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Impaired Sexual Activity in Male Adults with Partial Androgen Insensitivity

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Context: Choosing the sex of rearing of an XY neonate with a major sexual ambiguity and a mutated androgen receptor remains one of the more difficult questions of neonatal endocrinology. A direct consequence of this choice is the accomplishment of sexual function in adulthood. There is very limited knowledge of the sexual performance of patients with partial androgen insensitivity syndrome.

Objective: The objective of this study is to describe physical acts of sexuality in partial androgen insensitivity syndrome patients reared as males.

Design: We were able to obtain factual information regarding the sexual activity of 15 adult patients who had been reared as males and followed at our institution since birth. We evaluated their sexual performance using two validated questionnaires (Golombok-Rust Inventory of Sexual Satisfaction and International Index of Erectile Dysfunction).

Results: We documented a major impairment of all parameters of sexual activity.

Conclusion: This long-term insight into the consequences of male sex assignment will have to be balanced by a study of the consequences of female sex assignment. **(*J Clin Endocrinol Metab* 91: 3310–3315, 2006)**

IN XY NEONATES having mutations of the androgen receptor (AR) gene, partial androgen insensitivity syndrome (PAIS) encompasses a wide spectrum of masculinization defects ranging from minimal virilization (clitoromegaly) to perineo-scrotal hypospadias (1, 2). The more frequent phenotype is a very small penis with posterior hypospadias and none, one, or two testes palpated in the scrotum. The phenotype of PAIS can be estimated using an external masculinization score (EMS) ranging from 1–6. The calculation of the score is based upon the site of uretral opening, the severity of the micropenis, the degree of scrotal fusion, and the position of the gonads (3). In most reported series of patients, sex assignment is balanced between male and female with 35–67% of PAIS neonates reared as males, a varying choice that reflects the absence of consensus of pediatric endocrinologists on established criteria (4–6).

Hormonal, physical, and sexual development of PAIS patients has been carefully studied during infancy, childhood, and puberty (3, 4, 7, 8). In contrast, there are few reports regarding the facts of life in male or female adults with PAIS. The phenotypes of only 21 adult PAIS patients with mutated AR reared as males were reported in medical surveys published from 1993–2005, but with a limited description of their sexual life (9–19). Male infertility is considered by all authors to be almost constant (6, 10–13, 16, 18, 19). Whether or not the assigned sex proves to be the best choice in a neonate with PAIS thus remains very difficult to know. We suspect this ignorance to be detrimental to the quality of the medical decision regarding the sex of rearing. In the present study, we investigated 15 well-characterized PAIS patients with AR gene mutations, who were followed from birth to adolescence in our institution, then were carefully interviewed during adulthood. Our aim was to provide detailed information about the sexual acts that are usual in young adult males affected by PAIS. This information could help physicians and parents to decide which sex should be assigned to a child born with PAIS. However, it should be balanced by information obtained in adult PAIS patients reared as females. This study is under way. Sexual activity is obviously difficult to evaluate in PAIS male patients, largely because sexual acts have almost exclusively been characterized in males with normal genital anatomy (20–23). The main objective of the present report is simply to describe, as precisely as possible, the nature, frequency, and self-estimated quality of sexual activity in adult males with PAIS, without attempting to make any conclusion regarding their psycho-sexual or psycho-affective life.

Subjects and Methods

Subjects

We reviewed the files of 45 XY neonates with PAIS and mutations of the AR. All were initially referred to our clinic, the Pediatric Endocrinology Department of Paris V University in Saint Vincent de Paul Hospital, and were then followed at our institution. Twenty-eight of them (62%) were reared as males, and we were able to trace 22 of these in adult life. When they were informed of the sexual nature of the information we sought, 7 of 22 (31%) declined participation and 15 agreed to participate. Their ages ranged from 16–43 yr (median 24.3). External genitalia and gynecomastia were evaluated independently by

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Abbreviations: AR, Androgen receptor; EMS, external masculinization score; GRISS, Golombok-Rust Inventory of Sexual Satisfaction; IIEF-5, International Index of Erectile Dysfunction; PAIS, partial androgen insensitivity syndrome.

a pediatric endocrinologist and a urological surgeon. Penile length was measured in neonatal and adult ages. The EMS was calculated according to Ahmed *et al.* (3). A score of 12 occurs with normal male genitalia. All patients had reconstructive surgery of the hypospadias. Seventeen XY neonates with PAIS and mutations of AR were reared as females, but we were able to track only nine. We will study these nine in a separate analysis.

