoral arteries are susceptible to atherosclerosis which may in turn lead to erectile insufficiency. It has been postulated that this may be a contributory cause of female sexual arousal disorder, although vasodilators such as sildenafil have not yet been shown to be of benefit in the treatment of female sexual dysfunction.

2.3 Conclusion

The clitoris has been a controversial organ since its initial description and has variously been blamed for "unfeminine" behaviour. Indications for clitoral surgery may have changed, but perhaps the end-point of promoting femininity is not so different. The anatomy and physiology remains poorly understood with comparatively little research into structure and function. Recent studies have highlighted this paucity of data, and shown the clitoris to be a much more sizeable structure than previously thought, with dense neuronal networks covering the tunica and glans. Over the last 30 years it
has become more widely accepted that the clitoris plays a considerable role in sexual function, although the exact mechanisms still require further elucidation. To date, no role other than mediating sexual pleasure has been identified.
Chapter 3

The role of surgery in CAH

3.1 Genital Development

During normal fetal development the external genitalia consist of the labioscrotal swellings and the genital tubercle. By the 12th week of gestation the labioscrotal swellings have begun to differentiate into the labia majora, or have fused into the normal scrotum. Similarly the genital tubercle differentiates into the clitoris or penis. The urethra will either then be incorporated into the penis, or open separately onto the perineum.

![Diagram of normal development in utero of the female genital system](image)

Figure 3.1 Normal development in utero of the female genital system

3.1.1 Genital Development in women with CAH

When androgen excess occurs in utero, the female fetus will be virilised. This can occur to a varying degree; the labial folds may fuse, and take on a more rugose scrotal appearance; the clitoris may enlarge with a prominent glans, and bulky corpora. The vagina will open into the urethra in a high, medium or low position, and the urethra will then open onto the perineum as a single urogenital sinus. The upper vagina will develop normally, along with the uterus. The ovaries will develop and have the potential to function normally.
Virilisation was described by Prader in five stages. Stage 1 represents mild clitoromegaly only, whilst stage 5 consists of complete labial fusion, marked clitoromegaly, with the urethra opening at the tip of the clitoris. Girls with Prader 5 virilisation can be incorrectly assigned male at birth.

Figure 3.2. Prader stages of virilisation

Figure 3.3. Virilisation of a baby girl, with a single opening urethra/vagina, clitoromegaly, labial fusion and scrotalisation of the labial skin. This would be Prader stage 4.

3.2 Indication for treatment

Surgery for CAH may be considered as correcting both the external appearance of the genitalia, most notably the enlarged clitoris, and also the internal anatomical structures, by opening up the vaginal introitus. Most individuals are likely to need vaginal surgery at some stage in order to facilitate menstrual flow, and allow penetrative intercourse. However, surgery to the clitoris is more likely to be recommended for cosmetic rather than functional reasons. The majority of individuals will have clitoral and vaginal surgery carried out initially in early childhood. Some authors argue that to perform surgery in childhood is to prevent subsequent urinary tract
complications 47, although the evidence for this is limited, and is disputed elsewhere 48. Indeed, persistent urinary tract infections may be a complication of such surgery 49, and damage may be caused to the urethra during the operation leading to meatal stenosis 50. More often, surgery may often be recommended purely to relieve parental anxiety about the external appearance of the genital area, and in particular the clitoromegaly. Newman suggests that parents “are calmed” by the “promise of major corrective surgery within 3-6 months [of life]” 51. Yet adult patient peer groups argue that surgery causes sexual difficulties and are campaigning against the alieviation of parental distress being the main indication for childhood surgery 20. Rather, they prefer that operations for cosmetic enhancement are delayed until the individuals concerned are able to give an informed opinion.

However, it is argued that it is simply unacceptable for children to grow up with an unusual appearance to the genital area, and this could cause additional psychological trauma 52;53. As the policy of early surgery is so widespread, it is difficult to find any control group by which to assess this policy. To date, there remains no evidence that by not undergoing surgery in childhood, psychological trauma to the individual is increased.

3.3 Clitoral operations

There have been many types of operations described to reduce the size of the enlarged clitoris.
3.3.1 Total Clitorectomy

Initial surgical approaches involved removing the whole of the clitoris in an aim to achieve a female appearance to the genitalia. Jones and Jones in 1954 emphasised the need to extirpate the whole clitoris, rather than simply amputate the erectile bodies. They stated that remaining erectile tissue may become painful despite cortisol therapy, and therefore rooting out the whole of the clitoris was necessary. For reconstructive purposes they employed a roll of skin to make a "cosmetic clitoris".

Figure 3.4 Clitorectomy with cosmetic clitoris, reproduced from Jones and Jones, Am J Obstet Gynecol 1954.

Gross recommended an alternative method of clitorectomy, by amputating the erectile bodies and glans, whilst leaving the crura, which were then oversewn.

Figure 3.5 Clitorectomy proposed by Gross et al, reproduced from Surgery, 1966.
This approach was then widely adopted as the standard surgical procedure for the enlarged clitoris, and many adult women seen nowadays will have had this particular procedure carried out in early childhood.

3.3.2 Clitoral Recession

As an alternative to total clitorectomy, recession of the clitoral body was proposed, whereby improved cosmesis was obtained with minimal removal of clitoral tissue. In 1961 Lattimer described recessing the corpora under a skin bridge. The clitoral hood was removed and the shaft exposed. A midline tunnel was then made in the subcutaneous fat, coming out at the point where the labia minora fuse in the midline, just above the urethra. The glans was reduced in size by trimming the corona, and the whole clitoris was drawn through the tunnel with the tip of the glans exposed at the end. However, other authors felt this bent the clitoris into an abnormal position, which could compromise function. In 1970 Randolph and Hung proposed opening tissues over the mons and dissecting down to the pubic symphysis. The clitoral hood was removed and corpora exposed. The erectile tissue was divided from the suspensory ligament of the clitoris to free the body. Three sutures were inserted into the dorsum of the corporal fascia and into the pubic periosteum. Once tied, the whole clitoris was swung inwards and under the pubic bone, giving the appearance of a much smaller clitoral shaft. Clitoral recession procedures have however, fallen from favour. In 1982 Allen et al assessed 6 patients who had undergone clitoral recession procedures and found all had pain with erection. This and similar studies led to the general abandonment of clitoral recession, with reduction techniques becoming the preferred method.

Figure 3.6 Clitoral recession as described by Lattimer, J Urol, 1961.

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preferred option, although some authors were still recommending recession in the 1990s.

3.3.3 Clitoral reduction: glans amputation and grafting

Although the appearance of the clitoral area was deemed by surgeons to be much improved by total clitorectomy, some felt improvements on the technique could be made. Spence and Allen proposed a clitoral reduction technique rather than simple amputation, although it appears the primary motivation for this was to improve the refashioning of the urogenital sinus, rather than from any significant interest in subsequent clitoral function. Initially they experimented with incising the ventral aspect of the corpora, dissecting out the erectile tissue to the pubic arch, and then excising the entire shaft. The base of the glans was then sutured to the lower edge of the pubic symphysis, and the mucosal incision closed. However, this approach was thought to leave too much clitoral hood tissue, and a second technique was developed. This time the dorsum of the clitoral shaft was incised, the erectile bodies mobilised and removed. The glans, attached only to the urethral plate, was grafted onto the stumps of the erectile bodies.

Figure 3.7 Clitoral reduction showing the preferred technique of Spence and Allen, reproduced from Br J Urol 1973.

With both approaches, the vascular supply was interrupted, but this was seen as an advantage. Although the glans was noted to become dusky and
displayed signs of ischaemia during the post operative recovery time, this led to atrophy and shrinkage which, according to the authors, was beneficial in reducing the clitoris yet further to "a size more consistent with that of a normal female clitoris". For those concerned about possible subsequent function, the authors advised that "possession of a clitoris is not essential for orgasm in the female and one need not hesitate unduly to remove it if a useful purpose is thereby served".

3.3.4 Clitoral reduction: dorsal neurovascular bundle preservation

With the increasing awareness that the clitoris and particularly the glans may be important in orgasm and sexual function, Mollard proposed a new approach to clitoral reduction surgery in 1981, with the aim to preserve erogenous tissue and erectile capacity, whilst improving the external appearance. Rather than complete removal of the erectile tissue, a subtotal resection of the corpora was proposed, having made an incision over the dorsum of the clitoral hood. A cuff of skin was left attached to the glans, with the middle section of hood being removed. The dorsal neurovascular bundle was dissected out and preserved, and not divided as with previous techniques. The glans was then sutured to the corporal stump.
3.4 Clitoral surgery: current practice

Total clitorectomy is no longer thought to be performed in the UK, although may have been carried out as recently as 10 years ago. Certainly many adult women will have undergone this procedure, and a recent survey carried out in 2002 highlighted that this is still the case in parts of Europe. Of the 125 centres surveyed, 27 (13%) carried out total clitorectomy as first-line practice. The majority of clitoral surgery operations performed in the UK and USA are clitoral reduction procedures involving the division of the clitoris. However, recent studies looking at the neuroanatomy of the clitoris have demonstrated the nerve supply is more extensive than previously thought, and so may be preserved in the dorsal part of the clitoral hood. Mollard et al. Brit J Urol 1981.
centres surveyed, 27 (13%) carried out total clitorectomy as first-line practice. The majority of clitoral surgery operations performed in the UK and USA are clitoral reduction procedures along the lines of Mollard’s technique.

Figure 3.9. Clitoral reduction technique. First the clitoris is degloved and the erectile bodies exposed (right).

Figure 3.10. The separation of the dorsal neurovascular bundle (left), and removal of the erectile bodies to the level of the crura (centre). The glans is then repositioned on the stump of the erectile bodies and the tunica repaired (right).

However, recent studies looking at the neuroanatomy of the clitoris have demonstrated the nerve supply is more extensive than previously thought, as discussed in chapter 2. The main nerve is carried in the dorsal neurovascular bundle, but a dense neuronal network has been shown to fan out, perforating the whole of the tunica and glans. The only place where nerve fibres were not seen was at the 12 o’clock position on the glans. The
cut specimens were examined and divided nerve fibres were identified, leading the authors to conclude that even with modern techniques, significant numbers of nerves were divided, with unknown significance for resultant sexual function. A new technique was proposed, by incising along the ventral aspect of the corpora, and removing erectile tissue from within the tunica. In this way the external surface of the tunica was not disturbed. The dorsal neurovascular bundle was identified but was not lifted off from the tunica. After removal of the erectile tissue the glans was sutured to the corporal stumps, and the tunica closed horizontally.

Figure 3.11 Proposed surgery based on neuroanatomical studies. Reproduced from Baskin, JPEM 2004.

The aim was for optimal cosmetic appearance, but with the least disruption to the underlying neurovascular anatomy. Clearly, long-term results will not be available for some years.

3.4.1 Timing of clitoral surgery

The timing of surgery has become controversial. Many authors suggest clitoral surgery should be carried out as a child, citing relative ease of surgical correction compared with that in adolescents. Others suggest that neonatal correction is preferable for the avoidance of any memory of ambiguous genitalia and for relieving the anxiety of parents. It is also
argued that an oestrogenising effect from the mother still persists for the first 3-4 months after birth, and this would contribute to a better surgical result 64. However, if adequate steroid suppression in the treatment of CAH is not achieved, further virilisation will occur, and the clitoris may enlarge further. Therefore, if surgery is carried out early for cosmetic reasons, it is likely that further procedures will be deemed necessary to reduce the subsequent clitoral bulk. A long-term study assessing 44 patients, reported clitoral regrowth occurring in 39% of patients 65. Ten individuals had undergone 2 or more clitoral procedures, with one patient having had 4 separate clitoral reduction procedures. A stated aim of the surgical treatment of CAH is to limit the number of interventions required 17. This would suggest careful timing of the initial procedure, with consideration given to deferring surgery, rather than risking repeated operations.

3.4.2 Outcome measures: Cosmesis

There are few reports in the literature of outcome measures, and those that exist are often vague in the methodology (see table 3.1). Frequently only short-term outcomes such as post-operative cosmesis are reported 66. Bellinger discussed the cosmetic appearance of a glans reduction procedure. The series consisted of six patients with a mean follow-up of 20 months, and all cases were reported to have a "pleasing" cosmetic appearance. No details were published on how the appearance was rated, and all were assessed by the authors rather than parents/individuals. Although short-term information is of value, information on longer-term outcomes is required. Randolph et al conducted a study looking at long-term follow-up for 37 patients who had undergone clitoral recession surgery, 23 of whom had CAH 67. Follow-up consisted of an external examination by the authors, with a grading of excellent, satisfactory or unsatisfactory. Four patients were lost to follow-up. Of the remaining 19, 8 required further clitoral surgery to achieve satisfactory cosmesis. Two of these patients were then advised to have a third operation; one patient has declined, to the authors' surprise, despite the "disfiguring prominence of her clitoris". One study assessed 14 girls with a
mean age of 13.1 years who had undergone feminising genitoplasty procedures at centres of excellence, in early childhood. Six (46%) were considered to have unacceptable cosmetic appearance of the clitoris, either due to an enlarged glans or due to atrophy and shrinkage. Creighton et al studied 44 adolescents who had undergone feminising genitoplasty procedures in childhood between 1979 and 1995. 18 (41%) were judged to have poor cosmesis, with a further 18 only rated as satisfactory. Only 8 patients had a good cosmetic outcome, despite having surgery carried out at specialist centres.

Figure 3.12 Poor cosmesis in adolescence following childhood feminising genitoplasty

3.4.3 Outcome measures: Sensation

Others have suggested that clitoral sensation remains intact following surgery, and details on operative technique are given. Yet, on further reading it appears that all subjects were children at the time of publication and hence not yet sexually active, which makes such a claim difficult to substantiate. One study made more attempt to assess sensation following clitoral reduction, by testing the patient's awareness of a pinprick or light touch by a wisp of cotton, to the clitoral glans. Results were reported as sensation being present in all subjects. Although this does suggest an objective way of testing sensation in the nerves responsible for light touch, it is difficult to quantify a light touch. The amount of force used to elicit a positive response can have considerable inter- and intra-observer variability, leading to difficulties in reproducibility. In 1989 Hinderer reported the long-term outcomes of 9 patients who had undergone clitoral reduction surgery between 1973 and 1979. However, 3 patients were lost to follow up, and a
further 3 were not sexually active, leaving only 3 patients that could be assessed. Clitoral sensation and sexual function were reported as normal although no details on how such information was obtained were given. This paper was published with the recommendation that “satisfactory” sexual function can therefore be anticipated for all patients, yet clearly such claims are based on limited data.

3.4.4 Outcome measures: Sexual Function

Where function is considered, details on the assessment processes used are often sparse. Newman et al followed-up 12 patients who had undergone clitoral surgery for ambiguous genitalia and concluded that 10 had highly satisfactory social, psychological and sexual function, without clarifying how such conclusions were reached 51. One patient was described as having had “partial success” despite having pain with orgasm. Again, it is not clear by whose or which criteria such success is measured. The final patient has dyspareunia, but no details on orgasm are given, perhaps suggesting that penetrative intercourse ranks above orgasm capacity in the assessment of female sexual function. A study carried out in 1976 followed 12 patients who had undergone clitoral recession surgery, between 5 to 22 years previously 50. The results were presented as being cosmetically and functionally satisfactory, although the paper revealed only five patients had been sexually active. All reported erotic sensation with clitoral stimulation, although no details on orgasm are given. One patient required revision after 5 years, presenting with a painful enlarged clitoris. This illustrates the need for long-term follow up, showing that the results of clitoral surgery may change depending on the degree of suppression of androgens. This patient underwent a clitoral amputation, and was lost to further review. Of a study assessing 37 patients after clitoral recession 67, only 6 patients had been sexually active with a partner, and all reported achieving orgasm. Adolescents in the series reported “enjoyable sensations” during masturbation. Little other information on sexual function or sensation is given. Further studies have assessed whether neuronal pathways involved in
clitoral sensation and function remain intact after surgery, and these are considered in chapter 5.70,71.

Table 3.1 Details of outcome studies following feminising genitoplasty

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Name</th>
<th>Year</th>
<th>Follow-up</th>
<th>Study n</th>
<th>CAH n</th>
<th>Method of Assessment</th>
<th>Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cosmesis</td>
<td>Bellinger66</td>
<td>1993</td>
<td>20 months</td>
<td>6</td>
<td>3</td>
<td>External examination by surgeon</td>
<td>Small study, short term, prepubertal</td>
</tr>
<tr>
<td></td>
<td>Randolph67,68</td>
<td>1981</td>
<td>Up to 16 years</td>
<td>37</td>
<td>23</td>
<td>External examination by surgeon</td>
<td>No details of assessment, older surgical techniques</td>
</tr>
<tr>
<td></td>
<td>Creighton69</td>
<td>2001</td>
<td>13.2 years</td>
<td>44</td>
<td>21</td>
<td>External examination by authors</td>
<td>retrospective</td>
</tr>
<tr>
<td></td>
<td>Alizai69,70</td>
<td>1999</td>
<td>Up to 14 years</td>
<td>14</td>
<td>14</td>
<td>External examination by authors</td>
<td>mean age 13</td>
</tr>
<tr>
<td>Sensation</td>
<td>Sagehashi69,70</td>
<td>1993</td>
<td>Up to 3 years</td>
<td>4</td>
<td>4</td>
<td>External examination by author</td>
<td>Short term, prepubertal</td>
</tr>
<tr>
<td></td>
<td>Barrett71</td>
<td>1980</td>
<td>Up to 34 months</td>
<td>23</td>
<td>18</td>
<td>External examination by surgeons, tactile sensation to glans</td>
<td>Short term, prepubertal, so no sexual function data or objective sensation data</td>
</tr>
<tr>
<td></td>
<td>Hinderer71</td>
<td>1989</td>
<td>Up to 13 years</td>
<td>9 – only 6 after 2 years</td>
<td>9</td>
<td>External examination by surgeon, reported sexual function and sensation by subjects</td>
<td>Small numbers, only 3 sexually active, no objective sexual function or sensation</td>
</tr>
</tbody>
</table>
### 3.5 Vaginal Surgery

Urogenital sinus anomalies are variable in CAH, and may be classified in relation to the confluence of the vagina with the urethra. If the vagina joins the urethra within 2cm of the perineum it is considered a low urogenital sinus. However, if the vagina joins the urethra greater than 2cm from the perineum, or at the urethral sphincter it is defined as a high urogenital sinus. The majority of women with CAH will require some type of vaginal procedure in order to allow menstrual flow, and/or comfortable penetrative intercourse. The surgical approach and technique depends on the level of the urogenital sinus.

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Age Range</th>
<th>Sample Size</th>
<th>Methodology</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newman</td>
<td>1992</td>
<td>Up to 29 years</td>
<td>9</td>
<td>External examination by surgeon, reported sexual function and orgasm by subjects</td>
<td>Small numbers, no objective sexual function or sensation data</td>
</tr>
<tr>
<td>Sotiropoulos</td>
<td>1976</td>
<td>Up to 22 years</td>
<td>16</td>
<td>External examination by surgeon, and sexual function and erotic sensation reported by subjects</td>
<td>Only 5 sexually active, only 2 with intercourse</td>
</tr>
</tbody>
</table>
3.5.1 Low take-off vagina

The low-take off vagina has always been considered as a more straightforward anomaly to correct. For those with simple labial fusion, a vertical incision may be made in the perineum and the vagina exposed. This is an unusual scenario in CAH and the majority of patients with a low-take off vagina will require slightly more than this. A V-Y vaginoplasty is frequently utilised for the low take-off vagina and involves incising an inverted U just below the urogenital sinus. This skin flap is mobilised, and the underlying tissue then divided in the midline, up to the vaginal entry into the common channel. The skin flap is laid down and sutured to the edges of the sinus, creating an enlarged introitus, therefore allowing tampon use, and either dilator use, or intercourse. There have been variations on this technique in the hope this offers better subsequent cosmesis. Freitas Filho described an omega-shaped flap, with the aim of allowing the labia majora to overlap the neointroitus at the base \(^74\). It has been suggested that this would lead to improved cosmesis, although follow-up studies have not yet reported on this.

3.5.2 High take-off vagina

The high take-off vagina has presented more of a challenge to surgeons. A "pull-through" technique was suggested, whereby a perineal incision was made, and the vagina dissected out and pulled down to join the perineal skin.
flaps. This was usually performed later in childhood. This technique could be combined with an abdominal approach, where the upper vagina was mobilised, and passed down to the perineal incision. Further options included the use of free skin flaps, thigh flaps, or a section of bowel to bridge the gap between the lower end of the vagina and the perineum.

Pena described a posterior sagittal approach, disconnecting the vagina and bringing it down. Although this gives good access to the vagina, it involves a covering colostomy and subsequent closure. Hardy Hendren proposed a posterior sagittal approach with mobilisation and retraction of the rectum, with other authors further modifying this to provide visualisation, without dividing or mobilising the rectum.
Total urogenital sinus mobilisation has been proposed as an alternative to a pullthrough technique. Incisions are made around the urogenital sinus, with dissection carried out in the retropubic space until the sinus is mobile. Further dissection is then performed to open the vagina posteriorly, and the anterior wall is then separated from the urethra, and is closed in two layers. Jenak et al amend this by raising an omega posterior skin flap, for anastomosing with the mobilised vagina. They also suggest total mobilisation is only suitable for those with a urogenital sinus of less than 3cm in length. No long-term data is yet available for this procedure but it carries a significant advantage in allowing the surgery to be performed from a perineal approach, rather than necessitating division or mobilisation of the rectum.

3.5.3 Vaginal Autografts

Autografts have been used as an alternative to urogenital sinus mobilisation. Colon grafts have been used with sigmoid colon usually the preferred graft. The bowel is mobilised and a section of is swung down retaining its blood supply. A perineal opening is fashioned and the graft anastomosed to the neointroitus, with the proximal end being joined to the high vagina. The McIndoe-Reed procedure utilises a skin graft, usually taken from the thigh, to fashion a tube and implant into the pelvis, with anastomosis on the perineum. Both these methods are more commonly utilised for intersex conditions where the vagina has not developed, or for Rokitansky syndrome, and would usually be carried out on adult patients. However, some surgeons have used such techniques for the treatment of the high take off vagina in CAH. Surgery may often be carried out as a neonate, or small child. Outcome measures are sparse, and tend to refer to anatomical rather than functional accounts.
One study assessed a bowel graft vagina in women with Rokitansky syndrome, and suggested that sexual function was equivalent to that in normal women. Typical problems with bowel graft vaginas include excessive mucous production, necessitating the wearing of pads. Although the women in this study needed to use one to two pads a day, this was reported as a normal finding. Most of the women were having intercourse at least once a week, although there was little information on sensation and sexual satisfaction. Syed et al reported poor long-term outcomes for 18 children who had undergone colovaginoplasty, 3 of whom had CAH. Diversion colitis occurred in 3 patients 2-7 years after surgery, proving to be difficult to treat, with only one patient responding to short-chain fatty acids. One patient responded to steroid enemas and mesalazine, but one patient required surgical reduction of her graft in order to try and control the blood and mucus. The authors recommended the avoidance of bowel vaginas in this age group. Bowel neovaginas are also at risk of carcinoma development, with a mean of 19 years after surgery. Screening for neoplasia is notoriously difficult as standard histological tests are difficult to interpret, and there is little available information on what to expect at colposcopy.

3.5.4 One-stage procedure
Since the 1980s there has been an increasing trend to aim to carry out all surgery at the same time as a “one-stage” procedure. This would involve some form of clitoroplasty, and also a vaginal procedure to open up the introitus. Theoretically, this would avoid the need for further surgery, and also reassure parents that everything had been “fixed”. Passerini-Glazel proposed a one-stage combined clitorovaginoplasty which combined a clitoral reduction procedure and the usage of the redundant clitoral hood and the opened urogenital sinus to form a mucocutaneous vaginal tube. The upper vagina is freed transvesically, and passed down to meet the vaginal tube, and then anastomosed via the transvesical incision. The perineum is then sutured to the distal end of the newly created vagina. This technique utilises clitoral skin in the hope that this may enhance sensation in the neovagina.
However, the transvesical approach does risk further complications and the first case reported developed a vesico-vaginal fistula.

In order to avoid stenosis around the introitus some authors advocated subsequent post-operative vaginal dilation, carried out by the parents. Vaginal dilation therapy is a difficult task emotionally for postpubertal girls and women, but becomes highly questionable when needing to be performed by a parent on a child. Therefore, if postoperative dilation is an essential part of surgical management, the timing of such surgery should be readdressed.

3.5.5 Outcome measures

There is little long-term data on separate vaginal surgery and one-stage techniques. The vagina should be able to permit the flow of menstruation, tampon use, and also be suitably capacious and sensitive to allow pleasurable penetrative intercourse. In addition, the whole genital appearance should have a pleasing feminine appearance. Ideally, this should be provided by one procedure. Long-term studies suggest that further surgery is often needed to achieve some or all of these aims. Details regarding the assessment of the outcome are often sparse. One study considered the outcome to be “excellent” if the vagina was thought to be suitable for intercourse, and “satisfactory” if the vagina permitted menstrual flow but did not allow intercourse. A further study suggested an adequate outcome was achieved purely if successful penetrative intercourse could take place, with no information on pleasure or sensitivity.

One study found “successful cosmetic and early functional results” in children who had undergone a one stage procedure. Short-term data is of value, although should be reinforced with longer-term studies as the vagina effectively has no function in childhood. Conversely, a study following up 14 girls with CAH, 13 of whom had undergone feminising surgery in childhood showed 13 had varying degrees of introital stenosis, requiring further surgery. This concluded that despite specialist care in centres of excellence, total reconstruction could not be adequately achieved in one procedure.
childhood. Furthermore, repeated aggressive attempts at surgical correction limited subsequent successful reconstruction by resulting in excessive scar tissue and precluding the use of tissue expanders, leading to the recommendation that all vaginal surgery be deferred until after puberty.

Krege and colleagues also found an unacceptably high rate of vaginal stenosis in their follow-up of 25 patients, with 36% requiring surgical correction. In those who had further surgery, an increased level of anxiety regarding intercourse was noted, and in particular difficulties with orgasm. In addition, 2 patients had recurrent urinary tract infections, and 3 had malodorous vaginal discharge. Sotiropolous et al studied 32 patients who had undergone V-Y vaginoplasty or episiotomy for a low take-off vagina, 5 to 22 years previously and found that the majority required revision at puberty to allow subsequent intercourse. All had undergone surgery aged between 12 and 22 months. In addition, of the 9 patients that were menstruating, two developed obstruction with a haematocolpos, and needed formal drainage. A further smaller study looking at the long-term outcome of 8 women with CAH, 7 of whom had undergone one-stage procedures in a tertiary referral centre, found similar results, with 6 needing further surgery. Short-term studies seem to have strikingly different results to long-term outcomes. It is not clear why such apparently excellent short-term results do not appear to be matched in the long-term.

Gynaecological and Psychosexual Outcomes of Feminising Genital Surgery
3.5.6 Timing of vaginal surgery

Such poor long-term outcomes have led to a reassessment of the timing of vaginal surgery. As early as 1954, Jones recognised the difficulty in the optimal timing, acknowledging the possibility of subsequent vaginal stenosis with early surgery. Writing in 1976 Lattimer's group assessed 16 women out of an original group of 32, and concluded that whilst the clitoral surgery outcome was "satisfactory", the vaginal surgery results were so poor that vaginoplasty should not be performed before puberty. Many authors agree and are now calling for vaginal surgery to be deferred until after puberty. However, whilst Lattimer was advocating deferral of surgery, Hardy Hendren proposed that vaginal procedures should be performed separately on the older child, even if this resulted in further surgery in adolescence. This was thought to be preferable to the complete delaying of primary vaginoplasty until after puberty as a secondary procedure was considered to be "not a big undertaking" and would be significantly less disturbing to the individual than having a primary procedure at adolescence, yet no psychological evidence was presented to support this view. Currently, some authors state that with the development of new techniques, vaginal stenosis has decreased to negligible levels, and advocate surgery at six months of age, presumably on the understanding that stenosis will be avoided. Others suggest the child being unaware of the ambiguity is of great importance and recommend surgery at a few months of age to facilitate this. Rink argues that nearly all children could undergo genital reconstruction as a one-stage procedure very early in life and achieve "near normal cosmesis". The anatomical difference between the low and high vagina may also alter the timing of surgery with some suggesting early surgery for those with a low vaginal take-off, whilst late surgery is preferred for those with a high vagina. Ironically, some surgeons recommend the one-stage procedure followed by further introital surgery at adolescence, without acknowledgement that this could be considered two-stage surgery. In addition, the literature is lacking in information from the patients themselves, and whether they would prefer to have definitive vaginal surgery deferred...
until adolescence, or whether the common scenario of repeated vaginal surgeries is completely acceptable.

