

Transition in gender dysphoria: stopping puberty

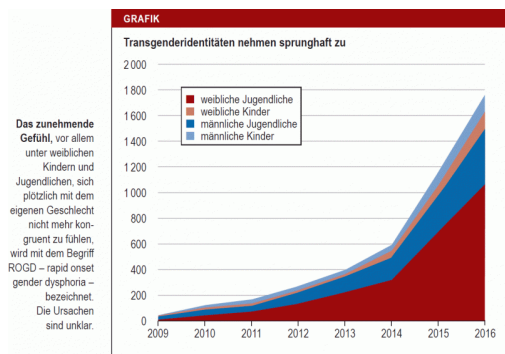
Drugs to block puberty are intended to buy time in the context of gender reassignment and help prepare for the transition . However , the evidence for their positive and negative effects is more than poor. Some countries ban them for children in this indication or require more rigorous safety screening.



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There is hardly an area in medicine in which such a striking increase in prevalence has been observed over the past decade as in the case of disorders of gender identity. What is meant by this is a condition in which the patient no longer feels that they belong to the gender assigned at birth and cannot identify with it. The terminology "sex assigned at birth" has replaced the concept of "biological sex" in scientific publications - although by no means everyone in the professional world wants to adopt it.

Most of those affected strive for the "opposite" gender, thus sticking to the binary concept of two genders. However, this has been expanded (*Box 1*) . Among those who wish to transition from female to male (transman) or vice versa (transwoman) there is a significant gender gap: 80% of them are girls who want to be "transformed" into a boy (1) . In many European and Anglo-American countries , the prevalence has consistently increased by more than 1000% since around the year 2000 (*Figure*) .



graphic

Transgender identities are skyrocketing

Mastectomies increased thirteenfold

The increase in registered minors seeking treatment was up to 4500% in some centers within a decade (2009–2018) (2). According to a recent US study, between 2013 and 2020, the number of mastectomies performed on girls aged 12 (to 17) years and older increased thirteenfold to adjust their physical appearance (3).

Increasing public media coverage of transgender people and gender-diverse children and adolescents has been identified as one of the reasons for this unusual increase in gender incongruity (4). However, there is debate as to whether the media reports trigger the s as a fashionable topic, similar to a Werther effect, or whether such identity disorders have always been more common and media reports merely encourage more people affected to seek help for the transition. In any case, the surprisingly high prevalence for a medical diagnosis some also interpret increases as a kind of "social contagion". In this context, the expression "rapid onset gender dysphoria" (ROGD) arose. Experts want to use this to describe the recent boom in the sudden turn away from their own gender, which is particularly rampant among girls. However, others reject the term ROGD (5, 6, 7). This shows how fluid the technical debate is.

Among pediatricians and child and adolescent psychiatrists there is currently a discussion as to whether and to what extent the pharmacological arrest of puberty development by so-called puberty blockers represents a medically safe and suitable therapeutic approach in view of the growing number of children who want this. With the medicinal blockade of the revolutionary hormonal, neuronal, mental and psychological developments that puberty brings with it, the path to the desired adjustment of a body designed for development into a woman to that of a man and vice versa begins in many cases.

Doubts about puberty blockage

The debate has recently become more and more controversial because countries that initially used puberty blocker therapy liberally according to the widely adopted Dutch model now no longer want to allow it in children or have raised the hurdles for its use significantly (Box 2). Medical committees justify the new restrictions with still unresolved doubts about safety and at the same time with the fact that more and more people affected who die as children. Drugs received, meanwhile, are filing public and legal complaints with

criticism that they were too quickly and too lightly placed on the gender reassignment track and are now suffering from the result (8).

In order to explain the current medical status of puberty blockers, Prof. Dr. medical Johannes Hebebrand, Medical Director of the Clinic for Psychiatry, Psychosomatics and Psychotherapy of Children and Adolescents at the LVR-Klinikum Essen, invited renowned German experts. First Prof. Dr. medical Florian Zepf, Head of the Clinic for Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy at Jena University Hospital, the thankless challenge of explaining the medical evidence for this. Because his conclusion is that the data is as sparse as it is unsatisfactory given the task of advising children, young people and their parents on the opportunities and risks of these drugs.

Zepf allowed himself to express his concern as a private opinion. For him, the question "When will I know that the young person has understood this for himself and his entire life?" is very difficult to answer in view of the highly complex evidence base, when in fact the experts themselves hardly derive any clear instructions for action from the data could.

