Controversias en el abordaje médico de la Insensibilidad a los andrógenos

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Introduction

DSD include a group of rare conditions

Rare conditions = often insufficient evidence to make informed decisions

especially if those are life changing

Decisions are based on :

1. evidence based medicine
2. consensus of experts' opinions
3. affected persons' experience

Providing care for individuals with DSD is best performed in a multidisciplinary setting

Introduction

Aim

Controversies in medical management of AIS

1. Gonadectomy

2. Hormone Replacement Therapy

Gonadectomy in AIS

Controversies regarding Gonadectomy in AIS

Remove gonads

- Cancer risk
- No use of gonad
- Musculinisation in PAIS

Delay gonadectomy until completion of puberty

- Spontaneous puberty
- Involved in decision making process

Defer Gonadectomy

- No need for HRT
- Fertility potential
- Better well being
- Better long-term outcomes

Current Clinical Practice

Clinical Endocrinology (2012) 76, 894–898 doi: 10.1111/j.1365-2265.2012.04330.x

ORIGINAL ARTICLE

Timing of gonadectomy in adult women with complete androgen insensitivity syndrome (CAIS): patient preferences and clinical evidence

Rebecca Deans*, Sarah M. Creighton†, Lih-Mei Liao† and Gerard S. Conway†

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- Of the 104 adult women with CAIS under review in the clinic, 16 (**15%**) have chosen to defer or decline gonadectomy
- The mean age of the women was 28 years (range 18–51 years)

Reasons given for deferring or declining gonadectomy

Reason given	*number*
Concern about the risks of the procedure	8
Surgery was not convenient because of academic commitments	6
Did not want to take hormone replacement throughout adult life either because of inconvenience, concern about side effects or worries that it might not work	6
Felt unable to make this decision as they had not yet come to terms with their diagnosis	5
Hoped their gonads could be used for future fertility	3
Unaware of any malignancy risk	1
Believed she had undergone a bilateral gonadectomy in adolescence but in fact had undergone a unilateral gonadectomy	1

Deans R, et al. Timing of gonadectomy in adult women with complete androgen insensitivity syndrome (CAIS): patient preferences and clinical evidence. Clin Endocrinol (Oxf). 2012 Jun;76(6):894-8. doi: 10.1111/j.1365-2265.2012.04330.x.

Current Clinical Practice

Original Paper

HORMONE RESEARCH IN PÆDIATRICS

Horm Res Paediatr
DOI: 10.1159/000493645

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Management of Gonads in Adults with Androgen Insensitivity: An International Survey

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An international survey among health care professionals through the I-DSD Registry, between 2015 and 2017.

- 22 Centres (18 European and 4 non-European centres)
- Data were collected on 166 women with CAIS and 26 men with PAIS.

CAIS - Attitudes towards Gonadectomy in Centres

1. Gonadectomy was performed on a routine basis **during childhood** in 18% of centres

2. Gonadectomy was routinely proposed **after puberty** in 54% of centres

3. 27% of centres reported not to propose gonadectomy on a routine basis at any age but to perform the procedure **according to individuals' preferences**

Tack LJW, et al. Management of Gonads in Adults with Androgen Insensitivity: An International Survey. Horm Res Paediatr. 2018;90(4):236-246. doi: 10.1159/000493645.

CAIS – Women older than 16 years with retained gonads

Of 166 women, 24 (**14.5%**) had retained gonads at the time of the survey

The median age of these women was 20 years (range: 16–48 years).

50% had abdominal and 25% had inguinal gonads; location was unknown in 25%

Reason given	***number***
Concern about the risks of the procedure	8
Surgery was not convenient because of academic commitments	6
Did not want to take hormone replacement throughout adult life either because of inconvenience, concern about side effects or worries that it might not work	5
Felt unable to make this decision as they had not yet come to terms with their diagnosis	4
Unaware or did not understand cancer risk	2

Men with PAIS - Attitudes towards Gonadectomy in Centres

1. Gonadectomy was performed on a routine basis **during childhood** in 6% of centres
2. Gonadectomy was performed **based on gonadal location** in 22% of centres
3. Gonadectomy was routinely proposed **after puberty** in 12% centres
4. The decision was made on a case by case basis **according to gonadal function and location** in 22% of centres

Only 35% of men had at least one retained gonad at the time of the survey

Tack LJW, et al. Management of Gonads in Adults with Androgen Insensitivity: An International Survey. Horm Res Paediatr. 2018;90(4):236-246. doi: 10.1159/000493645.

Current Clinical Practice

Clinical Study | A K Lucas-Herald and others | Gonadectomy in DSD | 184:6 | 791–801

Gonadectomy in conditions affecting sex development: a registry-based cohort study

Lucas-Herald AK, Bryce J, Kyriakou A, et al. Gonadectomy in conditions affecting sex development: a registry-based cohort study. Eur J Endocrinol. 2021 May 4;184(6):791-801. doi: 10.1530/EJE-20-1058.

I-DSD Registry study – included **cases who were over the age of 16.0 years** in January 2019

Gonadectomy in females with AIS

	CAIS	PAIS
All		
number	161	
Cases of gonadectomy	129 (80%)	
Age at presentation	15 years (0 – 32)	
Cases of gonadectomy		
Age at gonadectomy	16 years (0.3 – 68)	
Prior to specialist centre	6 (5%)	
Cases with retained gonads		
number	32 (20%)	
Age at presentation	14 years (0.1 – 51)	
Current age	27 years (17 – 86)	

Lucas-Herald AK, Bryce J, Kyriakou A, et al. Gonadectomy in conditions affecting sex development: a registry-based cohort study. Eur J Endocrinol. 2021 May 4;184(6):791-801. doi: 10.1530/EJE-20-1058.

Gonadectomy in females with AIS

	CAIS	PAIS
All		
number	161	29
Cases of gonadectomy	129 (80%)	24 (83%)
Age at presentation	15 years (0 – 32)	11 years (0.1 – 20)
Cases of gonadectomy		
Age at gonadectomy	16 years (0.3 – 68)	8 years (0.5 – 24)
Prior to specialist centre	6 (5%)	2 (8%)
Cases with retained gonads		
number	32 (20%)	5 (17%)
Age at presentation	14 years (0.1 – 51)	1 year (0.1 – 12)
Current age	27 years (17 – 86)	23 years (18 – 28)

Lucas-Herald AK, Bryce J, Kyriakou A, et al. Gonadectomy in conditions affecting sex development: a registry-based cohort study. Eur J Endocrinol. 2021 May 4;184(6):791-801. doi: 10.1530/EJE-20-1058.