3.6 Conclusions

Surgery for the correction of ambiguous genitalia has become an accepted part of treatment in CAH. Emphasis has been on technique and timing, rather than assessing the original need for such surgery. The majority of outcome studies are short-term, concentrating on appearance, and often are rated by those involved in the original procedure. Long-term results are sparse with some authors suggesting vaginal surgery should be deferred until after puberty in order to optimise results and limit the need for revision surgery. Clitoral surgery technique has been refined over the last 50 years, but long-term studies give little information on function and sensation. At present the only known function of the clitoris is in contributing to sexual pleasure, and it seems inappropriate that outcome studies do not assess this in detail. Recent work has suggested that all clitoral surgery risks neurological damage and that surgery should now only be reserved for those with severe genital ambiguity. Surgery is primarily performed in childhood for cosmetic rather than anatomical reasons. Without clear information regarding the long-term risk to sexual function, it cannot be assumed that surgery does not cause damage. Parents and clinicians should be clear about this when planning and agreeing to genital surgery in childhood.
Chapter 4
The Normal Appearance

4.1 Background

The main aim of genital surgery in CAH has been to restore “normality”, and produce a normal appearance. This is a natural legacy from John Money's work in the 1950s, as discussed in chapter 1. Yet, in order to achieve a normal appearance this suggests that such a thing exists. However, there is little data in the literature on what constitutes normality with regard to female genitalia. Information is necessary for those concerned with two distinct groups: those with an intersex condition, or congenital anomaly to the genital area, or those with no underlying condition who seek cosmetic alteration of the external genitalia.

4.1.1 Measurements in the Literature

Measurements of individual areas of the female genitalia exist. Weber et al assessed vaginal length in 104 women who had presented for gynaecological care, and found the average length to be 11.1cm +/- 1cm. The mean age of the group was 55.8 years, and the majority were postmenopausal. A further study measured the clitoral glans and body in 200 consecutive women presenting to a gynaecologist. They found the measurements were normally distributed, with a mean glans transverse diameter of 3.4+/-.1.0mm, mean glans longitudinal diameter of 5.1 +/- 1.4mm, and mean total (body and glans) length of 16 +/- 4.3mm. Recent work by O'Connell et al has shown the size and anatomy of the perineal area to be different from that classically presented in anatomical texts.

Dissections of 2 fresh and 8 fixed cadavers were carried out, with particular interest in the clitoris and the relationship with the urethra. They found that the urethra was embedded in the anterior vaginal wall and was intimately related to clitoral erectile tissue superiorly and bilaterally. In addition, the urethra, distal vaginal wall and clitoral erectile tissue were shown not to lie...
flat against the pubic rami, but projected for 3 to 6 cms internally. A recent study asked 50 women to self-rate the appearance of their genital area. Two-fifths of them indicated a clitoral size that would be regarded as normal by experts, with a further two-fifths rating the clitoris as larger than would be expected by clinicians. When asked about the vaginal introitus 16% rated this as inadequate for penetrative intercourse, yet all women were sexually active. This suggests some discrepancy in either professional or personal perception of the female genital area.

4.1.2 Representations in Anatomical text

Female anatomy is frequently represented in anatomical texts after prior discussion of standard male anatomy. Descriptive passages are often much shorter in length and structures routinely described with reference to the male genitalia assuming this to be the “standard” e.g. the clitoris is the homologue of the penis. Further work has reviewed the anatomy of the clitoris and revisited these descriptions to assess them for accuracy. Dissection of the perineum was performed on 22 female and 4 male cadavers, and further detailed dissection of the suspensory ligaments on 4 female and 2 male cadavers. These showed differences in the suspensory ligaments of the penis when compared with those of the clitoris which were found to be more substantial and complex than previously documented. The anatomical descriptions in the historical and current anatomy texts were found to be accurate for the penile ligament descriptions, but inaccurate in describing shape, extent, and orientation of the clitoral ligaments.

Anatomy tends to be viewed as a “stable” science where descriptions should not vary once recorded. However, representations of female genitalia in anatomical texts have varied significantly over the 20th century. As discussed in chapter 2, the 1901 edition of Gray’s Anatomy showed the clitoris to be a prominent, well labelled structure, comprising a prepuce, glans, and body. By the 1942 edition, the clitoris was poorly labelled, and was considerably smaller in proportion. This representation persisted (and persists): the
1986 edition of Snell’s Anatomy, a popular student text, does not even include the clitoris on the pelvic cross sections comparing male and female anatomy \(^9\).

4.1.3 Representations in the lay press

Books such as “Femalia” have tried to address the gap in knowledge of the normal appearance of female genitalia by publishing photos of normal female genitalia \(^7\). Although informative, pictures are posed, with fingers frequently distorting the natural lines of the anatomy. This serves as a useful text for those interested in normal appearances, but is less helpful in informing the clinician seeking accurate information about the normal configuration of the female genitalia. In 1982 a feminist self-help group aimed to reinterpret female anatomy, and produced a new textbook, “A New View of a Woman’s Body”, showing detailed images of the clitoris with extensive labelling of parts, as shown in chapter 2 \(^2\). The group used their own observations and experiences to draw on, and published the book as a “get to know your body” manual. The female anatomy is represented first, and comparisons with male anatomy then shown.

4.1.4 Necessity of measurements

Previously, standard measurements of different parts of the anatomy have been used to define “normality”. Yet, is it perhaps more important to utilise such information to display variation. Societal pressures on women to conform to a particular appearance are not new, with the desired shape of women having changed significantly over the twentieth century. Edwardian ladies occasionally had a lower rib removed to enable them to wear the latest bustle fashions. Yet only 20 years later, women were strapping down their bust to achieve a more boyish figure. Robert Latou Dickinson measured hundreds of women in his quest to discover “perfect measurements” rather than “deviant” anatomy \(^8\). He designed models called Norma and Normman which were a combination of the most desirable measurements. A more
recent study published in 2002 looked at the trends in height, weight, bust, waist and hip measurements in Playboy centrefold models, from 1953 to December 2001. For a commercial magazine such measurements may not represent the average woman, but instead suggests the perceived desirable shape that a woman should aspire to. Interestingly, weight did not change, but height and waist size increased, whilst bust and hip size decreased, showing a trend to a more androgynous shape. The emergence of plastic surgery as a speciality over the last 50 years, coupled with the increasing availability and affordability has enabled women to seek surgical solutions to perceived problems. Anything which is seen as a difference in female genitalia appearance is sometimes interpreted as a “problem”, being listed along with abnormal smears and irregular periods on advertisements for private clinics.

Figure 4.1 Advertisement for private gynaecology clinic listing female genital surgery alongside other gynaecological conditions.

Once an area has been self-identified as “abnormal” an immediate fix or cure can prove irresistible. Yet it is surprising that surgeons are able to offer a restoration of normal anatomy without a clear definition of what this may be.

4.2 Study Background

In order to try and address this gap in knowledge, a study to assess normal genitalia in healthy women was designed. Critical to this was the ability to undertake detailed measurements, and to record the external appearance.
using digital photography, so such information may be used for teaching and educational purposes. To achieve this, a steady influx of subjects was needed, and it was decided that a gynaecology operating list (with prior informed consent) presented the opportunities for detailed examination and photography, without undue embarrassment to the subjects concerned.

4.3 Methodology

Ethical approval for the study was obtained from the Joint Hospital and University Ethics Committee. Women having routine procedures, such as hysteroscopy or diagnostic laparoscopy, were given an information leaflet, and written consent was then obtained from the 50 women who chose to take part. Age, parity, ethnicity, use of systemic hormones and sexual activity history were recorded. Participants were excluded if they were non-English speakers without an interpreter present, were under the age of 18, were postmenopausal, or if they had previously undergone any surgery to the external genitalia. Women who had undergone female genital mutilation/cutting were also excluded. Once anaesthetised, women were placed in the lithotomy position. A digital photograph of the external genitalia was taken prior to skin preparation and draping for surgery. Measurements were taken, in accordance with the diagram in figure 4.2, and a vaginal swab used to measure vaginal length from the posterior vaginal fornix to the introitus.

Figure 4.2 Location of measurements taken from the genital area
Clitoral body length, clitoral glans width, and distance from the base of the glans to the anterior margin of the urethral orifice were recorded. Measurements were also taken of labia majora (length), labia minora (length and width), and distance from posterior fourchette to anterior anal margin (perineum). Rugosity and skin tone of the labia majora, and hair distribution according to Tanner's stages were noted. All examinations and photographs were taken by one of two researchers (NSC, or JL, a gynaecology senior house officer at UCL Hospitals) in order to minimise interobserver variability. Analysis of data was performed using SPSS (version 11.5), with Spearman's correlation and descriptive statistics as appropriate. A p value of <0.05 was deemed significant.

4.4 Results

Over an eight month period 58 women were invited to take part, and 50 agreed, giving an 86% acceptance rate. The commonest reasons for declining were embarrassment, or concern about a partner's reaction. All women were pre-menopausal, and aged between 18 and 50, with a mean of 35.6 (SD 8.7). The majority of women were white (n=37), with 5 asian women, 6 black women, 1 latin american woman, and 1 woman who was mixed race. Three women had never been sexually active. Twenty-nine women were nulliparous, and 18 were parous. Parity ranged from 1 to 8, with a mean of 2.5 (SD 1.5). Eleven women were taking systemic hormones, such as oral progestogens or the combined oral contraceptive pill. The range, mean, and standard deviation for all measurements are displayed in table 4.1, with the descriptive details in table 4.2.
Table 4.1 Measurements of genital area

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clitoral length / mm</td>
<td>5-35</td>
<td>19.1</td>
<td>8.7</td>
</tr>
<tr>
<td>Clitoral glans width / mm</td>
<td>3-10</td>
<td>5.5</td>
<td>1.7</td>
</tr>
<tr>
<td>Clitoris to Urethra / mm</td>
<td>16-45</td>
<td>28.5</td>
<td>7.1</td>
</tr>
<tr>
<td>Labia Majora length / cm</td>
<td>7.0-12.0</td>
<td>9.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Labia Minora length / mm</td>
<td>20-100</td>
<td>60.6</td>
<td>17.2</td>
</tr>
<tr>
<td>Labia Minora width / mm</td>
<td>7-50</td>
<td>21.8</td>
<td>9.4</td>
</tr>
<tr>
<td>Perineum length / mm</td>
<td>15-55</td>
<td>31.3</td>
<td>8.5</td>
</tr>
<tr>
<td>Vaginal length / cm</td>
<td>6.5-12.5</td>
<td>9.6</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Table 4.2 Description of genital area

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanner stage / n</td>
<td></td>
<td>4</td>
<td>46</td>
</tr>
<tr>
<td>Colour of genital skin</td>
<td>Same</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>compared with surrounding</td>
<td>Darker</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>skin / n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rugosity of labia / n</td>
<td>Smooth</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Marked</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

There was no statistically significant association between the any of the different genital measurements and age, parity, ethnicity, hormonal use, or history of sexual activity.

When clitoral to urethral distance was correlated with clitoral length, a negative association was shown, with Spearman's coefficient of -0.45 (p value <0.001).
Figure 4.3 Comparing and contrasting genital appearance, with especial reference to the differences in the clitoral hood, labia minora and rugosity. Images from participants in the study.
An association between a shorter clitoral to urethral distance and smaller labia minora length was also shown, as seen in figure 4.4.
4.5 Discussion

In general there are very few descriptions of female genitalia in the literature. By contrast, measurements for male genitalia are widely available and were published as early as 1899\textsuperscript{101}. There have been a few reports on clitoral size\textsuperscript{94,94,102} and vaginal length\textsuperscript{93} but very little information on labial size or other aspects such as genitalia colour and rugosity. Work by O'Connell et al and Rees and co-workers has focused upon the internal size, position and relationships to surrounding structures of the clitoris following post mortem dissections of external female genitalia rather than upon the external appearance\textsuperscript{31,32}. These studies illustrate the inaccuracies and lack of understanding surrounding female genital anatomy. This study shows the wide range of variation in genital measurements and descriptions for all parameters. Clearly, certain individual measurements may have implications for different populations, and these are considered below.

4.5.1 Vaginal Size

The mean vaginal length was at 9.6cm +/- 1.5cm with a wide range varying from 6.5 cm to 12.5cm. This is slightly shorter than has previously been described\textsuperscript{93}, and is interesting as the majority of women had been sexually active. For women born with vaginal hypoplasia, either as part of an intersex condition, or with congenital absence of the uterus, as with Rokitansky syndrome, this information is valuable. Standard treatment for these conditions include the opportunity to create a vagina, and for women who choose to do so passive dilator therapy is the first option. The main aim of this is to achieve sufficient vaginal depth for comfortable and satisfactory penetrative sexual intercourse. Dilation therapy was first described by Frank in 1938, and consisted of pressing a perspex tube against the vaginal dimple for 20 minutes three times a day\textsuperscript{103}. Increasing sizes were used and after 4 weeks sexual intercourse was attempted. Franks claimed a successful result, which meant a vagina suitable for penetrative intercourse, was created in 6-8 weeks. The Ingram modification was described in 1981 using body weight to apply vaginal pressure with the dilator mounted on a bicycle seat\textsuperscript{104}.
Continuous perineal pressure was applied to the vaginal dimple for two hours daily resulting in 82% of patients “able to experience coitus”\textsuperscript{105}. The Ingram method has not been widely utilised, and self-dilation treatment currently still follows the Frank technique utilising plastic moulds of increasing size with a detachable handle. Success rates, usually defined as the ability to have penetrative sexual intercourse have varied from 43% to 87%\textsuperscript{106-108}.

At the Middlesex Centre the dilator therapy programme is run by a specialist clinic nurse, with a consultant clinical psychologist, and consists of a series of appointments with both separately. Assessment sheets are completed at each visit, and vaginal length measured at regular intervals. Previously an approximate target of 10cm vaginal length was made, although penetrative intercourse dilates the vagina well, and would be encouraged from an earlier stage, if appropriate. The knowledge that vaginal length is so variable in sexually active women who had not complained of any sexual difficulty is reassuring for both patient and clinician, and perhaps reduces the need to attain an absolute measurement. Rather, this may permit the individual to reach a state of acceptance of their diagnosis, and promote psychological wellbeing in order to optimise therapy.

4.5.2 Clitoral Size

For women born with ambiguous genitalia, the clitoral size is often the most obvious anatomical variation. Stated aims of surgery are to reduce the size of the clitoris to a more “normal” size\textsuperscript{17,63}. Yet, this study illustrates the variation in women without intersex conditions. The length of the clitoral body was 19.1mm with the range from 5 to 35mm. Any measurement in the human body that can vary by a factor of seven suggests a wide degree of variability in different individuals. This is further supported by the study by Schober et al showing a significant proportion of women surveyed indicated their clitoral size was larger than would be expected\textsuperscript{95}. The role of clitoral surgery has perhaps been the most contentious part of the debate surrounding surgery for intersex conditions. It has long been proposed that such surgery is necessary in order to promote a normal and secure gender
identity\textsuperscript{5}, despite there being little evidence that this is the case\textsuperscript{109}. Indeed, to extrapolate further, it could be argued that all women need to have conformity in genital measurements in order to achieve stable gender identity. It is unlikely that such a theory would nowadays be generally accepted, but is not dissimilar to theories supporting current management of those born with intersex conditions. Feminising genitoplasty surgery often involves repositioning the urethra to open separately onto the perineum, and is usually relocated at the base of the clitoris. Yet, the average distance between the clitoris to the anterior margin of the urethra was found to be surprisingly large at 28.5mm. Even the smallest distance recorded was 16mm which is an appreciable distance away. The negative correlation between clitoral to urethral distance and clitoral size, where a larger clitoris may have the urethra positioned more closely to the clitoral base, suggests that there is a range of virilisation across normal subjects. This is further reinforced by the association between a shorter clitoral to urethral distance and smaller labia minora length as seen in figure 4.4. This would suggest that surgery performed specifically to relocate the urethral meatus close to the clitoris is unnecessary. In general, surgeons may feel more reassured in not offering surgery for mild and moderate clitoromegaly in having objective evidence of the range of normal appearance of the genital area. This knowledge may also be useful for healthy women without intersex conditions seeking cosmetic alteration of the size of the clitoris\textsuperscript{110}. With objective information about the range in the size of the clitoris, women may feel that surgical intervention is inappropriate, and be reassured that variation is entirely normal.

4.5.3 Labial Measurements

There is a steady demand for cosmetic procedures to “improve” the appearance in female genitalia – the so-called “designer vagina” trend. Amongst the more popular of these is reduction surgery of the labia minora, either to correct asymmetry, or to reduce the size bilaterally. Clinical indications for such surgery are stated as poor hygiene, and interference with intercourse, although there is little data in the literature to suggest how
This actually is further indications include where women complain of the labia rubbing against underwear or of embarrassment with sexual partners. However, a more common presentation appears to be “self-consciousness” of the women with an outcome measure of enhanced “self-esteem”. This underlying implication of labia needing to be less than a certain size, or otherwise being deemed abnormal is supported in the literature with some authors employing measurements to determine whether the labia are enlarged. Rouzier et al selected a size of 4cm as abnormally enlarged and therefore requiring surgical correction, although no additional information on how this value was chosen is given. There are reports in the literature about different techniques employed, but little on any follow-up. One study did send questionnaires to patients with a follow-up of up to 30 months. Yet there was little data on sexual function, with only a response required as to whether penetrative intercourse had taken place since the operation, and whether dyspareunia had occurred. Labial reduction surgery appears to provide a relatively easy solution to a problem, yet one abstract in the literature suggests this may be over-simplistic (the main article being in Dutch, and translation unavailable). The cases of three women seeking labial reduction surgery were discussed. When further questioning was undertaken exploring the issues behind their request, it became apparent that one woman was recently divorced and unconfident about her genital appearance. One woman was not aware of normal anatomy, and the final subject had a vulvar pain syndrome and a history of sexual abuse. As with the clitoral and vaginal measurements, labial dimensions have been demonstrated to vary considerably. This data provides an opportunity for women and clinicians to consider the anatomical variations before resorting to an irreversible and arguably unnecessary step.

4.6 Conclusions

The appearance of female genitalia varies enormously, yet little objective evidence of this exists. With the lack of robust information regarding “normality” it is surprising that “corrective” surgery can be offered.
Information on the wide range of measurements in normal genitalia will be of value to clinicians, to parents and patients with intersex conditions, and to healthy women seeking cosmetic alteration. This data will provide an objective reference tool, not least by emphasising that the women who took part in this study had not sought surgical correction for the natural differences in the configuration of the genital area.
Chapter 5

Genital Sensation Testing

5.1 Background

Clitoral sensation is increasingly accepted as being an important part of the female sexual response. It has become a stated aim in clitoral procedures that sensation must be preserved 80, although studies assessing this outcome are scarce.

5.1.1 Studies assessing Sensation

Von Frey filaments are used in neurological studies to assess touch and light pressure sensation, or to assess two point discrimination. These filaments were first described by von Frey in 1922, who used horse hairs attached to wax candles to assess skin sensitivity to pressure or touch 116. One study has used von Frey filaments to assess sensation to the clitoris, labia minora and majora and perineum in 32 women 117, the main aim being to derive reference ranges for normal women, and to verify the use of von Frey filaments as an investigative tool. 15 women were postmenopausal, and 14 had impaired sexual function according to self-rated measures. The investigators found those with sexual dysfunction and those who were postmenopausal had significantly less sensation in the genital area. They also argued that von Frey filaments represented a reproducible simple way of assessing genital sensation. One of the earlier outcome studies looking at sensation following surgery assessed 15 out of 23 children who had undergone feminising genitoplasty procedures 70. Sensation was measured by using a wisp of cotton wool, or a light pinprick, and was noted to be “present” in all 15 cases. This represents a limited assessment of sensation testing, with a light touch or pinprick difficult to quantify and compare. A more recent study has assessed light touch and vibration sensation to the clitoris one year following clitoral surgery 118. Eight subjects aged 17 or more were assessed using 3 different Von Frey fibres to elicit light touch to the clitoris. The results were compared with normal controls, and no difference was
found between the two groups. In addition, a vibrating rod was used to detect first sensation to increasing and decreasing vibration. Seven of the women had undergone one clitoral reduction procedure in childhood and had normal sensation. One woman had undergone a second operation aged 7, and was reported as having decreased sensation. This study also discussed psychosexual outcomes of the six sexually active women, but this merely commented on whether the women reported dryness or problems during intercourse. No details on orgasm, sensation or satisfaction were given. Schober et al considered sensation and function in a group of 50 volunteers who had no history of genital surgery. Women were asked to self-rate genital sensitivity, and intensity and ease of orgasm for various sites on the genital area. The clitoris and clitoral hood were found to be the most sensitive areas and were associated with comparative ease of achieving orgasm. However, this study was not correlated with objective measures of sensation. Investigations for female sexual dysfunction for non-intersexed women have employed a GenitoSensory Analyzer (Medoc, Israel) to assess genital sensation. This measures temperature sensation, and also vibration sensation using specifically designed probes suitable for male or female patients. Vardi et al measured clitoral and vaginal sensation on 89 paid volunteers, with normal sexual function determined by a questionnaire. Normative values were derived and stratified for age, with the clitoris proving to be more sensitive than the vagina for temperature change and vibratory sensation. In addition, clitoral sensitivity decreased slightly with increasing age, whereas anterior vaginal sensation did not.

5.1.2 Studies assessing neurological conduction

Other studies have employed somatosensory evoked potentials (SSEPs) to assess pudendal nerve conduction for women with multiple sclerosis and sexual dysfunction. Measurement of SSEPs is achieved by placing electrodes on the clitoris with repeated electrical stimulation applied via the skin surface or fine needle electrodes. The resulting potentials are recorded and reflect activation along the afferent somatosensory pathways. There is little data available regarding normal SSEP values, although one study has
assessed 20 female healthy volunteers to derive a reference range. In order to address the increasing controversy surrounding the potential neuronal damage caused during clitoral surgery, Gearhart et al studied 6 patients undergoing feminising genitoplasty. Three patients had CAH, one was diagnosed with androgen insensitivity, one patient had mixed gonadal dysgenesis, and the final patient had virilised due to an adrenal tumour. All were aged between 2 and 23 months of age, and were assessed in the operating theatre after anaesthesia was commenced. Unipolar electromyographic electrodes were placed on the dorsal aspect of the base of the clitoris, and responses were recorded. SSEPs of the clitoris were evaluated before and immediately after the procedure, and a comparison of the two values made. Following standard clitoral reduction surgery, incorporating removal of the erectile bodies with preservation of the glans and neurovascular bundle, the stimulation was repeated. In five of the patients, no difference was seen pre- or post-operatively. A slight prolongation was noted with the sixth patient, suggesting impaired pudendal nerve function, but this did not prove to be statistically significant. The authors concluded that nerve conduction and sensation were therefore retained. There are several issues with this study. The electrodes were placed at the base of the clitoris, and not at the tip, and therefore did not assess the more distal fibres to the glans. The authors acknowledged that information on nerve conduction is of limited value until the individuals are older and become sexually active. But more fundamentally, SSEPs assess the nerves to the dorsal column, which are responsible for sensation to touch, vibration and light pressure. It does not assess the spinothalamic tracts which provide sensation to temperature and pain. Therefore, this method does not adequately assess the dorsal nerve to the clitoris which carries sensation for light touch, vibration and temperature and pain. Despite evoked responses remaining unchanged following surgery, it is not possible to conclude that sensation is undamaged. This was further reinforced by a letter from Cheryl Chase in response to the paper, citing examples where women were found to have normal pudendal evoked responses, yet had sexual function difficulties and anorgasmia.
5.1.3 Studies assessing sexual outcome

Very few studies have linked sensation testing with objective measures of sexual function. One study measuring the evoked potentials on 14 women with multiple sclerosis, compared this with a questionnaire on sexual function. Electrodes were placed on the clitoral hood and at the base of clitoris between the labia minora and majora. Impaired evoked potential responses were associated with self-reported difficulties in arousal and achieving orgasm. However, the questionnaire used was simplistic, consisting of eight questions requiring a yes/no response. Examples include: “Are you satisfied with your sex life?” “Do you think you have problems with sexual function?” The questions had not been validated on a normal population, which leaves the data difficult to analyse. Furthermore there were no specific questions asking about orgasm or sensation.

5.2 Methodology

5.2.1 Study Design

Therefore a study assessing sensation to the clitoris and vagina in women with CAH was planned, along with an objective validated assessment of sexual function. This would consist of two parts: the first part would carry out sensation testing to the clitoris and vagina, and would ask participants specifically about their opinions regarding feminising genitoplasty surgery. Current debates in the literature include the appropriateness of surgery, and the timing of any treatments. However, there is little regarding the opinions of women with CAH, other than those involved in support groups. In order to examine the findings of the sensation testing, it is important to consider the viewpoint that the participants may hold. It was probable that the majority of women with CAH would have undergone surgery, in keeping with policies for the last 50 years. However, should there be any participants that had not, this would be an interesting group to study, although was likely to be small in
numbers. Recruitment of normal controls was therefore planned to establish a group for comparison.

The second part of the study would concentrate on sexual function. The design and results of this part are discussed fully in chapter 6. The study was approved by the UCL and UCLH Joint Hospital and University Ethics Committee.

5.2.2 Patient Cohort

Recruitment was planned from two places: a specialist service for women with intersex conditions, and from a specialist endocrinology clinic.

The Middlesex Centre at the Elizabeth Garrett Anderson Hospital is a multidisciplinary clinical service for adult women with intersex conditions, led jointly by gynaecology, endocrinology and psychology consultants. It is coordinated by a full-time clinical nurse specialist, and also can draw on the expertise of affiliated specialist surgeons in laparoscopy, paediatric surgery and adolescent urology. The clinic sees over 300 patients per year, with approximately one third of these being seen for the first time in the clinic. Some will have been under the care of paediatric services, but others will have a new diagnosis of an intersex condition made in the clinic. Due to the relatively rare nature of intersex conditions, patients are referred from a wide geographical area, mostly from over the south of England, but also from all areas of the United Kingdom and Eire, and individuals from other European cities. The Middlesex Centre has its own website on www.uchl.org/reprodev and is able to answer queries from individuals all over the world. Increasingly, intersexed women in the UK have accessed the website and requested referrals to the clinic, either having recently been diagnosed elsewhere, or in order to find out more about their particular diagnosis and any new treatment developments. The website also has information sheets about many different conditions for patients and families to access. The clinic is well supported by, and works closely with patient groups such as the AISSG, and CAH support groups (Children Living with Metabolic Diseases.
(CLIMB) and Adrenal Hyperplasia Network). Patients with a wide range of intersex conditions are seen in the clinic, and may require input from any or all of the clinicians. This varies over time, as different issues come to the fore. The clinic practices a policy of full disclosure of diagnosis and condition details, which may take place over several sessions. The Middlesex Centre now represents one of the world’s largest cohorts of intersex patients, and carries out research into many aspects of the care of intersexed individuals. Work has been presented at many national and international conferences by members of the clinic team.

The Endocrinology CAH Clinic is a tertiary referral service seeing patients with all types of CAH. It sees approximately 118 male and female patients a year, of which 16 will be new referrals. The women are under the care of a consultant endocrinologist and team of junior endocrinology doctors, and can be referred to The Middlesex Centre if additional gynaecological or psychological input were required.

5.2.3 Study Equipment

In order to assess clitoral sensation accurately, as discussed in chapter 2, both temperature and vibration/light touch sensation should be evaluated. A GenitoSensory Analyzer (GSA) (Medoc, Israel) was chosen as the most appropriate investigative tool. The GSA employs the method of threshold testing where the levels at first sensation are recorded.

Figure 5.1 GSA shown, with thermal probe positioned on the end of the adjustable arm. Patient response switch is lying across the computer.
This represents the standard neurological test used to assess sensation and to allow the detection of any impairment. This information may be compared with normal controls and therefore quantify the degree of deficit. The equipment is controlled by a computer which is positioned on a portable stand.

The GSA consists of two separate probes; one for temperature measurements and one for vibratory testing, with a feedback patient response switch. Temperature is generated by a closed water system, driven by a computer to heat and cool the probes appropriately.

**Figure 5.2.** The vibration (left) and thermal (right) probes in greater detail. Von Frey fibres for light touch are shown.

Each probe can be used externally on the clitoris and also inside the vagina. The probes are held by an adjustable arm, and therefore can be positioned correctly.

The temperature probe has a thermal button on the end for application to the clitoris, and a flat element on the cylinder for contact with the anterior vaginal wall. The vibration probe vibrates throughout its length, with an end button for clitoral application, or is placed in the vagina for vaginal sensation assessment.

The woman is positioned supine with her knees supported in lithotomy position therefore allowing the probes to be correctly positioned. The clitoral probe is placed firmly against the clitoral glans. It is then moved back slightly so not pushing as firmly but the woman is clearly able to feel it. Both the
thermal and vibratory clitoral probes are positioned in the same way. The thermal vaginal probe is positioned so the plate lies against the upper third of the anterior vagina. The vaginal vibration probe is inserted so the distal portion is in the upper third of the vagina.

