Associazione Medici Endocrinologi

Sabato 9 novembre 2013

8° Congresso Congiunto AME – ANIED

Aula 7, ore 9.00 - 17.00

Associazione Nazionale Infermieri in Endocrinologia e Diabetologia

Bari,
7-10 novembre 2013

ASPETTI MEDICI DEL DISTURBO DI IDENTITA' DI GENERE

Dr. Ettore Caroppo
ASL Bari
UOSD Fisiopatologia della Riproduzione Umana e P.M.A.
Conversano (Ba)

Pubmed search

Bari,
7-10 novembre 2013

- "*Transsexual*" = 867 articoli
- "*Gender identity disorder*" = 324 articoli
- "*Transgender*" = 907 articoli

PubMed

National Library of Medicine NLM

Sommario

Bari,
7-10 novembre 2013

- Definizione di disturbo di identità di genere (DIG)
- Teorie eziopatogenetiche e psicodinamiche
- Management del DIG
  - Il ruolo dell'endocrinologo
- Linee guida europee
  - DIG in età infantile e adolescenziale
  - la terapia ormonale
  - indicazioni alla chirurgia
- DIG e mortalità
- Conclusioni

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Disturbo di identità di genere (DIG)

Bari,
7-10 novembre 2013

Table 1 *Diagnostic and statistical manual of mental disorders*, 4th ed (DSM-IV) criteria for diagnosis of gender identity disorder[4]

- A strong and persistent cross gender identification (not merely a desire for any perceived cultural advantages of being the other sex)
- A persistent discomfort with his or her sex or a sense of inappropriateness in the gender role of that sex
- The disturbance is not concurrent with a physical intersex condition
- The disturbance causes significant distress or impairment in social or occupational or other important areas of functioning

Tugnet et al, Postgrad Med J 2007;83:638–642

Table 1. Diagnostic Criteria for Gender Identity Disorder.*

- Strong and persistent cross-sex identification (not merely a desire for any perceived cultural advantages of being the other sex)
  - Children (at least four criteria must be met)
    - Repeatedly stated desire to be a member of the other sex or insistence on actually being a member of the other sex
    - In boys, preference for cross-dressing or simulating female attire; in girls, insistence on wearing only stereotypically masculine clothing
    - Strong and persistent preferences for cross-sex roles in make-believe play or persistent fantasies of being a member of the other sex
    - Intense desire to participate in the stereotypical games and pastimes of the other sex
    - Strong preference for playmates of the other sex
  - Adolescents and adults (at least one criterion must be met)
    - Stated desire to be of the other sex
    - Frequent attempts to pass as the other sex
    - Desire to live or be treated as the other sex lives or is treated
    - Conviction of having the typical feelings and reactions of the other sex
- Discomfort with original sex or sense of inappropriateness in the role of that sex
  - Children (at least one criterion must be met)
    - In boys, assertion that penis or testes are disgusting or will disappear, assertion that it would be better not to have a penis, or aversion to rough-and-tumble play and rejection of male stereotypical toys, games, and activities; in girls, rejection of urinating in a sitting position, assertion that she has or will have a penis, assertion that she does not want to have breasts or menstruate, or marked aversion to normative feminine clothing
  - Adolescents and adults (at least one criterion must be met)
    - Preoccupation with getting rid of primary and secondary sex characteristics (e.g., request for hormones, surgery, or other procedures to physically alter sexual characteristics and simulate the other sex) or belief in having been born with the wrong sex
- No concurrent physical intersex condition
- Clinically significant distress or impairment in social, occupational, or other important areas of functioning

Incidenza del DIG

Bari,
7-10 novembre 2013

- 1/12.000 – 1/20.000
- Rapporto maschi/ femmine = 3/1

- Esordio: precoce nel 66% dei casi, tardivo nel 33% (di regola MTF)
- In età prepuberale maschi > femmine
- In età adolescenziale maschi=femmine
- Età adulta maschi>femmine per esordio tardivo MTF
- Transessualismo post-puberale generalmente non modificabile

Gooren LJ, New Eng J Med 2011

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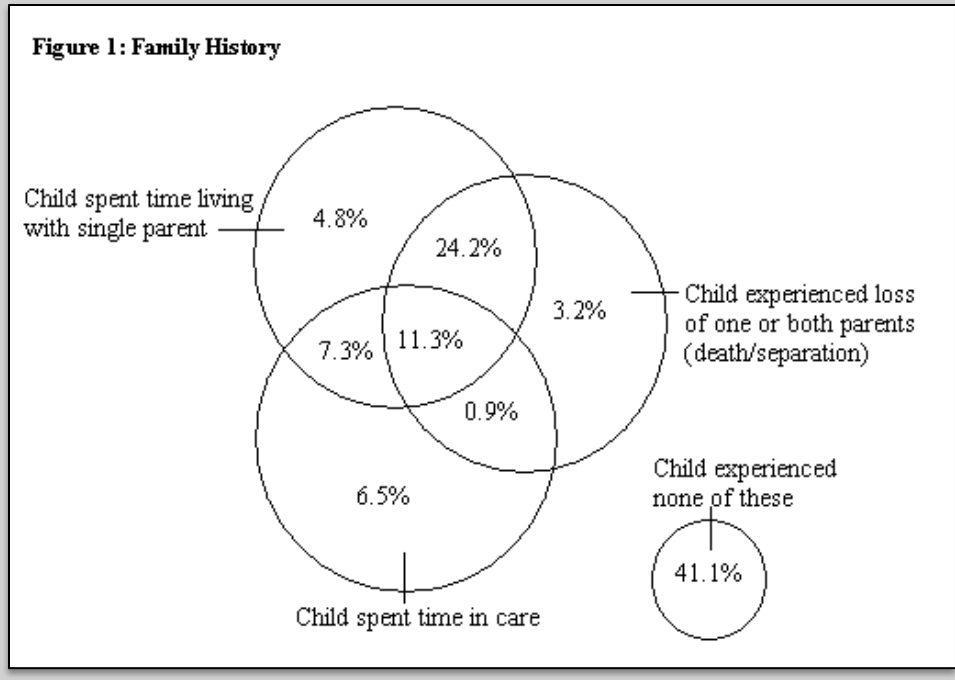
Teorie psicodinamiche