Evaluation of sexual activity at adult age

We used two questionnaires. One is the Golombok-Rust Inventory of Sexual Satisfaction (GRISS) for males, a multidimensional sexual function questionnaire designed to assess the existence and severity of sexual problems (20). The GRISS has been validated in European males (20, 21). It comprises 28 items that yield seven subscale scores for erection, ejaculation, sensuality, avoidance, satisfaction, frequency, and communication, which allows a breakdown of specific areas of sexual dysfunction. Scores on each of the GRISS subscales range from 1–9, such that scores of 1–4 reflect normal sexual functioning and scores of 5–9 indicate increasing levels of sexual dysfunction.

The second questionnaire is the Simplified International Index of Erectile Dysfunction (IIEF-5), a 15-item self-administered questionnaire used to assess erectile function. Six questions are related to erectile function, three to satisfaction with intercourse, two to orgasm, two to sexual desire, and two to overall satisfaction. Each question gives a score of 5 (22). We considered that the "premature ejaculation" subscale was not appropriate to our patients since they had no intercourse. In addition to the questionnaire approach, we used direct interviews with the patients, performed by C.B. and H.L.

The study protocol was approved by our Institutional Review Board for medical bioethics. All patients provided written informed consent.

Hormone measurements and genotyping

Serum testosterone, gonadotropins, anti-Müllerian hormone, and inhibin B were measured with standard radioassays. Testosterone measurements were performed on d 2–7, 30, 60, and 90 after birth and after human chorionic gonadotropin stimulation (three im injections of 1500 U every other day) as well as in adulthood. The response of LH and FSH to iv injection of GnRH (100 $\mu g/m^2$) was evaluated on d 60 after birth. Direct sequencing of the AR gene was performed after PCR using an Applied Biosystems 373A sequencer and Taq dye terminator kit (Applied Biosystems, Foster City, CA) as described (23).

Statistical analysis

Data are reported as mean ± SEM. χ^2 tests were used to compare the scores of the two questionnaires with the values in the normal reference population of adult males. Statistical significance was defined as $P < 0.05$.

Results

Neonatal characteristics

All neonates had posterior hypospadias. Table 1 shows the clinical, hormonal, and molecular characteristics of the studied patients at birth. Neonatal penile length averaged 16.3 ± 5 mm (range 10–25 mm). Ten patients received 50 mg of im testosterone enanthate three times per month during the first months of life, which was associated with a nonsignificant mean penile growth of 8 mm (range 5–10 mm). Four of 15 patients had scrotal testes, others had bilateral (six of 15) or unilateral (five of 15) cryptorchidism. The EMS of Ahmed *et al.* (3) averaged 2.8 (range 1–5) at birth, a value indicating severe undermasculinization, and showed no correlation with the AR genotype. Mean testosterone value was 3.1 ± 1 ng/ml, between 1 and 4 months of life (range 1.8–6.7 ng/ml); values were within the high normal range (8). Human chorionic gonadotropin stimulation raised testosterone levels to 11.5 ± 6 ng/ml (range 6.2–21.8 ng/ml). Basal LH was 4.8 ± 1 U/liter and peaked at 15.6 ± 2 IU/liter after GnRH stimulation. A small vagina was found at neonatal cystography in 11 of 15 patients (73%), with a mean length of 7.7 ± 1.4 mm (5–20 mm).