The method of threshold testing was applied, whereby the stimulus is changed in linear increments until first sensation is felt. The thermal probe starts at 37°C and will increase or decrease according to whether warmth or cold sensation is being assessed. Once the subject registers a change in sensation, a button is pressed which stops the test. The thermal probe has a safety cut-off at both 20°C and 50°C. The vibration probe has a fixed frequency of 100Hz and an amplitude range of 0 to 130 μm, and similarly the subject is asked to press the response switch as soon as vibration sensation is felt. Stopping the test gives the value at which first sensation is felt by the subject. The tests are repeated six times each for warmth, cold and vibration, to both the clitoris and the upper vagina. The mean of the six readings is calculated by the GSA, with this value representing the level of first sensation. Using six separate values and calculating the mean gives a more representative level of threshold sensation, rather than relying on one value alone.

Light touch was also assessed using Von Frey filaments (Semmes Weinstein Von Frey Anaesthesiometer, North Coast Medical Inc., USA). The fibres are designed so that when pressed against the skin until they bend, a constant reproducible amount of force is applied. The fibres are graded to provide a logarithmic scale of applied force, in grammes, from 0.008g to 300g. The clitoral glans was exposed, and Von Frey filaments applied starting from 0.008g until the subject was first aware of light touch. If in doubt, higher strength fibres would continue to be used, and then reduced to lower levels in order to be clear when sensation was first felt.

All participants with CAH in the sensation testing study, and therefore all those that were willing to undergo a genital examination, were invited to
complete a short questionnaire asking about their opinions regarding the role and timing of genital surgery. They were also asked to volunteer any good or bad experiences associated with surgery. The questionnaire consisted of 11 statements, with a five point Likert scale from “strongly agree” to “strongly disagree”. There were two further questions giving the scenario of a baby girl with CAH, and respondents were asked to offer advice about whether and when surgery should be carried out. The questionnaire is given in Appendix 1. As this questionnaire was specifically completed by those that underwent sensation testing, rather than as part of the postal questionnaire utilised in chapter 6, it is presented and discussed here.

5.2.4 Study Recruitment

To start the study, use was made of a clinical database of women with 21-OH CAH who had been under the care of The Middlesex Centre, or of the Endocrinology CAH Clinic. This would ensure that women were invited to take part even if they were not under the care of a gynaecologist. A mailshot letter and information leaflet were sent out to prospective participants inviting them to join the study, or be contacted by the main study investigator if they wished for more details. A second letter was sent out two weeks later if no response was received. Prospective recruitment of women from both The Middlesex Centre clinic and the Endocrinology CAH Clinic then commenced, with women being approached at the time of their routine appointment. They were given information sheets and invited to take part. Responses and comments were invited about the study, and women were advised they were free to participate in just one part if they chose. For those that attended The Middlesex Centre for the genital testing, travel expenses were reimbursed.

5.2.5 Operation details

As part of the postal questionnaire all participants were asked for permission to obtain previous hospital notes in order to ascertain which operations had been performed. Once permission was granted a copy of the consent form
was sent along with a request letter to the relevant medical records departments. If no reply was received this was followed up with a further letter, and phone call to ensure receipt of the original request. If photocopying charges were requested, this was met from the study fund.

5.2.6 Statistical Analysis

All statistics were analysed using SPSS version 11.5. Given the small sample numbers non-parametric testing methods were employed. The Mann-Whitney U test was used to calculate a p value, which was deemed significant at less than 0.05.

5.3 Results

In total 56 women were invited to take part in the study, with the breakdown of this shown in figure 5.3. A mailshot was sent to 39 women whose details were obtained from the clinical database of patients with an information sheet, and a response sheet to indicate if they wished to take part, would like further information before deciding, or wished to decline. 24 women agreed to take part in the study. Of these 24, three subsequently did not respond to any contact, two agreed to complete the questionnaire part only, and one agreed to both parts but subsequently was too busy when clinic appointments were offered. Ultimately 18 of the initial 39 women invited attended for testing. Of the 15/39 women that did not agree to take part in the study, 8 did not reply to the invitation and subsequent follow-up, 2 declined without giving a reason, 2 declined as they were working; one full time, and the other for A levels, 1 indicated she was not interested in the study, 1 pack was returned indicating the person was no longer resident at that address. Further attempts to obtain a valid address via the last listed general practitioner were unsuccessful. Finally one respondent declined stating “I am very embarrassed to show anyone my private parts even for medical reasons. I do not wish to be touched in that area.”
17 women were approached in clinic, and 16 agreed to take part in the study. Of these, two patients proved unresponsive to further contact, and one respondent lived in Scotland, and did not attend for routine clinic before the end of the study. Three others agreed to the questionnaire part of the study only. 10 women from clinic ultimately attended for testing. This gives a total recruitment rate into the first part of the study of 71% ((24+16)/56) with an attendance rate of 50% ((18+10)/56). Of the 28 patients that attended, 12 had a proven mutation consistent with a diagnosis of 21-hydroxylase CAH. For the other patients who had not undergone genetic testing, diagnosis had been made on clinical grounds.

Figure 5.3. Details of recruitment for the genital sensation testing

Nine normal controls were recruited to take part in the sensation testing part of the study. Three were friends of women with CAH taking part in the study, two were hospital members of staff who had heard about the study, and four were non-medical individuals who had heard about the study from friends working in the hospital. None of the normal controls had any endocrinological abnormality or any history of genital surgery. They were of a similar age range to the CAH group.
5.3.1 Clitoral Sensation Results

Four groups were identified for comparison: Clitorectomy (those who had undergone a clitorectomy or had no remaining identifiable glans tissue), Clitoral reduction, CAH without surgery, Normal Controls. The Kruskal-Wallis test was applied, with a p value of less than 0.05 deemed significant (see table 5.1 and figure 5.4).

Table 5.1 Difference in peri-clitoral sensation for operation types

<table>
<thead>
<tr>
<th>Clitoral Sensation test</th>
<th>Normal Controls Median (range) N = 9</th>
<th>CAH No surgery Median (range) N = 4</th>
<th>Clitoral Reduction Median (range) N = 9</th>
<th>Clitorectomy Median (range) N = 6</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warmth °C</td>
<td>39.2 (38.6-41.2)</td>
<td>40.0 (38.7-40.9)</td>
<td>42.8 (38.3-49.6)</td>
<td>47.0 (43.8-49.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>Cold °C</td>
<td>33.2 (30.9-35.1)</td>
<td>31.8 (30.6-32.5)</td>
<td>28.1 (24.7-32.0)</td>
<td>23.7 (20.1-30.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Vibration μm</td>
<td>1.83 (1.22-5.15)</td>
<td>3.04 (2.19-3.38)</td>
<td>3.00 (1.30-8.09)</td>
<td>5.36 (1.26-8.09)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

*Kruskal-Wallis test
A statistically significant difference was seen between the four groups, and is shown in figure 5.4. Those who underwent clitoral surgery had poorer results than those that did not or than the normal controls, with the group who had undergone clitorectomy having the worst results. The clitorectomy and clitoral reduction groups were then compared as shown in table 5.2.

Table 5.2 Comparison of clitoral sensation results between those who had clitorectomy and clitoral reduction procedures

<table>
<thead>
<tr>
<th></th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warmth</td>
<td>0.068</td>
</tr>
<tr>
<td>Cold</td>
<td>0.125</td>
</tr>
<tr>
<td>Vibration</td>
<td>0.376</td>
</tr>
</tbody>
</table>

*Mann-Whitney U test p value

No significant difference was seen between the operation types.
Given the small sample sizes when comparing operation types the results were also analysed in two larger groups; those with CAH were compared with normal controls. The Mann Whitney U test was applied, and a p value calculated (see table 5.3).

<table>
<thead>
<tr>
<th>Clitoral Sensation test</th>
<th>Normal Controls Median (range) N = 9</th>
<th>CAH subjects Median (range) N = 28</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warmth °C</td>
<td>39.2 (38.6-41.2)</td>
<td>42.4 (38.3-49.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Cold °C</td>
<td>33.2 (30.9-35.1)</td>
<td>29.9 (32.5-20.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vibration μm</td>
<td>1.83 (1.22-5.15)</td>
<td>3.00 (1.14-13.41)</td>
<td>0.039</td>
</tr>
</tbody>
</table>

*Mann-Whitney U test p value

The results showed a statistically significant difference for warmth, cold and vibration sensation when comparing the CAH group with the normal controls. In all three instances, sensation was poorer for the CAH group.

Secondly the results were compared between women who had undergone genital surgery, and those who had not (4 women with CAH plus the normal controls) (see table 5.4).

<table>
<thead>
<tr>
<th>Clitoral Sensation test</th>
<th>No Surgery Median (range) N = 13</th>
<th>Surgery subjects Median (range) N = 24</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warmth °C</td>
<td>39.3 (38.6-41.2)</td>
<td>43.3 (38.3-49.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cold °C</td>
<td>32.9 (30.6-35.1)</td>
<td>28.9 (20.1-32.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vibration μm</td>
<td>2.04 (1.22-5.15)</td>
<td>2.87 (1.14-13.41)</td>
<td>0.114</td>
</tr>
</tbody>
</table>

*Mann-Whitney U test p value

The results again showed a statistically significant difference for warmth and cold sensation, with sensation being poorer for those who had undergone
surgery. The clitoral vibration sensation also showed a difference, but this was not significant.
Difference in mean temperature sensation to warmth for clitoris between CAH group and Normal Controls

Difference in mean temperature sensation to cold for clitoris between CAH group and Normal Controls
5.00 - 0.00 - 3.00 - 2.00 - 1.00

Difference in mean vibration sensation for clitoris between CAH group and Normal Controls

Figure 5.5 Graphs showing the median and range of temperature and vibration sensation to the clitoris in the CAH group and Normal Controls. Some overlap is seen, but the values for CAH women have a much wider range indicating poorer sensation.

5.3.2 Vaginal Sensation Results

Fewer women with CAH were able to complete the vaginal sensation testing due to introital stenosis. In addition, some normal controls chose not to undergo vaginal testing. The vaginal thermal probe is slightly larger than the vibration probe, so whilst 16 CAH women and 6 controls were able to measure vaginal vibration, only 8 CAH women and 4 controls had thermal sensation to the vagina assessed. The groups were divided into those with CAH who had undergone surgery, those with CAH who did not have surgery,
and Normal Controls. The Kruskal-Wallis test was used to calculate a p value.

Table 5.5 Comparison of vaginal sensation results for CAH with surgery, CAH without surgery, and Normal Controls

<table>
<thead>
<tr>
<th>Vaginal Sensation test</th>
<th>Normal Controls</th>
<th>CAH subjects without surgery</th>
<th>CAH subjects with surgery</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (range)</td>
<td>Median (range)</td>
<td>Median (range)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N [ ]</td>
<td>N [ ]</td>
<td>N [ ]</td>
<td></td>
</tr>
<tr>
<td>Warmth °C</td>
<td>45.1 (42.2-48.3) [4]</td>
<td>46.7 (43.4-50.0) [2]</td>
<td>46.7 (39.8-50.0) [6]</td>
<td>0.782</td>
</tr>
<tr>
<td>Cold °C</td>
<td>29.1 (26.5-31.3) [4]</td>
<td>27.9 (25.8-30.0) [2]</td>
<td>27.3 (20.0-32.7) [5]</td>
<td>0.873</td>
</tr>
<tr>
<td>Vibration µm</td>
<td>2.34 (1.55-4.19) [6]</td>
<td>5.17 (4.77-5.56) [2]</td>
<td>3.87 (1.23-5.82) [14]</td>
<td>0.088</td>
</tr>
</tbody>
</table>

As the three groups had small study numbers, larger groups were also analysed with the Mann-Whitney U test used to calculate a p value. Firstly, the groups were divided into CAH and non-CAH participants.

Table 5.6 Comparison of vaginal sensation results for CAH and non-CAH participants

<table>
<thead>
<tr>
<th>Vaginal Sensation test</th>
<th>Normal Controls</th>
<th>CAH subjects</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (range)</td>
<td>Median (range)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N [ ]</td>
<td>N [ ]</td>
<td></td>
</tr>
<tr>
<td>Warmth °C</td>
<td>45.1 (42.4-48.3) [4]</td>
<td>45.8 (39.8-50.0) [8]</td>
<td>0.551</td>
</tr>
<tr>
<td>Cold °C</td>
<td>29.1 (26.5-31.3) [4]</td>
<td>27.3 (20.0-32.7) [8]</td>
<td>0.705</td>
</tr>
<tr>
<td>Vibration µm</td>
<td>2.34 (1.55-4.19) [6]</td>
<td>4.27 (1.23-5.82) [16]</td>
<td>0.090</td>
</tr>
</tbody>
</table>

*Mann-Whitney U test p value

No difference was observed between the CAH group when compared with the normal controls.

The results were then compared between women who had undergone genital surgery, and those who had not.
Table 5.7 Comparison of vaginal sensation results for surgery and non-surgery participants

<table>
<thead>
<tr>
<th>Vaginal Sensation test</th>
<th>No Surgery Median (range) N [ ]</th>
<th>Surgery subjects Median (range) N [ ]</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warmth °C</td>
<td>45.1 (42.4-50.0) [6]</td>
<td>46.7 (39.8-50.0) [6]</td>
<td>0.872</td>
</tr>
<tr>
<td>Cold °C</td>
<td>29.1 (25.8-31.3) [6]</td>
<td>27.3 (20.0-32.7) [6]</td>
<td>1.000</td>
</tr>
<tr>
<td>Vibration μm</td>
<td>2.76 (1.55-5.56) [8]</td>
<td>3.87 (1.23-5.82) [14]</td>
<td>0.585</td>
</tr>
</tbody>
</table>

*Mann-Whitney U test p value

Similarly, no difference was noted between the "surgery" and "non-surgery" group, although as the surgery refers to clitoral and lower vagina surgery the groups were not considered according to clitoral surgery type.

5.3.3 Von Frey filaments Results

The first sensation to Von Frey filaments was recorded, and the difference between the CAH and normal controls compared.

Table 5.8 Comparison of sensation to Von Frey filaments for CAH subjects compared with non-CAH participants

<table>
<thead>
<tr>
<th>Normal Controls Median /g (range) N [9 ]</th>
<th>CAH subjects Median /g (range) N [27 ]</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07 (0.08-0.40)</td>
<td>0.16 (0.02 - 6.0)</td>
<td>0.209</td>
</tr>
</tbody>
</table>

* Mann-Whitney U test p value

The groups were then divided into those who had undergone surgery, and those who had not (normal controls + 2 CAH participants).

Table 5.9 Comparison of sensation to Von Frey filaments for surgery subjects compared with those who did not have surgery

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0.16 (0.008 - 6.0)</td>
<td>0.16 (0.02-1.4)</td>
<td>0.917</td>
</tr>
</tbody>
</table>

Gynaecological and Psychosexual Outcomes of Feminising Genital Surgery
No difference was seen in first sensation using Von Frey filaments between the CAH and non-CAH groups, or surgery and non-surgery groups.

The groups were also analysed according to the type of surgery they had had, with four groups identified: Clitorectomy or no identifiable glans tissue, clitoral reduction, CAH no surgery, Normal Controls. The Kruskal-Wallis test was used to determine a p value.

<table>
<thead>
<tr>
<th>Table 5.10 Comparison of Von Frey sensation test for Normal Controls, CAH No Surgery, Clitoral Reduction and Clitorectomy groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Von Frey Sensation test /g</td>
</tr>
<tr>
<td>Normal Controls Median (range) N = 9</td>
</tr>
<tr>
<td>CAH No surgery Median (range) N = 4</td>
</tr>
<tr>
<td>Clitoral Reduction Median (range) N = 8</td>
</tr>
<tr>
<td>Clitorectomy Median (range) N = 6</td>
</tr>
<tr>
<td>P value*</td>
</tr>
<tr>
<td>0.2 (0.008-2.8)</td>
</tr>
<tr>
<td>0.9 (0.1-2.0)</td>
</tr>
<tr>
<td>0.2 (0.04-1.4)</td>
</tr>
<tr>
<td>0.8 (0.4-6.0)</td>
</tr>
<tr>
<td>0.050</td>
</tr>
</tbody>
</table>

A significant difference was observed, with those who had undergone clitorectomy or who had no clitoral tissue present having the poorest sensation to light touch.

5.3.4 Questionnaire

All 28 participants with CAH completed the questionnaire, indicating on a scale of 1 (strongly disagree) to 5 (strongly agree) whether they agreed with the statements. The median and mean responses to each question were calculated (table 5.11)
Table 5.11 Questionnaire on genital surgery given to CAH study participants

<table>
<thead>
<tr>
<th>Question</th>
<th>Likert Scale*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I have never thought about genital surgery</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>I think genital surgery is a good idea in CAH</td>
<td>4</td>
<td>3.7</td>
</tr>
<tr>
<td>I think genital surgery should not be performed</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>I would be angry if I had/have had surgery as a baby</td>
<td>1</td>
<td>2.3</td>
</tr>
<tr>
<td>I think genital surgery causes problems with sex</td>
<td>3</td>
<td>3.3</td>
</tr>
<tr>
<td>It is fine for parents to make the decision they think is best</td>
<td>4</td>
<td>3.1</td>
</tr>
<tr>
<td>I would be relieved if I had/have had surgery as a baby</td>
<td>3</td>
<td>3.1</td>
</tr>
<tr>
<td>It is fine for doctors to make the decision for surgery</td>
<td>2</td>
<td>2.9</td>
</tr>
<tr>
<td>I think a lot about the appearance of my genital area</td>
<td>5</td>
<td>3.4</td>
</tr>
<tr>
<td>It is important for the genital area to look completely female</td>
<td>4</td>
<td>3.8</td>
</tr>
<tr>
<td>Only the patient should make the decision for surgery</td>
<td>3</td>
<td>3.4</td>
</tr>
</tbody>
</table>

*Where 1 = strongly disagree and 5 = strongly agree

<table>
<thead>
<tr>
<th>Question</th>
<th>Most common response</th>
</tr>
</thead>
<tbody>
<tr>
<td>At what age should clitoral surgery be carried out?</td>
<td><em>Whenever patient requests</em></td>
</tr>
<tr>
<td>What would you advise the parents of a two month old girl with CAH with</td>
<td><em>To have an operation at this time</em></td>
</tr>
<tr>
<td>a large clitoris considering surgery to make the clitoris look smaller?</td>
<td></td>
</tr>
</tbody>
</table>

16 subjects had their notes traced (see below), and age of first surgery ascertained. No clear association was seen between the age of first surgery and whether subjects were angry at having undergone childhood surgery (Spearman’s correlation -0.045, p value 0.873). Similarly no relationship was observed between the age of first surgery and whether subjects were relieved at having undergone an operation as a child (Spearman’s correlation -0.009, p value 0.974).
5.3.5 Operative Results

Of the 28 women with CAH who took part in the sensation testing study, 4 had not undergone surgery. The remainder were asked for permission to trace their hospital notes. Written consent was obtained, as part of the postal questionnaire discussed in chapter 6. 22/24 women completed the questionnaire and gave permission. Details of the operation performed was obtained for 16/22 women, either by receiving a copy of the original operation note (12/16) or by clear details in hospital letters (4/16). Of the six participants whose operative details were not obtained, two participants were unable to recall where surgery had taken place, with no record in The Middlesex Centre notes. Records received for one participant did not have the original operation note present, although the other records were contemporaneous. A request for a set of notes for another respondent was returned as the hospital had since closed, and records from subsequent hospitals where the patient received care did not contain operative details. One request for notes was unsuccessful despite two letters, follow-up phone calls and faxes. Finally, one patient underwent her initial surgery in Hungary, having only moved to the UK in the last few years.

Figure 5.5 Details of obtaining operative records

The majority of participants had surgery carried out under the age of 4 (14/16), with 8/16 having initial surgery performed at less than 24 months of
age (see table 5.12). One subject had her surgery carried out in the late 1960s, four subjects in the 1970s, nine subjects in the 1980s, one subject in the 1990's and one woman in 2001. Four (4/16) women were documented as having clitoral removal, with a further eleven (11/16) having clitoral reduction procedures; of these eleven, six were documented as having "nerve sparing" procedures; three specified "glans preservation"; one reported "partial reduction" but the original operation note was unavailable, and one did not comment on the dorsal neurovascular bundle. The final participant (1/16) had an operation described rather confusingly as a "total clitoridectomy with ventral ¼ glans preservation".

Figure 5.6 Details of clitoral operations

Ten of the women had vaginal surgery at the same time as their clitoral operation, which in nine cases was a posterior flap vaginoplasty (see figure 5.7). One woman (1/10) had a longitudinal incision made posteriorly, apparently in the style of a Fenton's procedure. One participant did not have vaginal surgery until puberty, and one had deferred her surgery until the age of 19 when she underwent a hysterectomy (after lengthy counselling) for dysmenorrhea. One subject did not require vaginal surgery initially, having been diagnosed at the age of 3. A further participant underwent clitoral removal and labial reconstruction in 1968 and no mention of definitive
vaginal surgery. One woman underwent clitoral reduction aged 1 month for severe virilisation (having been incorrectly assigned male initially), and had a vaginal pullthrough procedure performed aged 4.

**Figure 5.7 Details of vaginal operations**

16 women

- Vaginal surgery at time of clitoral procedure
  - 9 posterior flap vaginoplasty
  - 1 Fenton’s procedure
- 1 vaginal surgery deferred
  - 1 u flap vaginoplasty at puberty
  - 1 hysterectomy aged 19
  - 1 labial reconstruction + clitorectom
  - 1 pullthrough aged 4

Gynaecological and Psychosexual Outcomes of Feminising Genital Surgery
5.4 Discussion

5.4.1 Recruitment

The final attendance rate for the testing part of the study of 50% may be considered low by some standards. However, given the sensitive nature of the study, a rate of around 50% may be expected and compares with other research carried out in this area \(^{126}\). By having sensation testing carried out on the clitoris and vagina, the study is clearly intrusive and needs to be performed as sensitively as possible. Women with CAH are less likely to be sexually active when compared with age-matched peers, and are also likely to reach sexual milestones at a later age \(^{128}\). Given that they are also dealing with the side-effects of long-term corticosteroid medication, such as short stature, truncal obesity, striae, and acne, in a society which tends to favour height, a slim figure and clear skin, many women with CAH can be shy about any medical examinations, but especially those of the genital area. It may also remind them of unpleasant examinations as a child. When considering this, it is perhaps surprisingly that the recruitment is as high as 50%. In comparison with other long-term studies in the literature looking specifically at results of surgery, the attendance rate is favourable \(^{51}:72\). Furthermore, when considering absolute numbers, the recruitment of 28 women with 21-OH CAH into one study represents a large cohort in the context of intersex research.

5.4.2 Clitoral Sensation

This study is the first in the literature to utilise objective measures of sensation for both large myelinated and small unmyelinated fibres. Pilot data looking at the first six patients demonstrated a significant difference when compared with the normative values generated by Vardi et al \(^{119}\), and therefore was published in 2004 ahead of the main study results \(^{129}\). This generated debate in the literature, with recommendations for prospective follow-up data \(^{130}\). The results from the completed genital testing study show the clitoral sensation to be significantly worse following genitoplasty surgery. Those with CAH who did not undergo any operation had results comparable
with normal controls. One participant who had undergone a clitoral reduction operation was unaware of the sensation of warmth on the clitoris until the probe reached 50°C, which is far hotter than bath water. Another participant was unable to sense cold until nearly 20°C, which is colder than many swimming pools. This suggests significant damage which may have occurred to the neurology of the clitoris. Although those who underwent clitorectomy had poorer results it is interesting that no significant difference was observed when compared with those who had newer clitoral reduction procedures. It is likely that this included preservation of the dorsal neurovascular bundle, although this is only documented clearly in 6 notes. The term "glans sparing" may refer to preservation of the neurovascular bundle, particularly as these women underwent procedures in the early 1980s in a specialist centre at a time when preservation of the dorsal neurovascular bundle was becoming standard. However, it may only refer to the glans being preserved for appearance and division of the neurovascular bundle might still have occurred. This is not clearly stated in the notes. A significant difference was observed when comparing those who had undergone any type of clitoral surgery with those who had not, and with normal controls. This result therefore strongly supports the view that impaired sensation is caused by surgery, and not an inherent effect of CAH.

The majority of participants in this study underwent operations in the early 1980s. It is often stated that caution should be used in assessing the results of surgery carried out years ago often implying that there is no value in performing follow-up studies on women who underwent operations in the 1970s or 1980s. Yet this is disingenuous for several reasons. Firstly, many women did undergo operations at this time, and to have knowledge of their current difficulties with sexual function gives valuable information, for those women and for clinicians who can then advise further care. Secondly, the majority of clitoral procedures are based along the nerve-sparing approach as described by Mollard in 1981 \(^6\), which has become the basis of current practice, and certainly was widely employed after 1985. Thirdly, although many centres in the west offer nerve-sparing reduction techniques, this is by
no means universal\textsuperscript{62}. Clitorectomy is still performed as first-line treatment in some countries, as discussed in chapter 3. With the development of the internet, access to scientific knowledge is now available in many countries which previously may not have subscribed to journals. Therefore information about the longer-term outcomes of surgical approaches such as clitorectomy is still of value. Finally, outcome data on surgery performed in the 1990s simply will not be available for another 5-10 years at the earliest. The main aim of clitoral surgery is for cosmesis without sacrificing function. Clearly these outcomes cannot be known until the woman is postpubertal and sexually active. Without long-term data on operations in the 1970s and 1980s to serve as a comparison, it will not be apparent whether significant advances have truly been made. Data from this study suggests this is not the case.

It is possible that genital sensation is partly associated with hormone levels. It has been suggested that vulval sensation is reduced after the menopause, as a reflection of reduced oestrogen levels\textsuperscript{117}. However, all participants in this study were premenopausal making reduced oestrogen levels less likely to be a cause of diminished sensation. It is not known whether genital sensation changes significantly with the menstrual cycle. Many participants did not have a regular menstrual cycle as an effect of their CAH, reducing the likelihood of this variable leading to significant bias. Furthermore, a study looking at vibration sensation to the clitoris on premenopausal women did not show any variation with the menstrual cycle or with serum oestradiol levels\textsuperscript{131}. There is little information in the literature regarding genital sensation and testosterone levels, but that which is present suggests that low androgen levels are more likely to be associated with reduced sensation\textsuperscript{132}. Women with CAH are more likely to have high testosterone levels, particularly if steroid suppression levels are not adequately met.

5.4.3 Vaginal Sensation

The results for the vaginal measurements are interesting in two ways. Firstly, in the number of women who were unable to undergo the assessment due to
a narrowed vaginal introitus. Only 8/28 in the CAH group (28%) were able to perform the thermal tests using a probe of approximately 2.8cm diameter, and 2 of these had not undergone surgery, leaving only 6/24 of the surgical group completing the tests. One of the surgical group and one of the CAH non-surgical group chose not to do the vaginal tests as they had not been sexually active. At least 23 women had undergone definitive surgery that should have resulted in a functional vagina, yet less than 25% clearly did, echoing poor results following vaginal surgery seen in other studies ⁴⁹,⁶⁵. The second interesting finding was the lack of difference in results when compared with the normal controls. Only 4 of the 9 controls chose to undergo the thermal testing, making this a small cohort with which to compare. Five of the normal controls declined for a variety of reasons: one person had female partners and did not wish for any penetrative investigation. Another had problems with ongoing vaginal candidiasis. A further control participant was menstruating, and two others did not wish for any internal investigation. However, although only four controls participated this does make the different groups reasonably comparable in numbers. The clitoral results could be argued to show a difference in sensation due to some effect of CAH and chronic steroid use. Yet the vaginal values make this an unlikely scenario, by illustrating the similarity in sensation in the upper vagina between the groups.

5.4.4 Von Frey Sensation

It is interesting that no difference was seen between the CAH and non-CAH or surgery and non-surgery groups for first sensation to Von Frey filaments, yet a difference was seen once the surgery groups were subdivided. This is in contrast to the vibration results, where no difference was seen once the surgery groups were divided into clitorectomy and clitoral reduction groups. Sensation to light touch is carried in the same nerve fibres as vibration, therefore it would be expected to see a similar difference to that seen with the vibratory results. However, vibratory sensation may be transmitted to subcutaneous and internal clitoral fibres whereas von Frey sensory testing is purely external, and may be performed over scar tissue. Therefore for those
that have no external clitoral tissue, poorer results may be expected. Conversely, where external clitoral tissue is present, some preservation of sensation exists. For one of the subjects who did not have external clitoral tissue, the original operation was intended to be a clitoral reduction operation. Glans shrinkage and atrophy can occur post operatively leading to total necrosis and sloughing of the glans. These results suggest that sensation would be impaired by such a complication, and therefore case selection remains important in order to minimise this risk. Given that the Von Frey filament testing was only repeated sufficiently to be clear that sensation was truly felt (typically two to three times once sensation was registered), it is likely that the vibration results are more accurate. In addition, no widely accepted reference ranges for Von Frey filaments to the clitoris exist. One study used 3 different fibres (0.068, 0.408 and 1.052g) to assess sensation to the clitoris in 8 women who had undergone reduction, and found no difference when comparing with normal controls. In contrast, Romanzi et al who argued that Von Frey filaments showed a difference in sensation over the vulva for certain patient groups. This thesis has not used Von Frey filaments to assess other areas on the vulva other than the clitoral glans, so it is not possible to conclude whether Von Frey filaments are able to detect a change in clitoral sensation. Further work could assess the clitoral hood and labia to see if those who have undergone surgery showed any difference in sensation.

