Gender identity disorders can manifest themselves in varying degrees of severity from early childhood onward. The affected children express a desire to belong to the opposite sex, or insist that they actually do belong to it. They display characteristic behaviors of the opposite sex, preferring playmates of the opposite sex as well as the clothing and games (including role-playing games) that typically pertain to it. They reject anything regarded as belonging to their biological sex (2, e2); as a result, the outside world, with its sociocultural gender stereotypes, perceives them as discordant to the sex they were born with. Even young children sometimes adamantly reject or deny their own sex. They may also express a desire to have the genitalia of the opposite sex, or even become convinced that they already have them. The designation “gender identity disorder in the strict sense of the term” is recommended for such severely affected children.

The DSM-IV-TR criteria for gender identity disorders (GID) in children and adolescents are reproduced in box 1 (e3). In the ICD-10, which is the classification system of the World Health Organization, “gender identity disorder of childhood” (F64.2) is included in Chapter F64, “gender identity disorders”; this chapter also contains “transsexualism” (F64.0), “dual-role transvestism” (F64.1), and “other” and “unspecified GID” (F64.8 and F64.9, respectively) (boxes 2 and 3). The diagnosis of gender identity disorder of childhood requires that the symptoms result from a complex biopsychosocial interaction. Only 2.5% to 20% of all cases of GID in childhood and adolescence are the initial manifestation of irreversible transsexualism. The current state of research on this subject does not allow any valid diagnostic parameters to be identified with which one could reliably predict whether the manifestations of GID will persist, i.e., whether transsexualism will develop with certainty or, at least, a high degree of probability.

Conclusions: The types of modulating influences that are known from the fields of developmental psychology and family dynamics have therapeutic implications for GID. As children with GID only rarely go on to have permanent transsexualism, irreversible physical interventions are clearly not indicated until after the individual’s psychosexual development is complete. The identity-creating experiences of this phase of development should not be restricted by the use of LHRH analogues that prevent puberty.

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**BOX 1**

**DSM-IV-TR: Gender Identity Disorder in Children (302.6) and Gender Identity Disorder in Adolescents or Adults (302.85)**

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:
     - Repeatedly stated desire to be, or insistence that he or she is, the other sex
     - In boys, preference for cross-dressing or simulating female attire; in girls, insistence on wearing only stereotypical masculine clothing
     - Strong and persistent preferences for cross-sex roles in make-believe play or persistent fantasies of being 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.
   - 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:
     - In boys, assertion that his penis or testes are 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
     - In girls, rejection of urinating in a sitting position, assertion that she has or will grow a penis, or 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.

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Holstein (7); no newer data are available. There are more boys than girls among the affected children, although this apparent asymmetry may well be due, in part, to the greater social acceptance of gender-atypical behavior in girls (e6). Though prospective studies are lacking, a consensus of opinion holds that gender identity disorders in children and adolescents are often associated with serious emotional and behavioral problems and with a high psychiatric comorbidity (1, 8) and also manifest a highly variable and plastic course because these patients’ psychosexual development is not yet complete (e2). The figure shows the possible courses of gender identity disorder, as well as its main differential diagnoses.

In view of the continuing diversity of scientific opinion on the subject, with mutually exclusive positions held by different parties, our goal in this article is to present the main manifestations of, and diagnostic criteria for, gender identity disorders and then to provide an overview of present hypotheses regarding its etiology, which remains unknown. We will then discuss the current, often heavily controversial debate on the “correct” therapeutic approach, and, in particular, the question of early hormonal treatment. Our discussion will necessarily include a fundamental consideration of the ethical and moral principles underlying medical treatment, with particular attention to developmental psychology. This article is based on a selective review of the literature, including an analysis of the current international guidelines, as well as on the authors’ own clinical experience and insights gained in a critical and constructive debate among experts from many countries in the framework of an international, interdisciplinary research association.

**Etiology and pathogenesis: neurobiological and (developmental) psychological aspects**

The development and maintenance of gender identity disorders is held to be a multifactorial pathological process, in which individual psychological factors exert their effects in concert with biological, familial, and sociocultural ones (e2). From the point of view of developmental psychology, it would be wrong to imagine that patients with GID constitute a homogeneous group with a uniform pathogenesis. Different theoretical conceptions imply different—complementary, not necessarily contradictory—notions of the possible causes of GID (e7).