Gonadectomy in males with AIS

	PAIS
All	
number	50
Cases of gonadectomy	3 (6%)
Age at presentation	29 years (3 – 54)
Cases of gonadectomy	
Age at gonadectomy	41 years (5 – 75)
Prior to specialist centre	1 (33%)
Cases with retained gonads	
number	47 (94%)
Age at presentation	0.3 years (0.1 – 20)
Current age	24 years (17 – 57)

Lucas-Herald AK, Bryce J, Kyriakou A, et al. Gonadectomy in conditions affecting sex development: a registry-based cohort study. Eur J Endocrinol. 2021 May 4;184(6):791-801. doi: 10.1530/EJE-20-1058.

Gonadectomy in conditions affecting sex development: a registry-based cohort study

- There was no change over time in the age at gonadectomy
- Gonadectomy was performed in 6% prior presenting to a specialist centre
- There were variations in practice between Low-Medium Income Countries and High Income Countries: the likelihood of retaining gonads for CAIS was greater in Low-Medium Income Countries

Lucas-Herald AK, Bryce J, Kyriakou A, et al. Gonadectomy in conditions affecting sex development: a registry-based cohort study. Eur J Endocrinol. 2021 May 4;184(6):791-801. doi: 10.1530/EJE-20-1058.

Controversies regarding Gonadectomy in AIS

18%	***54%***	***27%***
Remove gonads	**Delay gonadectomy until completion of puberty**	**Defer Gonadectomy**
• Cancer risk • No use of gonad • Musculinisation in PAIS	• Spontaneous puberty • Involved in decision making process	• No need for HRT • Fertility potential • Better well being • Better long-term outcomes

Gonadectomy 80 – 85%

Intact gonads 15 – 20%

Risk for Gonadal Cancer in AIS - Evidence

Author	Country	Year	Condition	Number of people	Pre-cancer	In situ cancer	Invasive cancer
Ahmed SF	UK	2000	CAIS	65	none	none	none
			PAIS	56	none	none	none
Hannema SE	UK	2006	CAIS	44	none	2	none
Cheikherald A	France	2008	CAIS	29	none	1	none
Audi L	Spain	2010	CAIS/PAIS	13	none	none	none
Nakhal RS	UK	2013	CAIS	25	none	3	none
Chaudhry S	UK	2017	CAIS	133		6	2
Cools M	Belgium	2017	CAIS	42	6	none	none
			PAIS	10	1	none	none

Tack LJW, et al. Management of Gonads in Adults with Androgen Insensitivity: An International Survey. Horm Res Paediatr. 2018;90(4):236-246. doi: 10.1159/000493645.

Risk for Gonadal Cancer in AIS - Evidence

Review article
https://doi.org/10.6065/apem.2040170.085
Ann Pediatr Endocrinol Metab 2021;26:19-23

Annals of Pediatric Endocrinology & Metabolism
apem

Complete androgen insensitivity syndrome and risk of gonadal malignancy: systematic review

Barros BA, et al. Complete androgen insensitivity syndrome and risk of gonadal malignancy: systematic review. Ann Pediatr Endocrinol Metab. 2021 Mar;26(1):19-23.

Systematic review of 15 studies, evaluating the gonadal aspect of a large number of women with CAIS

- A total of 456 women
- A low rate of malignancy was detected [6% of premalignant lesions, the majority (81%) after 12 years of age, and 1.3% of malignancies, all in adult women]

Risk for Gonadal Cancer in AIS - Evidence

Human Reproduction, Vol.32, No.12 pp. 2561–2573, 2017
Advanced Access publication on November 7, 2017 doi: 10.1093/humrep/dex300

human reproduction ORIGINAL ARTICLE *Reproductive genetics*

Malignant testicular germ cell tumors in postpubertal individuals with androgen insensitivity: prevalence, pathology and relevance of single nucleotide polymorphism-based susceptibility profiling

Cools M, et al. Hum Reprod. 2017 Dec 1;32(12):2561-2573.

STUDY QUESTION: What is the prevalence of malignant gonadal tumours

and its pre-malignant changes in late teenagers and adults who have AIS

- Material from 52 post-pubertal individuals with AIS was included
- The median age at surgery was 17.5 years (range: 14–54 years)

- Pre-malignant changes were present in 14% of individuals with CAIS and in 10% of those with PAIS at a median age of 16 years
- No malignant changes were found

Conclusion:

1. The prevalence of pre-malignant changes in individuals with AIS beyond puberty is around 15%.
2. Progression to malignancy appears to be rare
3. Therefore, the practice of routine prophylactic gonadectomy in adults with AIS appears questionable and the person's preference, after having been fully informed, should be decisive in this matter.

Risk for Gonadal Cancer in AIS - Evidence

1. There is a very low risk of malignancy before puberty

2. Older reports: The risk of gonadal tumour increases with age in CAIS and is estimated at 3.6% at 25 years and 33% at 50 years

Cools M, et al. Endocr Rev 2006;27:468-84.

3. Recent reports: Very low prevalence of malignancies, mostly localised

Is gonadectomy in adulthood necessary?

VS

What are the benefits from keeping the gonads?

Benefits from retaining gonads

1. Spontaneous puberty with physiological development of secondary sex characteristics

2. No need for Hormone Replacement Therapy - continuous and long-term hormone therapy is necessary to maintain sexual function, psychosocial well-being, and bone health

3. General well being is reported to be impaired after gonadectomy

4. Gonadectomy can lead to worsening of sexual function and high level of psychological stress in women

5. Effects on bone health

6. Preserving fertility

7. Involved in decision making process

Current Opinion

The conservative management of gonads in CAIS

Management of individuals with CAIS should be based on the holistic well-being of the child and the future adult, aiming at minimising physical and psychosocial risks, preserving potential fertility, respecting the individual's right to participate in the decisions that will affect them, and avoid irreversible treatments not essential for their health.

If gonadectomy is postponed, many new questions arise

- How does endocrine function develop in adulthood, and when does it decline?
- How many gonadal tumours will occur, and how will they affect the lives of the individuals?
- How to Identify a Gonad at Risk for Development of Malignancy?

Monitoring for gonadal cancer in CAIS

- If gonadectomy is not performed post-puberty, the malignancy risk will increase with age.
- The difficulty with conserving gonads is that there are **no available reliable screening tests** that detect early malignant change.
- The gonads are usually intra-abdominal and so are impalpable.
- Neither ultrasound nor MRI can reliably detect premalignant changes, and tumours markers are unspecific.
- This means that presentation with a gonadal malignancy may be late and with clinical symptoms.