5.4.5 Questionnaire

Opinions of patients are rare in the literature, except when associated with support groups. These have done much to raise the issues of patient concern with aspects of surgery, but some authors argue that such associations only represent the dissatisfied yet vocal minority. This data shows that surgery can cause damage to genital sensation, yet the majority of women that took part did not express strong opinions about their previous treatment (see appendix 1 for questionnaire).

The general view was that surgery was a good idea, that genital surgery should be performed in childhood, and that parents should be responsible for
making the decision for surgery. When asked to respond to the statement “I would be angry if I had/have had surgery as a baby”, the most common response was strongly in disagreement, although a wide range of answers was given. This indicates that although some were unhappy with childhood surgery, many respondents were not. However, when asked the converse view “I would be relieved if I had/have had surgery as a baby”, respondents were less sure, with the most common response being neutral. This may reflect that surgery was often performed before the individual was aware of any differences in the genital area, so was unclear why they should “be relieved”. Similarly, when asked to respond to the statement “Only the patient should make a decision for surgery”, the response was in the “not sure” zone. These paradoxical views seem to suggest that women accepted having undergone childhood surgery and therefore the decisions made by their parents, and also felt neutral about taking their own decisions about treatment.

Participants indicated it was important for the area to look completely female, and they thought a lot about the appearance of the genital area. This may be because the appearance did not fit with their own view of an acceptable outcome.

When considering whether genital surgery caused difficulties with intercourse the answer was neutral. A definition of “sex” was deliberately not given, but it may be that as many women had not been sexually active with a partner, they did not feel able to give an answer one way or another.
Two questions were posed asking when the ideal age for genital surgery would be:

At what age should clitoral surgery be carried out?
Please tick one box only

- □ Less than 1 year
- □ 1-5
- □ 5-10
- □ 10-13
- □ 14-18
- □ over 18
- □ whenever the parents choose
- □ whenever the patient requests

The most commonly given response was "whenever the patient requests". This is slightly at odds with the response to whether "only the patient should make the decision for surgery" which was neutral. Yet conversely when given a scenario of a child with CAH:

What would you advise the parents of a two month old girl with CAH with a large clitoris considering surgery to make the clitoris look smaller?

- □ To have an operation at this time
- □ To have the operation as a child
- □ To have an operation after puberty
- □ To put off the operation until she can give an opinion
- □ To put off the operation indefinitely
- □ Other thoughts

The majority of respondents would advise the parents to opt for surgery as a child. This may simply reflect the treatment which they themselves had undergone. Alternatively, it may be that in an ideal world, women felt they should make their own decisions, but in practice, all operations needed to be carried out in childhood, therefore passing responsibility back to the parents.

The views expressed by patients showed that the majority were not overly critical of past surgical treatments, further validating the sensation test.
results. If most women were upset about previous childhood operations it could be argued they may wish to have poor results in the sensation testing to prove a point. However, as the majority of women were content with past treatments, there would be no apparent advantage in poor test results.

5.5 Conclusions
These results show that sensation to the clitoris is markedly impaired in those who have undergone genital surgery. There is no obvious difference between clitorectomy and clitoral reduction techniques although the numbers in the groups are small. A significant difference, however, is observed when either group is compared with those who did not have operations and with the normal control group. Furthermore when sensation is measured for the upper vagina, where surgery did not take place, there is no difference between those who underwent surgery and normal controls. It is unlikely that this cohort of women with CAH represent a disenchanted group who are dissatisfied with their treatment; although a wish was expressed for the patient to be involved in treatment options, they would still advise parents to choose surgery in childhood for their affected child. This therefore makes such results particularly significant. Chapter 6 goes on to address the psychological and psychosexual outcomes of this group of women.
Table 5.12 Details of operations undergone by participants in study

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age at diagnosis</th>
<th>Age at first operation</th>
<th>Year of first operation</th>
<th>First operation</th>
<th>Outcome</th>
<th>Subsequent operation (age) [year]</th>
<th>Notes</th>
<th>Clitoral results ( t )</th>
<th>Vaginal results ( t )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(38.80 °C)</td>
<td>(41.65 °C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(33.36 °C)</td>
<td>(28.48 °C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2.23 μm)</td>
<td>(12.62 μm)</td>
</tr>
<tr>
<td>4</td>
<td>Birth</td>
<td>13 months</td>
<td>1981</td>
<td>Clitoral reduction (nerve sparing) and vaginoplasty</td>
<td>Enlarged clitoris and vaginal stenosis</td>
<td>Clitoral reduction (nerve sparing) and u-v vaginoplasty (15) [1996]</td>
<td>Radical revision genitoplasty required.</td>
<td>40.2</td>
<td>31.6</td>
</tr>
<tr>
<td>5</td>
<td>Birth</td>
<td>8 months</td>
<td>1982</td>
<td>Clitoral reduction and u flap vaginoplasty</td>
<td>Prominent clitoris</td>
<td>Clitoral reduction and vaginoplasty 970 [1988]</td>
<td>Assessed aged 15 – glans enlarged but not shaft</td>
<td>42.8</td>
<td>24.7</td>
</tr>
<tr>
<td>9</td>
<td>Birth</td>
<td>2 ½ years</td>
<td>1983</td>
<td>Partial reduction (no operation note)</td>
<td>UG sinus, large clitoris</td>
<td>Glans separated grafted onto (reduced) stump. U-V vaginoplasty. (14) [1995]</td>
<td>Good result- no further surgery required (17) [1998]</td>
<td>38.3</td>
<td>30.7</td>
</tr>
<tr>
<td>10</td>
<td>Birth</td>
<td>3 ¾ years</td>
<td>1972</td>
<td>Clitoral removal and opening of UG sinus</td>
<td>Not known</td>
<td>Further vaginal and labial surgery aged 10 [1978] and 13 [1981] – notes unavailable</td>
<td>Poor cosmetic outcome</td>
<td>43.8</td>
<td>20.5</td>
</tr>
</tbody>
</table>

§ Indicates subject number allocated for study for all CAH participants, including those who chose not to undergo sensation testing (n/32)\( t \) Normal upper limits of warmth, cold and vibration values in women under the age of 50 \(^{119}\). Numbers in bold are within normal published levels.

Gynaecological and Psychosexual Outcomes of Feminising Genital Surgery
<table>
<thead>
<tr>
<th></th>
<th>Birth</th>
<th>Age</th>
<th>Year</th>
<th>Type of Surgery</th>
<th>Outcome</th>
<th>Result</th>
<th>Age</th>
<th>Year</th>
<th>Type of Surgery</th>
<th>Outcome</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>15 years</td>
<td>16 years</td>
<td>2001</td>
<td>Clitoral reduction (nerve sparing) with u flap vaginoplasty</td>
<td>Good external result – small glans and clitoris</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>46.1</td>
<td>25.5</td>
</tr>
<tr>
<td>13</td>
<td>Birth</td>
<td>2 years</td>
<td>1974</td>
<td>Clitoral removal with u-v vaginoplasty</td>
<td>No vagina seen externally aged 13 [1985]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>45.0</td>
<td>26.9</td>
</tr>
<tr>
<td>14</td>
<td>Birth</td>
<td>11 months</td>
<td>1983</td>
<td>Clitoral reduction (nerve sparing) with flap u-v vaginoplasty</td>
<td>Highly scarred introitus aged 19 [2001]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>42.2</td>
<td>27.7</td>
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<tr>
<td>15</td>
<td>Birth</td>
<td>3 months</td>
<td>1974</td>
<td>?Clitoral removal (no operation note)</td>
<td>Williams vaginoplasty and hysterectomy 21 [1992]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>47.7</td>
<td>30.2</td>
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<tr>
<td>17</td>
<td>Birth</td>
<td>15 months</td>
<td>1984</td>
<td>Clitoral reduction with glans preservation, with opening of UG sinus (no operation note)</td>
<td>Painful erectile lump in vulva. Vaginal stenosis</td>
<td>Ileovaginoplasty 9 [1993], clitoroplasty and lump removal 9 [1993]</td>
<td></td>
<td></td>
<td></td>
<td>44.9</td>
<td>29.9</td>
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<tr>
<td>18</td>
<td>3 years</td>
<td>4 years</td>
<td>1984</td>
<td>Clitoral reduction with glans preservation (no operation note)</td>
<td>No clitoral tissue present</td>
<td>Fenton procedure 22 [2001]</td>
<td></td>
<td></td>
<td></td>
<td>49.6</td>
<td>20.1</td>
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</tbody>
</table>

Gynaecological and Psychosexual Outcomes of Feminising Genital Surgery
<table>
<thead>
<tr>
<th>No.</th>
<th>Birth</th>
<th>Age</th>
<th>Year</th>
<th>Operation Details</th>
<th>Stage</th>
<th>Age</th>
<th>Year</th>
<th>Details</th>
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</thead>
<tbody>
<tr>
<td>22</td>
<td>Birth</td>
<td>1 year</td>
<td>1982</td>
<td>Clitoral reduction (nerve sparing) with u-v vaginoplasty</td>
<td></td>
<td></td>
<td></td>
<td>Bifid scarred clitoris, rugose labia, vaginal stricture 16 [1997]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Scar tissue excised with clitoral reconstruction, u flap vaginoplasty 16 [1998]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Birth</td>
<td>10 months</td>
<td>1984</td>
<td>Clitoral reduction (nerve sparing) with u-v vaginoplasty</td>
<td></td>
<td></td>
<td></td>
<td>Very prominent clitoris 14 [1997]</td>
</tr>
<tr>
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<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>27</td>
<td>Birth</td>
<td>3 ½ years</td>
<td>1968</td>
<td>Clitoral removal and labial construction</td>
<td></td>
<td></td>
<td></td>
<td>Needs vaginoplasty</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>Birth</td>
<td>1 month</td>
<td>1982</td>
<td>Clitoral reduction (nerve sparing) and labial reconstruction</td>
<td></td>
<td></td>
<td></td>
<td>Further perineal pullthrough with abdominal mobilisation 4 [1986]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>High take-off vagina. Further u flap vaginoplasty 14 [1997]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Requires further surgery to excise buried erectile tissue in vulva</td>
</tr>
<tr>
<td>30</td>
<td>Birth</td>
<td>20 months</td>
<td>1974</td>
<td>Total clitoridectomy with ventral ⅓ glans preservation. Posterior flap vaginoplasty</td>
<td></td>
<td></td>
<td></td>
<td>Correction of urinary fistula 10 [1984]</td>
</tr>
</tbody>
</table>
Chapter 6

Psychosexual outcomes of women with CAH

6.1 Background

Theories about sexual development are controversial. It is generally accepted that parental and social influences are important; in addition the hormonal environment during fetal development may be implicated. Higher levels of testosterone have been shown to be associated with more typically masculine behaviour such as rough and tumble play in childhood, and has been suggested to lead to preferring female sexual partners later on. Women with CAH represent a group who have been exposed to higher levels of androgenic hormones in utero onwards, despite subsequent suppressive therapy, compared with other women. Psychologists and sociologists have attempted to assess differences in psychosexual development in childhood and as adults, especially in the following areas: childhood play behaviour, gender identity and sexual behaviour.

6.1.1 Juvenile play

Androgens are responsible for external genital development in utero, as discussed in chapter 1. They are also thought to be involved in early brain development, and particularly in areas which are involved in behaviour. Therefore, it is theorised that girls born with ambiguous genitalia may also behave in ways that are more typical for boys due to virilisation of the brain. As experiments involved in giving hormones to pregnant women would almost certainly be unethical, women born with CAH provide an excellent group to study the effects of prenatal androgens on subsequent gender characteristics. One mode of assessment is to observe the play behaviour exhibited by girls with CAH. Female-type play behaviour would include choosing dolls rather than cars, seeking female friends rather than male, whereas male behaviour includes a preference for rough-and-tumble play. Studies have shown that girls with CAH are likely to show more male-type play behaviour than unaffected girls, but not to the same degree as unaffected boys. It is argued
that these differences are due to brain virilisation, but it is possible that this is secondary to genital virilisation, and subsequent influence and reinforcement by peers and parents. It is thought that, despite parental belief to the contrary, boys and girls are reared differently\(^\text{134}\). Therefore, knowing whether a child is being reared female or male may lead to reinforcement or discouragement of certain behaviours as deemed appropriate.

6.1.2 Gender identity

The term gender identity refers to whether an individual feels they belong to a male or female gender. The majority of women with CAH seem to develop a female gender identity, despite genital virilisation. Berenbaum and co-workers assessed the gender identity of 43 girls with CAH using a questionnaire, and found that although the average scores were in between those of normal females and males, nearly 90% had results overlapping the unaffected female scores\(^\text{135}\). They concluded that gender identity does not solely depend on genital appearance, or the age at which corrective surgery was performed. Zucker et al conducted a study of 53 adult women with CAH, and found 3 were living in the male role\(^\text{136}\). However, 2 of these were initially assigned male at birth, and kept this role on diagnosis. The other participant chose to change to the male role during adolescence. The remaining 50 women were happy with a female gender identity. Money described 3 patients raised as male who developed male gender identities and successfully lived the male role, choosing to be sexually active with female partners\(^\text{137}\), whilst 4 other patients with a similar degree of virilisation were reared female, and reportedly developed female gender identities. Therefore, although the majority of women with CAH have a female gender identity, where a child is reared male, a male gender identity does seem to develop.

6.1.3 Sexual experiences and orientation

It has been argued that women with CAH are more likely to have a homosexual orientation than the normal female population. However, different studies have yielded different results. In 1984 Money studied 30 women with
CAH and of the 23 women who were prepared to indicate their orientation, almost 50% identified themselves as homosexual or bisexual. A control group consisting of 15 women with AIS and 12 women with Rokitansky syndrome only had 2 (7%) women who identified themselves as bisexual, although the background rates of same-sex orientation are not known for either of these conditions. Dittmann et al studied 34 women with CAH and compared them with 14 control sisters, and found that 20% of patients had experienced or desired same-sex relationships, whilst none of the control group expressed this wish. However, these findings are not consistent. Later work in 1996 suggested that CAH women did not have any more sexual experiences in same-sex relationships than peers. Kuhnle et al in 1997 studied 45 women with CAH and compared with 46 controls and found that women with CAH experienced social and sexual milestones later than age-matched controls, but did not show any increased preference for same-sex relationships.

When considering sexual experiences, May et al compared a group of CAH women with a group of diabetic women, arguing that both groups had grown up with a chronic condition, necessitating regular hospital attendances, and therefore were comparable. The CAH group were found to be less sexually experienced and have expressed a lower level of sexual interest than the diabetic group.

6.1.4 Sexual function

When comparing CAH women with diabetic women, May found that the women with CAH had specific sexual function difficulties with penetration, pain during intercourse, and orgasm. Yet, there is little information about the impact of genital surgery on sexual function and development. Berenbaum et al considered the timing of genital surgery and effect on subsequent gender identity and concluded there was no relationship between gender identity and timing of surgery, or of degree of virilisation. This article was published from the psychology department, with little input from surgeons, therefore giving limited information about other clinical considerations. There are few studies
in the literature assessing both clinical and psychological aspects of genital surgery for CAH.

6.2 Study design
Various study designs were considered in order to assess psychological aspects of CAH and having undergone genital surgery (or not) in childhood. A semi-structured interview would yield good information and allow the participants to raise topics of interest to themselves. This may bring up new areas of concern which had not previously been highlighted, and enable the interviewer to investigate new material. However, it would be difficult to quantify the data in ways that enable comparisons, and to validate the interview questions used. In addition, the nature of the topic may inhibit responses when in a face-to-face setting. Few individuals would be completely comfortable discussing aspects of sexual function, and even less so, if the answers were self-perceived as being different to the norm. A semi-structured interview may take longer than completing a questionnaire, and may require interim analysis in order to draw out common themes. Thematic analysis can be complex and ideally should be undertaken by experienced researchers. Care needs to be taken in conducting the interview to avoid leading the study subject, and can lead to problems with reliability.

A questionnaire study was considered to examine multiple psychological outcomes. It enables participants to answer only those sections they feel comfortable with, without feeling obligated to an interviewer. The questionnaires selected (as discussed below) could be validated and applicable to the chosen population. It also is consistent and reliable in asking every participant the same questions. Questionnaires may be offered at a clinic visit, but for the purposes of this study a postal questionnaire was chosen. Although this can risk reducing the completion rate, it was felt more appropriate given the sensitive topics involved. Participants might find it intrusive to be approached in a busy waiting room, or they could feel inhibited to work in the same room as a study investigator. A stamped addressed envelope was enclosed in order to maximise the response rate, along with a
letter from the study investigator to explain the relevance of the information requested.  

6.2.1 Questionnaire Structure

The whole questionnaire had several goals. It had to be reasonably quick to complete, yet give good amounts of information. The language needed to be simple to understand and the questionnaire clear to complete. Therefore it was not possible to ask about all aspects of living with CAH, but rather, needed to be targeted at specifics. For this reason and for methodological issues (e.g. validity) relating to retrospective psychological data, subjects were not specifically asked about play behaviour or childhood experiences in the past.

General details regarding medical and surgery background needed to be elicited in order to compare data, with particular emphasis on different operations that women may have undergone. As discussed earlier, some studies have shown that women with CAH reach sexual milestones later than peers, and may be more likely to choose female partners than the general population. Therefore, some assessment of sexual orientation and experience would be valuable to include in the questionnaire. Several aspects of sexual function were of particular interest as many clinically based studies assessing childhood surgery are carried out whilst subjects are still children, so clearly information regarding sexual function is limited. Previous research has shown that those who have undergone clitoral surgery have significantly increased levels of sexual function difficulties, and especially with orgasm. Therefore, measuring different aspects of sexual function, including orgasm would be important. A significant number of study participants did not have a current sexual partner, and some had never been sexually active with a partner, which needed to be taken into consideration when selecting questionnaires. Sexual function may be dependent on general psychological health, and some measure of wellbeing would be needed in order to interpret the results. In addition, women with CAH have endured a lifetime of monitoring and regular hospital attendances, and possibly hospital
admissions. Those with a chronic disease state may have a predisposition towards depression, and some tool to assess this would be of value. Gender identity may be connected with sexual function and quality of life, and some assessment of whether participants felt happy living a female role would be useful when considering the long-term outcomes of CAH treatment. Finally, the opportunity to review case notes would be invaluable, in order to assess the particular types of operations performed, and also to see how much individuals understood about their past medical history. Participants were all asked for their permission for access to their medical records, and were advised that all information would be discussed with them if they chose.

No individual questionnaire could fulfil all of these goals, so the most suitable structure was deemed to be a combination of general background information, and of validated tools. The whole questionnaire consisted of 10 sections, and individuals were asked to complete as much or as little of it as they felt comfortable with. Completion of the questionnaire represented consent. Several parts had the opportunity for free script to allow participants to elaborate if they wished. All women were sent or given a covering letter explaining the aim of the research and the nature of the questionnaire. They were advised to stop completing the questionnaire if any of the questionnaires caused offence or upset. They were also informed that taking part, or declining to participate had no effect on subsequent medical care, and that participation remained separate and completely confidential. Further details about each section are given below, and the whole questionnaire is given in appendix 2.

**Section 1: About You**
Participants were asked to give their age, their ethnic background, and to indicate if they were members of any support groups.

**Section 2: Diagnosis**
The type of CAH was recorded (i.e. "salt-wasting" etc), along with details of how the diagnosis was originally made, and at what age. Subjects were asked
to indicate if they had suffered any condition which may impair genital sensation, such as multiple sclerosis, depression, or diabetes.

Section 3: Surgery and Treatment
Medical treatment of CAH was recorded, followed by questions about surgical history, including type of operation, age at which they were performed. Individuals were also asked for their thoughts on the appearance of the genital area, and satisfaction with sensation, or any difficulties they had experienced since any operations. Participants were asked to record if they had a sexual partner, and to note any opinions regarding genital appearance given by their partner. General questions about urinary function were included in this section.

Section 4: Sexual Function
This section assessed sexual function, and used the Golombok Rust Inventory of Sexual Satisfaction (GRISS) to score responses. The GRISS consists of 28 questions referring to the frequency of sexual interests and activities on a five point scale from “never” to “always”. A global score is calculated to give an overall indication about general sexual function, and a score greater than 38 indicates general sexual function difficulties. In addition, the questions divide into seven subsets of Frequency, Communication, Sensuality, Vaginal Penetration Difficulties, Satisfaction, Avoidance and Orgasm. A score may be calculated for each, and a value greater than 5 in any area can indicate a particular difficulty. The GRISS was validated on 88 heterosexual couples in the UK who were receiving sex therapy. The GRISS can either be applied as a one-off assessment, or may be used over time to indicate a change in any particular areas. As the validation only occurred with heterosexual couples, in this study participants were asked to indicate if their current or most recent relationship was with a female partner. In addition, the GRISS was only suitable for those who had a current or previous sexual partner.

Section 5: Sexual Function
Section 5 also assessed sexual function using the Brief Index of Sexual Function for Women (BISF-W). This consists of 22 questions covering the
main areas of sexual desire, arousal, orgasm and satisfaction. Three areas are scored, for sexual desire, sexual activity, and sexual satisfaction. Importantly it also has an element assessing desire and fantasy, allowing those without a partner to respond, in contrast to some aspects of the GRISS. Questions were also asked on sexual orientation, comparing this with previous sexual experience, and whether the respondent has a current partner. Additionally, one question gives a measure of body image by asking about general satisfaction with the appearance of their body. The BISF-W was validated on 269 women in the United States, and consistency and reliability determined by repeated administration of the questionnaire.

Section 6: Hospital Anxiety
General anxiety and depression levels may be higher in those with a chronic condition, and the Hospital Anxiety and Depression Scale was used to assess levels of global psychological distress. This comprises 14 questions in total, with alternate questions relating to anxiety or depression. Each question has a statement and respondents are asked to indicate on a scale how like them this is. It is quick to complete, and was validated on 50 UK patients. Good separation of anxiety and depression symptoms was shown when originally tested on a sample group. Each question is scored from 0 to 3 with a higher score indicating a greater level of the symptom. A separate score is produced each for anxiety and for depression.

Section 7: Personal Identity
Mechanisms for the development of gender identity remain poorly understood, but hormones are thought to play a part. Therefore, with the exposure to higher than normal androgen levels in utero, women with CAH may develop more a male gender identity than would be expected. This questionnaire consisted of 12 statements, asking whether an individual would choose to be male or female, over the last 12 months, and over the whole of their life. The topic of gender identity can be a sensitive area for those born with ambiguous genitalia, and for the purposes of a postal questionnaire, the section was entitled “personal identity”.
Section 8: General Health Questions
As a general measure of psychological distress the General Health Questionnaire (GHQ) was included in the main questionnaire. This is a smaller version of the widely used GHQ\(^{146}\), and has 12 questions. Half of these pertain to health and the other half to illness. The GHQ has been validated in over 90 countries, and used in many different languages. This gives a general impression about background psychological health at the time of survey, and takes a few minutes to complete.

Section 9: Permission to obtain previous hospital notes
All participants were asked for permission to obtain previous hospital notes. In keeping with previous management, many patients were not aware, or at the very least, unclear about their previous surgical treatment. Therefore, accessing records pertaining to the original operations performed would give information about the type of genital surgery performed, and also allow an opportunity for the individual to receive feedback about their medical background, if they chose to do so. Equally, by not completing this section, participants were able to choose to remain anonymous whilst still providing valuable information for the study.

Section 10: Any comments
The last section on the questionnaire thanked all participants for taking part, and invited any comments. This could relate directly to the questions they had been asked, or more generally about different aspects of living with CAH.

Normal Controls
The questionnaire was slightly amended for normal controls, by omitting detailed questions on clitoral and vaginal surgery, and asking additionally about number and mode of delivery of any children. Sections 4 to 8 were otherwise identical.

6.3 Results
56 women in total were invited to take part in the study, and are the same cohort as discussed in chapter 5 (see figure 6.1). Details of 39 were obtained from a database of women with CAH under the care of the Middlesex Centre,
or under the care of a tertiary referral endocrinology clinic. These 39 women were sent two invitations in the post at the start of the project offering the opportunity to discuss the study further before agreeing to take part. The remaining 17 women were seen in person at either of the clinics. All participants were advised they could take part in one part only of the study (for example, completing just the questionnaire) if they chose. Of the original group of 39 women, 24 agreed to take part (63%). One subsequently declined, citing work pressures, and a total of 19 questionnaires were returned (19/39, 49%). Of the 17 women seen in clinic, 16 agreed to participate (94%). 13 questionnaires were returned from this group (13/16, 81%). In total, 32 questionnaires were received, from 56 invited participants (57%) (see figure 6.1).
Figure 6.1 Breakdown of recruitment into Questionnaire part of study

All normal controls who took part in the sensation testing were invited to complete the questionnaire. In addition, one participant who was not free to attend for testing completed the questionnaire, leading to 10 controls taking part. Some participants chose only to complete certain sections of the questionnaire, and the number of respondents therefore varies for each section.

6.3.1 Questionnaire Analysis and Results

32 questionnaires were received from the CAH group. 10 normal controls completed the questionnaire. All questionnaires were scored by the study investigator, who was blinded to the identity of individuals and sensation.
testing results, but not to CAH versus normal control status which was apparent from the questionnaires. As advised in the study information leaflet, respondents were free to ignore questions if they chose to. Therefore, the subject numbers vary slightly between questions, as indicated in the text. The results for each section are given below.

Section 1: About you
Participants were aged between 17 and 39, with a mean age of 25.3. The majority of (28/32) self-classified as white, with 1 black-african and 2 asian participants. One subject self-identified as Mediterranean. The majority of patients did not belong to a support group (25/31). One chose not to reply, and six were members of the CAH Support group.

Normal controls had a mean age of 25.3, with a range of 23-38. The mean ages of the two groups were comparable with no significant difference (p value 0.02).

Section 2: Diagnosis
25 patients stated their diagnosis as “CAH-salt-losing”. Four noted they had non-salt losing CAH, and 3 recorded themselves as late-diagnosis CAH. 25 patients were first brought to the attention of doctors at birth, either due to illness and/or genital ambiguity. The remainder (7/32) presented in adolescence due to one or more of amenorrhoea, difficulties with puberty or hirsuitism. 12 patients had a history of anxiety or depression, and 4 were still taking antidepressant medication. 2 patients had previous difficulties with lower back ache, although neither were undergoing active investigations at the time of questionnaire completion.

Section 3: Surgery and Treatment
All respondents except one were taking some form of steroid replacement, in the form of hydrocortisone or prednisolone, and some with additional fludrocortisone. 29 patients had undergone some form of surgery. Two respondents underwent surgery but did not indicate details. For the 27 patients where details were given 13/27 patients had procedures carried out
on the vagina and clitoris. 9/27 patients underwent operations to the clitoris only, with 4/27 having vaginal surgery only. One patient (1/27) with late-diagnosis CAH had a laparoscopy at the time of her diagnosis (aged 15), but no vaginal or clitoral surgery. Three patients did not have any surgery; two of these had late-diagnosis CAH with no noted genital changes, and one had non-salt losing CAH. This last respondent chose to remain anonymous, so further details are unclear.

Table 6.1 Self-reported surgical history: results for "Have you had any surgery related to your condition?"

<table>
<thead>
<tr>
<th>Numbers (n = 29)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clitoral Surgery</td>
<td>9 (31%)</td>
</tr>
<tr>
<td>Vaginal Surgery only</td>
<td>4 (14%)</td>
</tr>
<tr>
<td>Clitoral and Vaginal surgery</td>
<td>13 (45%)</td>
</tr>
</tbody>
</table>

Section 3: Surgery and Treatment; Results of Vaginal Surgery
Several participants responded to the questions regarding vaginal surgery, yet did not indicate they had actually undergone vaginal operations. As some respondents were anonymous, this discrepancy was difficult to resolve. Therefore results are presented as reported by study participants and no responses have been excluded.