In view of the still unsatisfactory state of the data, any generalizations should be made with caution.

Neurobiological genetic research has not yet convincingly shown any predominant role for genetic or hormonal factors in the etiology of GID (1). Some study findings were originally thought to suggest a possible effect of sex steroids in utero and an inadequate masculinization or defeminization of hypothalamic nuclei (“gender role centers”) because of pathologically altered maternal hormone levels (e8, e9); these findings are now viewed more critically (9). On the other hand, studies of gender identity in patients with various types of intersex syndrome (e.g., complete versus partial androgen receptor defects) have led to the formulation of a biological
**BOX 2**

**ICD-10 F64.2: Gender Identity Disorder of Childhood**

For girls:

A. Persistent and intense distress about being a girl, and a stated desire to be a boy (not merely a desire for any perceived cultural advantages to being a boy), or insistence that she is a boy.

B. Either (1) or (2) must be present:

   1. Persistent marked aversion to normative feminine clothing and insistence on wearing stereotypical masculine clothing, e.g. boys’ underwear and other accessories
   2. Persistent repudiation of female anatomical structures, as evidenced by at least one of the following:
      - Assertion that she has, or will grow, a penis
      - Rejection of urinating in a sitting position
      - Assertion that she does not want to grow breasts or menstruate.

C. The girl has not yet reached puberty.

D. The disorder must have been present for at least six months.

For boys:

A. Persistent and intense distress about being a boy and an intense desire to be a girl or, more rarely, insistence that he is a girl.

B. Either (1) or (2) must be present:

   1. Preoccupation with female stereotypical activities, as shown by a preference for either cross-dressing or simulating female attire, or by an intense desire to participate in the games and pastimes of girls and rejection of stereotypical male toys, games and activities
   2. Persistent repudiation of male anatomical structures, as indicated by at least one of the following repeated assertions:
      - That he will grow up to become a woman (not merely in role)
      - That his penis or testes are disgusting or will disappear
      - That it would be better not to have a penis or testes.

C. The boy has not yet reached puberty.

D. The disorder must have been present for at least six months.
**ICD-10 F64: Gender Identity Disorders (except F64.2 → see box 2)**

**F64.0 Transsexualism**
- A. Desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make one’s body as congruent as possible with one’s preferred sex through surgery and hormone treatment.
- B. Presence of the transsexual identity for at least two years persistently.
- C. The disorder is not a symptom of another mental disorder, such as schizophrenia, or associated with chromosomal abnormality.

**F64.1 Dual-role transvestism**
- A. Wearing clothes of the opposite sex in order to experience temporary membership of the opposite sex.
- B. Absence of any sexual motivation for the cross-dressing.
- C. Absence of any desire for a permanent change to the opposite sex.

**F64.8 Other gender identity disorders**
- F64.9 Gender identity disorder, unspecified

No specific criteria are defined for these diagnoses.

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hypothesis for the etiology of gender identity disorders, in which these are caused by hormone resistance restricted to the brain (10, 11). In addition, neuroanatomical findings in the dichotomous brain nuclei of transsexual patients provide further evidence for a biological component in the complex etiology of GID (12). Contrary to earlier assumptions, gender identity cannot be changed by external influences alone, i.e., attempts at so-called “re-education,” even when these attempts are begun as early as the first year of life (13); this implies an early, somatic determination of gender identity. Moreover, because bodily and genital sensations exert a major effect on psychosexual and gender-identity development, one must assume that the overall process involves an interaction of biological and psychosocial factors. Etiological and pathological influences should thus be sought in both areas (e10).

Multiple publications have concerned a possible traumatic etiology of gender identity disorders (14) and an overlap of the psychopathological findings in GID with those of borderline personality disorder (15, e11, e12, e13), although there is some controversy on the latter point (16). A profound disturbance of the mother-child relationship can often be empirically demonstrated and is postulated to be a causative factor (e14). The desire to belong to the opposite sex is held to be a compensatory pattern of response to trauma. In boys, it is said to represent an attempt to repair the defective relationship with the physically or emotionally absent primary attachment figure through fantasy; the boy tries to imitate his missing mother as the result of confusion between the two concepts of having a mother and being one (e15). In girls, the postulated motivation for gender (role) switching is the child’s need to protect herself and her mother from a violent father by acquiring masculine strength for herself (e16).