Characteristics in adult ages

Table 2 shows the clinical and hormonal characteristics of the patients in adulthood. Penile length averaged 40.6 ± 6 mm (range 30–50 mm), less than 5 SD values of the normal mean (133 ± 16 mm) of Caucasian males (24), with a diameter not exceeding 15 mm. Adult penile length was related to neonatal penile length, including the patients who received testosterone therapy ($r = 0.43$, $P < 0.05$). Marked gynecomastia occurred in 13 of 15 patients (87%) at a mean age of 13.7 ± 1.1 yr, leading to mastectomy in all. Adult testosterone level without treatment was 7.9 ± 1 ng/ml (range 6.2–10.9 ng/ml), compared with normal values of 3.4–10 ng/ml. Basal LH and FSH concentrations were 6.6 ± 0.6 and 5.1 ± 1.5 U/liter, and peaked at 30 ± 7 and 14 ± 5 IU/liter after GnRH stimulation. Mean anti-Müllerian hormone and inhibin B were 173 ± 61 pmol/liter and 95 ± 25 pg/ml, re-

TABLE 1. Clinical and hormonal characteristics of the studied patients at birth without any treatment

Patient no.	AR mutation	Penile length (mm)	Cryptorchidism	EMS	T (ng/ml)[a]	Basal LH (IU/liter)
1	Leu547Phe	10	Bilateral	1	3.7	2.9
2	Gly568Trp	10	Unilateral	2.5	3.9	8.4
3	Tyr571His	20	Bilateral	3	4.2	4.3
4	Ser597Thr	10	Bilateral	1.5	NA	NA
5	Arg607Gln	25	No	5	2.2	8.6
6	Ala645Asp	20	No	5	3.2	5.2
7	Pro671His	15	Unilateral	2.5	2.2	9
8	Tyr739Asp	15	Bilateral	1.5	3.1	3.2
9	Val746Met	15	Bilateral	2	4.4	4.6
10	Phe754Leu	25	No	5	1.8	2.5
11	Met780Ile	15	Unilateral	2.5	6.7	3.1
12	Arg788Ser	20	No	5	2.9	1.1
13	His885Tyr	20	Unilateral	3	2.8	5.2
14	Ser888Ser	15	Unilateral	2	2.1	4.8
15	Ser888Ser	10	Bilateral	1	NA	NA

NA, Not available; T, testosterone.
[a] To convert to SI units, multiply by 3.46.

TABLE 2. Clinical and hormonal characteristics of the studied patients in adulthood

Patient no.	Age (yr)	Penile length (mm)	Testosterone (ng/ml)[a]	Basal LH (IU/liter)	Testosterone treatment
1	19.5	45	6.6	8.5	No
2	16.1	40	7.5	5.2	No
3	22.2	50	9.5	8.5	No
4	43	30	6.7	5.8	Yes
5	22.3	50	6.2	5.1	Yes
6	17.1	45	8.2	4.6	Yes
7	23.4	40	7.3	7.4	No
8	16	40	6.2	3.2	No
9	18.6	35	7.8	8.3	No
10	24	35	7.2	6	No
11	34.8	35	7.2	6.5	No
12	25.6	45	7.6	7.4	No
13	26	45	10.9	4	No
14	17.2	40	9.4	7.8	Yes
15	38.5	35	11	11	No

[a] To convert to SI units, multiply by 3.46.

spectively, compared with normal range values of 11–84 pmol/liter and 135–150 pg/ml.

Four of 15 patients (27%) received im testosterone enanthate therapy without any significant or detectable effect. At time of study, 10 of 15 patients (67%) knew the PAIS diagnosis enough to understand the consequences of their disease. Five of 15 patients (33%) thought they had simple hypospadias.

Description of sexual acts

Although none of the participants ever attempted penile-vaginal intercourse, many had sexual activities. This is to be kept in mind to follow the scores evaluating sexual acts. The sexual function scores of the participants for each GRISS subscale are shown in Fig. 1. All men had one or more subscale scores reflecting sexual problems (score of 5 or above). The most prevalent areas of difficulty were noncommunication (15 of 15, 100%), avoidance (15 of 15, 100%), dissatisfaction with sexual acts (13 of 15, 86%), infrequency (13 of 15, 86%), and impotence (12 of 15, 80%). Differences with the normal population were highly significant for each score ($P < 0.001$).

