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Practice guidelines

Endocrine management of transgender adolescents: Expert consensus of the french society of pediatric endocrinology and diabetology working group

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ABSTRACT

Introduction: Requests for hormonal transition in minors are increasing. To date, there is no national recommendation to guide these practices in France. Therefore, the SFEDP (French Society of Pediatric Endocrinology and Diabetology) has commissioned a group of experts to draft the first national consensus on this topic.

Method: Each chapter was prepared by one to three authors who conducted a literature review, and it was then reviewed and revised by the group as many times as necessary to achieve a consensus position. The final document was reviewed by a group of external experts.

Results: A consensus position was reached regarding the multi-professional nature of support for trans youth, the prescription of molecules aimed at inhibiting endogenous hormone secretion, and the use of gender-affirming hormone therapies, as well as the importance of offering gamete preservation. Non-hormonal aspects of support and various considerations, including ethical ones, were also discussed.

Conclusion: This work constitutes an initial set of recommendations for professionals involved in the hormonal transition of trans youth. Additional recommendations under the auspices of the French High Authority for Health would be worthy of being drafted, involving all relevant stakeholders to establish comprehensive official national guidelines that would secure the support and rights of these young individuals, especially those under 16 years old, as well as the professionals involved in their care.

1. Introduction

The most recent definition of gender incongruence is from the ICD-11, which now classifies it under the category of "conditions related to sexual health". This definition varies depending on whether one is dealing with a prepubescent child (Tanner stage 1) or an adolescent (Tanner stage 2 and above) (Table 1). For the latter, the definition is the same as for adults.

Hormonal management of transgender minors started in 2013 in France [1] but had been established earlier in other countries [2–5]. Requests for support at pediatric age are increasing in France, as in most other countries [4,6]. The reasons for this increase are probably multifactorial, particularly related to the improvement of information, a better societal recognition and acceptance, as well as the establishment of specific support for minors.

The hormonal management of minors raises some societal controversies and ethical considerations from the medical community [7–10]. To date, guidelines have been published internationally [11–14], but not in France. The French National Authority for Health (HAS) published a report in 2009 on the subject, but it was only an overview of transgender care in the country [15]. In 2021, the French Ministry of Health requested a new report from the HAS, that should serve as guidelines for good practice. However, these recommendations will initially only concern adults and minors over 16 years old [16]. The lack of guidelines in the current French medical landscape puts professionals, trans youth and their families in great difficulty.

In response to these challenges, the French Society of Pediatric Endocrinology and Diabetology (SFEDP) supported the establishment of a working group of pediatric endocrinologists who worked on drafting these first French recommendations for supporting hormonal transition of transgender minors.

2. Methods

This work was carried out by the working group under the auspices of the SFEDP. The twenty authors come from 14 French teams and 1 Swiss team that provide care for trans youth. For specific points, collaboration with specialists from other medical disciplines was sought. Each chapter was prepared by one to three authors who conducted a literature review. It was then reviewed and revised by the group as many times as necessary to achieve a consensus position. This work began in November 2022 and concluded in June 2024. The final version was reviewed by four external reviewers.

The abbreviations used were defined upon first occurrence and are summarized in Appendix 1. Initially, the group aimed to use inclusive language, but due to readability and editorial guidelines, this project had to be abandoned [16].

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Table 1
Definitions of gender incongruence according to the international classification of diseases (version 11).

In children (Tanner stage 1)	In adolescents and adults (From Tanner stage 2)
Gender incongruence in childhood is characterized by a marked incongruence between an individual's experienced/expressed gender and the assigned sex. It includes :	Gender Incongruence in Adolescence and Adulthood is characterized by a marked and persistent incongruence between an individual's experienced gender and the assigned sex
A strong desire to be a different gender than the assigned sex	Which often leads to a desire to 'transition', in order to live and be accepted as a person of the experienced gender, through hormonal treatment, surgery or other health care services to make the individual's body align, as much as desired and to the extent possible, with the experienced gender.
A strong dislike on the child's part of his or her sexual anatomy or anticipated secondary sex characteristics and/or a strong desire for the primary and/or anticipated secondary sex characteristics that match the experienced gender.	
Make-believe or fantasy play, toys, games, or activities and playmates that are typical of the experienced gender rather than the assigned sex	Puberty must have started
The incongruence must have persisted for about 2 years	Gender variant behavior and preferences alone are not a basis to affirm gender incongruence
Gender variant behavior and preferences alone are not a basis to affirm gender incongruence	

3. Ethical considerations

3.1. General information

From an ethical standpoint, several questions remain debated. The issue of the age at which to initiate potential treatments involves two important concepts: the best interests of the young person and their autonomy in deciding on medical treatment. In pediatrics, the "best interest of the child" is a reference in decision-making [17], but it is often difficult to apply [18]. The interest here is twofold: to stop the distress caused by unwanted pubertal progression and to keep open the possibilities in terms of surgeries or fertility preservation that may one day be desired. The ability of a minor to express their needs and to have the capacity to give consent can also be questioned. However, other medical situations have already validated this possibility for fertility preservation before chemotherapy or in the context of differences in genital development [19,20]. Recently, studies aiming to assess whether transgender youth are competent to express their needs and consent before puberty suppression or gender-affirming treatment, report that the vast majority had thought at length about this treatment, understood its implications, and were therefore considered competent to make this decision [21,22]. Moreover, the percentage of young people or adults who have retransitioned remains low, at about 1 to 6% [3,23–25].

Uncertainties also persist regarding the long-term effects of hormonal treatments [8–10]. Although no severe adverse effects have been reported to date, the long-term medical and psychological effects must continue to be evaluated. It could be argued that since the risks of an early transition cannot be fully established in advance, it is impossible to give a valid informed consent. On the other hand, every new therapeutic proposal in medicine, and particularly in pediatrics, raises the question of the absence of long-term data. Moreover, a wait-and-see attitude in adolescence does not reduce psychological distress, increases the risk of committing suicide and can affect psycho-affective and cognitive development [1,26–30]. At the extreme, "conversion therapies" have been scientifically proven to be harmful [27] and have been banned in France since 2022.

Thus, medical support is now an option that should be considered in a personalized approach that takes into account the needs of each young person without a predefined protocol. Nevertheless, for a field that has such an impact on the future adult, hormonal transitioning in trans youth has been the subject of relatively little academic research until recent years. It is therefore essential that professionals supporting these young people work together at national and international levels to accumulate prospective data in order to provide these young people and their families with the most enlightened information as possible.

3.2. Information, reflection period and consent

The practitioner is required to provide clear, fair, and appropriate information based on contemporary scientific knowledge. Explanations regarding treatments will be given prior to prescription to allow for a sufficient reflection period before consent. These explanations will cover the modalities of prescription and monitoring of the treatment, its expected effects with their onset times and whether they are reversible or not, and potential side effects. The limited data on long-term effects will be discussed, as well as the potential socio-psychological repercussions of transitions. Dedicated information materials can be provided. The young person must be informed that they can interrupt their treatment at any time, and this will not affect their follow-up by the professionals supporting them.

The purpose of this information period is to allow the young person and their legal representatives to give their consent in an informed manner. The reflection period is also important and must be adapted to the understanding capacities of the different parties involved. Finally, the practitioner will ensure that the young person is able to give their consent freely [12,13]. In case of doubt about the ability of one or more parties to consent freely and informedly to the treatment, the practitioner may seek the advice of other professionals to support their analysis (ethics committee, lawyer, psychologist, etc.).

This consent (Appendix 2) must be written in a manner that is adapted for clear understanding. We recommend that it be handwritten on plain paper by each of the parties involved. A new written consent must be obtained for each hormonal treatment that is the subject of a multidisciplinary collegiate discussion (see **chapter 4.2**).