Other authors, in line with psychoanalytic theory, do not attribute the desire to belong to the opposite sex to any prior trauma. Rather, they postulate the formation of a classic neurotic compromise, in which the child symbolically achieves a symbiotic fusion with the loved parent by switching genders (15, e17, e18). Excessive identification with the opposite sex is said to help affected boys cope with fears of loss of maternal attention (17, e19, e20), while affected girls are said to identify with their fathers in order to compensate for a relationship with their mothers that they perceive to be deficient (18).

From the perspective of developmental psychology, psychopathology, and psychiatry, such maladaptive reactions can be seen as failed attempts to fulfill particular developmental tasks: separation from parents, establishment of an individual identity, and attainment of sexual maturity. Some adolescents, meanwhile, seem to view a gender switch as a universal problem-solving strategy when confronted by other, totally different developmental tasks, bearing no relation to the establishment of sexual identity, that they perceive as insurmountable. It seems clear that the manner of psychological processing of conflicts and traumatic experiences can be expected to vary greatly from one child or adolescent to another, depending to a major extent on temperamental factors and on the developmental stage that the individual’s cognitive, emotional, and social skills have reached (19).

Learning theory and concepts derived from it tend to favor a causative model in which the primary attachment figure(s) is (are) postulated to exert an exogenous-reinforcing, active-manipulative effect on the development of features typifying the opposite sex. This explanatory approach ascribes primary importance to a desire on the parent’s part for the child to be of the opposite sex (3). A high rate of psychological abnormalities in the parents of children with GID has been reported in more than one study (20, 21). It is essential, therefore, to explore thoroughly the psychopathology of the child’s attachment figures and their “sexual world view,” including any sexually traumatizing experiences they may have undergone, in order to discover any potential “transsexualogenic influences.” The same holds for overarching sociocultural variables. Presentations currently appearing in the mass media of ever younger patients describing their treatment in euphoric terms are a cause for concern. Two further reasons for the rising demand for sex changes among minors would appear to be the “feasibility delusion”—the notion that modern medicine can effect a sex change with no problem at all—and a tendency to view the choice of one’s own sex as a type of fundamental right (e10).

**Current scientific controversies: different treatment strategies**

A review of the scientific literature reveals two different scientific positions leading to different approaches to treatment.
Multiple longitudinal studies provide evidence that gender-atypical behavior in childhood often leads to a homosexual orientation in adulthood, but only in 2.5% to 20% of cases to a persistent gender identity disorder (3, 6, 22). Even among children who manifest a major degree of discomfort with their own sex, including an aversion to their own genitalia (GID in the strict sense), only a minority go on to an irreversible development of transsexualism (6). Irreversibility of the manifestations, however, is considered to be an indispensable requirement before the diagnosis of transsexualism can be made, or any body-altering treatments initiated. In England and Canada, in accordance with this view, hormonal treatment or surgery is not recommended until the patient’s somatic and psychosexual development is complete.

In other countries, however, the opinion prevails that it is appropriate to use LHRH (luteinizing hormone-releasing hormone) analogues, which block gonadotropin secretion and secondarily inhibit the sex steroids, for diagnosis and treatment (23). Using LHRH analogues is held to give the patient time to assess whether GID will persist, and to prevent the irreversible somatic changes corresponding to the sex of birth (particularly voice breaking and beard growth). This is supposed to bring relief and prevent psychiatric comorbidity (24). According to the standards of the Harry Benjamin International Gender Dysphoria Association (2001), "completely reversible" gonadotropin blockade is to be followed in a second and a third phase by "partially reversible" (estrogen/testosterone therapy) and irreversible surgical interventions (e2). The elevated risk of misdiagnosis if treatment is begun early is considered to be acceptable in view of the putatively better results of treatment for correct indications (e21). In the Netherlands, the minimal age for hormone therapy has been set at 12 years (e22).