The conservative management of gonads in CAIS

Childhood Puberty

Inform person/family about the condition and the low risk for cancer

No action required

Adulthood

- Inform person about the condition and the risk for cancer
- Check person's understanding and awareness

Explain pros and cons of gonadectomy

According to individual's preference

Surveillance

- Relocation of gonads in a more superficial region
- Monitoring with imaging
  Ultrasound every 6 – 12 months
- Tumour markers every 12 months
- MRI
- Gonadal biopsy

Gonadectomy

Tack LJW, et al. Horm Res Paediatr. 2018;90(4):236-246. doi: 10.1159/000493645.

SEEN Sociedad Española de Endocrinología y Nutrición
SOCIEDAD ESPAÑOLA DE DIABETES

Endocrinología, Diabetes y Nutrición

www.elsevier.es/endo

CONSENSUS DOCUMENT

Consensus guide on prophylactic gonadectomy in different sex development

Julio Guerrero-Fernández[a,b,*], Pilar González-Peramato[c], Amaia Rodríguez Estévez[d], María José Alcázar Villar[a,e], Laura Audí Parera[a,f], María Cristina Azcona San Julián[a,g], Atilano Carcavilla Urquí[a,b], Luis Antonio Castaño González[a,h], José María Martos Tello[a,i], Cristina Mora Palma[a,b], Maria Francisca Moreno Macián[a,j], Diego Yeste Fernández[a,k], Manuel Nistal[l]

Hormone Replacement Therapy in AIS

Gonadal function in girls and women with CAIS

Spontaneous Pubertal Pattern

Few data on spontaneous pubertal development in adolescent girls with CAIS are available

When gonads are not removed:

- The onset of puberty and pubertal growth spurt occur at the same age as in other girls

- Women with CAIS and removed gonads after puberty are taller than those who underwent gonadectomy before puberty (172 vs. 165 cm, respectively)

Gonadal function in girls and women with CAIS

After puberty

- A very distinct hormone profile is present
- Testosterone concentrations in the normal to upper male reference range
- Oestradiol concentrations are slightly increased relative to male references
- Oestradiol concentrations are below the female reference range

Hormone Replacement Therapy after Gonadectomy

Girls with CAIS

Pubertal Induction

- Adequate HRT should be administered in girls with CAIS and gonads removed before puberty
- Hormonal induction of puberty should usually be consistent with physiological breast development
- The sex steroid treatment should attempt to replicate normal tempo of puberty
- Usually oral or transdermal estrogens are used, beginning with low doses and gradually increasing

Hormone Replacement Therapy after Gonadectomy

Women with CAIS

- Women will require HRT continuously until approximately the age of 50
- The principles of use of HRT for women with CAIS are usually the same as for any other women
- The main **treatment goals** are to maintain secondary sex characteristics, a good quality of life, sexual function and optimal bone density and cardiovascular function
- Sex steroid replacement has traditionally been based on types of **estrogens**
- As women with CAIS do not have a uterus, progesterone is not required

Long-term trials looking at long-term benefits and risks of HRT in women with CAIS are not available

Data in aging women (post menopausal) should not be extrapolated to young adults

Hormone Replacement Therapy after Gonadectomy

Testosterone

- There is increasing interest from user groups
- Testosterone is the main endogenous sex steroid hormone secreted by gonads
- Interest in testosterone has developed through observations voiced particularly from women who experienced late gonadectomy:

  Reported greater vitality, libido and athletic performance prior to gonadectomy when they are 'running on testosterone' compared to after gonadectomy when their sex steroid balance is based on oestrogen

- **There are no known adverse effects of long-term exposure to testosterone in women with CAIS who have retained their gonads**

What is the ideal HRT?

Current Clinical Practice

Research

Open Access

J K Y Ko *et al.* | HRT choices in CAIS | **375**–379 | 6:375

Endocrine CONNECTIONS

Hormone replacement treatment choices in complete androgen insensitivity syndrome: an audit of an adult clinic

Jennifer K Y Ko, Thomas F J King, Louise Williams, Sarah M Creighton and **Gerard S Conway**

Department of Women's Health, University College London Hospital, London, UK

Correspondence should be addressed to G S Conway
Email
g.conway@ucl.ac.uk

Ko JKY, et al. Endocr Connect. 2017

- **125 women with CAIS who had gonadectomy**
- **The age at gonadectomy was 17 years (range: 0.1–53 years)**

- The median age at start of HRT was 18 years (range 8–41 years).
- The most common form of HRT was **oestrogen** in 96% or those requiring HRT

- **Testosterone** was used in 12% of women, either combined **estrogen and testosterone** treatment or **testosterone alone**
- Ten individuals had used testosterone therapy in the past but had discontinued. The reason for discontinuing was that no meaningful benefit was perceived.
- No side effects from testosterone were recorded

There was no theoretical or practical reason not to offer this option

Ko JKY, et al. Hormone replacement treatment choices in complete androgen insensitivity syndrome: an audit of an adult clinic. Endocr Connect. 2017 Aug;6(6):375-379.

Clinical Trial

Oestrogen versus androgen in hormone-replacement therapy for complete androgen insensitivity syndrome: a multicentre, randomised, double-dummy, double-blind crossover trial

Wiebke Birnbaum, Louise Marshall, Ralf Werner, Alexandra Kulle, Paul-Martin Holterhus, Katharina Rall, Birgit Köhler, Annette Richter-Unruh, Michaela F Hartmann, Stefan A Wudy, Matthias K Auer, Anke Lux, Siegfried Kropf, Olaf Hiort

Birnbaum W, et al. Lancet Diabetes Endocrinol. 2018 Oct;6(10):771-780.

Study design

- Eligible participants (age 18–54 years) with CAIS gave written informed consent
- Gonadectomy had to date back more than 1 year.

12 participants

Testosterone for 6 months
(and oestrogen dummy)

→

Oestrogen for 6 months
(and testosterone dummy)

5 participants

Oestrogen for 6 months
(and testosterone dummy)

→

Testosterone for 6 months
(and oestrogen dummy)

Double blind

Birnbaum W, et al. Oestrogen versus androgen in hormone-replacement therapy for complete androgen insensitivity syndrome: a multicentre, randomised, double-dummy, double-blind crossover trial. Lancet Diabetes Endocrinol. 2018 Oct;6(10):771-780.

Study design

- **Mental health-related quality of life** (MHRQoL) and **physical Health-related quality of life** (HRQoL) were measured with the standardised German version of the SF-36.15

- **Psychological wellbeing** was measured with the German version of the Brief Symptom Inventory (BSI)

- **Sexual functioning**, including six domains of desire, arousal, lubrication, orgasm, satisfaction, and pain, we used the German version of the Female Sexual Function Index (FSFI)

- **Laboratory investigations**

Birnbaum W, et al. Oestrogen versus androgen in hormone-replacement therapy for complete androgen insensitivity syndrome: a multicentre, randomised, double-dummy, double-blind crossover trial. Lancet Diabetes Endocrinol. 2018 Oct;6(10):771-780.