Bari,
7-10 novembre 2013

- Psicopatologie nei genitori
- Ansia nei bambini
- Picco di ormoni femminili nel cervello fetale durante un periodo cruciale dello sviluppo, risultante in un bambino biologicamente normale ma con identità femminile
- Bambino in crescita in stretta relazione con la madre, padre emozionalmente assente

- 75% degli adolescenti in cura presso una Gender Identity Clinic in UK riferiscono problemi relazionali con i propri genitori



Tugnet et al, Postgrad Med J 2007;83:638–642

Di Ceglie D. et al Int J Transgenderism, 2002 (1)

Studi neuroanatomici

Bari,
7-10 novembre 2013

Author	Results	Limits of the study
Emory, 1991	Nessuna associazione tra transessualismo e anatomia del corpo calloso	MRI senza analisi computazionale dell'immagine
Zhou, 1995	Studio autoptico. Transessuali MTF avevano una suddivisione centraledel nucleo della stria terminale di tipo femminile, con riferimento alle sue dimensioni	Campione esiguo (6 pz) Pazienti in terapia estrogenica
Kruijver, 2000	Studio autoptico. Transessuali MTF avevano una suddivisione centrale del nucleo della stria terminale di tipo femminile, con riferimento al numero dei suoi neuroni	Campione esiguo (6 pz) Pazienti in terapia estrogenica
Garcia-Falgueras and Swaab, 2008	Transessuali MTF avevano un volume e densità neuronale del nucleo interstiziale dell'ipotalamo anteriore di tipo femminile	Campione esiguo (11 pz) Pazienti in terapia estrogenica

MRI

Bari,
7-10 novembre 2013

Neuroimage. 2009 July 15; 46(4): 904–907. doi:10.1016/j.neuroimage.2009.03.048.

Regional gray matter variation in male-to-female transsexualism

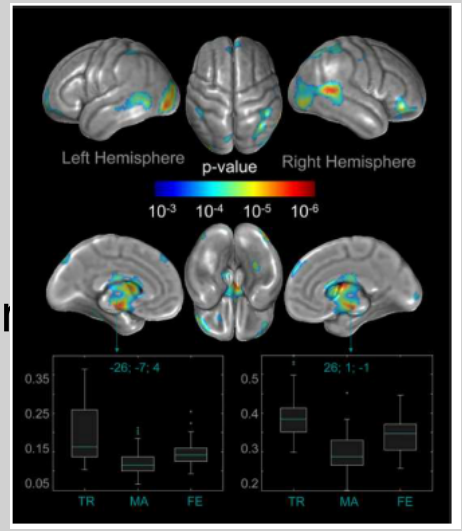
Eileen Luders[1], Francisco J. Sánchez[2], Christian Gaser[3], Arthur W. Toga[1,*], Katherine L. Narr[1], Liberty S. Hamilton[1], and Eric Vilain[2]

doi:10.1093/brain/awn276 *Brain* (2008), 131, 3132–3146

A sex difference in the hypothalamic uncinate nucleus: relationship to gender identity

Alicia Garcia-Falgueras[1,2] and Dick F. Swaab[1]

- 24 MTF-transessuali non in terapia ormonale
- 60 soggetti di controllo (30 uomini, 30 donne)
- High-resolution MRI in vivo co analisi computazionale delle immagini
- . Le dimensioni del corpo calloso erano più grandi nei MTF e nelle donne che negli uomini



MTF anomalie del nucleo interstiziale dell'ipotalamo femmino-simili

Bari,
7-10 novembre 2013

RC PSYCH ROYAL COLLEGE OF PSYCHIATRISTS

The British Journal of Psychiatry

BJPsych

Neuroimaging findings in post-traumatic stress disorder: Systematic review

ALASTAIR M. HULL

BJP 2002, 181:102-110.

Table 2 Magnetic resonance imaging studies of patients with post-traumatic stress disorder (PTSD)

Author (method)	Subjects	Control/comparison groups	Diagnostic criteria (method)	Results
Myslobodsky *et al*, 1995	10 CR-PTSD (gender not specified)	10 matched controls	DSM–III (PTSD symptom checklist)	Increased incidence of cavum septum pellucidum (a neurodevelopmental abnormality)
Bremner *et al*, 1995	26 CR-PTSD (all M)	22 non-CE matched controls (all M)	DSM–III–R (Mississippi Scale for CR-PTSD)	Reduced (R)HC volume, correlates with memory impairment (verbal memory component of Wechsler Memory Scale); no correlation with PTSD symptom severity, dissociation or CE severity
Gurvits *et al*, 1996	7 CR-PTSD (all M)	7 CE non-PTSD controls (all M); 8 non-CE controls (gender not specified)	DSM–III–R (CAPS)	Bilateral reduction in HC volume with statistically significant correlation between (L)HC volume and CE
Bremner *et al*, 1997*a*	17 survivors of CSA and/or physical abuse (12M; 5F)	17 case-matched controls (12M; 5F)	DSM–III–R (Early Trauma Inventory)	Reduced (L)HC volume correlates with abuse duration; trend for larger amygdala in PTSD; reduction in (R)HC not statistically significant
Stein *et al*, 1997	21 survivors of CSA (all F)	21 non-CSA (all F)	DSM–IV (CAPS)	Reduced (L)HC volume correlates with dissociative symptoms and to lesser extent PTSD symptoms
Canive *et al*, 1997 (FLAIR sequence)	42 CR-PTSD (all M)	20 controls (all M)	DSM–III–R (CAPS and Mississippi Scale for CR-PTSD)	Focal WMLs in 8 CR-PTSD subjects
De Bellis *et al*, 1999	44 maltreated children with PTSD (25M; 19F)	61 case-matched non-abused controls (36M; 25F)	DSM–III and DSM–IV (non-standardised measures)	No HC changes; smaller cerebral volumes and total corpus callosum measures correlate with PTSD; cerebral volume correlates with age of onset of trauma and negatively with duration of abuse
Bonne *et al*, 2001	10 miscellaneous trauma (3M: 7F)	27 TE controls (15M: 12F)	DSM–IV (CAPS at 6 months)	No reduction in HC volume at 1 week or 6 months post-trauma