The guidelines of the British Royal College of Psychiatrists (1998) (e5) and, analogously, those of the German Society for Child and Adolescent Psychiatry and Psychotherapy (2007) generally recommend against treatment with hormones of the opposite sex before the patient’s 16th birthday, yet they support the administration of (reversible) sex-steroid inhibitors at much earlier ages in rare, individual cases (25).

A relevant criticism of this approach is that the appropriate criterion for judgments of this type is the patient’s biological, rather than chronological, age. Physical and psychosexual development are already complete in some individuals by age 16, but most adolescents at this age are still in the process of establishing their sexual identity, and the diagnostic and therapeutic approach should accompany this process rather than overwhelm it. The authors have currently based their own approach on these considerations, working in a special interdisciplinary clinic for GID that was established in 2007 at the Charité Hospital in Berlin and that involves experts in adolescent psychiatry, sexual medicine, and pediatric endocrinology.

All of the 21 patients who received a new diagnosis of GID in our clinic up to mid-2008 (aged 5 to 17; 12 boys, 9 girls) had psychopathological abnormalities that, in many cases, led to the diagnosis of additional psychiatric disorders. As a rule, there were also major psychopathological abnormalities in their parents. The “motive for switching” among the 15 adolescents in the group was mainly a rejected (egodystonic) homosexual orientation (see figure), the development of which would have been arrested by puberty-blocking treatments.

The pros and cons of early hormonal therapy
Among the arguments in favor of early hormonal therapy are some that are beyond dispute and others of which the authors take a critical view. It is said that:

- Suppression of further somatosexual development rapidly alleviates the patient’s suffering.
- If puberty-blocking treatments and opposite-sex hormones are given early, then a sex-change operation performed later on in life will have a better cosmetic result.
The patient’s psychosocial and sexual functioning will improve, and psychiatric comorbidity will be prevented. In addition to these arguments, most advocates of early hormonal intervention assert that the effects of puberty-blocking treatment are totally reversible. This is true, however, only with respect to its physical effects, not with respect to the irreversible damage it does to the process of psychosexual development.

The counterargument to the claimed advantages of puberty-blocking treatment consists of the following disadvantages:

- A treatment of this kind changes the individual’s sexual experience both in fantasy and in behavior. It restricts sexual appetite and functionality and thereby prevents the individual from having age-appropriate (socio-)sexual experiences that he or she can then evaluate in the framework of the diagnostic-therapeutic process. As a result, it becomes nearly impossible to discover the sexual preference structure and ultimate gender identity developing under the influence of the native sex hormones (e10).

- Experience has shown that, in not a few cases, a strongly and resolutely asserted desire to change to the opposite sex becomes markedly neutralized over the course of time, and the individual later undergoes a homosexual "coming-out" (1, 3). In view of this fact, it must be understood that early hormone therapy may interfere with the patient’s development as a homosexual. This may not be in the interest of patients who, as a result of hormone therapy, can no longer have the decisive experiences that enable them to establish a homosexual identity.

- The parents’ psychological abnormalities (20) and their effect on the child can promote the consolidation of GIS (21). All psychodynamically relevant conflicts and "transsexualogenic" factors that may be present should be thoroughly analyzed and worked through in psychotherapy or family therapy; indeed, when this is done, there is a real chance that the patient will, in the end, no longer a desire a sex change. If a purely biologic approach is taken and a "rapid solution" with hormone therapy is initiated too early, these important aspects of the diagnostic and therapeutic process are likely to fall by the wayside.

- It is not known with any certainty at present how hormone therapy before the end of puberty might affect the further development of gender identity, or to what extent it might even iatrogenically induce persistence of GID. Thus, even in a case of treatment retrospectively judged to have been successful, one cannot necessarily assume that the patient’s transsexualism was a predetermined matter at the outset.

- Children and adolescents generally lack the emotional and cognitive maturity needed to consent to a treatment that will have lifelong consequences. The fact must be taken into account that children with GID have an above average prevalence of deficient social skills, behavioral abnormalities, and psychiatric comorbidities (5, 8) and are therefore particularly susceptible to the temptation of a supposedly rapid solution to all of their problems.