Results

	At Baseline
Mental Health	Lower
Physical Health	Higher
Psychological wellbeing	Lower
Sexual functioning	Lower

Testosterone

1. **is non-inferior to oestradiol in terms of quality of life and**
2. **may have beneficial effects on sexual functioning**

Birnbaum W, et al. Oestrogen versus androgen in hormone-replacement therapy for complete androgen insensitivity syndrome: a multicentre, randomised, double-dummy, double-blind crossover trial. Lancet Diabetes Endocrinol. 2018 Oct;6(10):771-780.

Clinical Trial

Endocrine (2022) 76:722–732
https://doi.org/10.1007/s12020-022-03017-8

ORIGINAL ARTICLE

Metabolic effects of estradiol versus testosterone in complete androgen insensitivity syndrome

Matthias K. Auer[1] · Wiebke Birnbaum[2] · Michaela F. Hartmann[3] · Paul-Martin Holterhus[4] · Alexandra Kulle[4] · Anke Lux[5] · Luise Marshall[2] · Katarina Rall[6] · Annette Richter-Unruh[7] · Ralf Werner[2,8] · Stefan A. Wudy[3] ·

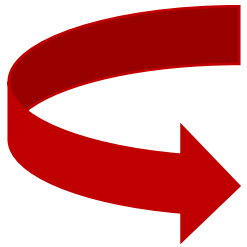
Both treatments resulted in a less favourable lipid profile, as there was a significant increase in total and LDL-cholesterol and a significant decrease in HDL-cholesterol. In addition, there was a significant increase in BMI in both groups.

There were no significant differences between both treatments in terms of metabolic and safety parameters

1. Testosterone treatment may have beneficial effects on sexual functioning and seems to be non-inferior to oestradiol in terms of quality of life

2. Both treatments resulted in a less favourable lipid profile and an increase in BMI

3. There were no differences between both treatments in terms of metabolic and safety parameters



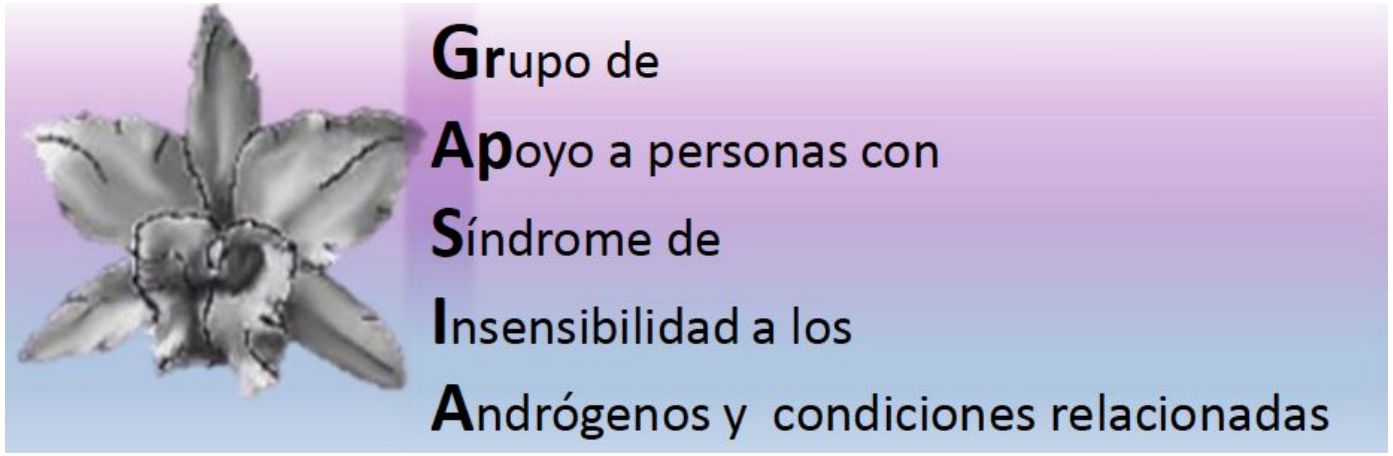
- **Testosterone was well tolerated and just as safe as oestrogen treatment**
- **It can be an alternative hormone substitution for women with CAIS, especially when sexual satisfaction is reduced**
- **Complementary treatment with oestrogens might be necessary for potential beneficial effects on bone metabolism**