4. Multiprofessional support

4.1. Team and/or care network

The affirmative approach recommended by the World Health Organization (WHO) [31] and by the main societies of psychology [32], psychiatry [33], and pediatrics [34] is defined by the recognition and support of gender identity and the simultaneous management of psychological, social, or medical aspects. The goal of gender-affirming care is to respond, in collaboration with the young people concerned, holistically to their needs and well-being in terms of mental, social, and medical health, allowing them to affirm their gender identity respectfully [12].

Given the diversity and specificity of the issues related to the care of these young people and their families, we recommend multiprofessional support by individuals trained in the support of transgender minors, [5,12,13,35–39] who will ideally be part of the same team or care network, including:

- child and adolescent mental health professionals
- physicians trained in pediatric endocrinology particularly on issues related to adolescence, growth, and puberty
- fertility specialists

and if possible, depending on local needs and resources, peer supporters, speech therapists, surgeons, nurses, lawyers, ethicists, sociologists, social workers, dermatologists, and gynecologists.

These professionals will need to work in conjunction with available resources that can offer local support (general practitioner, pediatrician, self-support and/or family support groups, psychologist, school medicine, adolescent centers, etc.).

4.2. Multiprofessional coordination meetings and therapeutics decisions

We recommend that each therapeutic decision related to **chapter 5** be collegially discussed in a multiprofessional meeting, especially when it concerns young people under 16 years of age. The minimal quorum for these meetings consists of at least one pediatrician specialized in endocrinology and one child psychiatrist who both will not necessarily be in charge of all the cases presented, but whose role will be to provide a specialized opinion when necessary. The case will be presented by at least one of the professionals accompanying the adolescent. Depending on local possibilities and the needs of the situations presented, other members of the team or care network may also participate, respecting medical confidentiality, as well as any person whose expertise can enlighten the discussions, including peer support groups.

In light of local logistical capabilities, particularly in terms of medical confidentiality, we advise offering the young person concerned the opportunity to be present or represented during discussions about their situation.

Progestogens and potential estrogen-progestogen combinations used for the induction of amenorrhea are excluded from these discussions and do not require collegial discussion.

5. Medical treatments

5.1. Point of attention

None of the medical treatment used in the context of hormonal transitioning have marketing authorization for this indication, but these molecules have been used for a long time in the pediatric population for other indications (precocious puberty, puberty induction…). Nevertheless, they have been used for hormonal transition in trans youth since the late 1980s in some countries, and their use in adults goes back even further [3,40,41]. In addition, off-label prescription is very common in pediatrics and child psychiatry.

It is important to specify before introducing the treatment and to regularly remind adolescents during follow-up that each treatment can be suspended or interrupted at any time if they wish, and that this will not alter the support they otherwise receive.

5.2. Reduction of endogenous hormones effects

5.2.1. In case of uncompleted physiological puberty

5.2.1.1. General. In adolescents that experience gender incongruence, the development of physiological pubertal characteristics can lead to increased distress, which may result in anxiety-depressive disorders, an alteration of psychological functioning sometimes complicated by self-harming or even suicidal behavior, leading to isolation and/or dropping out of school [12,36–38]. Since the mid-1990s, treatment with GnRH analogues (GnRHa) has been proposed to prevent further pubertal development and reduce these risks [14,40]. It has become common clinical practice as a first step in medical treatment of transgender adolescents.

We recommend that puberty suppression be offered by a multidisciplinary team or network trained in supporting transgender adolescents.

5.2.1.2. Indications. To initiate treatment with GnRHa, we recommend verifying [12,13]:

- The existence and persistence of gender incongruence as defined by the ICD-11 (Table 1), associated with distress expressed by the young person related to the appearance or development of secondary sexual characteristics
- The presence of at least Tanner stage 2 (onset of puberty), clinically and/or biologically confirmed by a professional trained in pediatric endocrinology, who will monitor the treatment

5.2.1.3. Contraindications. There are few contraindications for GnRHa [42]:

- Hypersensitivity to the active ingredient, to similar nonapeptides or decapeptides, or to any of the excipients listed in the composition.
- Ongoing pregnancy
- Hematological disease contraindicating any intramuscular injection. In this case, it is recommended to prefer the deep subcutaneous route.

5.2.1.4. Pre-therapeutic assessment. Before any further examination, medical interview will particularly focus on searching for:

- personal or family history of unexplained bone fragility
- history of hemorrhagic disease
- history of allergies
- psychiatric co-occurrences and/or neurodevelopmental disorders to organize follow-up when necessary
- adequacy of vitamin and calcium intake and lifestyle related to bone health (see **chapter 7.1**)

In the case of medical history that could lead to a risk associated with GnRHa, a possible adaptation of treatments should be discussed with the concerned specialists.

Further medical examinations to be carried out are summarized in Table 2. In case of an anomaly on initial bone mineral density (BMD) assessment, specialized investigations should be discussed.

5.2.1.5. Pharmacopoia and administration methods. The treatment consists of GnRHa injections. In France, there are two available molecules: triptorelin retard (DECAPEPTYL RETARD®, GONAPEPTYL®) and leuprorelin depot (ENANTONE®), which are administered by intramuscular or deep subcutaneous injection [42]. For each molecule, there is a monthly form, a quarterly form, and for triptorelin retard, a semi-annual form.

5.2.1.6. Monitoring and titration. Monitoring is primarily clinical. It focuses on assessing the cessation of pubertal progression and the young person's feelings. Their desire to continue treatment should be evaluated

Table 2
Additional examinations to be carried out before the initiation of GnRHa and during follow-up.

Before treatment initiation	Under GnRHa monotherapy	Under GAH in youth treated or having been treated with GnRHa
BMD *(or within the first 6 months of treatment)*	BMD every 12 to 24 months depending on initial Z-score	BMD every 12 to 24 months depending on initial Z-score until normalization
25.OH.D	25.OH.D every 12 months	25.OH.D every 12 months
LH, FSH ± LHRH test	LH, FSH within 48 h preceding the injection every 6 to 12 months	Other exams specific to GAH. See dedicated chapters.
Testosterone or estradiol (according to situation)	Testosterone or estradiol (according to situation) within 48 h preceding the injection every 6 to 12 months	

at each visit. Table 2 provides, as an indication, the modalities of paraclinical follow-up. BMD assessments should be performed more frequently in cases of significant bone demineralization at the initiation or during treatment. In case of clinical (progression of Tanner stage) or biological escape (increase in hormonal levels, especially at the end of the dose), the interval between GnRHa injections may be reduced.

5.2.1.7. Expected effects and adverse effects. **In the short to medium term**, the most common side effects of GnRHa are hot flashes, primarily in the first year of treatment, headaches, and sometimes mood changes or fatigue [13,14,43]. There may also be transient pain at the injection site, increased appetite, and moderate weight gain [44]. In rare cases, a granuloma or aseptic abscess can develop. A transient episode of metrorrhagia may occur after the first injection in young individuals with completed or nearly completed puberty.

In the long term, there is limited data available. Most of the knowledge comes from the experience of treating precocious puberty with GnRHa, which has a 40-year history and reassuring data [45,46]. In transgender youth, the use of GnRHa leads to a non-physiological situation of low levels of sex hormones at an age when puberty would normally occur. There is some experience with the use of GnRHa in older adolescents for other indications [45,47].

Effect on the Development of Secondary Sexual Characteristics: GnRHa can quickly stop the development of secondary sexual characteristics and are generally well-tolerated. The effect on the suppression of the hypothalamic-pituitary-gonadal axis is reversible upon discontinuation of treatment [48–50]. The suspension of the development of physiological secondary sexual characteristics provides the opportunity to continue exploring gender identity without the distress that pubertal progression would cause [12,13]. It also helps to avoid certain potential future surgeries or to make them less invasive (mastectomy, facial surgery) [10,51,52]. However, it is important to inform young individuals assigned male at birth that the use of GnRHa at an early stage of puberty may modify the possible surgical techniques in case of a future desire for vaginoplasty [52].