When asked to rate the results of vaginal surgery from “1 = totally unsatisfied” to “5 = totally satisfied”, eight patients out of 23 (34%) who responded said they were mostly or totally unsatisfied. However, a further 8 patients stated they were mostly or totally satisfied, and the median response was 3. When asked about any complications following vaginal surgery, 20 respondents indicated they had experienced at least one complication, with several giving more than one response. Four of these (4/20) had not previously given a history of vaginal surgery in earlier questions (see table 6.2). Twelve complained the vagina was too small for intercourse or narrow, with four having experienced complete closure of the vagina, rendering penetrative intercourse impossible. Six patients stated they had problems with lack of
lubrication during intercourse. Seven had also experienced problems with urinary tract infections or urinary symptoms. One patient had also developed a fistula, although had undergone surgical correction, and was currently asymptomatic.

The use of vaginal dilators had been discussed with 20 patients, with a further 11 indicating the subject had not been raised. Dilators were mostly suggested for post-operative therapy (11/20), although one patient was advised about their use pre- and post-surgery. Five patients were informed about dilators as an alternative to surgery, with two of these also advised to use dilators before and after any surgery they may choose to undergo. When asked about their opinion of the vagina post-surgery, six responded that it was “ok”. However, 11 stated they thought the vagina was too small or narrow, with a further four saying it was “tiny”. Ten participants felt a partner would notice it was different from other women, with ten women wanting the vagina to be bigger, longer or wider.

Table 6.2 Complications experienced following vaginal surgery

<table>
<thead>
<tr>
<th>Complication*</th>
<th>Numbers$\textsuperscript{§} (n = 20 respondents to question, although only 16 previously reported vaginal surgery)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Problems</td>
<td>2 (although neither reported vaginal surgery)</td>
</tr>
<tr>
<td>Persistent Discharge</td>
<td>2</td>
</tr>
<tr>
<td>Narrowing of the vagina</td>
<td>12</td>
</tr>
<tr>
<td>Complete Closure</td>
<td>4</td>
</tr>
<tr>
<td>Recurrent UTIs or leaking of urine</td>
<td>7 (1 did not report vaginal surgery)</td>
</tr>
<tr>
<td>Fistula</td>
<td>1</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>2</td>
</tr>
<tr>
<td>Intercourse difficulty due the vagina seeming too small</td>
<td>6 (1 did not report vaginal surgery)</td>
</tr>
<tr>
<td>Intercourse difficulty due to a lack of lubrication</td>
<td>6 (1 did not report vaginal surgery)</td>
</tr>
</tbody>
</table>

*As reported by participant

$\textsuperscript{§}Where 4/20 had not previously reported a history of vaginal surgery. Some respondents reported more than one complication
Section 3: Surgery and Treatment; Clitoral Surgery Results

Again, when asked separately about surgery to the clitoris, eight women (8/32) indicated they had never undergone clitoral surgery. This is at odds with the answers given earlier when asked about history of surgery (see table 6.1), where only 22 women indicated they had undergone clitoral procedures. Of the eight women who had not had clitoral surgery three (3/8) chose to remain anonymous, but of the remaining five, four had late-diagnosis CAH, and one had the salt-losing variant: further assessment of her operative notes showed she did undergo "glans sparing" clitoral surgery as an infant. Whether she was unaware of this fact or did not understand the question is unclear.

Of the 24 who stated they had undergone clitoral surgery, the majority (22/24) registered having undergone reduction procedures, with only two reporting clitoral removal. Only three women indicated they had undergone more than one operation to the clitoris. Of the 24 participants who gave a history of surgery, 2 chose to remain anonymous and therefore operation notes could not be traced or details verified. Operative details were obtained for 15/22, and showed that 10/15 had undergone at least two genital operations, with 7/15 undergoing two or more specific clitoral procedures. When all 24 patients were asked about their opinion on the appearance of the clitoris, rated from 1 = totally unsatisfied to 5 = totally satisfied, the median response was 3. Nine patients had rated the appearance at 1 or 2, but 11 were happier, rating 4 or 5, indicating they were mostly or completely satisfied with the appearance. Participants were then asked about the sensitivity of the clitoris using the same rating scale (see figure 6.2). The median response was 2, with 11 respondents rating 1 or 2, compared with only 5 rating 4 or 5.
Complications following clitoral surgery were reported by 13/24 women, with some women indicating more than one complication. Eight experienced difficulties with decreased sensation. Seven women indicated difficulties with orgasm, and 5 recorded clitoral pain as a complication. Three women experienced urinary difficulties following their surgery.

Table 6.3 Complications experienced following clitoral surgery

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number (Clitoral surgery n = 24, with complications for 13/24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections in the genital area</td>
<td>0</td>
</tr>
<tr>
<td>Pain during intercourse</td>
<td>5 (20%)</td>
</tr>
<tr>
<td>Leaking of urine</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Lack of sensation</td>
<td>8 (33%)</td>
</tr>
<tr>
<td>Difficulties with orgasm</td>
<td>7 (29%)</td>
</tr>
</tbody>
</table>

28 women responded when asked specifically about what they thought about their clitoris. Eight women thought their clitoris was “normal” or had no opinion (8/28). One wrote “It's a mess!”. Eleven women complained of lack of
sensation. Seven women felt their clitoris was too large, but the most common concern was that a partner would notice it was different from other women (12/28). Thirty women responded to the question regarding clitoral pain, with just over half (16/30) indicating they had never experienced this symptom. Five respondents were not sure, with one woman experiencing this very occasionally, four occasionally, and four women often experiencing clitoral pain, either when aroused or at other times. Of note, one of these four women had undergone a clitoral removal operation in the early 1970's, with the other three having clitoral reduction procedures either in the mid 1980's or early 1990's. Ten women (10/32) had a current partner, with eight out of nine responses indicating that their partner had never commented about the genital area, or that it made no difference. One respondent indicated that their partner thought there was a difference when compared with other women, but that it was not important. 29 women answered the question about overall genital appearance, with 12 indicating they felt the appearance was fine, or they were happy with it. Four had no opinion, although five were unhappy, with three hating their genital appearance. Ten respondents felt that partners would notice there was a difference when compared with other women.

Section 4: The GRISS questionnaire
19 subjects and all 10 normal controls completed the GRISS questionnaire, representing those who had been sexually active either with a current or previous partner. A raw score was calculated showing global sexual function difficulties, as seen in figure 6.3. A score of 5 or more in any of the subsets indicates a problem in that area, as shown in figure 6.4.
Figure 6.3 Global Sexual function difficulties comparing CAH with controls

Figure 6.4 Sexual Function subsets comparing CAH with controls, where a value greater than 5 indicates a difficulty in that area.

The sexual function scores for women with CAH and women without CAH (normal controls) were calculated and the Mann-Whitney U test applied to assess any differences (table 6.4).
Table 6.4 Sexual function scores for CAH vs normal controls

<table>
<thead>
<tr>
<th></th>
<th>Normal Controls n=10</th>
<th>CAH n=19</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median score* (range)</td>
<td>Median Score* (range)</td>
<td></td>
</tr>
<tr>
<td>Global Score</td>
<td>2 (1-4)</td>
<td>5 (1-9)</td>
<td>0.004</td>
</tr>
<tr>
<td>Infrequency of Intercourse</td>
<td>5 (1-7)</td>
<td>8 (1-9)</td>
<td>0.010</td>
</tr>
<tr>
<td>Non-Communication</td>
<td>5 (3-7)</td>
<td>4 (1-9)</td>
<td>0.907</td>
</tr>
<tr>
<td>Dissatisfaction</td>
<td>3 (1-4)</td>
<td>4 (1-9)</td>
<td>0.034</td>
</tr>
<tr>
<td>Avoidance</td>
<td>2 (1-7)</td>
<td>6 (1-9)</td>
<td>0.010</td>
</tr>
<tr>
<td>Non-sensuality</td>
<td>2 (1-6)</td>
<td>5 (1-9)</td>
<td>0.034</td>
</tr>
<tr>
<td>Vaginal penetration</td>
<td>1 (1-2)</td>
<td>5 (1-9)</td>
<td>0.003</td>
</tr>
<tr>
<td>difficulties</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anorgasmia</td>
<td>3 (2-9)</td>
<td>6 (3-9)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

†Mann-Whitney U test

*Score of 1 to 9, where a score greater or equal to 5 indicates a difficulty

All values except one showed a significant difference between the two groups, with the CAH group scoring higher (i.e. more sexual function difficulties) than the normal controls. No difference was observed for non-communication within a relationship.

The groups were then divided into those who had undergone surgery, and those who had never had genital surgery. This second group consisted of the 10 normal controls, with 3 women with CAH who had not had surgery. Table 6.5 shows the differences observed, with figure 6.5 illustrating Vaginal Penetration Difficulty and Anorgasmia scores.
Table 6.5 Sexual function scores for surgery vs non-surgery participants, with p value

<table>
<thead>
<tr>
<th></th>
<th>Non-surgery n=13</th>
<th>Surgery n=15§</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median score* (range)</td>
<td>Median Score* (range)</td>
<td></td>
</tr>
<tr>
<td>Global Score</td>
<td>2 (1-5)</td>
<td>5 (1-9)</td>
<td>0.006</td>
</tr>
<tr>
<td>Infrequency of Intercourse</td>
<td>5 (1-8)</td>
<td>8 (1-9)</td>
<td>0.007</td>
</tr>
<tr>
<td>Non-Communication</td>
<td>5 (2-7)</td>
<td>4 (1-9)</td>
<td>0.640</td>
</tr>
<tr>
<td>Dissatisfaction</td>
<td>3 (1-5)</td>
<td>4 (1-9)</td>
<td>0.045</td>
</tr>
<tr>
<td>Avoidance</td>
<td>3 (1-7)</td>
<td>6 (1-9)</td>
<td>0.029</td>
</tr>
<tr>
<td>Non-sensuality</td>
<td>2 (1-6)</td>
<td>5 (1-8)</td>
<td>0.068</td>
</tr>
<tr>
<td>Vaginal penetration difficulties</td>
<td>1 (1-2)</td>
<td>6 (1-9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anorgasmia</td>
<td>3 (2-9)</td>
<td>6 (3-9)</td>
<td>0.025</td>
</tr>
</tbody>
</table>

†Mann-Whitney U test
*Score of 1 to 9, where a score greater or equal to 5 indicates a difficulty
§1 respondent excluded as did not indicate a history of surgery

No difference is observed between the two groups for Communication difficulties. All other values show a significant difference, with sensuality problems approaching significance.
Mean response for Vaginal Penetration Difficulties

A score greater than 5 indicates a difficulty

Mean Score for Anorgasmia

Levels greater than 5 indicate difficulty

Figure 6.5 Differences observed in vaginal penetration difficulties between surgery (median 6) and non-surgery group (median 1), and for anorgasmia (median 6 and median 3 respectively).

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Finally, the groups were further divided into those with CAH who had undergone surgery, those with CAH who had not had surgery, and Normal Controls, as shown in table 6.6.

Table 6.6 Sexual Function Scores for Normal Controls, CAH no surgery and CAH with surgery

<table>
<thead>
<tr>
<th></th>
<th>Normal Controls (n=10)</th>
<th>CAH no surgery (n=3)</th>
<th>CAH with Surgery (n=15§)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global Score</strong></td>
<td>2 (1-4)</td>
<td>4 (1-5)</td>
<td>5 (1-9)</td>
<td>0.014</td>
</tr>
<tr>
<td><strong>Infrequency of Intercourse</strong></td>
<td>5 (1-7)</td>
<td>6 (3-8)</td>
<td>8 (1-9)</td>
<td>0.025</td>
</tr>
<tr>
<td><strong>Non-Communication</strong></td>
<td>5 (3-7)</td>
<td>5 (2-6)</td>
<td>4 (1-9)</td>
<td>0.896</td>
</tr>
<tr>
<td><strong>Dissatisfaction</strong></td>
<td>3 (1-4)</td>
<td>3 (2-5)</td>
<td>4 (1-9)</td>
<td>0.111</td>
</tr>
<tr>
<td><strong>Avoidance</strong></td>
<td>2 (1-7)</td>
<td>5 (4-7)</td>
<td>6 (1-9)</td>
<td>0.037</td>
</tr>
<tr>
<td><strong>Non-sensuality</strong></td>
<td>2 (1-6)</td>
<td>3 (2-6)</td>
<td>5 (1-8)</td>
<td>0.132</td>
</tr>
<tr>
<td><strong>Vaginal penetration difficulties</strong></td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
<td>6 (1-9)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Anorgasmia</strong></td>
<td>3 (2-9)</td>
<td>4 (3-6)</td>
<td>6 (3-9)</td>
<td>0.052</td>
</tr>
</tbody>
</table>

† Kruskal-Wallis test

*Score of 1 to 9, where a score greater or equal to 5 indicates a difficulty

§1 respondent excluded as did not indicate a history of surgery

A significant difference is still observed between the groups for global sexual functioning, infrequency of intercourse, avoidance, vaginal penetration difficulties and anorgasmia, with those who had undergone surgery having the poorer results. No difference is observed with dissatisfaction, or with non-sensuality. As with the previous groups, no difference is observed in communication within a relationship.

Section 5: The BISF-W questionnaire

32 CAH participants answered section 5, as did all 10 normal controls. The BISF-W questionnaire gave answers to 8 sections, depending on self-rating: sexual activity, sexual desire, sexual satisfaction, sexual activity in the last month, current sexual partner, orientation of past sexual experience, and
orientation of sexual fantasy, and general body image. No guidance is offered with the BISF-W as to what constitutes a difficulty in sexual function. Rather, the comparison of two groups should highlight any difficulty or difference in either group. Each section was analysed with the Mann-Whitney U test, and two groups analysed. Firstly, CAH participants were compared with normal controls (table 6.7), followed by those who had undergone surgery, compared with those who had not (CAH non-surgery and normal controls) (table 6.8).

Table 6.7 Comparison of sexual function for non-CAH versus CAH

<table>
<thead>
<tr>
<th></th>
<th>Non-CAH</th>
<th>CAH</th>
<th>P value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median Score (range)</td>
<td>Median Score (range)</td>
<td></td>
</tr>
<tr>
<td>Sexual activity</td>
<td>84 (10-156)</td>
<td>40 (1-133)</td>
<td>0.061</td>
</tr>
<tr>
<td>Sexual desire</td>
<td>13 (1-18)</td>
<td>12 (0-31)</td>
<td>0.723</td>
</tr>
<tr>
<td>Sexual satisfaction</td>
<td>21 (0-26)</td>
<td>8 (0-31)</td>
<td>0.156</td>
</tr>
<tr>
<td>Activity in last month</td>
<td>1 (0-1)</td>
<td>0 (0-1)</td>
<td>0.088</td>
</tr>
<tr>
<td>Current partner</td>
<td>1 (0-1)</td>
<td>0 (0-1)</td>
<td>0.088</td>
</tr>
<tr>
<td>Experience</td>
<td>1 (1-5)</td>
<td>1 (0-7)</td>
<td>0.619</td>
</tr>
<tr>
<td>Fantasy</td>
<td>1 (1-7)</td>
<td>2 (0-7)</td>
<td>0.170</td>
</tr>
<tr>
<td>Body image</td>
<td>2 (0-4)</td>
<td>2 (0-4)</td>
<td>0.683</td>
</tr>
</tbody>
</table>

‡Mann-Whitney U test
### Table 6.8 Comparison of sexual function for non-surgery versus surgery

<table>
<thead>
<tr>
<th></th>
<th>Non-Surgery</th>
<th>Surgery</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median Score</strong></td>
<td><strong>Median Score</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>(range)</strong></td>
<td><strong>(range)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1 Sexual activity</strong></td>
<td>78 (10-156)</td>
<td>42 (1-133)</td>
<td>0.135</td>
</tr>
<tr>
<td><strong>2 Sexual desire</strong></td>
<td>13 (1-18)</td>
<td>12 (0-31)</td>
<td>0.726</td>
</tr>
<tr>
<td><strong>3 Sexual satisfaction</strong></td>
<td>18 (0-26)</td>
<td>6 (0-31)</td>
<td>0.165</td>
</tr>
<tr>
<td><strong>4 Activity in last month</strong></td>
<td>1 (0-1)</td>
<td>0 (0-1)</td>
<td>0.035</td>
</tr>
<tr>
<td><strong>5 Current partner</strong></td>
<td>1 (0-1)</td>
<td>0 (0-1)</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>6 Experience</strong></td>
<td>1 (1-5)</td>
<td>2 (0-7)</td>
<td>0.343</td>
</tr>
<tr>
<td><strong>7 Fantasy</strong></td>
<td>1 (1-7)</td>
<td>2 (1-7)</td>
<td>0.189</td>
</tr>
<tr>
<td><strong>8 Body image</strong></td>
<td>3 (0-4)</td>
<td>2 (0-4)</td>
<td>0.699</td>
</tr>
</tbody>
</table>

†Mann-Whitney U test

1 Scored according to questionnaire. Higher value indicates more activity.
2 Scored according to questionnaire. Higher value indicates increased desire.
3 Higher value indicates increased satisfaction
4 1 = activity, 0 = no activity
5 1 = partner, 0 = no partner
6 Experience graded between 1 = completely heterosexual experience, and 7 = completely homosexual experience
7 Fantasy graded between 1 = completely heterosexual fantasy, and 7 = completely homosexual fantasy
8 Rated 0 – 4 where 0 = very satisfied with body, and 4 = very dissatisfied with body

For those with CAH no difference was shown regarding sexual desire, although the levels for sexual activity were approaching significance, with women with CAH having lower levels of activity. Participants are asked to rate sexual fantasy on a scale of 1 to 7 where 1 represents completely heterosexual and 7 is completely homosexual. Of the 30 participants with CAH who chose to answer that question, 12 rated themselves 4 or higher (40%), compared with only 1/9 of the controls (11%) who indicated a preference. When comparing those who had undergone surgery compared with those who had not, a past history of surgery was associated with a significantly reduced likelihood of having a current sexual partner, or having
been sexually active in the last month. No difference was observed in self-perceived body image between the groups.

Section 6: The HADS questionnaire
The HADS questionnaire gives a score for Anxiety and Depression, ranging from 0 to a maximum of 21. A value of less than 7 is considered within normal limits. A score of 8-10 is "borderline" for either symptom, and a value of 11 or more is considered abnormal. The results are shown in table 6.9. All 32 CAH participants completed the HADS, as well as 9 of the 10 normal controls.

Table 6.9 Results of Anxiety and Depression scoring

<table>
<thead>
<tr>
<th></th>
<th>Anxiety</th>
<th></th>
<th>Depression</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Borderline</td>
<td>Abnormal</td>
<td>Normal</td>
</tr>
<tr>
<td>CAH (n/32)</td>
<td>15</td>
<td>5</td>
<td>12</td>
<td>26</td>
</tr>
<tr>
<td>Normal controls (n/9)</td>
<td>5</td>
<td>-</td>
<td>4</td>
<td>9</td>
</tr>
</tbody>
</table>

A comparable number of participants showed a high level of anxiety with 37.5% of the CAH group and 44% of the control groups scoring in the abnormal range. 9% of the CAH group had a borderline score for depression, with an additional 9% scoring in the abnormal range.

The results were divided into normal scores and compared with borderline or abnormal scores. Firstly Normal Controls were compared with CAH women, as seen in table 6.10.

Table 6.10 Anxiety and depression scores for CAH women and Normal Controls

<table>
<thead>
<tr>
<th></th>
<th>Anxiety</th>
<th></th>
<th>Depression</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>P value*</td>
<td>Median</td>
<td>P value*</td>
</tr>
<tr>
<td></td>
<td>(range)</td>
<td></td>
<td>(range)</td>
<td></td>
</tr>
<tr>
<td>Normal Controls (n=9)</td>
<td>5 (2-12)</td>
<td>0.645</td>
<td>3 (0-7)</td>
<td>0.160</td>
</tr>
<tr>
<td>CAH (n=32)</td>
<td>8 (1-20)</td>
<td></td>
<td>4 (0-19)</td>
<td></td>
</tr>
</tbody>
</table>

* Chi squared test
Secondly those with CAH who had undergone surgery were compared with those with CAH who had not, and Normal Controls (table 6.11). Two CAH participants chose to remain anonymous and surgical details could not be verified. Therefore the data was excluded.

Table 6.11 Anxiety and depression scores for surgery versus non-surgery groups

<table>
<thead>
<tr>
<th></th>
<th>Anxiety</th>
<th></th>
<th>Depression</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>P value*</td>
<td>Median</td>
<td>P value*</td>
</tr>
<tr>
<td></td>
<td>(range)</td>
<td></td>
<td>(range)</td>
<td></td>
</tr>
<tr>
<td>Normal Controls (n = 9)</td>
<td>5 (2-12)</td>
<td>0.431</td>
<td>3 (0-7)</td>
<td>0.313</td>
</tr>
<tr>
<td>CAH Non-surgery (n = 4)</td>
<td>11 (9-14)</td>
<td></td>
<td>6 (3-10)</td>
<td></td>
</tr>
<tr>
<td>CAH Surgery (n = 28)</td>
<td>7 (1-20)</td>
<td></td>
<td>3 (0-19)</td>
<td></td>
</tr>
</tbody>
</table>

*Chi squared test

No significance was shown between the CAH and non-CAH participants, or between those who had undergone CAH surgery group, CAH non-surgery group and normal controls.

Section 7: The Personal Identity questionnaire
31 respondents with CAH completed the personal identity questionnaire, and 9 normal controls. The results were compared between those who had CAH and the control group.
### Table 6.12. Comparison of median response to gender identity questionnaire

<table>
<thead>
<tr>
<th>Questions</th>
<th>CAH</th>
<th>Non-CAH</th>
<th>p value*</th>
<th>CAH</th>
<th>Non-CAH</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Happy as a woman</td>
<td>Yes</td>
<td>Yes</td>
<td>0.904</td>
<td>Yes</td>
<td>Yes</td>
<td>0.796</td>
</tr>
<tr>
<td>Better to be a woman</td>
<td>Yes</td>
<td>Yes</td>
<td>0.505</td>
<td>Yes</td>
<td>Yes</td>
<td>0.090</td>
</tr>
<tr>
<td>Better to be a man</td>
<td>No</td>
<td>No</td>
<td>0.337</td>
<td>No</td>
<td>Sometimes</td>
<td>0.756</td>
</tr>
<tr>
<td>Felt more like a man</td>
<td>No</td>
<td>No</td>
<td>0.385</td>
<td>No</td>
<td>No</td>
<td>0.143</td>
</tr>
<tr>
<td>Nothing really good about being a woman</td>
<td>No</td>
<td>No</td>
<td><strong>0.054</strong></td>
<td>No</td>
<td>No</td>
<td>0.633</td>
</tr>
<tr>
<td>Happier living as a man</td>
<td>No</td>
<td>No</td>
<td>0.896</td>
<td>No</td>
<td>Sometimes</td>
<td>0.366</td>
</tr>
<tr>
<td>Dreams as a man</td>
<td>No</td>
<td>No</td>
<td>0.440</td>
<td>No</td>
<td>No</td>
<td>0.351</td>
</tr>
<tr>
<td>Wish to be a man</td>
<td>No</td>
<td>No</td>
<td>0.926</td>
<td>No</td>
<td>Sometimes</td>
<td>0.310</td>
</tr>
<tr>
<td>Not really felt like a woman</td>
<td>No</td>
<td>No</td>
<td>0.299</td>
<td>Sometimes</td>
<td>No</td>
<td><strong>0.140</strong></td>
</tr>
<tr>
<td>Mixed up about self</td>
<td>No</td>
<td>No</td>
<td>0.100</td>
<td>No</td>
<td>No</td>
<td><strong>0.037</strong></td>
</tr>
<tr>
<td>Dislike female anatomy</td>
<td>No</td>
<td>No</td>
<td>0.352</td>
<td>No</td>
<td>No</td>
<td>0.889</td>
</tr>
<tr>
<td>Wish to have male operation</td>
<td>No</td>
<td>No</td>
<td>0.590</td>
<td>No</td>
<td>No</td>
<td>0.263</td>
</tr>
</tbody>
</table>

* Mann-Whitney U test p value

Two questions showed a significant difference between the two groups, although the median responses were the same: "In the past 12 months have you ever felt that there was nothing really good about being a woman", and "Over the whole of your life have you ever felt mixed up about yourself, sometimes feeling more like a man and sometimes feeling more like a woman". In both cases the CAH group were more likely to agree with the statement.

**Section 8: The GHQ-12 questionnaire**

The GHQ-12 is scored 0-1-2-3 for each answer, giving a maximum of 36, where a higher level indicates poorer psychological health (see table 6.13). The results were analysed using the Mann-Whitney U test to compare CAH with non-CAH, and then those who had undergone surgery compared with those who had not.
Table 6.13 Comparison of GHQ-12

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (range)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAH (n=30)</td>
<td>15 (10-31)</td>
<td>0.079</td>
</tr>
<tr>
<td>Non-CAH (n=9)</td>
<td>13 (5-26)</td>
<td></td>
</tr>
<tr>
<td>CAH with Surgery (n=24)§</td>
<td>15 (10-31)</td>
<td>0.174</td>
</tr>
<tr>
<td>CAH no surgery (n=4)</td>
<td>20 (10-22)</td>
<td></td>
</tr>
<tr>
<td>Normal Controls (n=9)</td>
<td>13 (5-26)</td>
<td></td>
</tr>
</tbody>
</table>

Each question scores from 0-3, giving a maximum of 36. A higher score indicates a greater level of distress.

§Two respondents excluded as anonymous and unable to verify surgery details

No difference is observed between the CAH and non-CAH groups. When further divided into those with CAH who had undergone surgery, those with CAH who had not, and normal controls, again no difference is noted.

Section 9: Permission to obtain notes
As discussed in section 3, of the 24 participants who had undergone surgery 2 chose to remain anonymous. Of the remaining 22, hospitals were written to in order to obtain notes. If no reply was received, a further letter was sent, with a follow-up phone call. Operative details were obtained for 15/22, and showed that 10/15 had undergone at least two genital operations, with 7/15 undergoing two or more clitoral procedures.

Section 10: Any comments
Several participants chose to write comments about the questionnaires, the study in general, and living with CAH. These are considered in context in the discussion.

6.4 Discussion

Section 1: About you
The demographics of the CAH group show the mean age to be 25. The clitoral reduction procedure gained popularity in the early 1980s, and
represents the procedure that the majority of participants had performed. Only 4 individuals underwent a clitoral removal operation, all of which were carried out in the late 1960s to early 1970s. It is frequently stated that operative techniques have improved, and that caution should be used when judging the effects of previous operations, so it is useful to note that the vast majority of participants had the more modern clitoral reduction operations. Clearly, in judging the long-term outcomes of any operation with possible effects on sexual function, it is likely that a time-lag of at least 15 to 20 years will be encountered. This sample therefore represents an appropriate group to study. Although there is a statistically significant difference in the mean ages of the CAH group and the normal controls, this is unlikely to bias the results excessively. The majority of participants in both groups were in their 20s or early 30s, and with small samples it is hard to place considerable emphasis on this point. Some authors are concerned that adverse outcomes only represent a few angry and upset patients, who have become active in support groups. It could be argued that group members are more likely to be well-adjusted in seeking peer support, and therefore less likely to have a poor outcome following medical interventions. Nevertheless, it is important to be aware of potential bias, and it is interesting to note that of 32 participants, only 6 (19%) stated they were members of a support group. Again, this suggests that this group does not represent a particularly politically motivated sample, and should therefore give a more realistic impression of the issues facing women with CAH.

Section 2: Diagnosis
As would be expected, the majority of participants had their diagnosis made at birth (25/32). This would mean that regular hospital attendances and almost certainly steroid replacement medication would be commenced at a very early stage in life. All participants were clear about whether they had salt-losing or late-onset CAH. Genetic details were available for 15/32 (46%), and all confirmed the diagnosis. However, some indicated that they did not know much more about their condition than the name. One respondent commented, "Don't know any more about salt losing side as it's not really something I discuss when having appointments."
Another indicated she had salt-losing CAH,

"But I was not told about this for a long time".

Intersex conditions have historically been subject to much taboo and secrecy. Yet CAH represents a condition where sex assignment is deemed relatively straightforward, given the presence of female internal genitalia with an XX karyotype. In theory therefore, details of CAH were less likely to be withheld from an individual, except perhaps the genital ambiguity. One patient described this:

"I was never told about how many operations I've had, or even the surgery which was carried out when I was 16. I've found out more about my condition in the last 18 months than I have in my whole life."

It may be that individuals with CAH deliberately "shut-off" from learning more about an unpleasant condition. Having lived with a condition for so long, it may hark back to days of appointments with parents, where details were discussed over the head of the child. Questions about the condition may have been discussed between doctors and parents years earlier, and never revisited by the individual concerned.