**Conclusions**

The diagnosis and treatment of gender identity disorders in childhood and adolescence falls within the expertise of child and adolescent psychiatrists, who should, however, regularly call upon the expertise of colleagues in sexual medicine and pediatric endocrinology. Patients should not be forced into theoretical constructs; on the contrary, the currently debated pathogenetic concepts and attributions of causality should be critically evaluated in each individual case. It thus seems permissible, or even necessary, to make use of multiple explanatory approaches at the same time and to incorporate these into clinical therapeutic work. Family dynamic factors, in particular, have implications for treatment.

In the authors’ view, development inhibiting (LHHRH analogues) or body altering (estrogens/androgens) hormone therapy should not be initiated before the patient’s psychosexual development is complete, in view of the current lack of scientific data on these forms of treatment and the potential danger of aggravating a gender identity disorder. Somatosexual maturity is attained by girls at the menarche and by boys at the time of the first ejaculation; in either sex, the age at which this occurs is highly variable, ranging from 11 to 16 years. Consequently, there is also a great deal of variation with respect to the time at which psychosexual development can be said to be complete, and this is the relevant time for decision-making about hormone therapy.

The critical question of the determination of maturity and the linked question of establishing the indication for hormonal interventions are therefore not merely a matter of biological age. Rather, they must be answered on an individual basis for each patient, and in a process that is fundamentally interdisciplinary. There are no simple criteria, however, by which the completion of psychosexual development can be defined. The available empirical data on partner-oriented sociosexual developmental steps are not suitable for this purpose; they do make clear, though, that by age 17 (for example) one-third of adolescents have not yet had any experience of genital petting or coital intimacy (e23).

A uniform interdisciplinary approach to the care of children and adolescents with GID all across Germany is an important objective for the future. Once this has been accomplished, a multicenter study can be performed to put the care of these patients on a broader empirical basis. The primary objective must be to obtain a scientifically grounded answer, based on observations on the further developmental course of young patients who have established their sexual identities under the accompaniment of psychotherapy, to the question whether the early initiation of puberty-blocking or opposite-sex hormonal treatments might be appropriate—if not for all patients, then at least for a well-defined subgroup.
Gender identity disorders in childhood and adolescence

- Gender identity disorders of childhood (ICD-10 F64.2, DSM-IV 302.6) are only rarely the initial manifestation of a transsexual development (in 2.5% to 20% of cases). Nonetheless, because of the severe social isolation that they cause, they are often associated with a considerable degree of emotional stress for the affected children (and their parents), as well as with high psychiatric comorbidity, especially disturbances of affective and social behavior that require treatment. The presence of intersexual anomalies must be ruled out on clinical, genetic, and endocrinological grounds.

- The course of GID is highly variable and plastic. Gender identity disorders are often the forerunner of a homosexual orientation. In adolescence, the main differential diagnoses are sexual maturation disorder (ICD-10 F66.0) and a rejected (repressed or denied) egodystonic homosexual orientation (ICD-10 F66.1), as well as fetishes and transvestism (ICD-10 F65.1), severe personality disorders, and—less commonly—psychotic disorders.

- The guiding principle for the treatment of children with gender identity disorder is strengthening the patient’s feeling of belonging to the gender of birth without placing a negative value on his or her atypical gender-role behavior. The child’s parents, and usually also the school or kindergarten, must be involved in the treatment, and any comorbid psychiatric disorders must be dealt with appropriately as well.

- Adolescents should be treated in a diagnostic and therapeutic process that is open to multiple outcomes, utilizing the concepts of adolescent psychiatry and sexual medicine. This will enable the affected adolescents to resolve their own identity conflicts. The treating physician should assess the degree of persistence of the patient’s desire for a gender transformation while paying special attention to other unresolved developmental tasks and/or conflicts aside from the specific problem of GID.

- The diagnosis of a transsexual, i.e., irreversible, GID is permissible only when the individual’s psychosexual development is complete and after his or her sexual preference structure has been elucidated. A further prerequisite is that the sexual preference structure must have become established without any influence from extraneous hormones. It follows that the use of puberty-inhibiting LHRH analogues or sex steroids of the opposite sex during adolescence, at any chronological age, would seem to be appropriate only in rare cases for strict indications, when it is certain that nascent transsexualism is the correct diagnosis.

**Key messages**

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