Responses to the IIEF-5 questionnaire revealed that the patients with PAIS reared as males had grossly abnormal values ($P < 0.001$ *vs.* a normal population) (Fig. 2). Mean erectile function score (six questions with a maximal score of 5 for each) was 10 of 30 (moderate erectile dysfunction). The score of satisfaction with intercourse (three questions with a maximal score of 5 for each) was 0 of 15, reflecting the general absence of intercourse. The mean orgasmic function (two questions with a maximal score of 5 for each) score was 3 of 10 (severe dysfunction). The score of sexual desire was 4 of 10 (mild to moderate dysfunction). Mean overall satisfaction was 3 of 10 (severe sexual dysfunction).

During more personalized interviews, all participants identified their external appearance as male and reported a

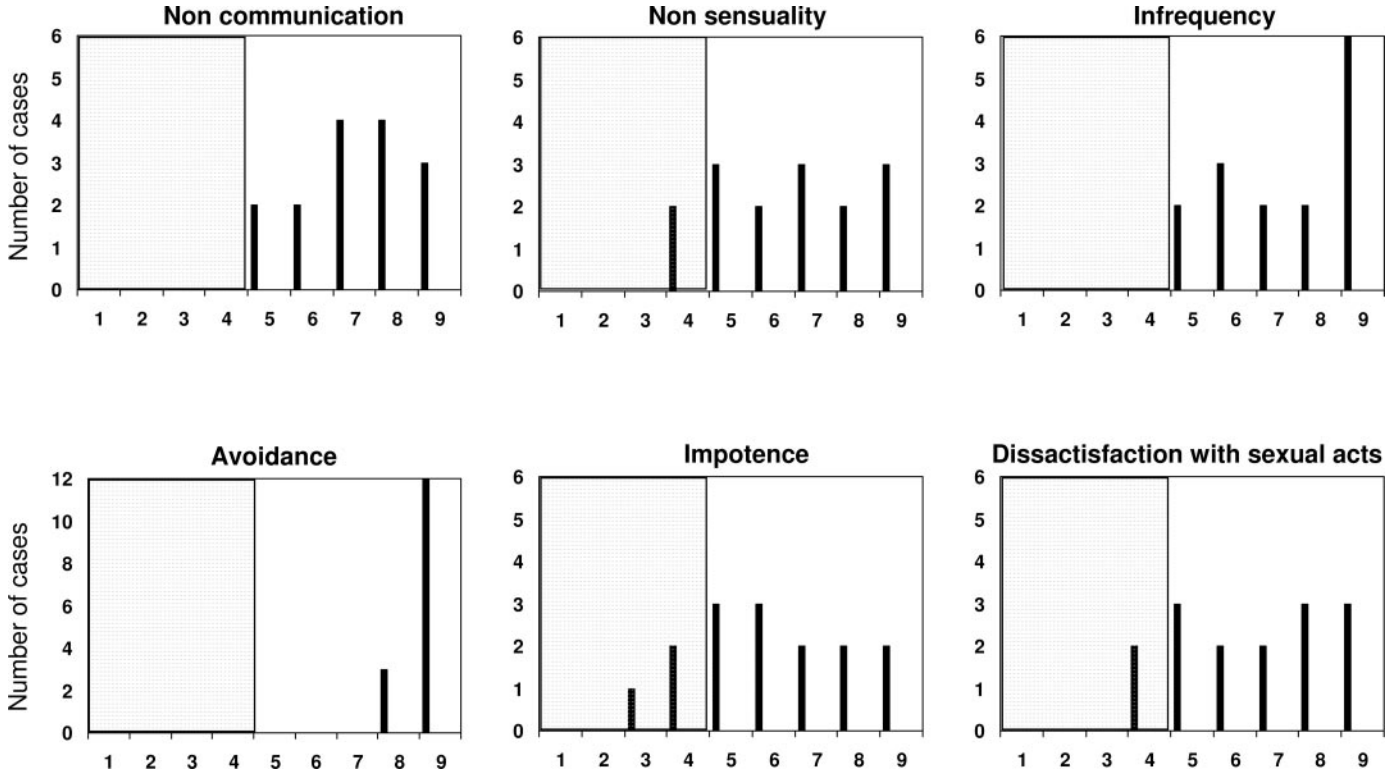

FIG. 1. Scores of sexual function in the 15 studied patients according to GRISS questionnaire. *Graphs* show the distribution of scores (from 1 to 9 on the x-axis) for each GRISS subscale, with the number of patients (y-axis) above each score. Note that ordinate scale is different for "avoidance" due to the large number of patients in the same defective situation. Normal scores range from 1–4 (*shaded area*) and abnormal scores are 5–9.

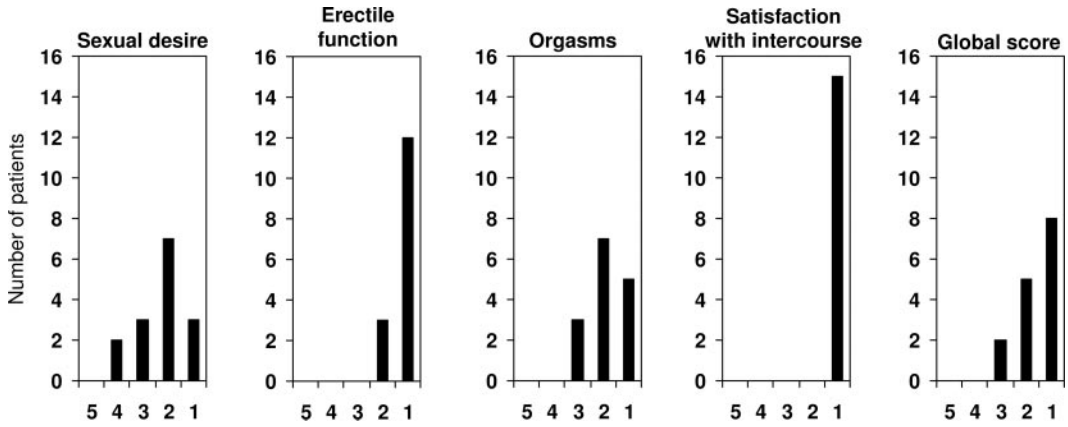

FIG. 2. Scores of sexual function in the 15 studied patients according to the simplified IIEF-5 questionnaire. *Graphs* show the distribution of scores for each IIEF-5 subscale. Scores ranging from 1–5 have been ordered on the x-axis to keep the same orientation (defects *rightward*) as Fig. 1. Dysfunction was classified into five categories based on the following scores: severe (5–7), moderate (8–11), mild to moderate (12–16), mild (17–21).

male heterosexual orientation. Complementary information regarding masturbation and oral sex were obtained from 14 of 15 participants (Table 3). One patient was married. None of the others has a partner established for life. After discussion with the patients, and because none of them was willing to father, a very rare possibility in the literature (16, 18), we did not feel entitled to propose seminal fluid analysis for the only purpose of clinical research.

Discussion