Conclusion

Controversies regarding Gonadectomy and Hormone Replacement Therapy

- Ensure safety
- Improve ability to monitor
- Gather evidence

A personalised approach to care



Thank you

Carla Diaz Juhl

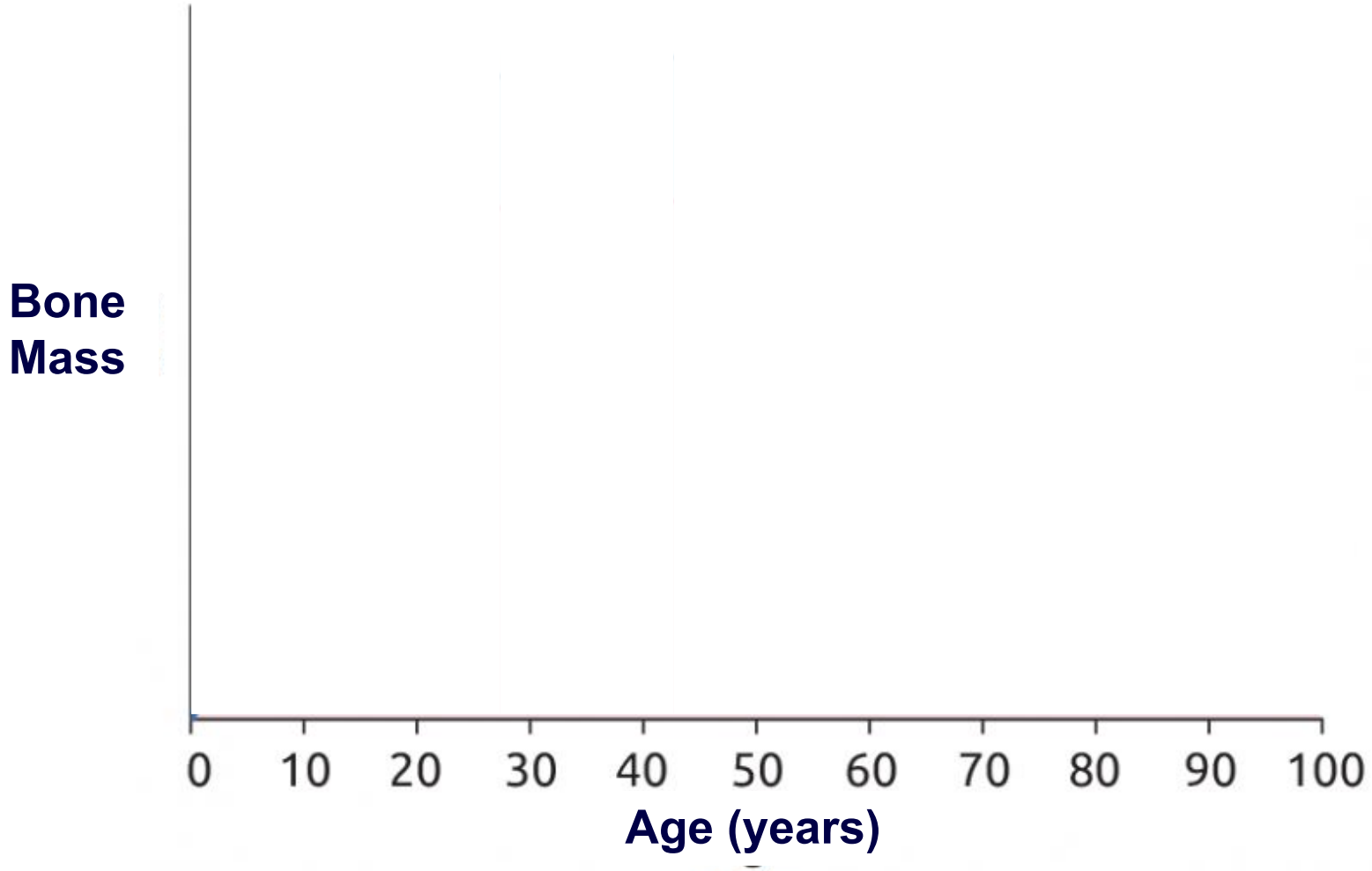
Yolanda

Marta

Hormone Replacement Therapy and Bone Health in AIS

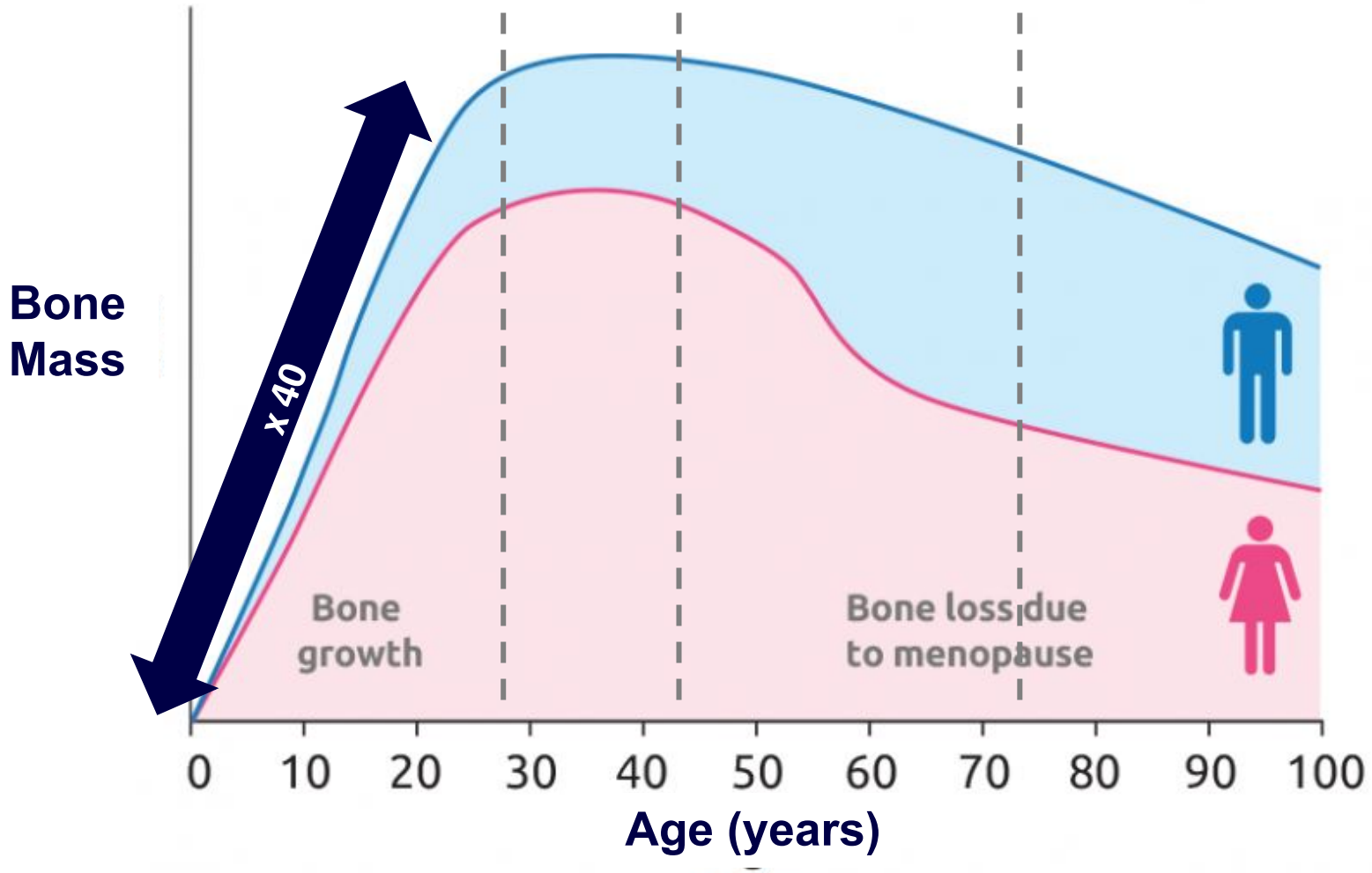
Bone Mineral Density