CR, combat-related; CE, combat-exposed; TE, trauma-exposed; HC, hippocampus; CSA, child sexual abuse; M, male; F, female; (R), right; (L), left; FLAIR, fluid attenuated inversion recovery imaging; CAPS, Clinician Administered PTSD Scale; WML, white matter lesion.

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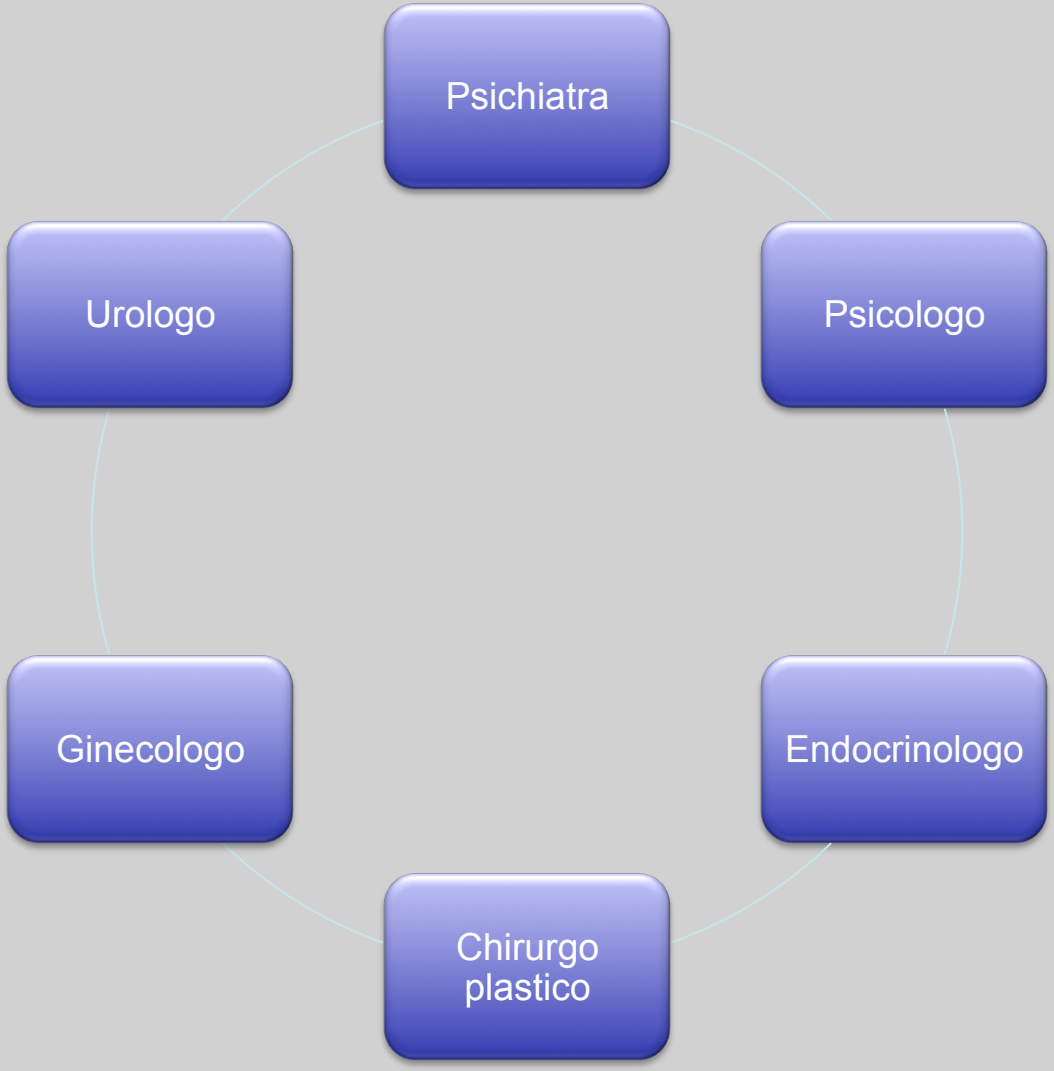
Approccio multidisciplinare al transessualismo

Bari,
7-10 novembre 2013



Il ruolo dello psichiatra

- Patologie psichiatriche, mutilazioni genitali, tentativi di suicidio in 1 paziente su 10 → diagnosi differenziale con psicosi e abuso di psicofarmaci/ stupefacenti
- Anamnesi psicosessuale (comportamenti tipici del sesso di origine/contrario nel periodo infantile, vestiario)
- Tentativi di uniformarsi alle aspettative culturali sul sesso di origine/contrario
- Vita affettiva/sessuale