It is interesting that 12/32 (37%) respondents had experienced depression and/or anxiety at some stage. It may be this relates to having a chronic condition, and one that tends to affect height and weight adversely to that favoured by society, which views being thin and tall as desirable for women. However, a significant proportion of the general population are thought to experience depression at some stage in their lives, and it may be that this reflects nothing more than the background expected rate for any UK population. Recent work suggested that women with CAH were psychologically well adjusted and showed no increase in psychiatric disorders when compared with the background population. However, this was a small study, with no control group, so additional studies would be required to assess this further.

Section 3: Surgery and Treatment; Vaginal Surgery

There are a wide variety of views expressed by those who have undergone some form of vaginal surgery. Interestingly, several women gave opinions
about the results of vaginal surgery without indicating they had undergone operations, leading to a discrepancy in the study numbers. It may be the question was misunderstood, with women believing they were being asked their opinions about their vagina, whether or not they had undergone surgery. Given the past policies of non-disclosure of diagnosis, it may be that women had undergone operations but remained ignorant of the fact and therefore did not give a history of having had surgery. It is also possible that women had undergone surgery but simply did not understand the procedures and therefore felt unable to comment whether they had undergone an operation. A third of women were mostly or totally dissatisfied with the results following surgery, which calls into question the aim of the surgery, and perhaps the expectations of the patient preoperatively, or involvement in vaginal dilation postoperatively. A further third indicated they were mostly or totally satisfied, with the remainder being neither satisfied nor dissatisfied. Of those that were unhappy with the results, presumably because surgery had not created an adequate introitus, all had undergone vaginal surgery prior to adolescence, and all but one before the age of 4. This is consistent with the findings of Creighton et al. who showed that the vast majority of women in their study who had undergone childhood surgery needed further operative procedures in adolescence. The main aim of vaginal surgery is to facilitate menstrual flow, and to allow comfortable penetrative intercourse. Yet five out of thirteen patients who had undergone vaginal surgery reported difficulties with intercourse due to the vagina seeming too small. This amounts to a failure rate of nearly 40%, which is challenging by any standard. In addition, it questions carrying out surgery 10 years or more before it may be necessary, even for menstruation. One woman commented:

"Scars from operation are very sore if touched causing a great deal of discomfort."

Five patients reported urinary difficulties, or problems with urinary tract infections, and this interesting finding has been assessed further in chapter 7. The majority of respondents had been offered vaginal dilator therapy at some stage, although this would not necessarily be first line treatment in CAH. The anatomical configuration with the vagina joining the urethra makes surgery necessary in most cases. However, stenosis can occur post-operatively, and
regular use of dilators can reduce this, so for dilator therapy to be offered to
the majority of patients is appropriate. The Middlesex Centre does have an
active dilation therapy programme, for various intersex conditions, so this may
represent a sample bias. An overriding theme which came out of the study
was the concern that a partner may consider the vagina to be different from
other women. As discussed in chapter 4, the normal anatomy of the genital
area and vaginal length varies considerably in the normal population, yet
10/32 (31%) expressed concern about a partner’s opinion. This suggests that
women may see an aim of vaginal surgery as not just the provision of a
functional vagina, but also to be considered “normal” by partners. This is a
significant finding, as for surgery to be truly successful, the vagina must not
only be of sufficient physical dimensions, but also should represent “normality”
to the woman. One woman commented:

“I would like it to be as normal as possible”.

Another indicated she thought a sexual partner would notice it was different in
appearance from other women and remarked:

“I myself work in the connection with the Adult Industry and the
difference I notice is very clear.”

Her employment involved packing videos for high street sex shops, and she
commented she felt different to pictures of other women. Yet interestingly, she
did not tick any other box requesting her vagina be made bigger, wider or
longer. Some women found it difficult to be reassured about normality, for
example:

”Although my gynaecologist says it is fine I am paranoid that “it”
wouldn’t fit. Still a virgin.”

An important part of the preoperative assessment could be exploring the
thoughts and expectations of surgery, and the realities of a surgical solution.
For example, patients may wish to be sexually active, but an operation is only
part of this process and is not in itself going to provide a satisfying and
fulfilling relationship. Therefore, continuing psychological work post-
operatively and potential involvement in a dilator programme may improve
satisfaction with vaginal surgery in the longer-term.
Section 3: Surgery and Treatment; Clitoral Surgery

Again, a lack of consistency was observed in the answers given to questions regarding surgical history. This may indicate a lack of information or understanding of personal medical history, or may simply be a confusion generated by the questionnaire. Overall respondents appeared to be generally happy with the appearance of the clitoris. The majority of participants felt that sensation was poor, although some were unclear:

"Lack of sensation but not had enough experience to know for sure."

The questionnaire did not make provision to ask if this were an acceptable trade off. Historically, doctors have felt this was acceptable, although activists have decried this, and argue that appearance is less important than sensation and function. Although 13 women reported complications following surgery, 17 did not. As discussed earlier, some respondents had not undergone clitoral surgery, so may have misunderstood the question, or answered in error. However, this still shows a significant proportion of those who had undergone clitoral surgery did not report complications. This may reflect the age at which surgery was carried out with individuals too young to remember, or it may be that the majority of respondents did not experience any post-operative difficulties. Eight women specifically commented on reduced sensation as a complication, and eleven also reported this when asked about complications. This is not routinely reported in the literature and is unlikely to form part of the post operative follow-up enquiries. Urinary difficulties were reported by three women, and this is further assessed in chapter 7. The most common worry reported by women was the opinion of partners – potential or actual. When asked about the appearance of the genital area in general one woman commented:

"Not generally happy but I think content, would like to know for sure that from someone else’s point of view that it is normal."

One woman commented that her opinion varied:

"It really depends on my mood, state of sexual arousal, the angle it’s viewed from etc. In general I think it’s ok, but I wish my clitoris looked a bit smaller and neater."

Yet when asked about partner opinion, the same respondent commented

"He seems to find them rather attractive!".
Of the nine women that responded, eight indicated their partner had never commented or noticed no difference:

"I think that over time I've got used to the way it looks and my boyfriend has never questioned any differences."

One woman had pre-empted her anxieties about her partner's opinion:

"She hasn't commented on my genitals as we spoke about it first."

Only one respondent indicated their partner had felt there was a difference, but even then, that this was unimportant. This suggests that the fears of the women were not realised, and rather, that partner selection was the critical choice.

When asked about the appearance of the genital area 8 of the normal controls reported this as "happy" or "fine". One of these respondents also put "unhappy", commenting:

"I know the above seems contradictory but sometimes I feel really good about it and sometimes I feel really bad"

Another commented:

"I am a bit self-conscious about having one v. long labium, but this has never actually been a problem"

One individual indicated she had "no opinion", and one did not answer.

Sections 4 and 5: Sexual function

The GRISS questionnaire showed a clear difference in global sexual function with the CAH group having greater difficulties. Only 3 women in the CAH group had not undergone genital surgery, and the results were very similar when they were included in the non-surgery group with the normal controls. When the groups were further divided into those who had undergone surgery, compared with both the non-surgery CAH group and the normal controls, sexual functioning was still significantly impaired for the CAH surgery group. Six of the seven subsets showed a significant difference when comparing the CAH women with normal controls. As expressed in section 3, anorgasmia was common, which is consistent with other studies. In addition, as found during the sensation testing in chapter 5, introital stenosis was a feature
leading to vaginal penetration difficulties. This echoes the findings in section 3, with women complaining the vagina did not seem big enough to allow penetrative intercourse. Mulaikal et al have argued that this is the main factor in the reduced fertility rates seen in women with CAH. As all women in this study were aged 17 or over, theoretically all should have undergone all the surgery they required to open up the lower vagina, even allowing for the almost inevitable second operation at adolescence. Yet the difference between the two groups was highly significant when considering the surgery vs non-surgery groups, with a p value of <0.001. This is consistent with the dissatisfaction with sexual function and tendency to avoid intercourse, as expressed by the surgery group. However, dissatisfaction was not significantly different when comparing the CAH surgery and CAH non-surgery groups with normal controls. Rather, a difference had been observed when the CAH group and normal controls were directly compared suggesting that genital surgery was not responsible for increased dissatisfaction. Rather, this could be an effect of CAH, and genital surgery could improve satisfaction.

A significant difference was seen in avoidance when comparing the three groups. Although those who had undergone surgery rated the highest in avoidance of intercourse with partners, those with CAH who had not had surgery still had markedly raised scores. It may be related to the difficulties of living with CAH, either in the changes in body habitus, or the stress of living with a chronic condition.

No differences were observed between the groups in communication with partners. Five of the nine normal controls indicated difficulties in this area, as did nine of the 19 subjects. This information is useful for women with CAH in that relationship anxieties are common, and not necessarily related to a history of surgery. Therefore, skills in communicating with partners are the stuff of normal life, and women with CAH are no different to any others in finding this a challenge.

The BISF-W questionnaire gave slightly different answers to the GRISS. This may reflect the increased response rate, given that the questionnaire did not
depend on the presence of a partner for completion. Yet, the non-surgical group were significantly more likely to have a sexual partner, and to have self-rated as sexually active in the last month. It is unclear why this is. It may be that women who have undergone surgery choose not to have partners, or simply that this reflects a level of concern about initiating relationships, and a sense of inevitability towards the relationship becoming sexual. From this study it is clear that this is not due to a lack of sexual desire. There was no difference between the two groups, suggesting that reduced sexual activity levels are more to do with lack of a partner rather than lack of desire. Initiating and negotiating relationships can be difficult for all. Women with CAH have usually been taking steroid medication for years, and as such often are short with truncal obesity, and other effects of androgenisation such as acne and hirsuitism. Society favours women who are tall and thin, and as such, women with CAH may find relationships difficult to embark upon. Yet, there was no difference between the two groups on body image. When considering previous sexual experience in terms of orientation, the majority of participants and controls had participated in heterosexual relationships, and there was no difference between the two groups (p=0.6). Yet, when asking about an imagined relationship, although the difference was still not significant, the responses were not the same, with more of the CAH group fantasising about same sex relationships. If the two groups had indicated that real relationships reflected the fantasy relationships, so those that fantasised about female partners went on to have relationships with female partners, the p value might have been expected to be similar. Instead the value was 0.17, suggesting that women with CAH may have heterosexual relationships in reality, but that fantasy was much more variable, with 40% of CAH respondents rating themselves as at least equally if not mostly homosexual in orientation. This is consistent with other papers in the literature and the aetiology and role of testosterone imprinting in utero is still hotly debated. This discrepancy in reality and fantasy may be due to the observance of societal convention, where heterosexual relationships are perceived as correct. Alternatively, it may represent lack of opportunity. Several participants with CAH had difficulty in employment, exacerbated by long periods of illness, and were still living in the parental home. As such, the opportunity to initiate same-sex relationships
was likely to be limited. Finally it may demonstrate the confusion that some women were experiencing about their own sexuality. One participant commented

"Held back from relationships completely for many years. Continue to struggle with sexual orientation. Much better re gender identity. Gay life too pressured and limited in some ways."

Sections 6 and 8: Hospital anxiety and GHQ-12
The Hospital Anxiety and Depression Scale did not show any difference between those who had CAH compared with those who did not, although as the control group for this was small, it is difficult to place significant emphasis upon this. Similarly, no difference was seen when comparing those who had undergone surgery with those with CAH who had not, and with normal controls. CAH is a condition where patients may become extremely unwell with simple ailments such as a cold or urinary tract infection, and it might have been expected that anxiety and depression levels would be high. On closer inspection the actual scores were relatively high with 37.5% and 18% of the patients scoring highly for anxiety and depression respectively, although this is similar to the normal control group. It has been suggested that women with CAH are genetically predisposed to anxiety or stress-related conditions as a result of a high ACTH drive. One study compared 18 women with CAH with controls with an endocrine condition such as Turner's syndrome, and found that the CAH group were more likely to suffer with obsessive-compulsive behaviour, interpersonal sensitivity and anxiety, although this did not reach significance. However, Kuhnle et al assessed 45 women with CAH and compared them with 46 age-matched controls, and found no significant difference in overall quality of life. They speculated that women with CAH have developed coping mechanisms through living with a chronic condition, and recommended further research to identify and strengthen these. Continued psychological input is recommended for those with CAH, and this result may reflect the success of this approach.
The GHQ-12 did show more of a difference between the CAH and non-CAH groups, with this approaching significance (p=0.079). This suggests that women with CAH do have more psychological difficulties, although not approaching levels sufficient for a diagnosis of anxiety or depression to be made. It is interesting that there was more of a difference for those with CAH compared with normal controls, than when comparing the CAH surgery and non-surgery groups with the normal controls. Surgery may be considered by some as a discrete episode in terms of seeing a surgeon preoperatively, having the operation, and a few postoperative consultations, and therefore contributing as greatly to general psychological functioning. In contrast, the management of CAH requires lifelong appointments, with little prospect of being discharged.

Alternatively, this may suggest that general questionnaires are less suitable for the investigation of those with chronic conditions. Other authors have commented on the difficulty in carrying out quality of life studies in intersex and suggest that intersexed patients may find completion of standard questionnaires difficult as they do not exactly fit the choices given. One respondent commented “I found some of the questions quite difficult to understand, for example (section 8) [GHQ-12] – the answers did not correspond very well to the question asked.”

This questionnaire is a general overview of psychological health, rather than being specifically for those with chronic conditions. This does underline the need for section 10, where patients are invited to give free comments regarding the questionnaires.

Section 7: Gender identity
The gender identity questionnaire shows clear similarities between the two groups, with the majority of respondents identifying with a female gender identity. This is consistent with other reports of women with CAH. Of the 24 responses asked for, only two showed a significant difference between the
CAH group and normal controls. The questions could be construed in different ways, and this could lead to differing responses: for example, "in the past 12 months have you ever felt that it would be better to be a man rather than a woman" could be interpreted as it being more advantageous to be male than female. For those who are ambitious in the world of work and employment this is almost certainly true, yet does not necessarily indicate a male gender identity. One normal control indicated that sometimes she felt it would be better to be a man, sometimes wondered if she would be happier living as a man, and sometimes had the wish or desire to be male, commenting  "this is about having babies!".

The vast majority of women with CAH appear to develop a female gender identity. However, one article has argued that although women may not wish to change to the male sex, there were reports of less satisfaction with the female sex. One respondent clearly identified with this view: "...it's not as simple as "I hate my body I want to be a man". I think for myself it's more a case of I find it difficult to relate to other women, as I feel I have nothing in common except a similar body. However, most stuff you can learn and I feel I have become quite a convincing liar."

A further study followed up 59 children with intersex conditions, of whom 18 had CAH and were reared female. Of the 18 children, 4 were classified as having general psychopathology according to DSM-IV, and two were considered to have gender identity disorder of childhood. However, this and other studies have argued there is no evidence that degree of virilisation or age at which corrective surgery is performed leads to difficulties with gender identity.

Section 10: Comments
Several respondents took the opportunity to complete section 10 with comments about the questionnaire, the study, or about living with CAH. Sexual function is clearly a sensitive area to investigate, yet many welcomed the opportunity to discuss this topic, and to contribute towards research for CAH.
• “Very glad to see someone is looking at CAH sexual function and identity. Currently a very difficult time for me personally.”
• “I’m very happy that finally a study is taking place to find out about how we (CAH patients) actually perceive ourselves. I feel this is extremely important if any developments regarding treatment/surgery are to be made. It’s a great idea.”
• “I would like to help with your study as much as possible.”
• “This questionnaire I think is a good idea so people with this condition can understand more about it.”
• “I hope by filling in this questionnaire that it helps children who are born with this condition. I wish I’d of had this help when I was growing up.”
• “This study is an excellent and long overdue necessity for all genital surgery not just intersex/CAH conditions.”

Clearly some women had taken a great deal of time and thought about the completion of the questionnaires, perhaps debating whether to take part.

• “I apologise for this questionnaire being sent in so late. I hope it can still contribute to your survey. Thanks.”

Some women worried about the value of their information.

• “Well the questionnaire I had no trouble taking part, but I’m not too sure how my answers can help your study, because the fact I’ve never have sexual intercourse means I have no experience whatsoever.”
• “I have not had a sexual partner, because I know with my condition it is not possible to participate in these activities at the moment.
• “Didn’t find all the questions very relevant as they assume you have had a sexual partner.”
Others welcomed the opportunity to discuss the operations and CAH, and viewed this as an opportunity to explore new treatment options.

- “I've found out more about my condition in the last 18 months than I have in my whole life. I knew I had low salt and just thought that my vagina would always be the same, now I know something can be done to change all that. I am seriously thinking about having the surgery, but I would like to come along to find out more about my genital area and ask some questions about the clitoris which I don't know much about at all.”

- “I have found out more about this condition in the short time I have been in contact with your department and by reading this questionnaire than I ever had in 25 years under the department I am under in my area. The more people with this condition know about it, I think the easier it is to come to terms with and understand why it has happened to them.”

- “I look forward to being tested to finally find out how much/little genital sensation I do have after the early surgery I had as a child.”

Others appreciated finding out about other women with the same condition.

- “I didn't realise there were groups or even people I could talk to about CAH. I suppose I should have tried to find out more but never pushed myself.”

Finally some women indicated there were other areas about CAH which bothered them more than the appearance of the genital area.

- “My main upset is stretch marks caused by change in medication which increased my weight dramatically. This is what has affected me most because as a young woman I am self conscious anyway but now I just cover myself up all the time.”
6.5 Conclusions

Women with CAH who have undergone genital surgery have decreased sensation to the clitoris, and also have increased sexual function difficulties when compared with the normal population. An overriding theme of the questionnaires was the desire to be “normal”, either self-perceived or given by partner opinion. Yet, on certain dimensions, there were similarities between the CAH and non-CAH groups. Both groups reported difficulties relating to sexual communication with partners, and both reported body image concerns. Women with CAH expressed the same levels of sexual desire but had lower levels of sexual activity.

For parents of children born with CAH, results from the current study are valuable for planning the care of their child. The results would also be of interest to those women who have already undergone surgery. Although childhood surgery is associated with more sexual difficulties, those who have undergone surgery may be reassured by the fact that the non-surgery group also shared some of their difficulties and concerns. Moreover, some of the difficulties reported by the CAH group are also shared by the non-CAH group. Psychological input focusing on relationship initiation and negotiation could benefit the adult woman with CAH, but some of the problems reported by adults are not specifically related to surgery, suggesting that regardless of decisions about childhood surgery, there are difficulties associated with living with CAH.
Chapter 7

CAH and Lower Urinary Tract Symptoms

7.1 Background
The development of the genitalia for females with CAH often results in a single urethra/vagina and labial fusion, as discussed in chapter 3. These anatomical changes may lead to incomplete emptying of the bladder with pooling of urine in the common urogenital sinus. This in turn may lead to reflux and subsequent urinary tract infections, or renal complications. Even if reflux does not result, the relative slowness of urethral emptying may cause post-micturition dribbling. A stated aim of the procedure is to prevent subsequent urinary tract infections and complications, yet there is little information available about the prevalence of urinary difficulties in women with CAH either before or after surgery. A feminising genitoplasty procedure involves division of the combined urethra/vagina into two separate openings, and theoretically should lead to a lower incidence of urinary difficulties.

The International Continence Society suggests that incontinence should be defined as a "condition in which involuntary loss of urine is a social or hygienic problem and is objectively demonstrable". One study looked at 12 patients with CAH and noted that 3 had urinary symptoms and incontinence. In addition, the average capacity of the bladder was noted to be approximately 86% of that expected for age. All but one patient had undergone some type of clitorovaginoplasty, with the remaining patient having had a clitoral removal and no vaginal procedure. This was a paediatric study, where the average age of the subjects was nine years, with data on adult outcomes awaited. A further study looking at the long-term outcomes of adult CAH patients showed two out of six subjects studied had some degree of incontinence; one was described as having "transient incontinence" for some years, and the second as experiencing urge and stress incontinence. Both had undergone feminising “one-stage” surgery in childhood, and had required further vaginal surgery in adolescence. Furthermore, two others of the six had suffered
repeated urinary tract infections after their initial "one-stage" surgery, which settled after subsequent vaginoplasty at adolescence.

As part of the study assessing clitoral sensation a questionnaire was sent to all participants, and reported in chapter 6 (appendix 2). One question asked specifically about the lower urinary tract, inviting women to indicate if they had ever experienced certain urological symptoms. The results showed 75% of all respondents had experienced at least one of the symptoms, with 50% having experienced two or more. Of the normal controls 60% had experienced one or more symptoms with only 30% having experienced two or more.

27. Have you ever experienced any of the following?
☐ Difficulty in holding your urine
☐ Passing urine frequently (more than every two hours)
☐ Leaking urine before getting to the loo
☐ Sudden feeling of needing to pass urine
☐ Sudden leakage of urine
☐ Getting up to pass urine more than once a night
☐ Leakage of urine on coughing or sneezing

taken from "What happens after surgery for CAH?" section 3, page 6

This represented a significant new discovery in considering the long-term outcomes of women with CAH, and further assessment was therefore planned to investigate this hitherto under-reported finding.

7.2 Methodology

7.2.1 Study design
Urinary symptoms are relatively common in the normal population, but prevalence increases significantly after the menopause and with a history of childbirth. However, there is little information available on the prevalence of urinary symptoms in a younger population. One subject with CAH had delivered one child by caesarean section, but all other women with CAH in the larger study were nulliparous and premenopausal. Therefore a case-control
study was planned, to compare lower urinary tract symptoms in women with CAH and an age-matched nulliparous population.

7.2.2 Data collection
The Bristol Female Lower Urinary Tract Symptoms (BFLUTS) Questionnaire was selected to be sent to participants, and is given in appendix 3 [153]. The BFLUTS has been designed to assess the prevalence of a wide range of urinary symptoms, but also to verify the degree of “bothersomeness” experienced by patients. It was validated on a UK population of 85 patients and 20 normal controls, and exhibited good differentiation between the two groups. The questionnaire consists of 34 questions; 9 on incontinence, 12 on other urinary symptoms, 4 regarding sexual function and 9 on quality of life. The BFLUTS takes approximately 15 minutes to complete, and is written in clear simple English.

7.2.3 Study Recruitment
At the time of planning, 27 women with CAH had already taken part in the clitoral sensation study, and all were approached inviting them to take part in this one further study. Recruitment to the clitoral sensation study was ongoing after completion of this additional urinary symptomatology study, with 28 women finally completing the sensation testing, as reported in chapter 5. Ethical approval was granted by the joint university and hospital ethics committee. Subjects were excluded if they had additional medical conditions which could have an effect on urinary symptoms, such as multiple sclerosis or diabetes mellitus.

Controls were recruited from hospital members of staff via a poster campaign, and were invited to participate if they were nulliparous and within the age-range of subjects (16-40 years). Anonymity was assured. Exclusion criteria for the control group were a history of previous urological or genital surgery, or taking medication which may lead to urinary symptoms, such as diuretics. Similarly, those with a medical condition which could cause urinary symptoms were also excluded.
Subjects and controls were sent the BFLUTS questionnaire and asked to complete it and return in a pre-paid envelope. Subjects were asked to give their name and date of birth, so that details regarding operative and medical history could be ascertained. Written consent was obtained from all subjects and a urology consultation was offered should they wish to undergo assessment of any symptom. One further follow-up letter was sent to subjects who had not responded to the initial letter and questionnaire. The control group were asked to give date of birth in order to ensure a comparable age group, but the questionnaire was otherwise anonymous. Controls were also asked for details of medications and any surgical history. For the control group completion and return of the questionnaire represented consent.

7.3 Results
27 subjects with 21-hydroxylase CAH were sent a postal questionnaire. 19 (70%) of these were completed and returned. The age range of subjects was 17-40 years, with a mean age of 26.8 years (SD = 7.35).

<table>
<thead>
<tr>
<th></th>
<th>CAH Subjects</th>
<th>Normal Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age range</td>
<td>17-40 (26.8)</td>
<td>21-39 (29.1)</td>
<td>0.26</td>
</tr>
<tr>
<td>Response rate</td>
<td>19/27 (70%)</td>
<td>22/31 (71%)</td>
<td>-</td>
</tr>
</tbody>
</table>

16 subjects had undergone feminising surgery, with operative details available for 12. Eight had undergone clitoral reduction between the ages of 11 months to 4 years, with 5/8 also having a u flap vaginoplasty. One had an ileovaginoplasty, another had a perineal pullthrough operation, and one had only required a Fenton’s procedure. Four subjects had undergone clitoral removal between the ages of 2 years and 4 months and 3 ½ years; of these, two had a u flap vaginoplasty, one had a colovaginoplasty, and one had not undergone any vaginal surgery.
Of the 12 women where operative details were available, 2 (16%) had undergone one clitoral/vaginal operation in their lives, 5 (42%) had needed two procedures, and 5 (42%) women had undergone three separate operations. Of the 8 subjects who had undergone clitoral reduction operations in infancy or early childhood, 6 (75%) required further surgery in adolescence.

31 members of staff responded to the advertisement and were given questionnaires and addressed envelopes, 22 completed questionnaires were received (71%). The age range of the control group was 21 - 39 years, mean age 29.1 years (SD = 5.19). There was no significance difference in the ages of the two groups (p=0.26). Three of the control group were excluded; one respondent gave a history of an inborn error of metabolism, one was taking nifedipine which has a potential side-effect of urinary frequency, and the third had a history of Polycystic Ovarian Syndrome. A summary of the results are in tables 7.1 and 7.2 below. Statistical analysis was performed using SPSS version 11.5. A p value of less than or equal to 0.05 was deemed significant. In view of the small numbers in different groups, Fisher's exact test was used.
Table 7.2 Urinary symptoms reported on the BFLUTS questionnaire for subjects and controls

<table>
<thead>
<tr>
<th>Urinary Symptoms</th>
<th>Subjects (n/%)</th>
<th>Controls (n/%)</th>
<th>Fisher's Exact Test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incontinence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urge</td>
<td>13 (68%)</td>
<td>3 (16%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Stress</td>
<td>9 (47%)</td>
<td>5 (26%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Nocturnal</td>
<td>7 (37%)</td>
<td>0 (0%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Unexplained</td>
<td>13 (68%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td>4 (21%)</td>
<td>1 (5%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Urgency</td>
<td>13 (68%)</td>
<td>8 (42%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Nocturia</td>
<td>4 (21%)</td>
<td>1 (5%)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Voiding</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete</td>
<td>13 (68%)</td>
<td>7 (37%)</td>
<td>0.10</td>
</tr>
<tr>
<td>emptying</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysuria</td>
<td>10 (53%)</td>
<td>5 (26%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Hesitancy</td>
<td>11 (58%)</td>
<td>4 (21%)</td>
<td>0.045</td>
</tr>
<tr>
<td><strong>Quality of Life</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse effect on life</td>
<td>9 (47%)</td>
<td>1 (5%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Restriction of fluid</td>
<td>8 (42%)</td>
<td>5 (26%)</td>
<td>0.49</td>
</tr>
</tbody>
</table>

7.3.1 Incontinence

The BFLUTS questionnaire discerns four categories of incontinence; urge, stress, nocturnal and unexplained. 68% of our subject group described experiencing urge incontinence to some degree, in contrast with 16% of the control group (Fisher’s Exact Test p=0.003). 47% of those with CAH had stress incontinence compared with 26% of the control group. (Fisher’s Exact Test = 0.31). Nocturnal incontinence was experienced by 7 of the CAH group (37%), whilst none of the normal controls complained of this symptom (Fisher’s Exact Test p = 0.003). Unexplained incontinence was not reported in any of the control group yet 13/19 (68%) of our subjects reported some degree of unexplained incontinence (Fisher’s Exact Test p<0.001).
7.3.2 Storage symptoms (frequency, urgency, nocturia)
Urgency was prevalent in both groups, with 68% (13/19) of subjects and 42% (8/19) of controls reporting this symptom. There was no significant difference between controls and subjects (p=0.19). Nocturia and frequency were only reported by 21% (4/19) of the subjects and one of the normal controls (1/19), with a p value of 0.16.

7.3.3 Voiding symptoms (incomplete emptying, dysuria, hesitancy)
Significant voiding symptoms were reported by both groups, with 10/19 (53%) of subjects and 5/19 (26%) of controls complaining of dysuria (p=0.18). However, the most prevalent emptying symptom reported by the subject group was hesitancy, with 11/19 (58%) of subjects experiencing this symptom, compared with only 4/19 (21%) of controls, p=0.045 (Fishers' Exact Test).

7.3.4 Quality of Life
When asked if their urinary symptoms had an adverse effect on their overall lives 9/19 of the subjects stated that their lives had been adversely affected to some extent compared with only one of the control group, p=0.06 (Fishers' Exact Test).

7.3.5 Sexual Function
The BFLUTS contains a brief assessment of sexual function and the effect of urinary symptoms upon it, within the Quality of Life section. As the majority of the subject group (74%) rated themselves as not sexually active they were unable to answer the sexual function questions due to the design of the questionnaire. Furthermore, as sexual function had already been fully assessed, this was not seen as the main aim of this study.
7.3.6 Others
Subjects were also offered the option of an out-patient appointment with a consultant urologist to discuss their symptoms, and any future management as appropriate. Only one subject requested a referral.