Effect on Mental Health: Several studies have shown an improvement in body satisfaction, behavioral and emotional problems, as well as a decrease in anxiety, depression and suicidality with GnRHa treatment, although not all changes are significant and there are methodological limitations in the studies [27,28,53–56]. Most of the youth on GnRHa in these studies continued their treatment with gender affirming hormones (GAH) [25,41,57].

Effect on neurodevelopment: Puberty is an important period for brain development. GnRHa treatments in transgender adolescents have no negative effect on the association between intellectual quotient and academic success [58] nor on executive function performances [59]. There are no long-term data yet, but studies on overall neurodevelopment are ongoing [60].

Effects on Statural Growth: Under GnRHa treatment, most youths experience a decrease in growth velocity, but a catch-up in statural growth has been described under GAH in two cohorts, related to the genetic target height [61,62]. Final height appears to be higher in trans boys treated with GnRHa at an early stage (Tanner stage 2–3), compared to those who received GnRHa at a later pubertal stage [61,63].

Effects on Bone Health: See chapter 7.1

Effects on Fertility: See chapter 6

5.2.2. When physiological puberty is completed

5.2.2.1. Why suppress the physiological production of sex steroids. When the initiation of medical transitioning occurs after the end of puberty, the challenge is no longer to inhibit pubertal physical transformations, which are mostly irreversible. However, some other body changes can be prevented or reduced:

- In trans girls, this suppression prevents the development of muscle mass, increased testicular volume, baldness, increased body hair, erections, and the presence of ejaculate.
- In trans boys, it prevents the accentuation of fat mass, the increase in breast size, and menstrual bleeding.

5.2.2.2. What can be proposed ?. **GnRHa**:

In trans girls, estrogens prescribed alone usually cannot inhibit the gonadotropic axis [64,65]. Furthermore, the physiological effects of testosterone can limit the effect of prescribed estrogens [66]. GnRHa can then be used to inhibit the secretion of endogenous testosterone until a possible orchidectomy in adulthood if desired [12,13].

In trans boys, synthetic testosterone has a powerful anti-gonadotropic effect [67,68]. This anti-gonadotropic role, however, only occurs at sufficiently high dosages (threshold varies from one individual to another). Therefore, GnRHa may be of interest in the early stages of testosterone treatment.

In both situations, the prescribing modalities, expected effects, and side effects of GnRHa are the same as those previously mentioned when used to inhibit ongoing puberty.

Spironolactone: In trans girls, spironolactone can be an alternative to GnRHa in certain situations. However, its effect is less potent than that of GnRHa. With this treatment, monitoring of potassium levels is recommended even though the risk of hyperkalemia in treated adult trans women does not seem increased [69]. Other side effects can include increased thirst, dehydration, hyponatremia, or a decrease in blood pressure. It is recommended to start at a low dosage (25 to 50 mg) and increase gradually (up to a maximum of 300 mg) [13].

Synthetic Progestogens: In trans boys, the use of microprogestogens in continuous intake can be proposed to allow amenorrhea [12]. They can be prescribed concurrently with testosterone if necessary. Although no study has been published to date, the use of dienogest may be considered in case of failure of microprogestogens. We do not recommend as a first-line treatment the use of macroprogestogens due to the reported risk of meningioma [70) nor the use of estrogen-progestogens which could worsen unwanted signs of feminization.

5.2.3. Point of attention

GnRHa used as monotherapy should only be continued for a limited period, as prolonged use could worsen adverse effects, particularly on bone mineralization, and could impact growth. Therefore, it is recommended to re-evaluate the benefit/risk balance of the treatment and to discuss the appropriate time to introduce GAH as part of regular monitoring.

For non-binary youth who do not plan to take sex steroids, treatments such as microprogestogens or spironolactone should be preferentially considered.

5.3. Gender-affirming hormone therapy (GAH)

5.3.1. GAH indications

The most recent international guidelines [12] suggest that GAH should be initiated in transgender adolescents whose gender incongruence has been confirmed according to the criteria outlined in the ICD-11 (Table 1). Additionally, these adolescents should demonstrate sufficient emotional and cognitive maturity to provide informed consent for treatment. Unlike strict age criteria, other factors such as the duration of gender incongruence, medical follow-up history, persistence of transition requests, psychological distress, and the individual's maturity level should be considered when determining the optimal timing for introducing GAH.

In situations where GAH is introduced before Tanner stage 5 (especially when GnRHa has been previously prescribed), suppression can be maintained upon the introduction of GAH to prevent the action of

Table 3
Additional tests to be performed before the initiation of testosterone and during follow-up.

Analysis	Before treatment	Every 6 months for the first 2 Years	Every 12 months	After 2 years of treatment: recommendations similar to the cisgender population
CBC	X	X	X	
ALT/AST	X		X	
Fasting glucose, HbA1c	X			X
Lipid profile	X	X		X
LH, FSH	X		X	
Total testosterone (residual level[a,c])	X	X	X	
Bone age	X		X	
Total testosterone (peak level[b])	Only in young people who have not finished growing If adverse effects occur; to investigate treatment compliance issues or to compare with residual levels in search of rapid treatment metabolism.			
Beta HCG	Only if risk factors are present			
STI screening	Only if risk factors are present			

[a] Residual level: measurement within 48 h preceding an injection.
[b] Peak level: measurement between day 2 and day 4 after an injection
[a,b]The difference between peak and residual levels as defined here only applies in cases of using testosterone enanthate, which is the main one used to date.
[c] An intermediate dosage 3 months after the introduction of hormone therapy is recommended.

Table 4
Pharmaceutical specialties containing testosterone available in the French pharmacopoeia: equivalences, minimum and maximum dosages, dosage increase steps.

	INN* Commercial name *Dosage*	Starting dose	Theoretical maximum dose[a]	Steps[b]
Intramuscular injection	**Testostérone enanthate** ANDROTARDYL® *1 mL = 250 mg*	25 to 50 mg every 3–4 weeks	100 to 200 mg every 2 to 4 weeks	25 mg every 3 to 6 months and/or reduction of the interval between two injections
	Testostérone undecanoate NEBIDO® TESTOSTERONE BESINS® *4 mL = 1000 mg*	No data. Due to its very long half-life, testosterone undecanoate is to be avoided in young people who have not completed their growth, for whom regular titration is necessary.		
Transdermal application	**Testosterone gel** ANDROGEL® *1 press = 20,25 mg*	1 pressure per two days	2 to 4 pressures per day	1 pressure / day every 3 to 6 months
	Testosterone gel FORTIGEL® 2% *1 press = 10 mg*	1 pressure per day	4 to 8 pressures per day	1 pressure / day every 3 to 6 months

* International Nonproprietary Name.
[a] The theoretical maximum doses are given purely indicatively due to the very strong inter-individual variability and the variable wishes of one person to another. Lower doses may be sufficient to achieve a satisfactory result in certain situations.
[b] The intervals are to be adapted according to the clinical response. For young people for whom growth has not yet completed, the longest intervals are to be preferred due to the effect of testosterone on bone maturation. Similarly, the intramuscular route is to be preferred due to greater flexibility, and because it is reimbursed. If the transdermal route is indispensable, then the formulation FORTIGEL® 2% allowing a greater range of progression is to be preferred.

endogenous hormones and the appearance or continued progression of secondary sexual characteristics in the undesired gender.

5.3.2. *Testosterone*

5.3.2.1. Contraindications. The contraindications for testosterone are few, often non-definitive, and mostly rarely applicable to young individuals [39,42]:

- Pregnancy, especially if carried to term, and breastfeeding
- Active hormone-dependent cancer (breast, endometrium)
- Unstable ischemic cardiovascular disease
- Hypersensitivity or allergy to any components of the treatment
- Personal history of liver tumor. Any potential multiple family history should be discussed on a case-by-case basis
- Severe cardiac, renal, or hepatic insufficiency

5.3.2.2. Pre-therapeutic assessment. Before any additional examination, the medical interview will particularly aim to identify:

- On a personal and family level:
  - History of hormone-dependent cancers or liver cancers.
  - History of cardiac, renal, or hepatic conditions.
  - History of thromboembolic events or coagulation disorders.
- On a personal level:
  - History of allergies.
  - Psychiatric co-occurrences in order to organize follow-up with a mental health professional when necessary.
  - Any situation that would alter the young person's understanding of and adherence to care.
  - Current medications in order to assess the risk of drug interaction.