Hope for instant solutions

In addition, the demands of those affected sometimes do not make it easy for the treatment teams. Some young people are clearly concerned with receiving an expert opinion as quickly as possible in order to be able to initiate the transition immediately. "What do you think of, questioning my wish?" - this is how they expressed their lack of understanding during the consultation, for example with regard to the clarification of psychiatric comorbidities or differential diagnoses.

Zepf does not consider the unequivocally formulated expectations to be an isolated case and suspects that specialist colleagues could also have something to do with it. This conflict between the desire for rapid implementation of therapies and careful medical consideration is now being discussed more and more often and internationally. So does Dr. Celso Arango, Director of the Gregorio Marañón Child and Adolescent Psychiatric Clinic at the University of Madrid, makes exactly these claims for what are downright characteristic behaviors of children and adolescents.

Classically adolescent, magical

If they hoped to get quick and easy relief from their ailments by being trans, it was "classic-adolescent, magical, the 'here-and-now fix,' frontal lobe disinhibition, acting rather than thinking," he said in one Interview (9). The overly compliant, uncritical yielding to such demands in large transgender clinics, such as the Tavistock Center in London, has ultimately discredited the therapies as such and makes a careful evaluation of the clinics necessary in the future (10).

The puberty blockers are substances that stop a maturation process that brings with it immense somato-psychic changes in everyone's life. According to Zepf, behind this blockade - as a rule, analogues of the gonadotropin-releasing hormone (GnRH) are used for

this purpose, which are also used in the diagnosis of precocious puberty - is the idea, according to Zepf, of buying time for the development of one's identity, so that one does not already have to go through the Being pushed into a certain physical development during puberty.

GnRH analogues act on the hypothalamic-pituitary axis, they prevent the secretion of gonadotropins from the pituitary gland. If this releases less luteinizing (LH) and follicle-stimulating hormone (FSH), this blocks the development of the gonads and thus the secretion of sex hormones such as estrogen and testosterone. This slows down the development of secondary sexual characteristics - the budding of the breasts in women or the deep voice in men - and thus relieves those affected who otherwise feel uncomfortable because of the manifestation of characteristics of the non-preferred sex.

It can also help reduce the risks of other gender reassignment measures. If a female breast grows less quickly, this can save or make it easier to tie off in order to flatten the breast. Such binding measures (chest binding) are in turn associated with constant pain and rib fractures that increase over time ([11](#)). At the same time, the blockade of puberty is the basis for later using opposite-sex hormones such as testosterone or estrogen to further advance an adjustment from woman to man and vice versa .

Penis replacement and neovagina surgery

In a third step, the body can finally be surgically adjusted. This occurs, for example, through penile amputation and plastic construction of a neovagina, through mastectomy, and through the –often unsatisfactory– construction of a penis replacement (penoid) from tissue from other body regions with or without lengthening of the urethra or a mini-penis from the clitoris (metoidoplasty) ([12](#) , [13](#) , [14](#)).

With regard to these corrective operations, the first disadvantages of blocking secondary sexual development are already becoming apparent: If not enough penile and scrotal skin can grow because the development of male characteristics has been slowed down in boys who want to transition , there will not be enough material later for the plastic one Construction of a neovagina available ([15](#)). Because of this ambivalent situation, other variants of the extremely numerous vaginoplasty techniques are now being proposed – however, the optimal surgical solution has not yet been found ([16](#)).

Sobering study results

For what puberty blockers are able to achieve at the beginning of such a cascade of measures, Zepf extensively cited the NICE report ([17](#)) as the most important scientific key witness source. This was published in March 2021 and already revealed the deficits of the research situation in the selection of studies : Of 525 studies on the topic, only 9 qualified for an analysis. Of these, 5 were retrospective and 3 longitudinal observational studies, one had a cross-sectional design.

Significant positive effects were rare. An influence on gender dysphoria could not be demonstrated. Regarding mental health, adolescents' depression was reduced, but their

anxiety or anger was not reduced. The quality of life could not be influenced either. Overall, Zepf summarized, the reliability of the statements - the level of evidence - was very low. In detail, for example, there was no influence on body image and none on satisfaction with subsequent surgical interventions. If one summarizes the results, their clinical value is questionable. Changes could also be due to other influences (confounders), bias or coincidence.

Risks of puberty blockers

On the possible side effects of gender reassignment therapies, Dr. medical Alexander Korte, Senior Physician at the Clinic and Polyclinic for Child and Adolescent Psychiatry, Psychosomatic Medicine and Psychotherapy at the LMU Munich, in his lecture. There are also insufficient studies and no clear evidence for this .