Tugnet et al, Postgrad Med J 2007;83:638–642

Il ruolo del chirurgo

Bari,
7-10 novembre 2013

- Valutazione e cura delle patologie chirurgiche preesistenti
- Valutazione/informazione al paziente sui possibili risultati della chirurgia e sulle complicanze peri/postoperatorie
- Gonadectomia, isterectomia, mastectomia
- Neovagina/falloplastica
- Mastoplastica
- Protesi peniena
- Chirurgia cosmetica/estetica

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Il ruolo dell'endocrinologo

- Diagnosi differenziale tra DIG e disordini dello sviluppo sessuale
- Valutazione di disordini dello sviluppo puberale
- Valutazione/cura delle patologie internistiche pre-esistenti
- Terapia ormonale
- Ruolo decisionale pre-chirurgia
- Follow up

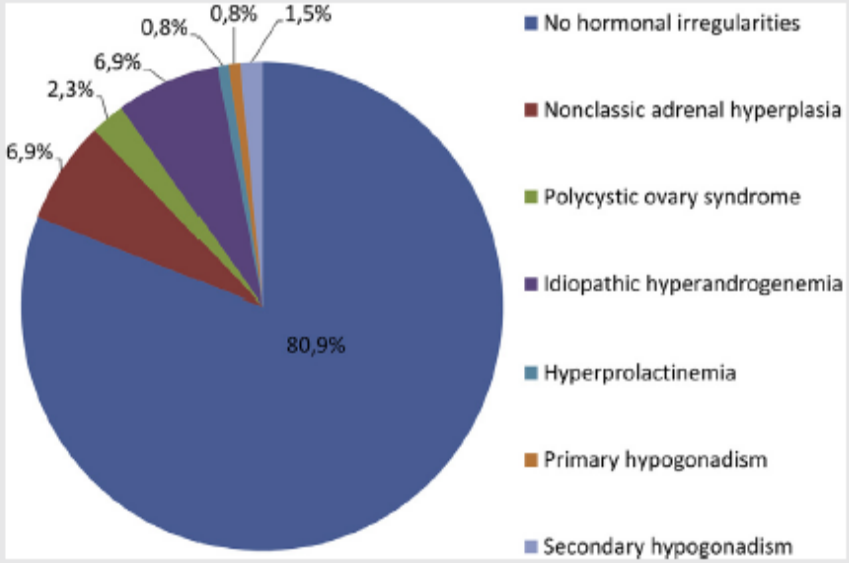
Twenty years of endocrinologic treatment in transsexualism: analyzing the role of chromosomal analysis and hormonal profiling in the diagnostic work-up

Matthias K. Auer, M.D.,[a] Johannes Fuss, M.D.,[b] Guenter K. Stalla, M.D.,[a] and Anastasia P. Athanasoulia, M.D.[a]

[a] Department of Internal Medicine, Endocrinology, and Clinical Chemistry, Max Planck Institute of Psychiatry, Munich; and [b] Department of Psychiatry and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim/University of Heidelberg, Mannheim, Germany

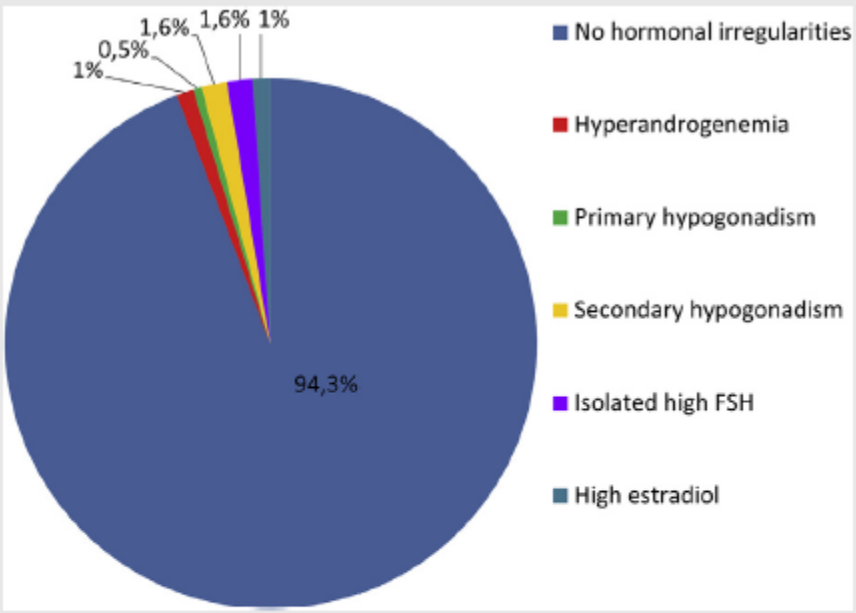
Alterazioni ormonali

Bari,
7-10 novembre 2013



Hormonal irregularities in female-to-male individuals (FtM) at first presentation. Hormonal disturbances were present in 25 subjects (19.1%) of the FtM group. Hyperandrogenemia was the most common diagnosis (16%), owing to a high prevalence of biochemically confirmed nonclassic adrenal hyperplasia (NCAH) in nine subjects (6.9%). PCOS was less common, with three cases (2.3%), and in nine patients (6.9%) no definite cause for hyperandrogenemia according to our criteria could be identified, and it was therefore referred to as idiopathic. Secondary hypogonadism was seen in two patients (1.5%) one of whom was suffering from anorexia nervosa (0.7%) and the other from hyperprolactinemia (0.7%).

Auer. Chromosomal analysis in transsexuals. Fertil Steril 2013.



Hormonal irregularities in male-to-female individuals (MtF) at first presentation. Two patients presented with hyperandrogenemia (1%), one with primary hypogonadism (0.5%), and three from secondary hypogonadism (1.6%). Two patients (1%) presented with elevation in E_2 levels and three with isolated high FSH (1.6%).