In the case of a history that could induce a risk in connection with hormone therapy, a possible adaptation of treatments should be discussed with the concerned specialists. The additional examinations prior to the introduction of testosterone are summarized in Table 3.

5.3.2.3. Pharmacopoia and administration methods. The testosterone-based specialties available in the French pharmacopoeia are summarized in Table 4. For a long time, testosterone enanthate was the only formulation reimbursed by french social security system. Since recently, testosterone undecanoate is also reimbursed. Both are administered intramuscularly.

Table 5
Effects of testosterone and estimated onset times.

Effect	Expected onset	Maximum expected onset after…
Facial and body hair**	3 to 6 months	4 to 5 years
Facial morphology*	6 to 12 months	Unknown
Increase in muscle mass and strength	6 to 12 months	2 to 5 years
Redistribution of fat mass	1 to 6 months	2 to 5 years
Cessation of menstrual bleeding	1 to 6 months	Not applicable
Clitoral enlargement*	3 to 6 months	1 to 2 years
Vaginal atrophy**	1 to 6 months	1 to 2 years
Voice deepening*	6 to 12 months	1 to 2 years

* Irreversible effects after stopping treatment.
** Partially reversible effects upon stopping treatment.

5.3.2.4. Monitoring and titration. Table 3 provides, as an indication, the modalities of paraclinical follow-up. The expert group agrees on the importance of starting treatment at a low dose and of a gradual titration until the optimal dose is reached, in order to obtain the desired effects while ensuring good tolerance [12,13,39] (Table 4). The rate of dose increase will depend on several factors, including the clinical and biological response to treatment, as well as the patient's feelings. Particular attention will be paid to young people whose growth is not complete, especially those who have received puberty-blocking treatment. For these young people, we recommend an initial dosage of 25 mg of testosterone enanthate every 3–4 weeks and a slower progression of titration as well as an annual follow-up of bone age to estimate the impact of treatment on bone maturation and adjust the titration speed if necessary [12,71]. We also recommend monitoring total testosterone plasma concentrations (peak or residual) with the goal of achieving average concentrations corresponding to the usual laboratory standards for the corresponding Tanner stage.

In the event of an excessively high peak, a reduction in dosage should be considered. Conversely, the gradual increase in plasma concentrations can be achieved either by shortening the intervals between injections or by increasing the doses.

For young people whose growth is complete, we also recommend a gradual titration of testosterone due to the potential effects of testosterone on mood. However, the initial dosage can be higher (50 or 75 mg every 3–4 weeks) and the titration up to the adult dose can be accelerated.

5.3.2.5. Expected and adverse effects. The expected effects are those related to masculinization. It is important to take the time, before the introduction of treatment, to educate the young person and their family about the relatively long and progressive nature of a hormonal transition [13]. The speed and order of appearance of the treatment's effects vary from one individual to another.

Table 5 summarizes all these effects, their estimated onset times, and whether they are reversible or irreversible [13]. These data are based on the observation of treatment in adults. Therefore, it is possible that the onset times may be longer in young people who will have a more gradual hormonal titration.

The main potential adverse effects [13,42] of testosterone are mood changes, irritability, sleep disturbances, liver function test abnormalities, lipid profile abnormalities, increased hematocrit, weight gain, reactions at the injection site, allergic reactions, the appearance of baldness or acne.

In the case of somatic or psychological adverse effects, differential diagnoses must be ruled out before affirming the responsibility of testosterone. These situations should ideally be discussed with the concerned specialists to consider a possible therapeutic adaptation. All possibilities should be explored to allow the continuation of hormone therapy, given the negative psychological impact that stopping treatment could cause.

Regarding cardiovascular risk, short-term data are reassuring [72]. There are currently no long-term data in young transgender individuals on testosterone, but the data in the adult transgender population are reassuring [73,74].

Rare cases of liver tumors have been described in studies involving derivatives of testosterone not used in France and which were used at high doses [75–77].

5.3.2.6. Other attention point. If a treatment aimed at therapeutic amenorrhea has been prescribed, it is recommended, if the adolescent wishes, to continue this treatment until sufficient residual levels of total testosterone are obtained to prevent the return of bleeding (generally, residual levels around 2–3 ng/mL). In situations where bleeding persists, treatments aimed at amenorrhea can be continued as long as necessary.

5.3.3. Estrogens

5.3.3.1. Contraindications. The contraindications for estrogens are relatively few, often relative, and, for the most part, rarely apply to young transgender individuals [39,42]:

- Known or suspected hormone-dependent malignant tumor.
- History of venous thromboembolic events.
- Recent or ongoing history of arterial thromboembolic events.
- Known thrombophilia or other coagulation disorders.
- Acute liver disease or history of liver disease, until normalization of hepato-cellular function.
- Porphyria.
- Hypersensitivity or allergy to any components of the treatment.

5.3.3.2. Pre-therapeutic assessment. Before any further examination, the medical interview will particularly focus on searching both personally and within the family for:

- History of hormone-dependent or liver cancers.
- The search for venous or arterial thromboembolic events. Multiple family histories should prompt a specialized consultation before starting treatment.
- History of liver conditions or coagulation disorders.
- Current medications to assess the risk of drug interaction.
- History of allergies.
- Psychiatric co-occurrences to organize follow-up with a mental health professional when necessary.
- Any situation that would alter the young person's understanding of and adherence to care.
- Current medications in order to assess the risk of drug interaction.

In the case of a history that could induce a risk in connection with hormone therapy, a possible adaptation of treatments should be discussed with the concerned specialists.

The additional examinations prior to the introduction of estrogens are summarized in Table 6.

5.3.3.3. Pharmacopoia and administration methods. It is recommended

Table 6
Additional tests to be performed before the initiation of estrogens and during follow-up.

Analysis	Before treatment	+ 6 months	+ 12 months	Every 12 months
ALT/AST	X	X	X	X[a]
Fasting Glucose, HbA1c	X	X	X	X
Lipid Profile	X	X	X	X
25-OH-Vitamin D	X		X	X
Total testosterone at 8am	X		X	X
Estradiol	X	X	X	X[a]
LH, FSH	X		X	X
Prolactine	X[b]		X	X[a]
BMD	X[c]		X[c]	X[c,d] or every two years[d]
Bone age	X[e]		X[e]	X[e]
STI Screening	Only if risk factors are present			

[a] At the start of treatment and every 6 months thereafter for each dosage change. Possibility of discontinuing monitoring if stable over several successive dosages.
[b] Estrogen therapy may increase prolactin levels, hence the importance of having a baseline level before treatment.
[c] Only in association with a treatment by GnRHa.
[d] Once a year if initial demineralization is present. Every two years otherwise. Continue until normalization of DMO, then according to adult follow-up recommendations.
[e] Only in young individuals who have not completed their growth.

Table 7
Pharmaceutical preparations based on 17-beta-estradiol available in the French pharmacopeia: equivalences, minimum and maximum dosages, dosage increase steps.