In the meantime , the influence of a puberty blockade on bone health is being examined more and more closely. "GnRH analogues delay the increase in bone density in the growth phase, which is critical for peak bone mass," stated Korte. A recent pilot study of children (mean age 10.9 years) who received GnRH analogues showed that after 12 months of dosing, they achieved lower bone mass than control children (mean age 11.7 years) and fat mass was higher in bone marrow (18). Since subsequent hormone administration with sex hormones also has an unfavourable effect on bone health ,advised to pay attention to calcium and vitamin D supplementation in children and adolescents undergoing puberty blockade and afterwards and to recommend appropriate sport (19). Korte explained that irreversible consequences are to be feared if GnRH administration is followed by therapy with steroid sex hormones in order to induce opposite-sex characteristics (20). " The s always goes hand in hand with a permanent loss of reproductive abilities," emphasized the child and adolescent psychiatrist.

Because GnRH administration is almost always replaced by later sex hormone administration , studies also address the associated metabolic consequences. It has been shown that trans women in particular gain significant weight after starting sex steroid hormone administration (21). Possible negative effects such as a higher risk of type 2 diabetes are also being discussed; trans men are particularly affected here, as their risk of type 2 diabetes is higher than that of cis women (22).

This is not surprising for endocrinologists. This is because patients with polycystic ovary syndrome (PCOS) have a pathological GnRH pulse frequency, which means that more androgens are released. Masculinization , which is undesirable in PCOS patients, can lead to facial hair growth and sub-/infertility, but is also characterized by insulin resistance and significantly increased metabolic risks (23).

Neural and cognitive effects

The influence of early hormone administration on psychosocial-cognitive development has also not been adequately researched. A study with 8 trans girls and 12 trans boys showed, for example, that the trans girls performed worse on functional tasks after therapy than untreated trans boys or cis-gender controls (24). In an extensive individual examination of

a trans girl during the transition, magnetic resonance imaging (MRI) showed before, and 22 and 28 months after therapy with puberty blockers that the white matter did not increase to the extent expected for puberty (25th). The white matter is used, among other things, for faster neuronal signal transmission. Twenty-two months after puberty suppression, working memory scores had fallen by more than two standard deviations. Furthermore, sex-specific effects on the volume of the amygdala and gray matter are known from animal studies (26). In children who received GnRH analogues because of precocious puberty, reductions in IQ were measured in the Hamburg-Wechsler intelligence test, especially in the action part (performance IQ) (27 , 28).

A current publication with a cohort of 72 adolescents shows how difficult it is to identify clear effects here. At the (mean) age of 12.78 years, they were included in treatment with puberty blockers and subsequent administration of sex hormones and were re-examined at the (mean) age of 20.4 years (29). The conclusion is that the association between IQ before treatment and the degrees achieved is similar to that in the normal population - and therefore no negative influence of the treatment is noticeable.

However, it is striking that almost half of the group treated achieve higher levels of education (high school or university), while only a good third of the general population achieves the s. That would actually be a positive effect. However, the authors themselves admit that IQ was not measured in the same way as in other studies. They failed to show a preliminary comparison between the IQ scores of comparison group and treated subjects. If the latter were significantly higher with their IQ, there is an inclusion bias that undoubtedly leads to better degrees - which makes the results worthless. After all, of 119 children who should have taken part, 47 were previously excluded.

Last but not least, Korte pointed out sexual functional limitations such as anorgasmia after gender reassignment therapies. The clinical evidence for this is overwhelming, even though no studies have yet been published. This taboo problem would severely limit the quality of life of those affected.

Rate of suicidal thoughts decreases

Prof. Dr. medical In his presentation, Georg Romer appealed that not blocking puberty also entailed risks. He pointed out that those affected suffer from suicidal thoughts much less frequently than if they were denied this therapy (30). However, it could not be shown that the number of attempted and executed suicides is actually decreasing, only the mental preoccupation with suicide (31).

Romer received approval for the fact that psychological suffering arises in the case of persistent transsexuality if the unwanted body changes have become irreversible. However, there was no clear consensus among the experts on the number of people affected who really need it. While Romer considers this proportion to be high, Korte pointed out that many transition wishes could also be due to the difficulty of facing one's own homosexuality.

The question of comorbidity was also discussed critically. Romer saw the high proportion of comorbidities such as depression, anxiety disorders, autism and other psychiatric diagnoses as a reaction to the problems associated with the transition or its refusal. Zepf pointed out that little is known about the causal relationships. It is also conceivable that another psychiatric illness is also present, which in turn requires its own treatment. In view of the unanswered questions, it was also suggested by the audience that puberty blockers should only be administered within the framework of studies. *dr medical Martina Lenzen-Schulte*

Diagnoses and terms: de-pathologization, gender fuck and eunuchs

- **ICD-10 gender identity disorder**

Until the end of 2021, this old coding summarized the “gender identity disorders” under F64, which mostly still appear in statistics in the years before 2022; in this system, sexual deviance was still considered a pathology.