Auer. Chromosomal analysis in transsexuals. Fertil Steril 2013.

Disordini dello sviluppo puberale

Bari,
7-10 novembre 2013

Pubertal and menstrual cycle irregularities in treatment-naïve patients.

	n	%
Female-to-male		
Pubertal irregularities present	5	3.8
Premature menarche	2	1.5
Delayed menarche	3	2.3
Menstrual irregularities after menarche present	14	10.7
Oligomenorrhea	8	6.1
Polymenorrhea	1	0.8
Secondary amenorrhea	5	3.8
Male-to-female		
Pubertal irregularities present	10	5.2
Delayed oigarche	5	2.6
Cryptorchidism	3	1.6
No pubertal voice change	2	1

Auer. Chromosomal analysis in transsexuals. Fertil Steril 2013.

Chromosomal profile of the patient group.

	n	%
Female-to-male (FtM)		
Karyotype available	56	53.3
Unremarkable karyotype 46,XX	53	94.6
Abnormal karyotype	3	5.4
45,X[10]/47,XXX[6]/46,XX[98]	1	1.8
45,XXder(14;22)(q10;q10)	2	3.6
Hair root analysis available	49	46.7
Barr body positive	49	100
Barr body negative	0	0
Overall chromosomal abnormality in the FtM group	3	2.9
Male-to-female (MtF)		
Karyotype available	83	30.4
Unremarkable karyotype 46, XY	82	98.8
Abnormal karyotype	1	1.2
47,XXY[a]	1	1.2
Hair root analysis available	83	30.4
Barr body positive[a]	1	1.2
Barr body negative	82	98.8
Overall chromosomal abnormality in the MtF group	1	0.6

[a] Same patient.

Auer. Chromosomal analysis in transsexuals. Fertil Steril 2013.

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Linee guida europee

Bari,
7-10 novembre 2013

SPECIAL FEATURE

Clinical Practice Guideline

Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline

Wylie C. Hembree, Peggy Cohen-Kettenis, Henriette A. Delemarre-van de Waal, Louis J. Gooren, Walter J. Meyer III, Norman P. Spack, Vin Tangpricha, and Victor M. Montori*

J Clin Endocrinol Metab. September 2009, 94(9):3132–3154

Raccomandazioni generali

Bari,
7-10 novembre 2013

- La diagnosi di DIG va posta da uno specialista in salute mentale
- Data l'alta frequenza di remissione del DIG dopo la pubertà, è controindicato un completo cambiamento del ruolo sociale e il trattamento ormonale nei bambini prepuberi
- I medici devono far comprendere ai pazienti gli effetti reversibili e quelli irreversibili della soppressione ormonale (GnRH) e della terapia ormonale per il cambiamento del sesso
- I pazienti transessuali vanno informati sugli effetti sulla fertilità dei trattamenti ormonali prima di dare inizio alla soppressione della pubertà negli adolescenti e alla terapia ormonale

TABLE 2. DSM-IV-TR diagnostic criteria for GID (3)

A. A strong and persistent cross-gender identification (not merely a desire for any perceived cultural advantages of being the other sex).
   In children, the disturbance is manifested by four (or more) of the following:
   1. Repeatedly stated desire to be, or insistence that he or she is, the other sex.
   2. In boys, preference for cross-dressing or simulating female attire; in girls, insistence on wearing only stereotypical masculine clothing.
   3. Strong and persistent preferences for cross-sex roles in make-believe play or persistent fantasies of being the other sex.
   4. Intense desire to participate in the stereotypical games and pastimes of the other sex.
   5. Strong preference for playmates of the other sex.

   In adolescents and adults, the disturbance is manifested by symptoms such as a stated desire to be the other sex, frequent passing as the other sex, desire to live or be treated as the other sex, or the conviction that he or she has the typical feelings and reactions of the other sex.
B. Persistent discomfort with his or her sex or sense of inappropriateness in the gender role of that sex.
   In children, the disturbance is manifested by any of the following:
   1. In boys, assertion that his penis or testes is disgusting or will disappear, or assertion that it would be better not to have a penis, or aversion toward rough-and-tumble play and rejection of male stereotypical toys, games, and activities.
   2. In girls, rejection of urinating in a sitting position, assertion that she has or will grow a penis, assertion that she does not want to grow breasts or menstruate, or marked aversion toward normative feminine clothing.

   In adolescents and adults, the disturbance is manifested by symptoms such as preoccupation with getting rid of primary and secondary sex characteristics (*e.g.* request for hormones, surgery, or other procedures to physically alter sexual characteristics to simulate the other sex) or belief that he or she was born the wrong sex.
C. The disturbance is not concurrent with a physical intersex condition.
D. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Codes based on current age:
302.6 GID in children
302.85 GID in adolescents or adults

Specify whether (for sexually mature individuals):
Sexually attracted to males
Sexually attracted to females
Sexually attracted to both
Sexually attracted to neither

The Telegraph

Bari,
7-10 novembre 2013

With his blonde pigtails and purple tutu, Zach Avery, now five, has been living as a girl for more than a year - after he first refused to live as a boy when he turned three.

Little Zach was just three when he began refusing to live as a boy, instead choosing to wear pink dresses and ribbons in his long, blonde hair - because he has Gender Identity Disorder (GID).

And the primary school he attends in Essex has even changed the kids' toilets to gender-neutral Unisex in support of Zach since his official diagnosis last year, aged four.

Zach is one of the youngest in Britain ever to be diagnosed with GID - meaning he feels like he's a girl trapped in a boy's body.

Mum Theresa Avery, 32, said Zach used to be a 'normal' little boy but suddenly at the end of 2010, he decided he wanted to live as a girl.