Pharmaceutical formulations[a]			Starting doses If growth is not completed	Starting doses If growth is terminated	Theoretical maximum dose[b]	Steps[c]
Treatments (commercial names)		Available dosages				
PATCHES	DERMESTRIL®	25 ; 50 ; 100 µg	6,25 µg / day ($^1/_4$ of a 25 µg patch)	25 to 50 µg / day	100 to 200 µg / day	If growth is not yet complete: Increase by 25 to 50% every 6 months If growth is complete: Increase by 50 to 100% every 3 to 6 months
	DERMESTRIL SEPTEM®	25 ; 50 ; 75 µg				
	THAIS®	25 ; 50 µg				
	THAISSEPT®	25 ; 50 µg				
	FEMSEPT®	50 ; 75 ; 100 µg				
GELS	OESTRODOSE®	0,75 mg / press	0,25 to 0,5 mg (1 pressure[d] or 1 bag[d] every 1 to 2 days)	0,5 to 1 mg/days	3 to 4 mg/day (4 to 8 pressures[e] / day)	
	ESTREVA®	0,5 mg / press				
	DELIDOSE®	0,5 or 1 mg				
PER OS	PROVAMES®	1 or 2 mg	0,25 to 0,5 mg / day	0,5 to 1 mg / day	4 to 6 mg / day	
	OROMONE®	1 or 2 mg				

[a] Equivalences: 1 mg of 17-beta-estradiol orally – 0.75 mg of 17-beta-estradiol in gel – 25 to 37 µg of 17-beta-estradiol in patches.
[b] Some young individuals do not need the maximum dose to achieve optimal effects.
[c] The intervals should be adapted based on the clinical response. For young individuals whose growth has not yet completed and wish to optimize it, the increase should be more slowly progressive. Therefore, it is preferable, in these situations, to choose smaller increments of increase and longer intervals of increase.
[d] For young individuals whose growth has not yet completed and wish to optimize it: choose the pharmaceutical formulation where the concentration by pressure is the lowest (for the brands mentioned, it is ESTREVA®).
[e] According to the prescribed formulations.

Table 8
Effects of estrogens and estimated onset times.

Effect	Onset	Maximum effect after
Redistribution of body fat	3 to 6 months	2 to 3 years
Decrease in muscle mass and strength[a]	3 to 6 months	1 to 2 years
Increase in skin softness and less greasy skin	3 to 6 months	Unknown
Decrease in libido[a]	1 to 3 months	3 to 6 months
Decrease in spontaneous erections[a]	1 to 3 months	3 to 6 months
Breast development*	3 to 6 months	2 to 3 years

[a] Individual variability in response, particularly dependent on whether or not there is a concomitant anti-androgenic treatment (the most powerful effect to expect is in association with GnRHa).
[*] Irreversible effect after cessation of estrogen.

to use preparations based on 17-beta-estradiol, which is chemically and biologically identical to endogenous estradiol. The transdermal route has a more favorable cardiovascular and thromboembolic profile than the oral route [12,13,78–81] and should therefore be favored as much as possible, especially for young people with personal or family history of cardiovascular, thromboembolic, or hepatic conditions. However, it is important to note that there does not seem to be an advantage of one form over the other in terms of effectiveness on the transition [12,13,39].

Other forms of estrogens available are not recommended [12,82–85].

The specialties based on 17-beta-estradiol available in the French

Table 9
Most common adverse effects of feminizing hormone therapy adapted from the VIDAL (French Reference for Medical Treatments) and common practice of the SFEDP expert group.

	Frequent effects >1/100 ; < 1/10	Possible effects >1/1000 ; < 1/100	Notable but rare or indeterminate frequency
Immune System-Related		Allergy, Hypersensitivity	
Metabolism and Nutrition	Weight gain or loss		
Psychiatric Disorders	Nervousness, Insomnia	Mood Change	Libido Change
Nervous System	Headache	Vertigo, Visual Disturbance	
Cardiovascular		Palpitation, increased blood pressure	Vein or artery thromboembolism, increased cardiovascular and coronary risk
Gastrointestinal	Abdominal pain, diarrhea, nausea	Dyspepsia	
Skin[a]	Skin rash, Itchiness, Dry Skin	Erythema, urticaria, skin discoloration	
Liver		Hepatic Function Abnormality	
Musculoskeletal	Dorsal pain		
Tumors			Breast cancer, Benign or Malignant Hormone-Dependent Tumor
Endocrine			Prolactin increase, galactorrhea
Fertility			Fertility issues which could persist after cessation of treatment

[a] Effects primarily observed with transdermal forms, mainly at the application sites.

pharmacopoeia with their dose equivalents are detailed in Table 7 [42,80].

Considering the effect of estrogens on the maturation of growth cartilages [86,87] in young people who have not yet finished their growth and wish to optimize it, they must be introduced at very low doses. In the absence of a suitable galenic form, the treatment can be modulated if necessary by cutting the patches or administering the gel or oral forms every other day [80].

5.3.3.4. Monitoring and titration. Table 6 provides, as an indication, the modalities of paraclinical follow-up. Table 7 provides, as an indication, the dosages at initiation, the stages of increase and the expected maximum doses; understanding that these are highly variable from one person to another and depend on the individual's expectations in terms of desired effects but also on treatment tolerance [12,13,39]. The dosage and the speed of titration must therefore be adapted to each young person, and follow-up must be regular. The expert group agrees on the importance of starting treatment at a low dose and of a gradual titration until the optimal dose is reached, in order to obtain the desired effects while ensuring good tolerance. The rate of dose increase will depend on several factors, including the clinical and biological response to treatment as well as the young person's feelings. We also recommend monitoring plasma estradiol concentrations with the goal of achieving average concentrations corresponding to the usual laboratory standards for the corresponding Tanner stage. Particular attention will be paid to young people whose growth is not complete, especially those who have received puberty-blocking treatment [86,87]. For these young people, a slower progression of titration and an annual follow-up of bone age are recommended. However, it is important to specify that the impact of 17-beta-estradiol at physiological doses on height reduction seems modest [88]. For young people whose growth is complete, the initial dosage can be higher and the titration up to the adult dose faster [13].

5.3.3.5. Expected and adverse effects. The expected effects are those related to feminization. It is important to take the time, before the introduction of treatment, to educate the young person and their family about the relatively long and progressive nature of a hormonal transition [13]. The speed and order of appearance of the treatment's effects vary from one individual to another.

Table 8 summarizes all these effects and their estimated onset times [13]. These data are based on the observation of treatment in adults. Therefore, it is possible that the onset times indicated may be longer in young people who will have a more gradual hormonal titration.

The main adverse effects are summarized in Table 9 [13,42] and are similar to those observed in cisgender adolescents and adults.

The prescriber will also be vigilant to the risks of drug interactions, particularly with cytochrome P450 inducer medications [42].

A moderate increase in prolactin is expected under estrogens, hence the interest in measuring it before starting treatment. Rare cases of prolactinoma have been described [89]. As a result, the worsening of hyperprolactinemia over several successive controls will prompt the discussion of performing a hypothalamic-pituitary MRI.

In the case of somatic or psychological adverse effects, differential diagnoses must be ruled out before affirming the responsibility of estrogens. These situations should ideally be discussed with the concerned specialists to consider possible therapeutic adaptations. All possibilities should be explored to allow the continuation of hormone therapy, given the negative psychological impact that stopping treatment could have.

5.3.3.6. Other attention point. Since the negative feedback of estrogens on the gonadotropic axis is only partial, the addition of GnRHa or another treatment aimed at suppressing endogenous hormones is often necessary alongside the prescription of estrogens (see **chapter 5.2**).

6. Gamete preservation and fertility

6.1. Impact of treatments on fertility

To date, no study has analyzed the long-term impact on fertility of gender-affirming hormone treatment in transgender adolescent.

The treatment prescribed to suppress endogenous hormones (mainly GnRHa) puts the gonad function at rest in a reversible manner. Treatment with estrogens or testosterone can also contribute to this reversible rest of the gonadotropic axis, while also having a direct impact on the gonads. The complete long-term reversibility of this effect has not yet been established. Histologically, tissue changes are observed in the specimens from ovariectomies (collagenization of the tunica albuginea, stromal hyperplasia, polycystic appearance) [90] and orchidectomies (peritubular fibrosis, maturation arrest) [91] of trans adults under GAH. However, numerous cases of spontaneous pregnancies have been reported after cessation of hormonal treatments in adult trans men [92,93]. In trans women, spermatogenesis may be partially preserved, and therefore spontaneous fertility is theoretically possible, although no study on the subject exists to our knowledge [94]. It is thus possible for trans youth who started treatment after puberty to regain their gonadal reproductive function if they wish to stop treatment to explore and preserve their fertility. It should be noted that the information available to date suggests a less favorable perspective regarding the negative

impact of estrogens on the testicle than that of testosterone on the ovary [94–97]. To date, there are only rare histological or functional data in adults who started treatments at the onset of their puberty [98].