Because many neonate endocrinologists may not be fully aware of consequences of PAIS in adult life, we think it has become mandatory to assess the sexual phenotype and function of adult patients to improve our knowledge about the lifelong problems of intersex patients. When designing this study, we considered that the identification of an AR gene mutation was a prerequisite for the diagnosis of PAIS, since other XY intersex syndromes without androgen insensitivity can result in phenocopy of PAIS (25), but may not have comparable effects on sexuality. Several studies in the literature reported adult male phenotypes in patients born with ambiguous genitalia and PAIS. We found that no more than 21 such cases were analyzed, with information about sexuality only available in seven patients. Data were scarce and no details were given. Four of seven patients were simply said to have "an active sexual life" (Table 4). In contrast, the current evaluation shows poor anatomical and functional results in all studied PAIS reared as males. From all information given by the interviewed patients, it appeared that the severely reduced penis size had a major negative impact upon their self-confidence for engaging in sexual acts with a partner. From late childhood to end of adolescence, a period of active sexual concerns in boys, penile length remained smaller than 50 mm in all studied patients, which impaired the initiation of sexual experiences in 14 of 15 patients. In the studied adults, penile length remained extremely small, with a markedly reduced erectile capacity. However, this does not mean that phallus size is solely responsible for the limitation of sexual acts. Despite obvious anatomical limitations, the mechanisms of sexual dysfunction in the studied patients remain unclear. It will be important in this respect to study patients without AR mutations born with micropenis or hypospadias to determine whether the deficient sexual function that we observed is the result of an abnormal phallus and androgen resistance or just an abnormal phallus. According to the results of the two specialized questionnaires, sexual acts were extremely limited in both frequency and nature, in all participants. We are conscious that our observations are limited to considerations of facts and acts and do not reflect all aspects of sexuality in their complexity. A weakness of the present observations is that we assessed sexual function only at a single point in time, and that longitudinal studies would give a more accurate assessment of adulthood sexuality.