He became obsessed with the girly kids' TV character Dora the Explorer and started dressing in girls clothing

Zach Avery: the boy, 5, who wanted to be a girl

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- I pazienti transessuali vanno informati sugli effetti sulla fertilità dei trattamenti ormonali prima di dare inizio alla soppressione della pubertà negli adolescenti e alla terapia ormonale

Human Reproduction, Vol.27, No.2 pp. 483–487, 2012
Advanced Access publication on November 28, 2011 doi:10.1093/humrep/der406

human reproduction ORIGINAL ARTICLE *Infertility*

Reproductive wish in transsexual men

Katrien Wierckx[1,*,†], Eva Van Caenegem[1,†], Guido Pennings[2], Els Elaut[3], David Dedecker[1], Fleur Van de Peer[1], Steven Weyers[4], Petra De Sutter[4], and Guy T'Sjoen[1]

Table II Relationship and reproductive characteristics.

Currently in relationship ($n = 50$)	
Yes	32 (64.0)
No	18 (36.0)
Sexual orientation after SRS ($n = 50$)	
(mainly) Attracted to females	43 (86.0)
Bisexual	2 (4.0)
(mainly) Attracted to males	5 (10.0)
Children ($n = 50$)	
Yes	11 (22.0)
No	39 (78.0)
Desire to have children ($n = 50$)	
Yes	27 (54.0)
In the past	4 (8.0)
No	19 (38.0)
Considered freezing of germ cells before transition ($n = 48$)	
Yes, but it was technically not possible	2 (4.2)
Yes, but I have never spoken about this with a health care provider	9 (18.8)
No	37 (77.1)
Would have considered freezing germ cells, if technique had been available ($n = 48$)	
Yes	18 (37.5)
No	30 (62.5)

Results are presented as *n* (%).

Trattamento ormonale

Bari,
7-10 novembre 2013

- ADOLESCENTI
- Soppressione dello sviluppo puberale negli adolescenti riconosciuti idonei e pronti alla attribuzione ormonale del sesso desiderato
- Soppressione dello sviluppo puberale allo stadio Tanner 2-3
- Induzione dello sviluppo puberale del sesso opposto a 16 aa, con incremento graduale della posologia ormonale
- Chirurgia:

  - test di vita reale soddisfacente

  - paziente soddisfatto degli effetti della terapia ormonale

  - paziente desideroso di cambiamento definitivo dei caratteri sessuali secondari

  - età ≥ 18 anni

TABLE 6. Description of tanner stages of breast development and male external genitalia

For breast development:

1. Preadolescent.
2. Breast and papilla elevated as small mound; areolar diameter increased.
3. Breast and areola enlarged, no contour separation.
4. Areola and papilla form secondary mound.
5. Mature; nipple projects, areola part of general breast contour.

For penis and testes:

1. Preadolescent.
2. Slight enlargement of penis; enlarged scrotum, pink texture altered.
3. Penis longer, testes larger.
4. Penis larger, glans and breadth increase in size; testes larger, scrotum dark.
5. Penis and testes adult size.

TABLE 7. Estradiol levels in female puberty and testosterone levels in male puberty during night and day

Tanner stage	Nocturnal	Diurnal
Estradiol (pmol/liter)[a]		
B1	<37	<37
B2	38.5	56.3
B3	81.7	107.3
B4	162.9	132.3
B5	201.6	196.7
Testosterone (nmol/liter)[b]		
G1	<0.25	<0.25
G2	1.16	0.54
G3	3.76	0.62
G4	9.83	1.99
G5	13.2	7.80
Adult	18.8	17.0

Data represent median of hourly measurements from 2400–0600 h (nocturnal) and 1200–1800 h (diurnal).

TABLE 5. Hormone therapy for adolescents

Adolescents are **eligible** and ready for GnRH treatment if they:

1. Fulfill DSM IV-TR or ICD-10 criteria for GID or transsexualism.
2. Have experienced puberty to at least Tanner stage 2.
3. Have (early) pubertal changes that have resulted in an increase of their gender dysphoria.
4. Do not suffer from psychiatric comorbidity that interferes with the diagnostic work-up or treatment.
5. Have adequate psychological and social support during treatment, AND
6. Demonstrate knowledge and understanding of the expected outcomes of GnRH analog treatment, cross-sex hormone treatment, and sex reassignment surgery, as well as the medical and the social risks and benefits of sex reassignment.

Adolescents are **eligible** for cross-sex hormone treatment if they:

1. Fulfill the criteria for GnRH treatment, AND
2. Are 16 yr or older.

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TABLE 8. Follow-up protocol during suppression of puberty

Every 3 months
- Anthropometry: height, weight, sitting height, Tanner stages
- Laboratory: LH, FSH, estradiol/testosterone

Every year
- Laboratory: renal and liver function, lipids, glucose, insulin, glycosylated hemoglobin
- Bone density using dual-energy x-ray absorptiometry
- Bone age on x-ray of the left hand

TABLE 9. Protocol induction of puberty

Induction of female puberty with oral 17-β estradiol, increasing the dose every 6 months:
- 5 μg/kg/d
- 10 μg/kg/d
- 15 μg/kg/d
- 20 μg/kg/d
- Adult dose = 2 mg/d

Induction of male puberty with intramuscular testosterone esters, increasing the dose every 6 months:
- 25 mg/m^2 per 2 wk im
- 50 mg/m^2 per 2 wk im
- 75 mg/m^2 per 2 wk im
- 100 mg/m^2 per 2 wk im

TABLE 10. Follow-up protocol during induction of puberty

Every 3 months
- Anthropometry: height, weight, sitting height, Tanner stages
- Laboratory: endocrinology, LH, FSH, estradiol/testosterone

Every year
- Laboratory: renal and liver function, lipids, glucose, insulin, glycosylated hemoglobin
- Bone density using dual-energy x-ray absorptiometry
- Bone age on x-ray of the left hand

These parameters should also be measured at long term. For bone development, they should be measured until the age of 25–30 yr or until peak bone mass has been reached.