6.2. Legal aspects

Universal access to sexual and reproductive health is part of the WHO's objectives. In France, gamete preservation is performed by reproductive biologists and physicians responsible for the Centers for the Study and Conservation of Human Eggs and Sperm (CECOS). The bioethics law states that any minor preparing to receive treatment with potentially gonadotoxic effects must be able, if they wish, to benefit from fertility preservation.

Given the current limited knowledge regarding the impact of hormonal treatments on the gonads and reproductive functions, we recommend that gamete preservation be offered before any hormonal treatment (GnRHa or GAH) for transgender adolescents and re-offered regularly, including during treatment (especially before gonadectomy if considered in adulthood), in case of initial refusal [12,13,99], as the desire for parenthood and fertility preservation increases with age [100].

6.3. Information and decision making

We recommend a dedicated consultation with a fertility specialist. Clear and complete information must be provided regarding the possibilities of gamete preservation. There is no obligation to preserve before starting hormonal treatment, but there is an obligation on the part of the medical team to provide information. On this occasion, it will be important to emphasize the many and different possibilities of accessing parenthood if this were one day the wish of the young person concerned. It will also be necessary to inform them about the conditions for reusing the preserved gametes depending on the advances in science and current legislation.

The young person must be supported through the different stages of preservation and prepared for the technical realization as well as a possible failure. Psychological support for the preparation and realization of this fertility preservation should be offered.

6.4. Practical implementation

Gamete preservation can only be considered after a detailed evaluation of the Tanner stage (clinical and/or biological).

6.4.1. At the beginning of puberty

Gamete preservation is not possible at the beginning of puberty. In this case, the preservation of gonadal tissue may be discussed. It is important to keep in mind that techniques for the *in vitro* maturation of immature germ cells remain largely experimental [101]. Furthermore, the *in vivo* reuse of testicular tissue is currently not possible [101]. Given the lack of knowledge about the long-term impact of hormonal treatments on the gonads at this stage of maturation and the very hypothetical future use of cryopreserved tissue, there is currently no consensus for proposing tissue cryopreservation for young people at the beginning of puberty. This proposal can be made on a case-by-case basis, depending on requests, centers, and in agreement with the national CECOS committee. Moreover, the possibility of stopping anti-gonadotropic treatment to perform gamete preservation must be weighed against the risk of resuming the development of secondary sexual characteristics (loss of the benefit of stopping pubertal development).

6.4.2. Puberty in progress or completed

6.4.2.1. Oocyte preservation. Preservation in this situation often requires hormonal treatments for ovarian stimulation and medical procedures often considered "invasive" by individuals. It should be offered but is rarely requested by the minors concerned [100]. It can be reconsidered later on.

6.4.2.2. Sperm preservation. It is necessary to wait until the young person is at approximately Tanner stage 3 of puberty to observe mature spermatozoa in the ejaculate [102]. Additionally, ejaculatory possibilities may be limited by testosterone levels and difficulties with masturbation [103]. If self-preservation at CECOS is not possible, a surgical attempt to extract spermatozoa or freeze testicular tissue under general anesthesia can be proposed. This does not currently have consensus in France and must be discussed on a case-by-case basis and in agreement with the national CECOS committee.

Anti-gonadotropic treatment, due to its central action, induces a decrease in spermatogenesis. A cessation of GAH prior to any fertility preservation is recommended. Given the duration of a spermatogenesis cycle [104], the cessation of hormonal treatment should ideally occur at least three months beforehand.

7. Non-hormonal support

7.1. Bone health

7.1.1. Bone mass: variation and evaluation

BMD is primarily assessed by dual-energy X-ray absorptiometry (DEXA). The value mainly used is that of the spine (L1-L4). The hip can be used when there is no more growth cartilage. Reference values depend on age, sex, and the device used. Interpretation must take into account height and bone age in cases of incomplete puberty [105].

Treatment with GnRHa will naturally slow down the progression of the BMD Z-score and the acquisition of bone mass that would have occurred with physiological puberty. There is no real loss of bone mineral content in the medium term [106–108]. There will be a new acquisition of bone mass and an increase in BMD with the introduction of GAH [107,109]. However, this increase in BMD does not always allow for normalization, especially if treatment with GnRHa was started late during physiological puberty (Tanner stage 4–5), particularly in trans girls [110]. On the other hand, it seems that trans individuals who benefited from puberty suppression at the beginning of puberty achieve a BMD comparable to that of the experienced gender at the end of the transition [111].

Monitoring BMD is essential in the management of a transgender adolescent under GnRHa, following a schedule proposed in Table 2. We recommend interpreting this BMD by referring to the pediatric reference values of the gender assigned at birth for transgender youth before the start of GAH, and then to the experienced gender for transgender youth who have started GAH [112].

Trans youth have an average BMD before the onset of puberty that is lower than that of the general population [106,113], regardless of treatment. This is probably related to the consequences of dysphoria: less physical activity, eating disorders, and/or poor dietary balance. In the case of low bone mineralization (corrected Z-score < -2 SD) before or during treatment, specialized investigations should be considered to rule out other causes.

7.1.2. Calcium intake: assessment and supplementation

We recommend the consumption of 3 to 4 servings of calcium per day [114]. Dietary intake can be assessed by a dietitian or simply by using the Faderlone self-questionnaire. In case of insufficient intake, a calcium prescription should be made.

7.1.3. Vitamin D: assessment and supplementation

Vitamin D deficiency is very common among young people: up to 60% in the general population and up to 90% in the transgender

population [115,116], which should therefore be considered a risk population according to the French Society of Pediatrics guidelines [115]. We therefore recommend systematic vitamin D supplementation according to one of the following modalities:

- Daily dose administration: between 800 and 1600 IU per day (approximately 1200 IU/day).
- Or intermittent dose administration: 50,000 IU every 6 weeks or 100,000 IU every 3 months. The curative treatment modalities for vitamin D deficiency are comparable to the general population [117].

7.1.4. Physical activity

See chapter 7.3

7.2. Sexual health

7.2.1. General

The WHO defines sexual health as a state of physical, emotional, mental, and social well-being related to sexuality, regardless of sex, gender, or sexual orientation. The development of sexual health includes respecting the sexual rights of all individuals, the right to express sexualities or diverse sexual practices safely, meaning free from discrimination and violence. Support in sexual health should allow for discussion and information on respecting free choice, consent, sexual functioning, and pleasure.

7.2.2. Adolescence and sexuality

7.2.2.1. Practitioner's approach. We recommend a kind, non-judgmental, and welcoming attitude to encourage the young person to discuss questions about sexuality, intimacy, and their needs.

For effective communication, it seems important to agree on the terminology used by the young person for their own body rather than the usual medical terminology [118]. The diversity of sexual practices should be taken into consideration. It is also essential to respect each individual's pace in discovering their sexuality.

If the young person has already had sexual experiences, it is possible to discuss the body parts involved in these experiences to better prevent the risks of sexually transmitted infections (STIs) and pregnancy. The issue of behaviors at risk should be addressed freely and without prejudice [119].

We recommend dedicating a specific consult time during which the young person can be seen alone, but also accompanied by their partner if they wish. We also recommend, when necessary, referring the young person to a specialized sexual health consultation.