Distinct phases during life



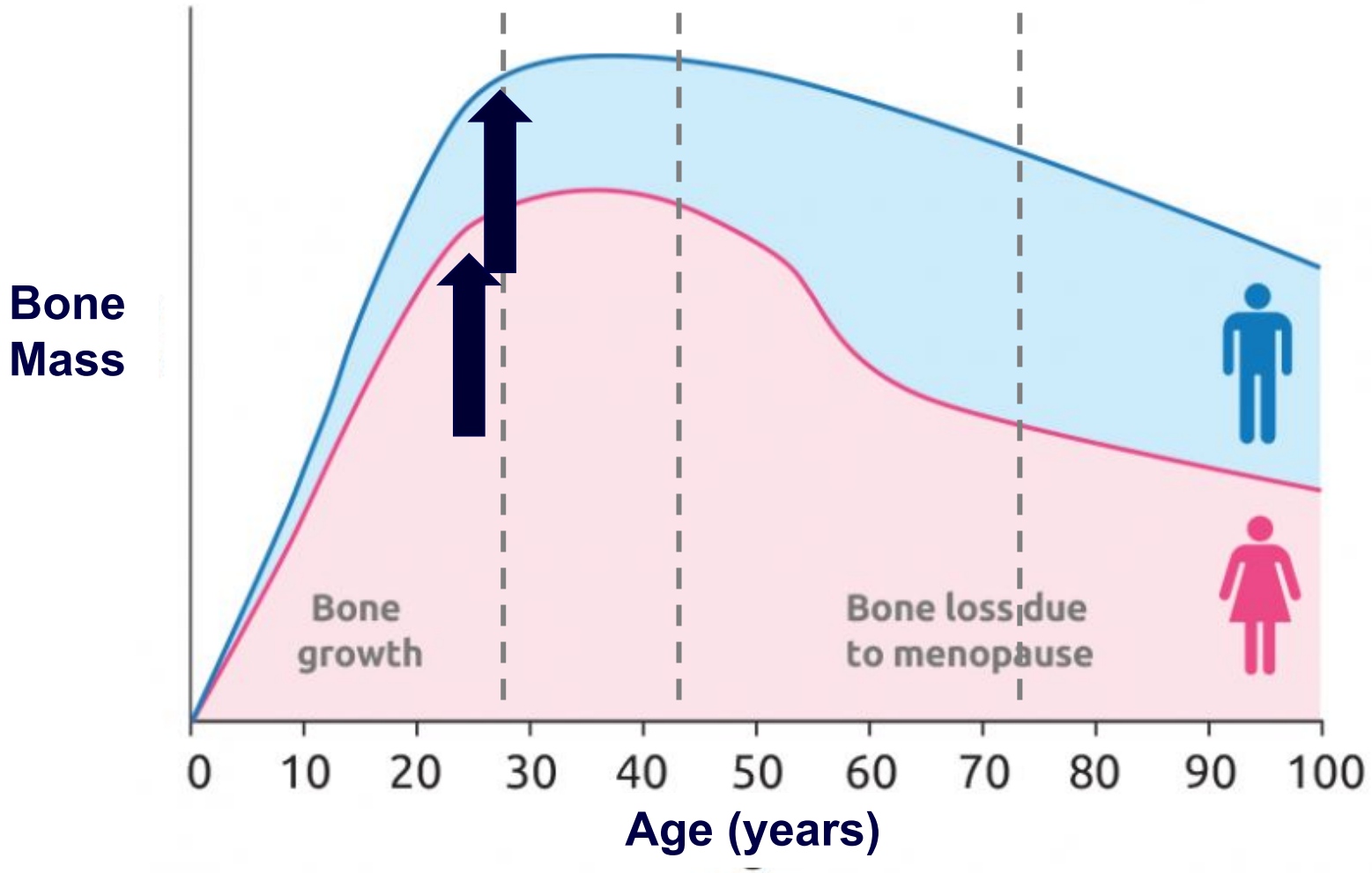
Bone Mineral Density

Bone mass increases by 40 times from birth to adulthood



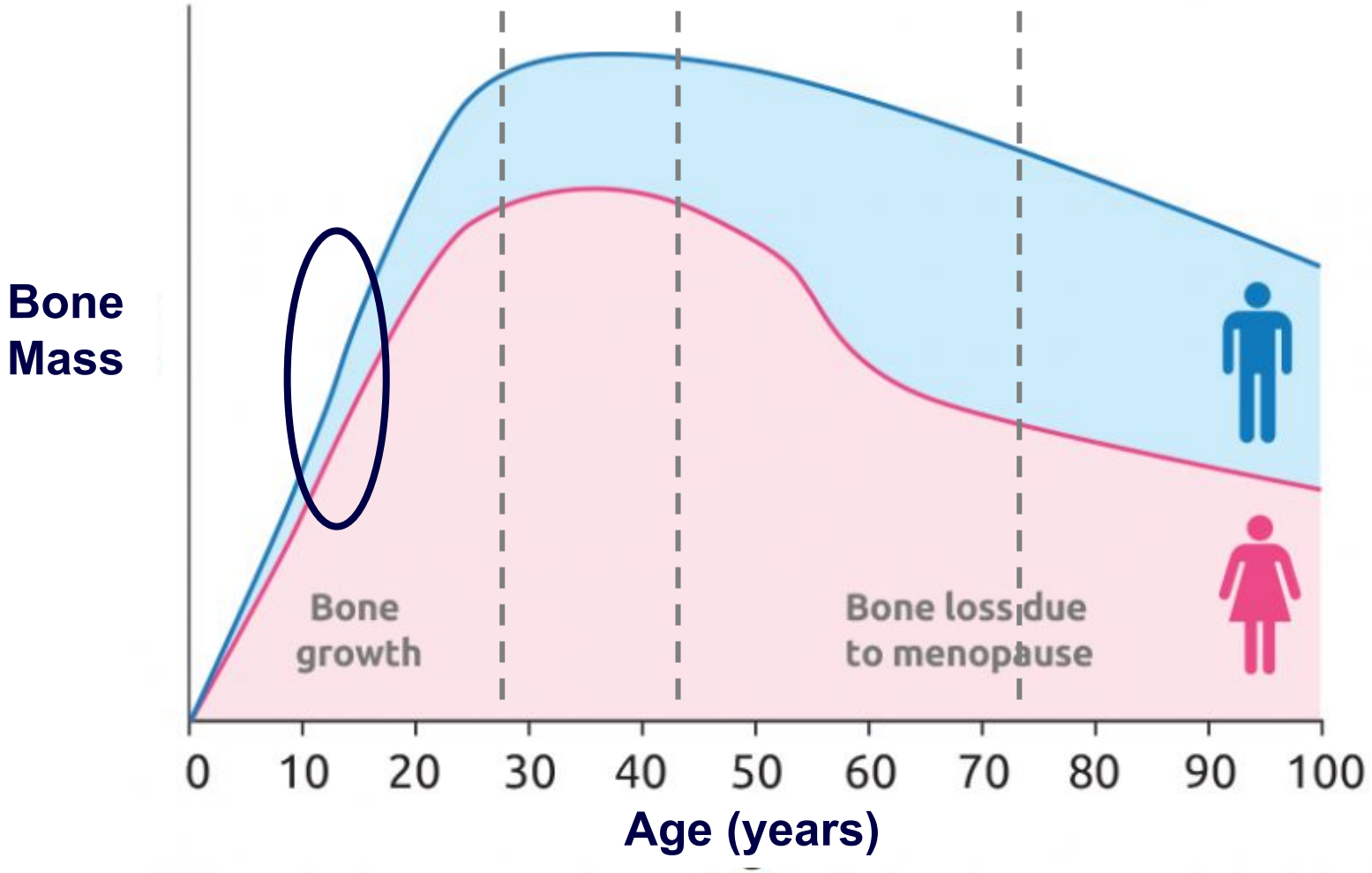
Bone Mineral Density

Peak bone mass is achieved at 3rd decade of life



Bone Mineral Density

40-60% of peak bone mass is gained during adolescent years, mainly during pubertal growth spurt