On the other hand, it is very likely that general "Quality of Life" questionnaires that are more and more used in medical studies do not have the psychological finesse and the degree of sensitivity that are necessary to detect specific difficulties with respect to sexual life. In addition, these declarative questionnaires are opened to a previsible source of bias, the underestimation of sexual deficiencies, leading to the conclusion questionable to us that intersex patients have a nearly normal quality of life (26). The relationship between sexual satisfaction and sexual dysfunction has recently been explored using the IIEF questionnaire with reference to nor-

TABLE 3. Main information derived from personalized interviews

	No. of patients	Frequency score for those who have sexual acts
Masturbation		
Self	5/14	1-2-3-3-3
Partner	0/14	
Oral sex		
Receiver	2/14	2-3
Donor	4/14	2-2-3-3

These criteria intended to bridge the gap between sexual acts that can only be performed by adult males with a functional penis anatomy (the GRISS and IESS-5 questionnaires), and sexual acts that can be performed even in the absence of a functional penis. Frequency scores were derived from the IESS-5 questionnaire (0, no; 1, almost never or never; 2, a few times; 3, sometimes; 4, most times; 5, most always or always).

TABLE 4. Recent data collected from all available studies in the literature regarding adult phenotype of adult PAIS with hypospadias reared as males

Ref.	Sex assignment	Age (yr)	Adult penile length (cm)	Sexual intercourse	Testosterone (ng/ml)	AR mutation
10	M	15.2	8.5	NA	NA	Val866Leu
19	M	19	4	Yes	NA	Met780Ile
11	M	16	3	No	NA	Glu772Gly
11	M	18	3	No	NA	Arg608Lys
12	M	23	7.5	No	NN	Arg607Gln
13	M	30	NA	NA	14.2	Val911Leu
14	M	37	5.5	NA	16.3	Leu712Phe
9	M	23	Small penis	NA (married)	7	Gln771Glu
9	M	19	Small penis	Yes	NA	Tyr562H
9	M	21	2.5	NA	10	del > 6kb intron 2
15	M	30	5	NA	9.4	Tyr571His
16	M	17	3	NA	NA	Arg840Cys
16	M	20	3.2	Yes, fathered at 27 yr	16.2	Arg840Cys
16	M	22	4	NA	9.6	Arg840Cys
16	M	22	4	NA	13.5	Arg840Cys
17	M	24	5.5	NA	1.75	Arg855His
17	M	16	3.2	NA	1.57	Tyr602Phe
17	M	22.5	7.4	Yes	10.2	Arg840His
17	M	25	6	NA	11	Tyr763Cys
18	M	14	6	NA	8.7	Trp751stop (somatic)
18	M	17	4.5	NA	1.53	Met895Thr (somatic)

mative data from a healthy population (27). In comparison, PAIS patients in the current report have very severe scores of sexual dysfunction. Not unexpectedly, 31% of the PAIS males who have been tracked refused to participate, indicating that physical aspects of male sexuality are a very sensitive subject. The observations of the present study should only be taken as a preliminary contribution to a more informative and more extensive investigation of all aspects of sexual activity in patients with PAIS. We undertook the current study with the main objective of helping sex assignment at birth. Note in this respect that the current study does not provide any insight into whether rearing PAIS individuals as girls would result in a better adult sexual function and satisfaction. Because the evaluation of female sexual dysfunction requires specific approaches and yet remains difficult (28), such patients reared in the female sex will be studied in a separate analysis. The number of such cases that we have been able to track, as well as data from the literature, remain too limited for the moment. It is only when the sexual life of PAIS patients reared as girls has been evaluated that the analysis of adult sexuality will start to take place in the complex predictive deliberation leading to sex assignment at birth.