- **ICD -11 gender incongruence (GI):**

The designation stands for a “condition related to sexual health” and does not represent a mental disorder; what is meant is an incongruity between the at birth and the experienced gender, which to a desire for transition in order to live and be accepted as a person of the experienced gender.

- **DSM 5 Gender Dysphoria (GD):**

Persistent distress resulting from gender mismatch with impairment of mental health.

- **Transgender ¹ people Means people whose psychological gender identity** does not match their birth-assigned gender; usually the “other” gender is aimed at by means of transition . ¹ This is not a medical term category.

- **Non-Binary ¹ Gender Identities**

This serves as a sort of umbrella term for a spectrum of gender identities that are not feminine or masculine.

¹ This is also not a medical term. But around the XIII. Social Code contains the wording “transident, non-binary and intersex young people”; the wider range of terms includes expressions such as agender, bi-, tri- and pangender, demi-boy or demi-man, demi-girl or demi-woman, also genderqueer and genderfuck.

- **Eunuch as a new gender identity**

According to the World Professional Association for Transgender Health (WPATH), there should be a “man-to-eunuch” variant as a valid transgender identity in the future; people with non-functional testicles, those who wish their

testicles to be non-functional or those who are aiming for a penile amputation are eligible.

- **New, planned AWMF-S3 guideline**

This uses the terms "gender incongruence, gender dysphoria and trans-health" in the title and, similar to ICD 11, would also like to completely de-pathologize trans -identity.

(Lit. Reg. No. 1, [34](#) , [35](#))

Looking abroad: Blockade of the puberty blockade

Thirty years ago, a team at the Amsterdam Center of Expertise on Gender Dysphoria began developing the Dutch model of child and adolescent transition support , which has been adapted by centers in Los Angeles, Chicago and San Francisco. It includes giving puberty blockers early in puberty from age 12 (Tanner stage 2–3); some children are treated from the age of 10. Sex hormones for opposite-sex sexual maturation (cross-sex hormones) can be administered from the age of 16. From the age of 18 or 19, irreversible surgical adjustment operations should be included in the therapy considerations.

The World Professional Association for Transgender Health (WPATH) recently advocated lowering the age for cross-sex hormone administration to 14 years. Gender dysphoric girls should be able to have their breasts removed at 15 , gender dysphoric boys should be allowed to have their testicles removed at 17.

In the years that followed, many countries followed the Dutch guidelines, although recently there have been signs of turning away or at least more restraint. At the beginning of 2022, the Swedish National Board of Health and Welfare (NBHW) updated the guidelines for treating gender dysphoria decided that the risks of hormone administration outweigh the benefits. Administration at an age younger than 18 has been heavily regulated and is now only possible in a research setting, for example in studies. In the summer of 2022, the Florida Medical Association decided that puberty blockers, hormones, and surgeries should no longer be offered to under-18s. Similar initiatives exist in Arkansas, Alabama, Oklahoma and Tennessee. Finland had already broken with the WPATH recommendations in 2020 and strictly limited the use of puberty blockers. The French national medical academy took a position on the subject in February 2022 and called for more caution when using gender reassignment therapies in children and adolescents; there, mastectomy is allowed from the age of 14. In England might the recent criticism of a lack of due diligence in diagnosis and therapy decisions in the Tavistock Center in London also lead to a reorientation and to greater restraint.

All initiatives have one thing in common: the growing number of those affected who want a "detransition" - a return from the adjustment - who are now making their suffering from the transition public or suing therapists, have led to a review of medical action. Furthermore, it is admitted that there is far from enough evidence to be able to

assess the long-term outcome and possible damage of early therapy with often irreversible consequences. The design for such studies is currently being developed, several have only recently been launched and results are not expected for the next few years at the earliest.

Therefore, more and more expert recommendations now emphasize that first-line therapy must be psychological and psychiatric. Finally, the ability of those affected to understand is discussed. So far, it has not been investigated whether children or young people can even understand the impact of puberty blockers. Available data on the ability of different age groups (of 9, 14, 18 and 21-year-old subjects) to give informed consent to other medical issues had shown that 14-year-olds were just as capable of assessing risk and benefit like 21-year-olds. But the 9-year-olds weren't nearly as good at it.