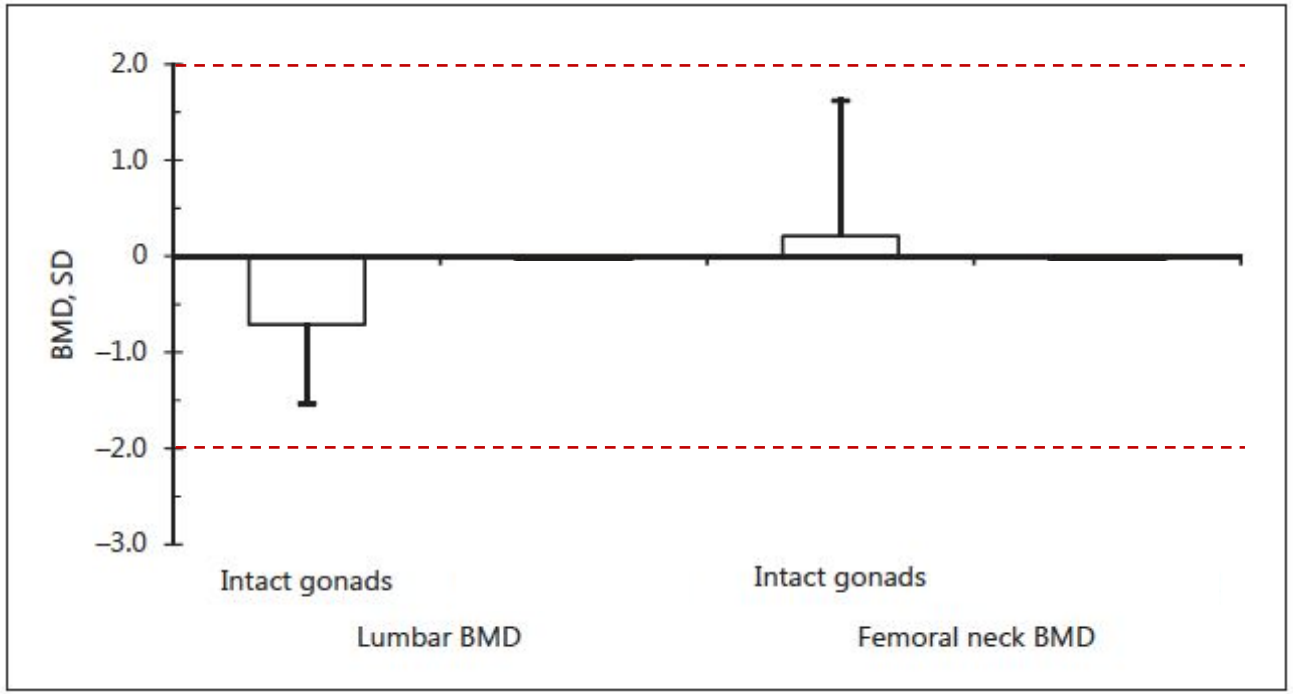
Sex steroids (testosterone, oestradiol) are essential for bone health

- Testosterone is the main androgen hormone secreted by the gonads in CAIS
- It is also considered as a pro-hormone, as it is metabolised to oestradiol.

- Reduced bone mineral density (BMD) has been reported in adult women with CAIS
- The low BMD may be due to the impaired androgen action, but removing gonads contributes to this finding
- Osteoporosis risk is a concern for women living with CAIS

Bone Health in women living with CAIS and Intact Gonads

Bone Mineral Density (BMD) in 10 adult women with CAIS and intact gonads

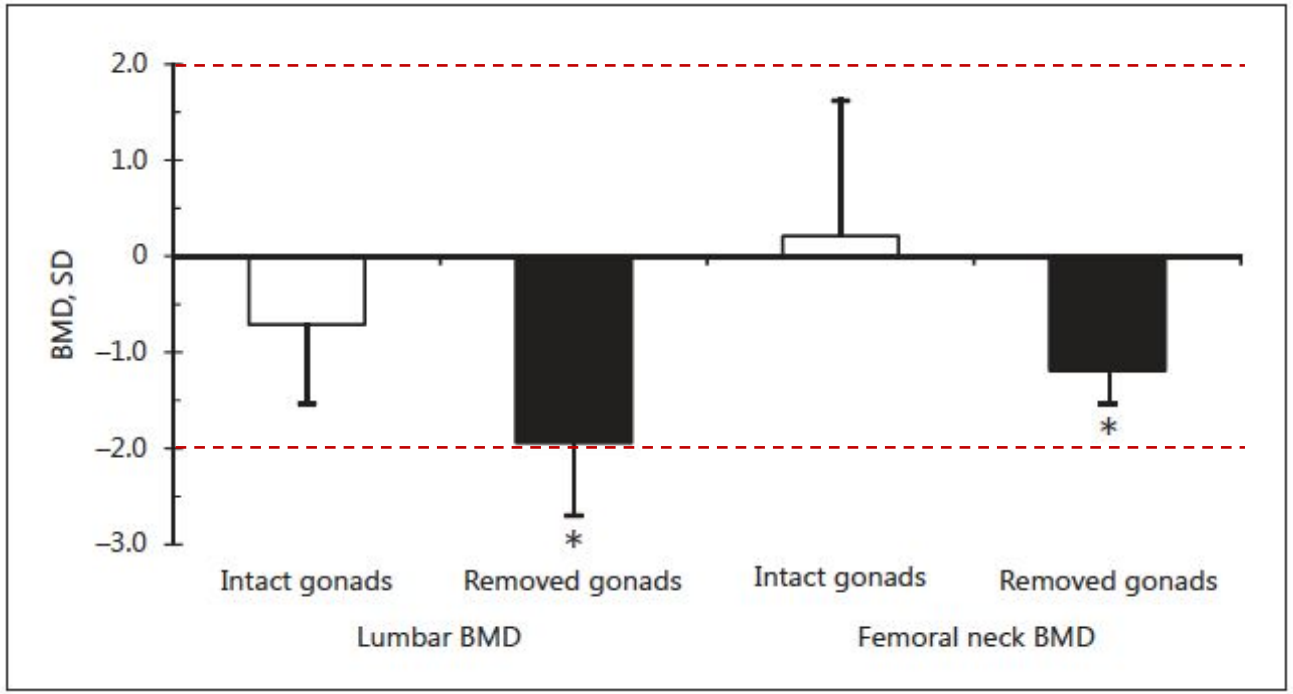


1. Lumbar BMD values were below the mean while femoral BMD was slightly above the mean.
2. **No woman showed Osteoporosis**

Bertelloni S, et. Bone Mineral Density in Women Living with Complete Androgen Insensitivity Syndrome and Intact Testes or Removed Gonads. Sex Dev. 2017;11(4):182-189.