7.4 Discussion
7.4.1 Data collection
Various modalities were considered when designing the optimum method of data collection. Urodynamic testing is considered the gold standard when assessing urological symptoms and this would yield important information about diagnosis and potential treatment options. However, none of the women had ever volunteered details about any lower urinary tract symptoms and had not sought clinical advice and treatment. Urodynamics is an invasive and uncomfortable procedure. In addition, it requires a specialist urodynamics nurse to be present, and an experienced person to interpret the results accurately. Urodynamics was therefore considered an inappropriate choice for a primary study although if future studies were indicated, this should be used to assess symptoms further.

A structured interview was considered as a possible alternative. This would give the advantage of being able to ask general questions, but also to ask further individual questions depending upon answers given. Themes are identified and drawn out and can highlight areas which require future research. This would give a high level of information, and allow detailed assessment of symptomatology and effect on quality of life. However, structured interviews can be time-consuming and difficult to interpret. It requires the patient to attend the hospital for an interview of approximately one hour. Furthermore, research suggests that individuals are less likely to be honest about potentially embarrassing symptoms when discussing them face-to-face or over the telephone. Rhodes et al assessed differences in reporting of urinary symptoms by healthy men via structured interviews or self-completed questionnaires. The questionnaires reported more symptoms

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than were recorded in the structured interviews. It was suggested the questionnaires were more accurate for individuals who had never sought medical treatment for their symptoms.

A postal questionnaire study was therefore planned, with all participating women in the main study being invited to take part. Postal questionnaires are widely used in clinical research as they allow access to a larger number of participants and are relatively cheap to administer. However, bias may be introduced if the response rate is poor. Edwards et al conducted a metanalysis on factors which increase the response to postal questionnaires. Many areas were identified which led to an improved return rate, including financial inducement, using a shorter questionnaire, enclosing a stamped addressed return envelope, precontact with the study subjects, follow-up with non-responders, and the study being university rather than industry sponsored. Response was also enhanced if the questionnaire was deemed an interesting topic, considered user-friendly, and an explanation for non-response was requested. However, response rates were lower if sensitive questions were introduced, such as in this case. It was important that the results were relatively easy to interpret and therefore communicate to others. Choosing a well-known questionnaire would make the study more applicable and readily understandable to clinicians. In addition, the questionnaire needed to be validated, in order that those with urinary symptoms were correctly identified and shown to have different responses to those with no difficulties. Ideally the questionnaire should have been validated on a UK population. The reporting of embarrassing symptoms may change culturally and internationally depending on what is deemed appropriate in different settings.

### 7.4.2 Results

Bladder symptoms appeared to be common among the patient group. Significantly more urinary symptoms were noted in the case group when compared with the normal controls. A recent large epidemiological study showed the prevalence of incontinence to be between 10% and 21% for ages...
20-39 \cite{155}, which is in keeping with the result from the control group. However, it shows the CAH group have experienced significantly higher levels of incontinence than would otherwise be expected. This is in contrast to the findings in a recent study, where 41 women with CAH completed a questionnaire which asked, in part, about urinary symptoms \cite{156}. None of the women reported any urinary incontinence, although 8 had experienced "noteworthy" urinary tract infections during their lives, compared with none of the control group. These findings are surprising, as some incontinence would be expected for women in this age group. However, there was a significant difference in urinary tract infections between the two groups. Details are not supplied regarding the control group, although it would be considered unusual that a population of normal women did not suffer any urinary tract infections.

It is unclear why women with CAH should have significantly increased lower urinary tract symptoms when compared with their peers. Danismend and colleagues suggest their finding of a reduced bladder capacity could be responsible for the symptomatology observed \cite{152}. They suggest this may be an effect of the in-utero virilisation, with a more male-like bladder developing. This could lead to storage problems, with frequency, urgency and nocturia being particularly troublesome. Although slightly more of the subject group experienced storage difficulties, there was no significant difference between the two groups. Others suggest that urethral function may have been compromised in some way by feminising surgery, and have highlighted this as an area that requires further attention \cite{89}.

Alternatively, the endocrinological effects caused by CAH may predispose to urinary symptoms, with increased levels of hormones present. Oestrogen, progesterone and androgen receptors are present at the bladder neck, although their interaction with the autonomic nerves which govern continence, is not clear \cite{152}. Progesterone receptors are present elsewhere in the bladder and urethra, and the general effects are to decrease detrusor tone and urethral resistance therefore having a negative effect upon the lower urinary tract \cite{157}. Elevated progesterone levels found in those patients with poorly controlled CAH may therefore have an effect upon bladder function \cite{158}. This
may account for symptoms of stress incontinence, but the most prevalent form of incontinence seen in our subjects was urge incontinence. The effects of progesterone would not necessarily cause this. It may be that long-term steroid replacement required for the treatment of CAH contributes to urinary symptomatology. However, replacement therapy has been practiced for approximately 50 years, and so far no such side-effects are documented.

A simplistic explanation for the lack of data available in the literature is that individuals may be reluctant to seek medical advice, preferring instead to “cope”. Urinary incontinence is an embarrassing symptom and one which patients may be reluctant to discuss. The majority of women with CAH do not routinely have reviews with a gynaecologist or urologist, and therefore may not feel it appropriate to discuss such symptoms during a consultation with an endocrinologist. Nevertheless, it seems unlikely that our subjects with CAH would significantly differ in their reporting of urinary symptoms compared with normal controls, who presumably would also find incontinence an embarrassing symptom. Furthermore, the choice of a postal questionnaire is designed to reduce this impact, and would also apply equally to the control group, making differences observed more significant.

The effect of a single problem on the overall quality of life of an individual is difficult to assess, particularly where there are co-existing disease states, yet 9/19 patients reported an adverse impact on their daily lives as a direct result of their urinary symptoms. This was significantly different to the control group. With a symptom such as nocturnal incontinence, this would clearly have an impact on relationships. Yet, when offered the opportunity of a referral to a urologist for further evaluation and discussion of their symptoms, only one of the nine chose to take this up. It is unclear why this should be the case. It may be that women with CAH simply expect to have urinary problems and accept the situation, having developed coping mechanisms. Alternatively, it may be that there is an erroneous general belief that the only option available to improve symptoms is some form of surgical intervention. Women with CAH have frequently undergone repeated genital surgeries, and may choose to put up with urinary symptoms rather than risk requiring additional operations.
Parents and patients are led to understand that one aim of having surgery in childhood is to avoid operations later in life, yet this is rarely the case. The majority of women with CAH will require surgery to the genital area in adolescence, regardless whether they have undergone a “one-stage” procedure as an infant, or not. A further aim of surgery is to avoid subsequent urinary complications. Adult patients may therefore feel if one or more aims of the original surgery were not achieved, subsequent aims are not likely to be met either. Incontinence is unpleasant but not life-threatening, and individuals may be concerned about risking surgery for urinary symptoms. The wide range of surgical procedures available for the treatment of incontinence also suggests that there is a lack of consensus as to which procedure is most effective.

One further explanation for the lack of evidence of lower urinary tract problems in patients with CAH could be the discrepancy between the patient’s and doctor’s perception to the severity of symptoms. One study looked at clinician-assessed quality of life parameters for an individual and compared this with patient self-reported scores. Overall the doctors assessments tended to underestimate the symptoms experienced by the patient, and in particular the degree of bothersomeness.

The design of the study may have led to the positive findings. The normal controls were recruited from members of staff at the hospital. Despite assurances of confidentiality they may have been reluctant to divulge any personal medical information. Members of the CAH group have already participated in the genital sensation study, and therefore may feel sympathetic towards the aim of the study. Although the majority declared themselves satisfied with their previous treatment (see chapter 5, section 5.4.5), they may have been more likely to express the presence of symptoms as they were aware of the study intention.

A degree of prudence should be employed when basing further management on urinary symptoms. Further detailed evaluation should be employed prior to the commencement of an intervention, and urodynamics would be necessary.
in order to assess the nature of any symptoms. One paper assessing the long-term outcomes of women with CAH found of the two patients experiencing incontinence, only one had an abnormal urodynamic assessment. In the quality of life study previously discussed, although the patient self-reported quality of life questionnaire yielded significantly more symptoms, this did not correlate well with objective findings of urinary incontinence.

Finally, as with other measures of long-term outcomes of feminising genitoplasty procedures, attributing urinary difficulties to surgery should be accompanied by an element of caution, as surgical techniques may have improved in the twenty years or so, since many of the subjects underwent surgery. This is argued in the recent consensus statement on the management of 21-Hydroxylase deficiency. However, these new findings suggest that a significant number of women with CAH who underwent feminising genitoplasty now have urinary difficulties. Until further long-term outcome results are available for the paediatric patients operated upon in the late 1980s and 1990s, it is not appropriate to extrapolate that outcome measures are significantly improved, and an enquiry regarding bladder function should form part of the care of all adult women with CAH.

7.5 Conclusions

This study shows women with CAH are more likely to suffer from urinary symptoms, particularly incontinence, when compared with an age matched population of controls. A significant number of patients report a negative impact on their daily lives as a result of their urinary symptoms. At present the underlying cause is unclear. Surgery does not protect against the development of urinary symptoms, and may be implicated in the aetiology. Further research is needed with urodynamic investigations to assess the type and degree of incontinence. More open dialogue is required with women with CAH to identify those who would benefit from further investigation and treatment to improve their lower urinary tract symptoms.
Chapter 8

Thesis Conclusions

8.1 Review of Thesis
This thesis is the world’s largest series assessing women who have undergone childhood genital surgery as part of the long-standing management for those born with intersex conditions. All participants in this thesis had CAH, and data cannot necessarily be extrapolated to those with different intersex conditions. Long-term outcomes have remained unevaluated for the last 50 years, until now. To date, the clitoris and its role in female sexual function remains poorly understood. The aims of childhood surgery of restoring normality, preserving normal sensation, improving psychosexual outcomes and preventing lower urinary tract problems have all been examined.

8.1.1 Normal appearance
This is the first time that detailed measurements have been taken of the normal female genital area. A wide variation in appearance is shown, with a range of virilisation occurring across normal subjects. Importantly, none of the participants had expressed concern with the appearance of the genital area. Such findings change the perception of “normality” and therefore have implications for the judgement of whether surgical correction is required to ensure conformity to the normal female appearance.

8.1.2 Long-term outcomes on Clitoral Sensation
Objective long-term data for those with intersex conditions is sparse. This study of adult women with the same condition evaluating the outcomes of childhood intervention provides much needed information for individuals, parents and clinicians. Sensation testing shows significant impairment to the clitoris in those who underwent feminising operations. Subjects were unaware of temperatures approaching 50°C or 20°C, where normal controls were sensing temperature changes at 39°C and 32°C. Those who had undergone a
clitorectomy or where no identifiable glans tissue was present had the worst results. However, although those who had undergone newer clitoral reduction techniques had better sensation, this was not significant when compared with those who underwent clitorectomy. Furthermore, a significant difference was observed when both surgical groups were compared with those who had CAH but had not undergone surgery and with normal controls. Where measured, the values for the upper vagina did not show a difference suggesting strongly that the effects observed were a direct result of previous surgery. Clitoral reduction procedures are thought to convey a major advance over older clitorectomy operations in preserving sensation. This research suggests such confidence is misplaced, and any form of clitoral surgery causes damage to sensation. The only known role for the clitoris is in mediating sexual pleasure and contributing to sexual sensation. As genital surgery damages this function, the need for such operations will increasingly be challenged. Further evaluation will also be necessary to assess the long-term outcomes where surgery is delayed until puberty, or deferred indefinitely.

8.1.3 Long-term Psychosexual outcomes
Women with CAH do have increased difficulties with sexual function when compared with controls. Vaginal penetration difficulties are common amongst those who have undergone surgery. Anorgasmia is also significantly more likely for those with a history of clitoral and genital operations. No difference was seen between different operation types although the numbers were too small to be clear on this. Women with CAH had increased levels of avoidance, and although this was greater for those who had undergone surgery levels were still high for those who had not. Dissatisfaction is high in women with CAH when compared with unaffected women, although satisfaction was improved in the CAH surgery group. Interestingly, no difference was observed for issues with body image (p = 0.69), with sexual desire (p = 0.73) or with partner communication (p = 0.64). Women with CAH often reported concerns regarding any unusual appearance to the genital area, and the opinion that partners may give. Yet, those in a relationship reported only positive
experiences, either with partners not having noticed or commented, or by only giving favourable opinions. These findings are important for women with CAH, suggesting that many issues which may arise are similar to those experienced by all, regardless of a history of surgery.

8.1.4 Long-term outcomes on Lower Urinary Tract Symptoms

Urinary symptoms were found to be common amongst the group that had undergone surgery. There is a significant difference in lower urinary tract symptoms for the surgery group when compared with age matched controls. This unexpected finding needs further evaluation. Definitive urodynamic studies should be performed, with a clear diagnosis identified.

8.2 Limitations of the Thesis

This thesis has assessed 28 women with the same condition. In the context of intersex research this represents a large cohort, particularly when considering a single condition. The recruitment rate was 50% overall, which compares favourably with other follow-up studies, and is high given the sensitive nature of the study. It could be argued a 50% recruitment rate may introduce bias by only those with poorer outcomes choosing to take part. However, even if the other 50% of women who were not recruited all had perfect results, these findings would still be remarkable and deserve further evaluation. From the limited feedback given by non-participants, it suggests that not all non-participants are entirely happy with the outcomes of their operations.

The vaginal measurements were limited by few subjects being able to take part. However, the fact that so many women could not accommodate the vaginal probe was significant. The main aim for vaginal surgery, apart from allowing menstrual flow, is to facilitate comfortable penetrative intercourse. These results clearly show that this was not possible for a significant number of participants.
8.3 Recommendations for Clinical Practice

8.3.1 Type of surgery

Chapter 3 illustrates the various operations for reduction of the enlarged clitoris, with many authors attempting to refine the procedure. Yet, as recent work has shown, any surgery is likely to disrupt nerves fibres. This therefore leads to the question of how necessary surgery really is. The clitoris has only one known function which may be damaged by essentially cosmetic surgery. This function is not required until after adolescence, so to perform irreversible damaging procedures in childhood for an organ whose function may not be assessed, is inappropriate. Parental pressure may be the strongest indication for performing surgery in infancy. Yet these decisions are being made on a background of anxiety and concern about their child's health, and parents are understandably desperate for their child to be as healthy as possible. Parents may erroneously associate feminising surgery as somehow "curing" their child. Yet, it is essential that parents appreciate that further operations are nearly always required in adolescence despite surgery in infancy, and that such operations risk damage to sexual sensation and function. This information should be discussed with parents as part of ongoing care for their child, and prior to any surgical planning.

In past decades clinicians have been the driving force behind childhood surgery suggesting this is a crucial part of the care of girls with CAH, and have been critical of parents or patients who do not wish to have surgery performed. This is implicit in the language used in the literature. One study commented about a patient who had undergone initial feminising clitoral reduction surgery as a child, and was deemed to have an enlarged clitoris.

"The final patient in this group has adamantly refused further surgery in spite of the disfiguring prominence of her clitoris."

This suggests the option of declining surgery was not in keeping with clinical recommendations, and was seen as unconventional at the very least.
Clear education and information is therefore required, along with the emphasis that operations should not be seen as an essential part of treatment. Surgery represents an irreversible treatment, whilst the option of deferring such interventions can be revisited. The normal appearance of the female genital area has been shown to vary considerably. Therefore surgery and its inherent long-term risks to sexual function should be reserved for those with major virilisation only, with conservative treatment for mild and moderate virilisation.

### 8.3.2 Timing of clitoral surgery

A recent commentary discussed aspects of living with CAH, and argued that the pressure of surgery to “normalise” the genitalia placed a heavy psychological burden on individuals. The article went on to question what was “normal” if everyone was individual and different, and implied that surgery should be performed when the individual was able to participate in the discussion. This suggests that surgery should not be performed until adolescence at the earliest in order for the individual to begin to appreciate the potential risks of surgery. A clitoris which may have appeared larger than usual in childhood could appear of more normal size following puberty. At this time the development of labial fat pads and pubic hair alters the appearance of the genital area considerably, therefore rendering previous surgery for cosmesis unnecessary.

For those born with major virilisation, surgery in childhood may be appropriate. However, potential risks to sensation and function should be explained to parents, along with the understanding that further operations are likely to be necessary. Furthermore, if steroid control is not optimised, clitoral enlargement will occur despite surgery.

### 8.3.2 Timing of vaginal surgery

The poor long-term outcomes of childhood vaginal surgery strongly argue that definitive surgery should be deferred until after adolescence. The vast
majority of those that undergo surgery in childhood are likely to require further procedures in adolescence. The only non-cosmetic procedure a female with CAH may require is vaginal surgery should they wish to have penetrative intercourse. Clitoral surgery is only required for cosmesis. Therefore offering definitive surgery until adolescence allows an individual to make a decision about cosmetic surgery at this time, and to begin to understand the implications regarding sexual function surgery. To carry out surgery when an individual chooses, also makes them more likely to comply with post-operative dilation therapy and to have a better long-term outcome.

8.3.3 Care of women with CAH
The care of adult women with CAH is best met through a multidisciplinary approach. The necessity of steroid replacement and monitoring by an endocrinologist is not disputed. However, few women have access to a gynaecologist for assessment and advice. This thesis illustrates the specific difficulties women may face, and a specialist gynaecological opinion is essential in order to offer appropriate operations as needed, or, potentially more importantly to advise on the limitations of a further surgical approach. Finally, psychological input is crucial. Women with CAH face many specific issues, and long-term psychological access is critical in contributing to the well-being of individuals. The best scenario is a multidisciplinary clinic where women may see relevant clinicians as needed. The selection of clinicians needed may change for individuals as they encounter different life events.

8.4 Recommendations for Future Research
It is essential that prospective long-term research is continued, including assessment of those children who have surgery delayed until adolescence, or indefinitely. It is not ethical for such children to be randomised into surgery-only or psychology-only groups. Therefore observational studies should be commenced, with children entered onto a register and followed throughout childhood and adolescence.
Any operative details could be accurately recorded, with long-term outcomes assessed once the individual was sexually active. This approach involves a great deal of commitment by clinicians, but can be achieved in a tertiary referral centre, with handover care from paediatricians.

Further qualitative research with thematic analysis can identify areas of concern for women with CAH and inform debate. The use of semi-structured interviews could enable themes to be examined in greater depth and give the opportunity to explore concerns expressed by women with CAH. A commonly expressed concern in this thesis was the opinion of partners, either present or future. Research involving partners of women with CAH could further assess sexual function and psychosexual development, and provide important information for those with CAH, and especially those that have undergone feminising genitoplasty procedures.

8.5 Final Conclusions

Feminising genitoplasty surgery has a significantly detrimental effect on sexual sensation and function. The vast majority of surgery is performed for cosmetic reasons, and most women will undergo more than one procedure. The normal appearance of the female genital area varies considerably and surgery should not be performed for mild or moderate virilisation. Contrary to some reports surgery does not protect against subsequent urinary difficulties, and this should not be used as the main indication for surgical procedures. Ideally all children born in the UK with an intersex condition should be entered into a prospective multicentre observational study and followed from childhood, through adolescence and to adulthood.
Reference List


Appendix 1

CAH Attitudes to Surgery

There are lots of different issues about the type and timing of surgery to the clitoris, for women with CAH. We would like to know what your views are.

The following are statements about having surgery to the clitoris. Please put down your initial feelings about the statements, as this gives an accurate idea of your thoughts about surgery.

Please read the following questions and indicate how much you agree with them, where 1 means very strongly disagree and 5 means very strongly agree.

<table>
<thead>
<tr>
<th>strongly disagree</th>
<th>strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have never thought about genital surgery</td>
<td></td>
</tr>
<tr>
<td>I think genital surgery is a good idea in CAH</td>
<td></td>
</tr>
<tr>
<td>I think genital surgery should not be performed</td>
<td></td>
</tr>
<tr>
<td>I would be angry if I had/have had surgery as a baby</td>
<td></td>
</tr>
<tr>
<td>I think genital surgery causes problems with sex</td>
<td></td>
</tr>
<tr>
<td>It is fine for parents to make the decision they think is best</td>
<td></td>
</tr>
<tr>
<td>I would be relieved if I had/have had surgery as a baby</td>
<td></td>
</tr>
<tr>
<td>It is fine for doctors to make the decision for surgery</td>
<td></td>
</tr>
<tr>
<td>I think a lot about the appearance of my genital area</td>
<td></td>
</tr>
<tr>
<td>It is important for the genital area to look completely female</td>
<td></td>
</tr>
<tr>
<td>Only the patient should make a decision for surgery</td>
<td></td>
</tr>
</tbody>
</table>
At what age should genital surgery be carried out?
Please tick one box only

☐ Less than 1 year  ☐ 1-5  ☐ 5-10
☐ 10-13  ☐ 14-18  ☐ over 18
☐ whenever parents choose
☐ whenever patient requests

What would you advise the parents of a two month old girl with CAH with a large clitoris considering surgery to make the clitoris look smaller?

☐ To have an operation at this time
☐ To have the operation as a child
☐ To have an operation after puberty
☐ To put off the operation until she can give an opinion
☐ To put off the operation indefinitely
☐ Other thoughts

If you have had clitoral surgery are there any good or bad experiences that you especially remember?

Good experiences

Bad experiences

Many thanks for your continued help with our study!
APPENDIX 2
SECTION 1: About You

1. How old are you? ...............  

2. Which ethnic group do you belong to?  
☐ Asian ☐ Chinese  
☐ White ☐ Mixed  
☐ Black, African  
☐ Black, other  
☐ Other .....................  

3. Are you a member of any Patient Support Groups?  
☐ Yes ☐ No  
If yes please tick  
☐ Adrenal Hyperplasia Network  
☐ CAH Support Group  
☐ Other (please specify)  
........................................

SECTION 2: Diagnosis  
Please answer the following questions to the best of your current knowledge  

1. What is the name of your condition?  
☐ Don't know  
☐ CAH salt losing  
☐ CAH non-salt losing  
☐ CAH late-onset  
☐ Other, please specify  
........................................
........................................
........................................
........................................
........................................

2. How was your condition first brought to the attention of doctors?  
☐ My condition was noticed at birth OR my sex was not clear when I was born  
☐ I was short for my age in childhood  
☐ I started puberty earlier than usual  
☐ I had problems with hair growth or acne  
☐ Investigated when I didn't have periods  
☐ Investigated because of fertility problems  
☐ Investigated because of sexual problems  
☐ Other, please specify  
........................................
........................................
........................................
........................................
........................................

Your answers will remain confidential
3. At what AGE was this?


4. Have you ever suffered with any of the following conditions?
- Diabetes
- Multiple Sclerosis
- Lower Spine Abnormalities
- Depression
- Any psychiatric illness (please specify)

SECTION 3: Surgery and Treatment

5. Are you taking any of the following drug treatments?
- Prednisilone
- Hydrocortisone
- Dexamethasone
- Fludrocortisone
- Dianette pill
- Oral contraceptive pill
- Hormone replacement therapy
- Spironolactone
- Cyproterone acetate (not Dianette)
- Flutamide
- Viagra
- Vaginal oestrogen cream
- other drugs (please specify)

6. Have you had any surgery related to your condition?
- Yes
- No (please go to question 11)
- Don't know (please go to question 11)

7. To the best of your knowledge have you ever had any of the following operations?
Please indicate how old you were at the time

- Examination under anaesthetic to look at the genital area
- Operation to reduce the size of the clitoris
- Operation to remove the clitoris completely
- Stretch of the vagina under anaesthetic
- Operation to enlarge or open the vagina
- Operation to create a vagina

Your answers will remain confidential
1. Laparotomy (i.e. cut the tummy to look inside) Age
2. Laparoscopy (i.e. looking inside the tummy with telescopes) Age
3. Operation to move the urethra (urine passage) Age
4. Operation to correct bladder or bowel abnormalities Age
5. Other operation (please specify) 

8. If you have had surgery to enlarge or create a vagina please give as much detail about the method(s) used by answering the questions below. 
(If you have not had any vaginal surgery, please go to question 11)

Name of Surgeon

Date of surgery

Hospital

Type of surgery (if known)

Hospital number (if known)

9. How satisfied are you with the results of your vaginal surgery at present on a scale of 1 to 5 (1 being totally unsatisfied and 5 being totally satisfied)?

Please circle your response: 1  2  3  4  5

10. Please tick any of the following complications that you have experienced at any time following vaginal surgery.
☐ No problems
☐ Persistent vaginal discharge
☐ Narrowing (stenosis) of the vagina
☐ Complete closure of the vagina
☐ Recurrent urinary tract infections (eg cystitis)
☐ Abnormal connection between vagina and bladder/bowel/other areas (usually called fistula)
☐ Pain with sexual intercourse (dyspareunia)
☐ Difficulty with sexual intercourse due to the vagina seeming too small or not being able to allow penetration.
☐ Difficulty with sexual intercourse due to lack of lubrication
☐ Problems with leaking of urine
☐ Other, please specify

Your answers will remain confidential
11. Has anyone ever suggested you try vaginal dilators? (these are hollow or solid moulds that you put in the vaginal area and with gentle pressure use to create a vagina)
please tick more than one if appropriate
□ No
□ Yes, without mentioning vaginal surgery
□ Yes, as an alternative to vaginal surgery
□ Yes, although I had previously had unsuccessful vaginal surgery
□ Yes, pre-operatively with vaginal surgery
□ Yes, pre and post-operatively with vaginal surgery
□ Yes, post-operatively with vaginal surgery

12. What do you think of your vagina at the moment?
please tick as many as appropriate
□ Never considered it / no opinion
□ Larger than average
□ Seems ok / 'normal'
□ Smaller than average
□ It is narrow
□ It is short
□ It is small
□ It is tiny or non-existent
□ A sexual partner would notice that it is different from other women
□ I would like it bigger
□ I would like it wider
□ I would like it longer
□ Other (please specify)

13. Have you ever had surgery to the clitoris?
□ Yes
□ No please go to question 22

14. Please tell us at which hospital this was, and names of surgeons if known.
Name of Surgeon

Date of surgery

Hospital

Your answers will remain confidential
Type of surgery (if known)
..........................................................................................................................
Hospital number (if known)
..........................................................................................................................

15. How old were you for the first operation?
..........................................................................................................................

16. What procedure did you have?
☐ Clitorectomy – complete removal of the clitoris
☐ Clitoral reduction – surgery to make the clitoris smaller
☐ Clitoral skin removal – surgery just to remove the skin around the clitoris
☐ Don’t know

17. Have you had further surgery to the clitoris?
☐ Yes
☐ No please go to question 19

18. Please list any subsequent operations you have had to your clitoris, with the hospital and surgeons name if you know this, along with the date.
Operations (if known)..........................................................................................................................
Date ..........................................................................................................................................................
Surgeons ..................................................................................................................................................
Hospital ..................................................................................................................................................
Hospital number (if known)
..........................................................................................................................

19. How satisfied are you with the appearance of your clitoris following surgery on a scale of 1 to 5? (1 being totally unsatisfied and 5 being totally satisfied.)
Please circle your response: 1 2 3 4 5

20. How satisfied are you with the sensitivity of your clitoris following surgery on a scale of 1 to 5? (1 being totally unsatisfied and 5 being totally satisfied.)
Please circle your response: 1 2 3 4 5

21. Please tick any of the following complications that you have suffered at any time following clitoral surgery
☐ infections to the genital area
☐ pain in the clitoral area during sexual intercourse
☐ leaking of urine
☐ lack of sensation
☐ difficulty with orgasm
☐ other (please specify) ..................................................................................................................

Your answers will remain confidential
22. What do you think of your clitoris? please tick as many as appropriate
☐ It is small
☐ It is large
☐ It is normal
☐ It is tiny or non-existent
☐ It is not sensitive enough
☐ It is too sensitive
☐ A sexual partner would notice that it is different from other women
☐ I would like it bigger
☐ I would like it smaller
☐ Other, Please specify

23. Have you ever suffered from painful sensations in the clitoral area, either when aroused or at other times?
☐ Don't know
☐ Yes, very occasionally
☐ Yes, occasionally
☐ Yes, often
☐ No

24. What do you think of the appearance of your genital area in general? please tick as many as appropriate
☐ I am generally happy with it
☐ I am generally unhappy with it
☐ I hate my genital area
☐ No opinion
☐ Everything seems fine
☐ A sexual partner would notice that it is different from other women
☐ Other, please specify

25. Do you currently have a regular sexual partner?
☐ Yes
☐ No please go to question 27

26. Has your partner ever commented the appearance of your genitals? Please tick as many that apply
☐ Never commented
☐ Commented they are no different to other women
☐ Commented they are different but not important
☐ Has suggested you might need to see a doctor for treatment
☐ Other thoughts

Your answers will remain confidential
27. Have you ever experienced any of the following?
☐ Difficulty in holding your urine
☐ Passing urine frequently (more than every two hours)
☐ Leaking urine before getting to the loo
☐ Sudden feeling of needing to pass urine
☐ Sudden leakage of urine
☐ Getting up to pass urine more than once a night
☐ Leakage of urine on coughing or sneezing

28. How much tea, coffee and alcohol do you drink a day?
Cups of tea............................
Cups of Coffee......................
Alcohol (eg two glasses wine) ......................