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References

1. **Quigley CA, De Bellis A, Marschke KB, el-Awady MK, Wilson EM, French FS** 1995 Androgen receptor defects: historical, clinical, and molecular perspectives. Endocr Rev 16:271–321
2. **Griffin JE** 1992 Androgen resistance. The clinical and molecular spectrum. N Engl J Med 326:611–618
3. **Ahmed SF, Cheng A, Dovey L, Hawkins JR, Martin H, Rowland J, Shimura N, Tait AD, Hughes IA** 2000 Phenotypic features, androgen receptor binding, and mutational analysis in 278 clinical cases reported as androgen insensitivity syndrome. J Clin Endocrinol Metab 85:658–665
4. **Migeon CJ, Wisniewski AB, Gearhart JP, Meyer-Bahlburg HF, Rock JA, Brown TR, Casella SJ, Maret A, Ngai KM, Money J, Berkovitz GD** 2002 Ambiguous genitalia with perineoscrotal hypospadias in 46,XY individuals: long-term medical, surgical, and psychosexual outcome. Pediatrics 110:e31
5. **Migeon CJ, Wisniewski AB, Brown TR, Rock JA, Meyer-Bahlburg HF, Money J, Berkovitz GD** 2002 46,XY intersex individuals: phenotypic and etiologic classification, knowledge of condition, and satisfaction with knowledge in adulthood. Pediatrics 110:e32
6. **Deeb A, Mason Y, Lee YS, Hugues IA** 2005 Correlation between genotype, phenotype and sex of rearing in 111 patients with partial androgen insensitivity syndrome. Clin Endocrinol (Oxf) 63:56–62
7. **Lee PA, Brown TR, La Torre HA** 1986 Diagnosis of the partial androgen insensitivity syndrome during infancy. JAMA 255:2207–2209
8. **Bouvattier C, Carel JC, Lecointre C, David A, Sultan C, Bertrand AM, Morel Y, Chaussain JL** 2002 Postnatal changes of T, LH and FSH in 46,XY infants with mutations in the AR gene. J Clin Endocrinol Metab 87:29–32
9. **Boehmer AL, Brinkmann O, Bruggenwirth H, Van Assendelft C, Otten BJ, Verleun-Mooijman MC, Niermeijer MF, Brunner HG, Rouwe CW, Waelkens JJ, Oostdijk W, Kleijer WJ, van der Kwast TH, de Vroede MA, Drop SL** 2001 Genotype versus phenotype in families with androgen insensitivity syndrome. J Clin Endocrinol Metab 86:4151–4160
10. **Hiort O, Huang Q, Sinnecker GH, Sadeghi-Nejad A, Kruse K, Wolfe HJ, Yandell DW** 1993 Single strand conformation polymorphism analysis of androgen receptor gene mutations in patients with androgen insensitivity syndromes: application for diagnosis, genetic counseling, and therapy. J Clin Endocrinol Metab 77:262–266
11. **Tincello DG, Saunders PT, Hodgins MB, Simpson NB, Edwards CR, Hargreaves TB, Wu FC** 1997 Correlation of clinical, endocrine and molecular abnormalities with in vivo responses to high-dose testosterone in patients with partial androgen insensitivity syndrome. Clin Endocrinol (Oxf) 46:497–506
12. **Weidemann W, Peters B, Romalo G, Spindler KD, Schweikert HU** 1998 Response to androgen treatment in a patient with partial androgen insensitivity and a mutation in the deoxyribonucleic acid-binding domain of the androgen receptor. J Clin Endocrinol Metab 83:1173–1176
13. **Knoke I, Jakubiczka S, Lehnert H, Wieacker P** 1998 A new point mutation of the androgen receptor gene in a patient with partial androgen resistance and severe oligozoospermia. Andrologia 31:199–201
14. **Holterhus PM, Sinnecker GH, Hiort O** 2000 Phenotypic diversity and testosterone-induced normalization of mutant L712F androgen receptor function in a kindred with androgen insensitivity. J Clin Endocrinol Metab 85:3245–3250
15. **Foresta C, Bettella A, Ferlin A, Garolla A, Moro E, Baldinotti F, Simi P, Dallapiccola B** 2002 Response to local dihydrotestosterone treatment in a patient with partial androgen-insensitivity syndrome due to a novel mutation in the androgen receptor gene. Am J Med Genet 107:259–260
16. **Chu J, Zhang R, Zhao Z, Zou W, Han Y, Qi Q, Zhang H, Wang JC, Tao S, Liu**