Bone Health in women living with CAIS and Removed Gonads

Bone Mineral Density (BMD) in 43 adult women with CAIS and removed gonads



1. Significantly reduced lumbar and femoral neck BMD
2. **BMD was significantly lower in comparison with BMD of women with intact gonads**

Bertelloni S, et. Bone Mineral Density in Women Living with Complete Androgen Insensitivity Syndrome and Intact Testes or Removed Gonads. Sex Dev. 2017;11(4):182-189.

Causes of impaired Bone Health

Usual HRT schemes may be not optimal for bone health

- Young women with CAIS may require higher doses of substitutive therapy than the recommended premenopausal adult daily dose
- The route of administration may also affect the BMD status
- Poor compliance with HRT

Current Evidence

Clinical Study | G Gava and others | Bone and metabolism in adult CAIS | 181:6 | 711–718

Bone mineral density, body composition and metabolic profiles in adult women with complete androgen insensitivity syndrome and removed gonads using oral or transdermal estrogens

Gava G, et al. Eur J Endocrinol. 2019 Dec;181(6):711-718

Aims of the study:

1. to assess bone health in 32 adult women with CAIS and removed gonads compared with healthy controls
2. to evaluate the effects of two types of oestrogen therapy (transdermal estradiol gel 2mg or oral estradiol valerate 2mg) on bone health

Results

1. Bone health in adult women with CAIS and removed gonads compared with controls

- BMD was significantly lower in all sites in the CAIS group when compared with the controls
- CAIS group: 56% had lumbar osteopenia and 25% had lumbar osteoporosis
- CAIS group: 53% had femoral osteopenia and 9% had femoral osteoporosis

Gava G, et al. Bone mineral density, body composition and metabolic profiles in adult women with complete androgen insensitivity syndrome and removed gonads using oral or transdermal estrogens. Eur J Endocrinol. 2019 Dec;181(6):711-718

Results

2. Effects of transdermal estradiol gel 2mg ***VS*** oral estradiol valerate 2mg on bone health

- Transdermal administration of estrogens was associated with better total body BMD in comparison to oral administration.
- BMD values were positively associated to the duration and the route of oestrogen administration and to serum oestradiol levels.

Gava G, et al. Bone mineral density, body composition and metabolic profiles in adult women with complete androgen insensitivity syndrome and removed gonads using oral or transdermal estrogens. Eur J Endocrinol. 2019 Dec;181(6):711-718

How to optimise Bone Health in CAIS

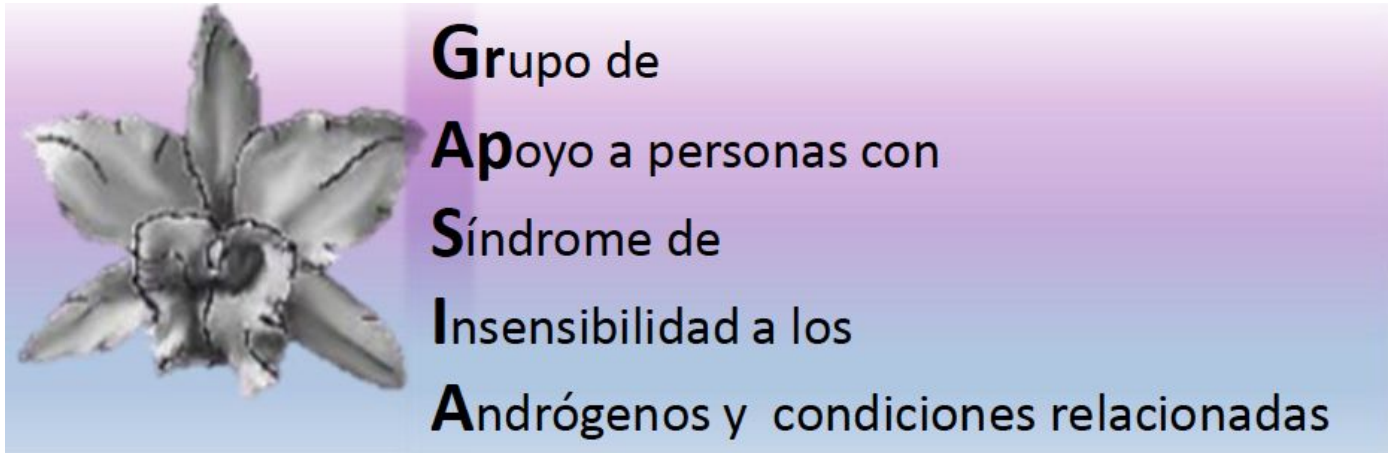
A. The maintenance of gonads may represent a strategy – additional oestrogens (?)

B. When gonads have been removed, hormone replacement therapy must be optimised

- Compliance
- Doses of oestrogens should be guided by BMD
- Use of transdermal oestrogen deliveries
- Testosterone (?)
- HRT should be administered until the age of menopause, although extended therapy can be considered in women with low BMD

C. Optimise general factors (physical activity, vitamin D status, calcium, body weight, smoking, drinking)

Women with CAIS may have a specific bone phenotype: female or male reference values could be inadequate, and only the assessment of the fracture rate in large samples will permit a true estimation of bone risk.



Thank you

Carla Diaz Juhl

Yolanda

Marta

Management of gonads in PAIS

- In girls with PAIS, concerns about both the possibility of virilisation during puberty and potential risk of gonadal neoplasia have contributed to the longstanding practice of early gonadectomy
- There is insufficient data to inform clinical judgement regarding long-term risks from retention vs. removal of gonads. Therefore, prophylactic gonadectomy should not be a foregone conclusion.
- Consideration should be given to retaining the gonads on an individual basis, with fully informed consent regarding the known and unknown risks of retention vs. removal.
- Regular surveillance should be provided by the most sensitive means available
- Surgical relocation of gonads to a position to facilitate monitoring and biopsy with detailed histological analysis to assess the presence of neoplasia

The basic ethical principle of keeping options open for the future should be considered when faced with life altering decisions regarding irreversible gonadal interventions in PAIS