29. Do you smoke?
☐ Yes
☐ No

Your answers will remain confidential
### SECTION 4: Sexual Function

This is a test designed by psychologists to assess a person's sexual functioning.

Please answer the questions thinking about your current relationship. If you are not in a relationship at the moment please answer according to the last relationship you had.

It has been designed and tested exclusively on heterosexual individuals. If your current or most recent relationship was with a female partner please circle option F in the questions where this choice is given.

### SCORING SCALE:
Please circle your response according to the scale:

A= Never  B= Hardly ever  C= Occasionally  D= Usually  E= Always  F= I have only had gay relationship(s)

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<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>1. Do you feel uninterested in sex?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>2. Do you ask your partner what they like or dislike about your sexual relationship?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>3. Are there weeks in which you don't have sex at all?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>4. Do you become easily aroused?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>5. Are you satisfied with the amount of time you and your partner spend on foreplay?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>6. Do you find that your vagina is so tight that your partner's penis can't enter it?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>7. Do you try to avoid having sex with your partner?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>8. Are you able to experience an orgasm with your partner?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>9. Do you enjoy cuddling and caressing your partner's body?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>10. Do you find your sexual relationship with your partner satisfactory?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>11. Is it possible to insert your finger into your vagina without discomfort?</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
</tbody>
</table>

Your answers will remain confidential
A= Never    B= Hardly ever    C= Occasionally    D= Usually    E= Always    F= I have only had gay relationship(s)

12. Do you dislike stroking and caressing your partner’s penis?    A B C D E F

13. Do you become tense and anxious when your partner wants to have sex?    A B C D E

14. Do you find it impossible to have an orgasm?    A B C D E

15. Do you have sexual intercourse greater than twice a week?    A B C D E

16. Do you find it hard to tell your partner what you like and dislike about your sexual relationship?    A B C D E

17. Is it possible for your partner’s penis to enter your vagina without discomfort?    A B C D E F

18. Do you feel there is a lack of love and affection in your sexual relationship with your partner?    A B C D E

19. Do you enjoy having your genitals stroked and caressed by your partner?    A B C D E

20. Do you refuse to have sex with your partner?    A B C D E

21. Can you reach orgasm when your partner stimulates your clitoris during foreplay?    A B C D E

22. Do you feel dissatisfied with the amount of time your partner spends on intercourse itself?    A B C D E

23. Do you have feelings of disgust about what you do during love making?    A B C D E

24. Do you find that your vagina is rather tight so that your partner’s penis can’t penetrate very far?    A B C D E F

25. Do you dislike being cuddled and caressed by your partner?    A B C D E

26. Does your vagina become moist during love-making?    A B C D E

27. Do you enjoy having sexual intercourse with your partner?    A B C D E

28. Do you fail to reach orgasm during intercourse?    A B C D E

Your answers will remain confidential
This questionnaire covers material that is sensitive and personal. Your response will be kept completely confidential.

Please answer the following questions by choosing and circling the most accurate response for the past month.

1. Do you have a sexual partner? Yes
   No

2. Have you been sexually active during the past month? Yes
   No

3. During the past month how frequently have you had sexual thoughts, fantasies, or erotic dreams?
   (0) Not at all
   (1) Once
   (2) 2 or 3 times
   (3) Once a week
   (4) 2 or 3 times per week
   (5) Once a day
   (6) More than once a day

4. Using the scale to the right indicate how frequently you have felt a desire to engage in the following activities during the past month?
   (An answer is required for each even if it may not apply to you.)
   .... Erotic Kissing .... Masturbation alone .... Mutual masturbation .... Petting and Foreplay .... Oral sex (giving or receiving) .... Vaginal penetration or intercourse .... Anal sex
   (0) Not at all
   (1) Once
   (2) 2 or 3 times
   (3) Once a week
   (4) 2 or 3 times per week
   (5) Once a day
   (6) More than once a day

5. Using the scale to the right indicate how frequently you have become aroused by the following sexual experiences during the past month.
   (An answer is required for each even if it may not apply to you.)
   .... Erotic Kissing .... Dreams or Fantasy .... Masturbation alone .... Mutual masturbation .... Petting and foreplay .... Oral sex (giving and receiving) .... Vaginal penetration or intercourse .... Anal sex
   (0) Have not engaged in this activity
   (1) Not at all
   (2) Seldom, less than 25% of time
   (3) Sometimes, about 50% of time
   (4) Usually, about 75% of time
   (5) always became aroused

Your answers will remain confidential
6. Overall, during the past month, how frequently have you become anxious or inhibited during sexual activity with a partner?

(0) I have not had a partner
(1) Not at all anxious or inhibited
(2) Seldom, less than 25% of the time
(3) Sometimes, about 50% of the time
(4) Usually, about 75% of the time
(5) Always became anxious or inhibited

7. Using the scale to the right, indicate how frequently you have engaged in the following experiences during the past month?
(An answer is required for each even if it may not apply to you.)

.... Erotic Kissing (0) Not at all
.... Sexual Fantasy (1) Once
.... Masturbation alone (2) 2 or 3 times
.... Mutual Masturbation (3) Once a week
.... Petting and foreplay (4) 2 or 3 times per week
.... Oral sex (giving and receiving) (5) Once a day
.... Vaginal penetration or intercourse (6) More than once a day
.... Anal sex

8. During the past month, who has usually initiated sexual activity?

(0) I have not had a partner
(1) I have not had sex with a partner during the past month
(2) I have usually initiated activity
(3) My partner and I have equally initiated activity
(4) My partner has usually initiated activity

9. During the past month, how have you usually responded to your partner's sexual advances?

(0) I have not had a partner
(1) Has not happened during the past month
(2) Usually refused
(3) Sometimes refused
(4) Accepted, reluctantly
(5) Accepted, but not necessarily with pleasure
(6) Usually accepted with pleasure
(7) Always accepted with pleasure

Your answers will remain confidential
10. During the past month, have you felt pleasure from any forms of sexual experience?

(0) I have not had a partner  
(1) Have had no sexual experiences during the past month  
(2) Haven't felt any pleasure  
(3) Seldom, less than 25% of the time  
(4) Sometimes, about 50% of the time  
(5) Usually, about 75% of the time  
(6) Always felt pleasure

11. Using the scale to the right, indicate how often you have reached orgasm during the past month with the following activities

.... In dreams or fantasies  
.... Erotic Kissing  
.... Masturbation alone  
.... Mutual Masturbation  
.... Petting and foreplay  
.... Oral sex (giving or receiving)  
.... Vaginal penetration or intercourse  
.... Anal sex

(0) I have not had a partner  
(1) Have not engaged in this activity  
(2) Not at all  
(3) Seldom, less than 25% of time  
(4) Sometimes, about 50% of time  
(5) Usually, about 75% of time  
(6) Always reached orgasm

12. During the past month, has the frequency of your sexual activity with a partner been:

(0) I have not had a partner  
(1) Less than you desired  
(2) As much as you desired  
(3) More than you desired

13. Using the scale to the right, indicate the level of change, if any, in the following areas during the past month.

(A n answer is required for each, even if it may not apply to you.)

.... Sexual interest  
.... Sexual arousal  
.... Sexual activity  
.... Sexual satisfaction  
.... Sexual anxiety

(0) Not applicable  
(1) Much lower level  
(2) Somewhat lower level  
(3) No change  
(4) Somewhat higher level  
(5) Much higher level

Your answers will remain confidential
14. During the past month, how frequently have you experienced the following?
(An answer is required for each, even if it may not apply to you.)

.... Bleeding or irritation after vaginal penetration or intercourse (0) Not at all
.... Lack of vaginal lubrication (1) Seldom, less than 25% of time
.... Painful penetration or intercourse (2) Sometimes, about 50% of time
.... Difficulty in reaching orgasm (3) Usually, about 75% of the time
.... Vaginal tightness (4) Always
.... Involuntary urination
.... Headaches after sexual activity
.... Vaginal infection

15. Using the scale to the right, indicate the frequency with which the following factors have influenced your level of sexual activity during the past month.
(An answer is required for each, even if it may not apply to you.)

.... My own health problems (e.g. infection, illness) (0) I have not had a partner
.... My partner’s health problems (1) Not at all
.... Conflict in the relationship (2) Seldom, less than 25% of time
.... Lack of privacy (3) Sometimes, about 50% of time
.... Other (please specify) (4) Usually, about 75% of the time
........................................ (5) Always

16. How satisfied are you with the overall appearance of your body?

(0) Very satisfied
(1) Somewhat satisfied
(2) Neither satisfied nor dissatisfied
(3) Somewhat dissatisfied
(4) Very dissatisfied

17. During the past month, how frequently have you been able to communicate your sexual desires or preferences to your partner?

(0) I have not had a partner
(1) I have been unable to communicate my desires or preferences
(2) Seldom, about 25% of the time
(3) Sometimes, about 50% of the time
(4) Usually, about 75% of the time
(5) I was always able to communicate my desires or preferences
18. Overall, how satisfied have you been with your sexual relationship with your partner?

(0) I have not had a partner
(1) Very satisfied
(2) Somewhat satisfied
(3) Neither satisfied nor dissatisfied
(4) Somewhat dissatisfied
(5) Very dissatisfied

19. Overall, how satisfied do you think your partner has been with your sexual relationship?

(0) I have not had a partner
(1) Very satisfied
(2) Somewhat satisfied
(3) Neither satisfied nor dissatisfied
(4) Somewhat dissatisfied
(5) Very dissatisfied

20. Overall, how important a part of your life is your sexual activity?

(0) Not important
(1) Somewhat unimportant
(2) Neither important nor unimportant
(3) Somewhat important
(4) Very important

21. Circle the number that corresponds to the statement that best describes your sexual experience.

(1) Entirely heterosexual
(2) Largely heterosexual, but some homosexual experience
(3) Largely heterosexual, but considerable homosexual experience
(4) Equally heterosexual and homosexual
(5) Largely homosexual, but considerable heterosexual experience
(6) Largely homosexual, but some heterosexual experience
(7) Entirely homosexual

22. Circle the number that corresponds to the statement that best describes your sexual desires.

(1) Entirely heterosexual
(2) Largely heterosexual, but some homosexual desire
(3) Largely heterosexual, but considerable homosexual desire
(4) Equally heterosexual and homosexual
(5) Largely homosexual, but considerable heterosexual desire
(6) Largely homosexual, but some heterosexual desire
(7) Entirely homosexual

Your answers will remain confidential
SECTION 6: Hospital Anxiety

INSTRUCTIONS:
Doctors are aware that emotions play an important part in most illnesses. If your doctor knows about these feelings he/she will be able to help you more. This questionnaire is designed to help your doctor to know how you feel. Read each item and underline the reply which comes closest to how you have been feeling in the past week.

Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought out response.

I feel tense or wound up
   Most of the time
   A lot of the time
   From time to time, occasionally
   Not at all

I still enjoy the things I used to enjoy
   Definitely as much
   Not quite so much
   Only a little
   Hardly at all

I get a sort of frightened feeling as if something awful is about to happen
   Very definitely and quite badly
   Yes, but not too badly
   A little, but it does worry me
   Not at all

I can laugh and see the funny side of things
   As much as I always could
   Not quite so much now
   Definitely not so much now
   Not at all

Worrying thoughts go through my mind
   A great deal of the time
   A lot of the time
   From time to time, but not too often
   Only occasionally

I feel cheerful
   Not at all
   Not often
   Sometimes

Your answers will remain confidential
Most of the time
Read each item and underline the reply which comes closest to how you have been feeling in the past week.

I can sit at ease and feel relaxed
  Definitely
  Usually
  Not often
  Not at all

I feel as if I am slowed down
  Nearly all the time
  Very often
  Sometimes
  Not at all

I get a sort of frightened feeling like “butterflies” in the stomach
  Not at all
  Occasionally
  Quite often
  Very often

I have lost interest in my appearance
  Definitely
  I don’t take as much care as I should
  I may not take quite as much care
  I take just as much care as ever

I feel restless as if I have to be on the move
  Very much indeed
  Quite a lot
  Not very much
  Not at all

I look forward with enjoyment to things
  As much as I ever did
  Rather less than I used to
  Definitely less than I used to
  Hardly at all

I get sudden feelings of panic
  Very often indeed
  Quite often
  Not very often
  Not at all

I can enjoy a good book or radio or TV programme
  Often
  Sometimes
  Not often
  Very seldom

Your answers will remain confidential
SECTION 7: Personal Identity

Please answer these questions about how you have been feeling about yourself over the last 12 months, and tick the most appropriate response.

<table>
<thead>
<tr>
<th>Questions 1-12</th>
<th>Yes</th>
<th>Sometimes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the past 12 months have you felt happy as a woman</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In the past 12 months have you ever felt that it is better to be a woman than to be a man</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In the past 12 months have you ever felt that it would be better to be a man than to be a woman</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In the past 12 months have you felt more like a man than like a woman</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In the past 12 months have you felt there was nothing really good about being a woman</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In the past 12 months have you ever wondered if you would be happier living as a man than as a woman</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>In the past 12 months have you ever had dreams in which you were a man</td>
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<td></td>
<td></td>
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<tr>
<td>In the past 12 months have you ever had the wish or desire to be a man</td>
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<tr>
<td>In the past 12 months have you ever felt that you did not really feel like you were a woman</td>
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<td></td>
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<tr>
<td>In the past 12 months have you ever felt mixed up about yourself, sometimes feeling more like a man and sometimes feeling more like a woman</td>
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<tr>
<td>In the past 12 months have you ever felt that you did not like your body because of your female anatomy (eg having breasts or having a vagina)</td>
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<td></td>
</tr>
<tr>
<td>In the past 12 months have you ever wished to have an operation to change your body into a mans (eg to have your breasts removed or to have a penis)</td>
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</tbody>
</table>
Please answer these questions about how you have been feeling about yourself over the whole of your life, and tick the most appropriate response.

<table>
<thead>
<tr>
<th>Questions 13-24</th>
<th>Yes</th>
<th>Sometimes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over your life have you felt happy as a woman</td>
<td></td>
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<td></td>
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<tr>
<td>Over your life have you ever felt that it is better to be a woman than to be a man</td>
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<tr>
<td>Over your life have you felt more like a man than like a woman</td>
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<tr>
<td>Over your life have you felt there was nothing really good about being a woman</td>
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<tr>
<td>Over your life have you ever wondered if you would be happier living as a man than as a woman</td>
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<td>Over your life have you ever had dreams in which you were a man</td>
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<tr>
<td>Over your life have you ever had the wish or desire to be a man</td>
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<td>Over your life have you ever felt that you did not really feel like you were a woman</td>
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<td>Over your life have you ever felt mixed up about yourself, sometimes feeling more like a man and sometimes feeling more like a woman</td>
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<td>Over your life have you ever felt that you did not like your body because of your female anatomy (eg having breasts or having a vagina)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Over your life have you ever wished to have an operation to change your body into a mans (eg to have your breasts removed or to have a penis)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Your answers will remain confidential 198
SECTION 8: General Health Questions

We should like to know if you have had any medical complaints and how your health has been in general, over the last few weeks. Please answer ALL of the questions by simply underlining the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, rather than those you have had in the past.

It is important that you try to answer ALL the questions.

A = Better than usual   B = Same as usual   C = Less than usual   D = Much less than usual

Have you recently:

1. Been able to concentrate on whatever you're doing? A B C D
2. Lost much sleep over worry? A B C D
3. Felt that you are playing a useful part in things? A B C D
4. Felt capable of making decisions about things? A B C D
5. Felt constantly under strain? A B C D
6. Felt you couldn't overcome your difficulties? A B C D
7. Been able to enjoy your normal day-to-day activities? A B C D
8. Been able to face up to your problems? A B C D
9. Been feeling unhappy and depressed? A B C D
10. Been losing confidence in yourself? A B C D
11. Been thinking of yourself as a worthless person? A B C D
12. Been feeling reasonably happy, all things considered? A B C D

Your answers will remain confidential
SECTION 9: Permission to obtain previous hospital notes

We would like to be able to view your medical records from other hospitals where you have had procedures carried out. This is to be able to identify exactly which type of surgery you had. Also we can check any specialist investigations you may have had for your type of CAH. This helps make our study more accurate.

To do this we would like your permission to be able to look at your notes from other hospitals where you have been a patient.

If you agree to this, please fill in the consent form below.

Full Name (Current)
.................................................................................................................................
Previous names or surname used
.................................................................................................................................
Date of birth
.................................................................................................................................
Current Address
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................

Hospitals where you have been treated
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................

Hospital numbers (if known)
........................................................................................................................................
........................................................................................................................................

I give permission for Dr Naomi Crouch, of University College London, to view my hospital case notes.

Signature ................................................................................................................................
Date .......................................................................................................................................
Many thanks for completing the questionnaire!

Your answers will remain confidential, and no identifying features will be published

SECTION 10: Any comments

Finally, if we could ask you for any comments you may have regarding the questionnaires, the study in general, or other points you wish to make.

Please use the space below, and over the page, to let us know any comments you may have.

Thank you for your time and support. We hope to have our results available in 2003. Copies will be sent to all the support groups and people who have participated, and will also be available from Dr. Crouch (UCL, Department of O&G, 86-96 Chenies Mews, London WC1E 6HX, UK)

Advice and support for anyone who has CAH is available from

- Adrenal Hyperplasia Network
  www.ahn.org
  Offers support for all with CAH, especially teenagers and young adults.

- CAH support group
  www.cah.org.uk
  Provides support for families, children and young adults with CAH. Support group of CLIMB (Children Living with Inherited Metabolic Diseases).
APPENDIX 3

Name.................................................  Patient No   
Date...............................................  Date of Birth

URINARY SYMPTOMS QUESTIONNAIRE

We are trying to find out how much of a problem your urinary symptoms are to you. We would be grateful if you could help us by filling out this questionnaire.

When answering the questions think about the symptoms you have experienced in the past month.

You will see that some questions ask if you have a problem occasionally, sometimes or most of the time.

Occasionally = less than one third of the time
Sometimes = between one third and two thirds of the time
Most of the time = more than two thirds of the time

Please tick one box for each question

<table>
<thead>
<tr>
<th>1. During the day, how many times do you urinate on average?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 6 times □</td>
</tr>
<tr>
<td>7 to 8 times □</td>
</tr>
<tr>
<td>9 to 10 times □</td>
</tr>
<tr>
<td>11 to 12 times □</td>
</tr>
<tr>
<td>13 or more times □</td>
</tr>
</tbody>
</table>

How much of a problem is this for you?

not a problem □
a bit of a problem □
quite a problem □
a serious problem □

<table>
<thead>
<tr>
<th>2. During the night, how many times do you have to get up to urinate, on average?</th>
</tr>
</thead>
<tbody>
<tr>
<td>none □</td>
</tr>
<tr>
<td>1 □</td>
</tr>
<tr>
<td>2 □</td>
</tr>
<tr>
<td>3 □</td>
</tr>
<tr>
<td>4 or more □</td>
</tr>
</tbody>
</table>

How much of a problem is this for you?

not a problem □
a bit of a problem □
quite a problem □
a serious problem □
<p>| | | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Do you have to rush to the toilet to urinate?</td>
<td>never □</td>
<td>occasionally (less than one third of the time) □</td>
<td>sometimes (between one and two thirds of the time) □</td>
<td>most of the time (more than two thirds of the time) □</td>
<td>all of the time □</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How much of a problem is this for you?</td>
<td>not a problem □</td>
<td>a bit of a problem □</td>
<td>quite a problem □</td>
<td>a serious problem □</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 4. Does urine leak before you can get to the toilet? | never □ | occasionally □ | sometimes □ | most of the time □ | all of the time □ |
| How much of a problem is this for you? | not a problem □ | a bit of a problem □ | quite a problem □ | a serious problem □ |

| 5. Do you have pain in your bladder? | never □ | occasionally □ | sometimes □ | most of the time □ | all of the time □ |
| How much of a problem is this for you? | not a problem □ | a bit of a problem □ | quite a problem □ | a serious problem □ |
6. How often do you leak urine?
   - never □
   - once or less per week □
   - 2-3 times per week □
   - once per day □
   - several times per day □

   How much of a problem is this for you?
   - not a problem □
   - a bit of a problem □
   - quite a problem □
   - a serious problem □

7. Does urine leak when you are physically active, exert yourself, cough or sneeze?
   - never □
   - occasionally (less than one third of the time) □
   - sometimes (between one and two thirds of the time) □
   - most of the time (more than two thirds of the time) □
   - all of the time □

   How much of a problem is this for you?
   - not a problem □
   - a bit of a problem □
   - quite a problem □
   - a serious problem □

8. Do you ever leak urine for no obvious reason and without feeling that you want to go?
   - never □
   - occasionally □
   - sometimes □
   - most of the time □
   - all of the time □

   How much of a problem is this for you?
   - not a problem □
   - a bit of a problem □
   - quite a problem □
   - a serious problem □
9. How much urinary leakage occurs?

- No leakage
- Drops/pants damp
- Dribble/pants wet
- Floods, soaking through to outer clothing
- Floods, running down legs or onto floor

10A. Do you have to change your underclothes or wear protection because of your leakage?

**YES/NO**

If NO please go to question 12
If YES please answer below

- Change underclothes
- Panty liners/mini pads
- Maxi/super sanitary towels
- Nappies/Incontinence products
- Other; please specify

10B How many times a day do you change the above items because of leakage

- No change required
- 1
- 2-3
- 4-5
- More than 5 times

11. Do you need to change your outer clothing during the day because of urine leakage?

- never
- occasionally
- sometimes
- most of the time
- all of the time

12. Is there a delay before you can start to urinate?

- never
- occasionally (less than one third of the time)
- sometimes (between one and two thirds of the time)
- most of the time (more than two thirds of the time)
- all of the time

**How much of a problem is this for you?**

- not a problem
- a bit of a problem
- quite a problem
- a serious problem
13. Do you have to strain to urinate?
   never □
   occasionally □
   sometimes □
   most of the time □
   all of the time □

   How much of a problem is this for you?
   not a problem □
   a bit of a problem □
   quite a problem □
   a serious problem □

14. Do you stop and start more than once while you urinate without meaning to?
   never □
   occasionally □
   sometimes □
   most of the time □
   all of the time □

   How much of a problem is this for you?
   not a problem □
   a bit of a problem □
   quite a problem □
   a serious problem □

15. Do you leak urine when you are asleep?
   never □
   occasionally □
   sometimes □
   most of the time □
   all of the time □

   How much of a problem is this for you?
   not a problem □
   a bit of a problem □
   quite a problem □
   a serious problem □
<table>
<thead>
<tr>
<th>16.</th>
<th>Would you say that the strength of your urinary stream is...</th>
<th>1 2 3 4 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>not reduced □</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>reduced a little □</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>quite reduced □</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>reduced a great deal □</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>no stream □</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>How much of a problem is this for you?</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>not a problem □</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>a bit of a problem □</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>quite a problem □</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>a serious problem □</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>17.</th>
<th>Have you ever blocked up completely so that you could not urinate at all and had to have a catheter to drain the bladder?</th>
<th>1 2 3 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no □</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>yes, once □</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>yes, twice □</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>yes, more than twice □</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>18.</th>
<th>Do you have a burning feeling when you urinate?</th>
<th>1 2 3 4 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>never □</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>occasionally (less than one third of the time) □</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>sometimes (between one and two thirds of the time) □</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>most of the time (more than two thirds of the time) □</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>all of the time □</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>How much of a problem is this for you?</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>not a problem □</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>a bit of a problem □</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>quite a problem □</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>a serious problem □</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>19.</th>
<th>How often do you feel that your bladder has not emptied properly after you have urinated?</th>
<th>1 2 3 4 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>never □</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>occasionally □</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>sometimes □</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>most of the time □</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>all of the time □</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>How much of a problem is this for you?</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>not a problem □</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>a bit of a problem □</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>quite a problem □</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>a serious problem □</td>
<td>4</td>
</tr>
</tbody>
</table>
20. Can you stop the flow of urine if you try while you are urinating?
   Yes, easily □
   Yes, with difficulty □
   No, cannot stop it flowing □
Sexual Matters

Please think about the past month

21. Do you have pain or discomfort because of a dry vagina?
   
   not at all □
   a little □
   somewhat □
   a lot □

   How much of a problem is this for you?
   
   not a problem □
   a bit of a problem □
   quite a problem □
   a serious problem □

22. To what extent do you feel that your sex life has been spoilt by your urinary symptoms?
   
   not at all □
   a little □
   somewhat □
   a lot □

   How much of a problem is this for you?
   
   not a problem □
   a bit of a problem □
   quite a problem □
   a serious problem □

23. Do you have pain when you have sexual intercourse?
   
   not at all □
   a little □
   somewhat □
   a lot □

   How much of a problem is this for you?
   
   not a problem □
   a bit of a problem □
   quite a problem □
   a serious problem □
24. Do you leak urine when you have sexual intercourse?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>not at all</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a little</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>somewhat</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>a lot</td>
<td></td>
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</tr>
</tbody>
</table>

How much of a problem is this for you?

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>not a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a bit of a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>quite a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a serious problem</td>
<td></td>
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</tr>
</tbody>
</table>
### Lifestyle

Please think about the past month

#### 25. How often do you pass urine during the day?

- Hourly □
- Every 2 hours □
- Every 3 hours □
- Every 4 hours or more □

**How much of a problem is this for you?**

- Not a problem □
- A bit of a problem □
- Quite a problem □
- A serious problem □

#### 26. Do you cut down on the amount of fluid you drink so that your urinary symptoms improve, and you can do the things that you want to do?

- never □
- occasionally □
- sometimes □
- most of the time □
- all of the time □

**How much of a problem is this for you?**

- not a problem □
- a bit of a problem □
- quite a problem □
- a serious problem □

#### 27. To what extent have your urinary symptoms affected your ability to perform daily tasks (e.g. cleaning, DIY, lifting objects)?

- not at all □
- a little □
- somewhat □
- a lot □

**How much of a problem is this for you?**

- not a problem □
- a bit of a problem □
- quite a problem □
- a serious problem □
28. Do you avoid places and situations where you know a toilet is not nearby (e.g. shopping, travelling, theatre, church)?

<table>
<thead>
<tr>
<th>Option</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>never</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>occasionally</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sometimes</td>
<td></td>
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<tr>
<td>most of the time</td>
<td></td>
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<tr>
<td>all of the time</td>
<td></td>
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</tbody>
</table>

How much of a problem is this to you?

<table>
<thead>
<tr>
<th>Option</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>not a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a bit of a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>quite a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a serious problem</td>
<td></td>
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</tr>
</tbody>
</table>

29. Do your urinary symptoms interfere with physical activity (e.g. walking, dancing, swimming)?

<table>
<thead>
<tr>
<th>Option</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>not at all</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a little</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>somewhat</td>
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</tr>
<tr>
<td>a lot</td>
<td></td>
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</tbody>
</table>

How much of a problem is this to you?

<table>
<thead>
<tr>
<th>Option</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>not a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a bit of a problem</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>quite a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a serious problem</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

30. How much do your urinary symptoms interfere with your social life (going out, meeting friends and so on)?

<table>
<thead>
<tr>
<th>Option</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>not at all</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a little</td>
<td></td>
<td></td>
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<tr>
<td>somewhat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a lot</td>
<td></td>
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</tr>
</tbody>
</table>

How much of a problem is this to you?

<table>
<thead>
<tr>
<th>Option</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>not a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a bit of a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>quite a problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a serious problem</td>
<td></td>
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</tbody>
</table>

31. Overall, how much do your urinary symptoms interfere with your life?

<table>
<thead>
<tr>
<th>Option</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>not at all</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a little</td>
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<tr>
<td>somewhat</td>
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<td></td>
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</tr>
<tr>
<td>a lot</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
32. How long have you had urinary symptoms that bother you?
   - less than 1 year □
   - 1-2 years □
   - 2-3 years □
   - more than 3 years □

33. If you had to spend the rest of your life with your urinary symptoms as they are now, how would you feel?
   - Perfectly happy □
   - Pleased □
   - Mostly satisfied □
   - Mixed feelings □
   - Mostly dissatisfied □
   - Very unhappy □
   - Desperate □

34. Which of your urinary symptoms bother you most at the moment? (please list the symptoms that bother you most below. Please describe the symptoms in your own words, or write the number of the question that comes closest to describing them):
   1. 
   2. 
   3. 

THANK YOU FOR YOUR HELP

If you have any comments you would like to make about the questionnaire or your urinary symptoms please use the space below