X, Luo Z 2002 Male fertility is compatible with an Arg 840 Cys substitution in the AR in a large chinese family affected with divergent phenotypes of AR insensitivity syndrome. J Clin Endocrinol Metab 87:347–351
17. **Melo KF, Mendonca BB, Billerbeck AE, Costa EM, Inacio M, Silva FA, Leal AM, Latronico AC, Arnhold IJ** 2003 Clinical, hormonal, behavioral and genetic characteristics of androgen insensitivity syndrome in a Brazilian cohort: five novel mutations in the androgen receptor gene. J Clin Endocrinol Metab 88:3241–3250
18. **Köhler B, Lumbroso S, Leger J, Audran F, Grau ES, Kurtz F, Pinto G, Salerno M, Semitcheva T, Czernichow P, Sultan C** 2005 Androgen insensitivity syndrome: somatic mosaicism of the androgen receptor in seven families and consequences for sex assignment and genetic counseling. J Clin Endocrinol Metab 90:106–111
19. **Rodien P, Mebarki F, Mowszowicz I, Chaussain JL, Young J, Morel Y, Schaison G** 1996 Different phenotypes in a family with androgen insensitivity caused by the same M780I point mutation in the androgen receptor gene. J Clin Endocrinol Metab 81:2994–2998
20. **Rust J, Golombok S** 1986 The Golombok Rust Inventory od Sexual Satisfaction (GRISS). In: Milne D, ed. Interpersonal difficulties. Windsor, UK: NFER-Nelson; 51–59
21. **Golombok S, Rust J, Pickard C** 1984 Sexual problems encountered in general practice. Br J Sex Med 11:171–175
22. **Rhoden EL, Teloken C, Sogari PR, Vargas Souto CA** 2002 The use of the simplified International Index of Erectile Function (IIEF-5) as a diagnostic tool to study the prevalence of erectile dysfunction. Int J Impot Res 14:245–250
23. **Gottlieb B, Trifiro M, Lumbroso R, Pinsky L** 1997 The androgen receptor gene mutation database. Nucleic Acids Res 25:158–162
24. **Schonfeld WA, Beebe GW** 1942 Normal growth and variation in the male genitalia from birth to maturity. J Urol 48:759–777
25. **Boehmer AL, Brinkmann AO, Sandkuij LA** 1999 17β-Hydroxysteroid deshydrogenase 3 deficiency: diagnosis, phenotypic variability, population genetics, and world-wide distribution of ancient and de novo mutations. J Clin Endocrinol Metab 84:4713–4721
26. **Warne G, Grover S, Hutson J, Sinclair A, Metcalfe S, Northam E, Freeman J, Murdoch Childrens Research Institute Sex Study Group** 2005 A long term outcome study of intersex conditions. J Pediatr Endocrinol Metab 18:555–567
27. **Mallis D, Moisidis K, Kirana PS, Papaharitou S, Simos G, Hatzichristou D** 2006 Moderate and severe erectile dysfunction equally affect life satisfaction. J Sex Med 3:444–449
28. **Basson R** 2006 Sexual desire and arousal disorders in women. N Engl J Med 354:1507–1514

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