7.2.2.2. Impact of hormonal treatments on sexuality. Healthcare professionals must inform young people and their families about the possible impact of GAH treatments on sexual functioning, gather their expectations, and ensure their understanding. These treatments can affect mood, sexual desire, the ability to have an erection or ejaculation, and vulvovaginal sensitivity; which can have an impact on sexual function and pleasure. This information may change the young person's desire for certain treatments, the possibilities and limitations of which will have been discussed.

7.2.2.3. Contraception. Testosterone is not a reliable contraceptive, especially at low doses [12,13,39]. This fact must be regularly reminded to the concerned youth. In case of sexual activity with a risk of pregnancy, we recommend the use of contraception (condom, pill, hormonal implant, intrauterine device, etc.).

In the absence of concurrent use of GnRHa or specific strongly antigonadotropic molecules, 17-beta-estradiol does not lead to a complete suppression of the gonadotropic axis. Therefore, there remains a possibility of spermatogenesis, even if partial, and thus of fertility [94]. We recommend mechanical protection in case of sexual intercourse with a risk of pregnancy and/or appropriate contraception for the partner.

7.2.2.4. Prevention of sexually transmitted infections (STIs). The goal is to provide essential information on STI prevention, screening, and treatment in the context where their prevalence is higher in the adult transgender population than in the general population (no studies in minors) [120]. Promoting HPV vaccination is important. In case of a history of risky sexual encounters, we recommend undergoing screening tests. Concerns related to body image, the intensity of dysphoria, and sometimes stigma can negatively impact self-esteem and the ability to assert one's desires or negotiate condom use, for example. Healthcare professionals should emphasize that condom use is necessary for STI prevention.

7.2.3. Gynecological and genital follow-up

The initiation of gynecological follow-up in young trans individuals should be considered and regularly proposed in their care. Dedicated gynecological consultations for this support are increasingly being offered to provide a reassuring welcome for young trans individuals. The topics addressed will be tailored to the age and needs of each young person. It will also be an opportunity to discuss contraception and sexual health, raise awareness of the importance of long-term gynecological follow-up, and explain its procedures. For trans men, the goal is to provide support in managing potential gynecological symptoms (bleeding, pelvic pain, vaginal dryness, etc.).

The HPV vaccination should be systematically offered [121], regardless of hormonal transition [122]. In the long term, we recommend gynecological follow-up for breast and cervical cancer screening, as well as testicular and prostate follow-up according to the recommendations currently in place for the cisgender population. [12, 123–128].

7.3. Lifestyle

Generally, the advice on a healthy lifestyle does not differ from that given to the general population. However, particular attention must be paid to bone, metabolic, and cardiovascular health in the long term. To minimize risks, the adolescent should be encouraged to adopt a balanced diet, engage in regular physical activity, and abstain from smoking or using other recreational drugs.

A balanced diet should be adapted to energy expenditure. Indeed, obesity can not only increase the risk of long-term complications but also hinder or complicate any surgical interventions that may be desired. The intake of vitamin D and calcium should be optimized to promote bone health and development (**see chapter 7.1**). Moreover, eating disorders are found with increased frequency among young trans individuals [129). It is important to search for and address them.

It is important to help adolescents find physical activities in which they feel safe and comfortable. Sports that require gender-based groups can cause or exacerbate dysphoria or lead to eligibility issues, especially at the level of competition [130]. Practical questions such as the use of locker rooms may require special attention.

The consumption of tobacco, alcohol, and drugs is higher among adult transgender individuals [131]. There has been no study conducted among minors. This consumption can be associated with increased risks of cardiovascular and thromboembolic diseases, particularly under long-term hormone therapy [132]. If surgery is desired in the future, young people should be informed that nicotine can hinder the healing of surgical sutures.

7.4. Social

In France, if the adolescents and their family wish, medical support

for trans youth can be fully reimbursed by the health insurance funds under the long-term illnesses category (also called "ALD 31"). This request can be made by any doctor accompanying the young person.

Administratively, the change of first name at the Civil Registry is possible at the town hall and no longer requires medical certificates. This process will then allow for the new first name to be added to all official documents (identity card, passport, etc.). However, this process still requires the consent of legal representatives. The administrative change of gender at the Civil Registry can, for the time being, only occur after reaching majority age or obtaining emancipation and requires a hearing in court.

At the educational level, the Ministry of National Education has issued a circular [133] facilitating the integration of trans youth into schools by allowing, among other things, the use of first names and pronouns in common use even before the administrative changes at the Civil Registry have been completed.

We recommend, as soon as it seems necessary and feasible, to direct adolescents and their family towards peer support groups, social workers, or any person or organization capable of assisting them in these procedures.

The contribution of peer support groups should be considered as soon as resources exist at the local level, both concerning administrative questions and for the more global support of the young people and their families. If resources do not exist, referral to structures in other localities or national organizations should be considered. Discussion groups for young people and/or their families, which can be organized by associations and/or medical teams, have also shown their usefulness in this support [134,135].

7.5. Dermatological treatment

Several dermatological situations may prompt trans youth to seek consultation [136].

Acne may be triggered or worsened by testosterone. The treatments in this case do not differ from those used in cisgender youth. In the event of oral isotretinoin use, it will be important to discuss contraception [42].

Hair removal may be desired, particularly on the face in case of persistent facial hair. Several techniques can be used: electrolysis, laser [136]. They should ideally be performed after hormonal suppression when it is desired.

7.6. Voice and communication therapy

This support aims to assist young people who wish to work on their voice and/or communication style [137].

This support is generally provided by speech therapists; however, other professionals such as vocal coaches, theater professionals, singing teachers, gesture experts, can play a complementary role that is not to be overlooked.

The targets are tone, intonation, resonance, articulation, speech rate, phrasing, elocution, language level, and non-verbal communication. It will be important for voice professionals to sensitize the adolescents about vocal health.

7.7. Methods of concealing secondary sexual characteristics

7.7.1. Binders

Many trans boys experience dysphoria related to the chest. In this context, some use a binder to compress the chest [138].

The use of binders can, however, lead to discomfort, pain, or shortness of breath during physical activities [12]. Prolonged use can cause chest, shoulder, or back pain, particularly poor posture of the back, gastric or thoracic compression, excessive sweating, skin lesions, and acne [139]. To minimize these side effects, we recommend:

- Using a binder designed for this purpose
- Not layering multiple binders
- Ensuring it is well-fitted. It should not be too tight and must not hinder breathing or cause pain
- Reducing as much as possible the duration of wear during the day (ideally less than 8h per day)
- Not sleeping with a binder
- If possible, having days without wearing a binder.

We do not recommend the use of adhesives or bandages that can cause skin lesions and have a negative impact on any potential future surgery.

7.7.2. Tucking technique

Tucking is a practice used by trans girls to conceal external genital organs. It often involves the retraction of testicles into the inguinal canals, as well as the backward positioning of the penis and scrotum, typically using special clothing and/or adhesives [140,141].

The adverse effects reported by those who practice this are testicular and/or penile pain [140,141].

The use of adhesives can lead to additional adverse effects such as itching, skin rashes, infections, and other skin lesions; and is therefore discouraged [140,141].

Retracting the testicles into the inguinal canal causes reversible thermally induced alterations in sperm production upon cessation of tucking [142]. Therefore, it is necessary to inform young people practicing this technique that spermatogenesis can be altered and fertility preservation less effective. If there is a desire to preserve gametes, we recommend not practicing tucking for about three months before collection to optimize sperm quality.

8. Handover of care to adult medicine

Hormonal treatment requires long-term medical follow-up. The handover from pediatric to adult care is therefore an important phase, with a risk of discontinuation of care [143]. Proper preparation of this handover aims to reduce the number of interruptions in medical follow-up [23).

We recommend that this handover occurs after the end of growth and/or when the hormonal treatment has reached doses close to those used in adults. It should be adapted to local organization and the specific needs of each young person who must feel ready for this change. Some pediatric services have established handover structures (dedicated place, specific support program). It seems appropriate that trans youth could benefit from these structures.