Trattamento ormonale

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- ADULTI
- L'endocrinologo deve confermare la diagnosi di DIG e la sussistenza dei criteri di eligibilità al trattamento ormonale
- Le patologie che possono essere aggravate dalla terapia ormonale devono essere individuate e corrette prima di cominciare il trattamento
- I livelli plasmatici degli ormoni del sesso desiderato/opposto devono essere mantenuti nei limiti della norma
- L'endocrinologo deve valutare l'esordio e la durata delle modificazioni fisiche indotte dal trattamento ormonale

TABLE 4. Hormone therapy for adults

Adults are **eligible** for cross-sex hormone treatment if they (28):

1. Fulfill DSM IV-TR or ICD-10 criteria for GID or transsexualism (see Tables 2 and 3).
2. Do not suffer from psychiatric comorbidity that interferes with the diagnostic work-up or treatment.
3. Demonstrate knowledge and understanding of the expected outcomes of hormone treatment, as well as the medical and social risks and benefits; AND
4. Have experienced a documented RLE of at least 3-month duration OR had a period of psychotherapy (duration specified by the MHP after the initial evaluation, usually a minimum of 3 months).

Adults should fulfill the following **readiness criteria** before the cross-sex hormone treatment. The applicant:

1. Has had further consolidation of gender identity during a RLE or psychotherapy.
2. Has made some progress in mastering other identified problems leading to improvement or continuing stable mental health.
3. Is likely to take hormones in a responsible manner.

Follow up e indicazioni alla chirurgia

Bari,
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- FOLLOW UP
- Esami ormonali ogni 3 mesi per il primo anno, quindi 1-2 volte/anno
- Monitoraggio di PRL in MTF
- Valutazione dei fattori di rischio cardiovascolare nei T in terapia ormonale
- BMD in caso di rischio di osteoporosi, soprattutto nei pazienti che sospendono la terapia dopo la gonadectomia
- MTF non a rischio per cr mammario devono comunque sottoporsi a screening
- MTF in terapia estrogenica devono sottoporsi a screening per patologie e cr della prostata
- FTM devono valutare i rischi e i benefici di sottoporsi a isterectomia e annessiectomia

- Indicazioni alla chirurgia
- Parere positivo dello psichiatra/ psicologo e dell'endocrinologo
- L'intervento di riattribuzione chirurgica del sesso desiderato va effettuato dopo almeno un anno di terapia ormonale continuata e ben sopportata dal paziente
- L'endocrinologo deve aver risolto tutti i problemi medici del paziente prima di inviarlo al chirurgo, e deve collaborare col chirurgo per stabilire la terapia ormonale ottimale da seguire durante e dopo l'intervento

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TABLE 11. Medical conditions that can be exacerbated by cross-sex hormone therapy

Transsexual female (MTF): estrogen
Very high risk of serious adverse outcomes
Thromboembolic disease
Moderate to high risk of adverse outcomes
Macroprolactinoma
Severe liver dysfunction (transaminases >3 × upper limit of normal)
Breast cancer
Coronary artery disease
Cerebrovascular disease
Severe migraine headaches
Transsexual male (FTM): testosterone
Very high risk of serious adverse outcomes
Breast or uterine cancer
Erythrocytosis (hematocrit >50%)
Moderate to high risk of adverse outcomes
Severe liver dysfunction (transaminases >3 × upper limit of normal)

TABLE 12. Hormone regimens in the transsexual persons

	Dosage
MTF transsexual persons[a]	
Estrogen	
Oral: estradiol	2.0–6.0 mg/d
Transdermal: estradiol patch	0.1–0.4 mg twice weekly
Parenteral: estradiol valerate or cypionate	5–20 mg im every 2 wk 2–10 mg im every week
Antiandrogens	
Spironolactone	100–200 mg/d
Cyproterone acetate[b]	50–100 mg/d
GnRH agonist	3.75 mg sc monthly
FTM transsexual persons	
Testosterone	
Oral: testosterone undecanoate[b]	160–240 mg/d
Parenteral	
Testosterone enanthate or cypionate	100–200 mg im every 2 wk or 50% weekly
Testosterone undecanoate[b,c]	1000 mg every 12 wk
Transdermal	
Testosterone gel 1%	2.5–10 g/d
Testosterone patch	2.5–7.5 mg/d

TABLE 13. Masculinizing effects in FTM transsexual persons

Effect	Onset (months)[a]	Maximum (yr)[a]
Skin oiliness/acne	1–6	1–2
Facial/body hair growth	6–12	4–5
Scalp hair loss	6–12	[b]
Increased muscle mass/strength	6–12	2–5
Fat redistribution	1–6	2–5
Cessation of menses	2–6	[c]
Clitoral enlargement	3–6	1–2
Vaginal atrophy	3–6	1–2
Deepening of voice	6–12	1–2

[a] Estimates represent clinical observations. See Refs. 81, 92, and 93.

[b] Prevention and treatment as recommended for biological men.

[c] Menorrhagia requires diagnosis and treatment by a gynecologist.