It will be necessary to direct the young person to a doctor familiar with the care of transgender individuals. This handover should be coordinated with other specialists who accompany them, especially if other follow-ups must continue into adulthood, ideally within the same healthcare network when possible.

The key points to address during this period are as follows (Appendix 3):

- Ensure that the young person has received and understood the necessary information regarding their health, including:
  - Their current treatment, known long-term effects, suspected or unknown, and existing medical or surgical treatments and their indications.
  - Recommended long-term follow-up
  - Questions of fertility and parenthood
  - The existence of organized screening programs for certain cancers from a certain age in adults for which they may not always receive

an automated invitation due to the registered administrative sex at social security.
- Support the acquisition of knowledge and skills necessary for the practical management of treatments and the course of care.
- Inform again about the existence and function of support groups, lawyers, social workers, occupational health services. Provide the means for the young person to contact them if needed.
- Reassess psycho-social aspects and the potential need for support in these areas.
- Reassess questions of fertility and sexual health.
- Address the concept of a trusted person.
- With the consent of the concerned individual, provide in writing all useful information to the adult reference physician. Multidisciplinary coordination meeting minutes can be attached.
- Provide precise and clear information, especially about organs in situ, to allow appropriate management of situations such as acute abdominal pain, and cancer screening.
- The modalities of handover between pediatrician and adult physician will depend on local possibilities and organization (joint consultation, alternating consultation periods, joint participation in a multidisciplinary consultation…).
- In all cases, it is up to the pediatric team to direct the young person to adult correspondents, organize their first appointment, and ensure its effective implementation. It should be specified to the young person to recontact the pediatric team if they encounter difficulties

9. Conclusion

This work constitutes the first national guidelines concerning the endocrinological support of trans youth in France. It complements the existing international recommendations and was written in parallel with the recommendations of the European Society for Pediatric Endocrinology (ESPE) expert group, which will be published soon. It is set against a backdrop of a general lack of reference text to guide practice in France. The document was written by a workgroup composed almost exclusively of pediatric endocrinologists, which is its main limitation. Recommendations written under the auspices of the HAS by a broader college of professionals involved and associations representing concerned individuals are awaited. In the meantime, the structuring, identification, and training of actors involved in supporting these young persons, especially those under 16 years old, is crucial to ensure their safety and rights. It is essential that all stakeholders work together, but also with public authorities, to make the support offer clear for adolescents and their families, uniform across the territory, and to allow the accumulation of prospective data in order to continue improving the care of trans youth.

Conflicts of interests

FB: support to attend a national or international conference from Merck, Sandoz, Pfizer, Ipsen; CL: support to attend a national or international conference from Merck, Pfizer, Sanofi; ÉF (Élodie): support to attend a national or international conference from Pfizer, Merck, participation in scientific advisory boards or symposium presentations/moderation for Sanofi, Pfizer, Merck; CB: support to attend a national or international conference from Merck, Sanofi, Pfizer, Sandoz, Ipsen; CA: support to attend a national or international conference from Sandoz, Pfizer, participation in scientific advisory boards or symposium presentations/moderation for Pfizer, Ipsen, Merck; MA: support to attend a national or international conference from Sandoz, Sanofi; AC: support to attend a national or international conference from Ipsen, Merck, Pfizer, Sandoz, participation in scientific advisory boards or symposium presentations/moderation for Merck; SC: support to attend a national or international conference from Sandoz, Merck, participation in scientific advisory boards or symposium presentations/moderation for Pfizer, Merck; MD: support to attend a national or international conference from Ipsen; EF (Eva): support to attend a national or international conference from Sandoz, Merck, Pfizer; MH: support to attend a national or international conference from Ipsen, Sanofi; BLL: support to attend a national or international conference from Sandoz, Merck, Sanofi, Novartis, participation in scientific advisory boards or symposium presentations/moderation for Merck; ASL: support to attend a national or international conference from Merck, Sandoz, Ipsen, Pfizer, participation in scientific advisory boards or symposium presentations/moderation for Merck, Pfizer; SR: support to attend a national or international conference from Merck, participation in scientific advisory boards or symposium presentations/moderation for Merck; MAT: support to attend a national or international conference from Pfizer, Sanofi, Sandoz, participation in scientific advisory boards or symposium presentations/moderation for Merck; VV: support to attend a national or international conference from Sandoz, Pfizer, Merck, participation in scientific advisory boards or symposium presentations/moderation for Pfizer, Merck; LM: support to attend a national or international conference from Besin Healthcare, Sandoz, Pfizer, participation in scientific advisory boards or symposium presentations/moderation for Ipsen, Merck, Lilly; KB, CD: no conflict of interests.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.arcped.2024.08.003.

Appendix 1. LIST OF ABBREVIATIONS

BMD: Bone Mineral Density
CECOS : French acronym for Centers for the Study and Conservation of Human Eggs and Sperm
GAH : Gender-affirming Hormone
GnRHa : Gonadotrophin Releasing Hormone Analogue
SFEDP : French acronym for ‘‘French Society of Pediatric Endocrinology and Diabetology’’
STI : sexually transmitted infections
WHO : World Health Organization

Appendix 2. – MODEL OF CONSENT

For the young person:
I, undersigned (first name last name), born on (date of birth), attest having received from Dr. xxx, all the information concerning puberty blockers / estrogens / testosterone treatment, its expected reversible and irreversible effects, and its potential side effects, notably the impact on fertility, growth

and bone metabolism, and future surgeries (for puberty blockers) and having understood them. I have taken note of the information sheet on the treatment and have been able to ask all the questions I had. I wish to benefit from this treatment.

Date, place, signature

For the holders of parental authority:

We, undersigned, mother/father/legal representative of xxx, attest having received the same information concerning the treatment with puberty blockers / testosterone / estrogens, its expected reversible and irreversible effects, and its potential side effects, notably the impact on fertility, growth and bone metabolism, future surgeries (for puberty blockers) and having understood them. We have taken note of the information sheet on the treatment with GnRH analogues (puberty blockers)/testosterone/estrogens and have been able to ask all our questions. We wish for our child to benefit from this treatment.

Date, place, signatures of all holders of parental authority

Appendix 3. - DOCUMENT OF PREPARATION FOR THE HANDOVER TO ADULT CARE

Inspired by the document of the Endocrine Society (endocrinetransitions.org)

This form can be filled out by the young person alone or during the consultation to help the team better understand their knowledge about their health, their use of the healthcare system, and the areas in which additional support seems necessary. It should not be hesitated to use this questionnaire well in advance of the actual handover to adult medicine in order to support autonomy.

SKILLS AND LIFE SITUATION	**The situation suits me**	**I need support**
I feel comfortable asking questions to my care team		
My family supports me in my transgender journey		
I live openly in my affirmed gender without any issues		
I can advocate for my interests		
I have sufficient housing and food		
I have enough money to meet my needs		
I can name 1 to 2 people who can help me achieve my health goals		
I know who to contact if I'm feeling down or have suicidal thoughts		
I know who to turn to in case of difficulties		
I know who to contact if someone abuses me or tries to harm me		
I am covered by social security		
I have health insurance		
I have a means of getting to my doctor (public transport, vehicle…)		
MY KNOWLEDGE	**I am comfortable**	**I need to deepen**
I can explain to others what my medical needs are		
I know which medications I take, when to take them, and at what dose without being reminded		
If I have allergies, I know what I'm allergic to (including medications)		
I know where I can find the name and phone number of my doctor		
I make my own medical appointments		
Before a visit, I think about the questions to ask my doctor		
Before a visit, I know it's necessary to bring a list of medications I'm taking		
I am aware of the potential side effects of hormone therapy		
I know how to request a referral to another doctor or specialist if needed		
I know where my pharmacy is and what to do when I run out of medication		
I know where to go for blood tests or other exams if prescribed by the doctor		
I know when it's necessary to contact my care team		
I know how to contact my care team if needed		
I know how to update my health card		
I know how to contact social security and my insurance company		
I know how to log in to 'Ameli' website		

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