TABLE 14. Feminizing effects in MTF transsexual persons

Effect	Onset[a]	Maximum[a]
Redistribution of body fat	3–6 months	2–3 yr
Decrease in muscle mass and strength	3–6 months	1–2 yr
Softening of skin/decreased oiliness	3–6 months	Unknown
Decreased libido	1–3 months	3–6 months
Decreased spontaneous erections	1–3 months	3–6 months
Male sexual dysfunction	Variable	Variable
Breast growth	3–6 months	2–3 yr
Decreased testicular volume	3–6 months	2–3 yr
Decreased sperm production	Unknown	>3 yr
Decreased terminal hair growth	6–12 months	>3 yr[b]
Scalp hair	No regrowth	[c]
Voice changes	None	[d]

[a] Estimates represent clinical observations. See Refs. 81, 92, and 93.

[b] Complete removal of male sexual hair requires electrolysis, or laser treatment, or both.

[c] Familial scalp hair loss may occur if estrogens are stopped.

[d] Treatment by speech pathologists for voice training is most effective.

TABLE 15. Monitoring of MTF transsexual persons on cross-hormone therapy

1. Evaluate patient every 2–3 months in the first year and then 1–2 times per year afterward to monitor for appropriate signs of feminization and for development of adverse reactions.
2. Measure serum testosterone and estradiol every 3 months.
   a. Serum testosterone levels should be <55 ng/dl.
   b. Serum estradiol should not exceed the peak physiological range for young healthy females, with ideal levels <200 pg/ml.
   c. Doses of estrogen should be adjusted according to the serum levels of estradiol.
3. For individuals on spironolactone, serum electrolytes (particularly potassium) should be monitored every 2–3 months initially in the first year.
4. Routine cancer screening is recommended in nontranssexual individuals (breasts, colon, prostate).
5. Consider BMD testing at baseline if risk factors for osteoporotic fracture are present (*e.g.* previous fracture, family history, glucocorticoid use, prolonged hypogonadism). In individuals at low risk, screening for osteoporosis should be conducted at age 60 and in those who are not compliant with hormone therapy.

TABLE 16. Monitoring of FTM transsexual persons on cross-hormone therapy

1. Evaluate patient every 2–3 months in the first year and then 1–2 times per year to monitor for appropriate signs of virilization and for development of adverse reactions.
2. Measure serum testosterone every 2–3 months until levels are in the normal physiological male range:[a]
   a. For testosterone enanthate/cypionate injections, the testosterone level should be measured midway between injections. If the level is >700 ng/dl or <350 ng/dl, adjust dose accordingly.
   b. For parenteral testosterone undecanoate, testosterone should be measured just before the next injection.
   c. For transdermal testosterone, the testosterone level can be measured at any time after 1 wk.
   d. For oral testosterone undecanoate, the testosterone level should be measured 3–5 h after ingestion.
   e. Note: During the first 3–9 months of testosterone treatment, total testosterone levels may be high, although free testosterone levels are normal, due to high SHBG levels in some biological women.
3. Measure estradiol levels during the first 6 months of testosterone treatment or until there has been no uterine bleeding for 6 months. Estradiol levels should be <50 pg/ml.
4. Measure complete blood count and liver function tests at baseline and every 3 months for the first year and then 1–2 times a year. Monitor weight, blood pressure, lipids, fasting blood sugar (if family history of diabetes), and hemoglobin A1c (if diabetic) at regular visits.
5. Consider BMD testing at baseline if risk factors for osteoporotic fracture are present (*e.g.* previous fracture, family history, glucocorticoid use, prolonged hypogonadism). In individuals at low risk, screening for osteoporosis should be conducted at age 60 and in those who are not compliant with hormone therapy.
6. If cervical tissue is present, an annual pap smear is recommended by the American College of Obstetricians and Gynecologists.
7. If mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society.

TABLE 17. Sex reassignment surgery eligibility and readiness criteria

Individuals treated with cross-sex hormones are considered eligible for sex reassignment surgery if they:

1. Are of the legal age of majority in their nation.
2. Have used cross-sex hormones continuously and responsibly during 12 months (if they have no medical contraindication).
3. Had a successful continuous full-time RLE during 12 months.
4. Have (if required by the MHP) regularly participated in psychotherapy throughout the RLE at a frequency determined jointly by the patient and the MHP.
5. Have shown demonstrable knowledge of all practical aspects of surgery (*e.g.* cost, required lengths of hospitalizations, likely complications, postsurgical rehabilitation, *etc.*).

Individuals treated with cross-sex hormones should fulfill the following readiness criteria prior to sex reassignment surgery:

1. Demonstrable progress in consolidating one's gender identity.
2. Demonstrable progress in dealing with work, family, and interpersonal issues, resulting in a significantly better state of mental health.

Sommario

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Transessualismo e mortalità

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- 324 T già sottoposti a riattribuzione chirurgica di sesso dal 1973 al 2003 in Svezia
- Mortalità T > non T stesso sesso di origine (aHR 2.8, 95% CI 1.8-4.3), particolarmente per suicidio (aHR 19.1, 95% CI 5.8-62.9)
- T dopo SRS alto rischio di suicidio (aHR 4.9; 95% CI 2.9–8.5) e ricoveri in psichiatria (aHR 2.8; 95% CI 2.0–3.9).
- FTM rischio elevato di condanne per crimini

Long-Term Follow-Up of Transsexual Persons Undergoing Sex Reassignment Surgery: Cohort Study in Sweden

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Conclusioni degli autori:
SRS, nonostante riduca l'entità della disforia di genere, non è "la terapia" del DIG. Sono necessarie cure adeguate psicologiche/pischiatriche post-chirurgia per ridurre il rischio di mortalità dei pazienti

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Conclusioni

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- Eziopatogenesi DIG
- DIG in età infantile – reversibile – nessuna cura
- DIG in età adolescenziale e adulta – valutazione multidisciplinare
- Endocrinologo responsabile di diagnosi differenziale, terapia ormonale, indicazione alla chirurgia, follow up
- La chirurgia non è “il trattamento” del DIG

ONIG

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