

## ARTICLE

FUNCTIONAL STATE OF ADRENAL GLANDS IN BOYS AND GIRLS  
AT PUBERTARY AGE

Maria V. Shaykhelislamova, Natalia B. Dikopolskaya, Gulfia A. Bilalova\*, Maria Yu Fomina,  
Timur L. Zefirov

Institute of Fundamental Medicine and Biology, Kazan Federal University, 18, Kremlyovskaya Street, Kazan,  
420008, RUSSIA



## ABSTRACT

Considering the sexual characteristics of the morphological and functional state of the child's body during normalization of physical and mental stress should be fundamental in critical periods of development, one of which is puberty. The physiological hyper function of the pituitary-adrenal system, which occurs already at the beginning of puberty, is characterized by an increase in the secretion of cortisol and testosterone - markers of activation of the sexual development of children. However, excessive, inadequate age and sexual characteristics of the body load against the background of functional instability of the endocrine system can lead to metabolic disorders and growth retardation. The study of the functional state of the adrenal glands in children aged 11-15 years showed that the level of excretion of hormones of the adrenal cortex (AC) and their metabolites depends on the age and stage of puberty (SoP) of adolescents. It was established that the content of 17-ketosteroids (17-KS) and 17-oxysteroids (17-OCS) at the beginning of the puberty period changes insignificantly, more significant shifts of these parameters and pronounced sex differences are recorded on SoP III and V. Androgens of the adrenal cortex spasmodically increase at the last SoP. However, puberty in girls occurs earlier than in boys. The functional activity of the adrenal glands depends on the level of puberty of adolescents, while in the group of boys and girls at different SoP, it has its own characteristics and is manifested by different ratios of glucocorticoid and androgenic function of AC.

## INTRODUCTION

**KEY WORDS**  
adrenal cortex, androgens,  
glucocorticoids, puberty,  
boys, girls.

The hormonal regulation of its adaptive activity plays a fundamental role in the development of the organism. The puberty of a person is extended in time and occurs later than the formation of other functional systems [1]. It is the basis for the principle of systemic genesis, according to which, during the individual development of the organism, the selective maturation of functional systems occurs, with the leading adaptive result being a useful one [2].

Considering the sexual characteristics of the morphological and functional state of the child's body during normalization of physical and mental stress should be fundamental in critical periods of development, one of which is puberty. The physiological hyper function of the pituitary-adrenal system, which occurs already at the beginning of puberty, is characterized by an increase in the secretion of cortisol and testosterone - markers of activation of the sexual development of children [3]. However, excessive, inadequate age and sexual characteristics of the body load against the background of functional instability of the endocrine system can lead to metabolic disorders and growth retardation [4]. In biomedical studies, to assess the function of AC, one of the metabolites of corticosteroids, 17-CS in daily urine, is determined. In women - all 17-CS of adrenal origin, while in men 2/3 of the total amount are metabolic products of corticosteroids, and 1/3 are hormones of the gonads [1]. It is known that analogues of sex hormones, both male and female, are produced in the reticular area of the AC, since AC and the sex glands develop from a common embryonic germ. The AC androgens include androstenedione, 11-hydroxyandrostenedione and dehydroepiandrosterone. Their biological activity is low; however, they can turn into active forms of hormones and participate in the formation of secondary sexual characteristics in men. The AC androgens are produced in persons of both sexes but in small quantities [7]. Determination of glucocorticoid function is carried out by studying the content of 17-OCS in biological fluids [2].

It has been established that before puberty, a gradual increase in 17-CS excretion is observed without significant sex differences [5]. During prepubertal period, the release of sex hormone metabolites increases spasmodically in both sex groups, however, it is significantly higher in girls than in boys. A more significant increase in androgens is observed in girls at the beginning of puberty, which is probably due to the property of androgens to enhance the cytotropic effect of estrogens [6]. With the progression of puberty transformations, with an increase in the secretion of the gonadal precursors of 17-CS in boys, a sharp increase is observed [7]. Literature data on the age-related dynamics of the excretion of cortisol and its metabolites in children, as a rule, do not reflect the influence of puberty on the formation of glucocorticoid function of the adrenal glands [8]. The available data are contradictory in nature, the state of the adrenal glands in the vast majority of works is evaluated without taking into account the reserve capabilities of the body of boys and girls, which makes it difficult to differentiate between normalizing physical and mental stress of adolescents.

\*Corresponding Author  
Email:  
g.bilalova@mail.ru

Based on the foregoing, the objective of the work was formulated - the study of age-gender characteristics of glucocorticoid and androgenic function of AC in children during puberty.

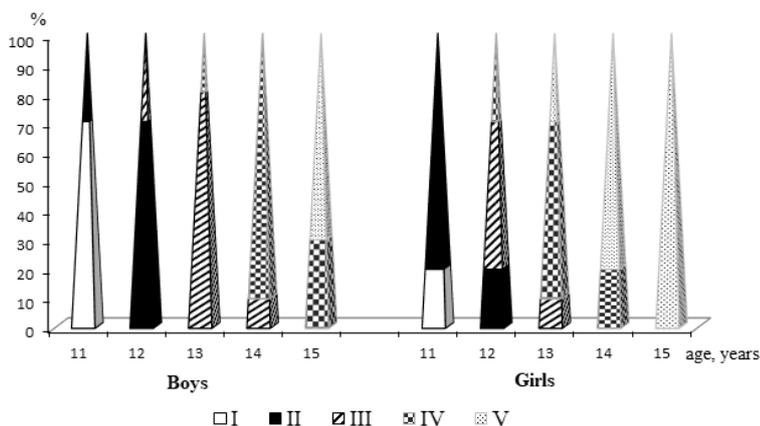
## MATERIALS AND METHODS

The study involved 80 children of 11-15 years old of both sexes without chronic diseases, at different stages of puberty. The method of sampling and analyzing daily urine was used. Written consent from the subjects was taken and the study was approved by the Kazan University ethical committee

Children were divided according to SoP using the method of J. Tanner [9]. The functional state of the adrenal cortex was evaluated by the level of excretion of 17-KS and 17-OCS with urine. Quantitative determination of 17-KS was carried out by the colorimetric method based on W. Zimmerman reaction modified by M.A. Krekhova [10]. Urine was collected without a preservative and stored in a cold place at t 0-12°C. The optical density was measured on a FEK - 56PM photo electro calorimeter at a wavelength of 500 nm. The determination of 17-OCS was carried out according to the method of R.N. Silber, C.C. Porter modified by N.A. Yudaev and M.A. Krekhova (1960), based on the reaction with phenyl hydrazine after enzymatic hydrolysis [10]. The optical density of the solution was measured on an SF-16 spectrophotometer at a wavelength of 410 nm in 10 mm thick cuvettes.

## RESULTS

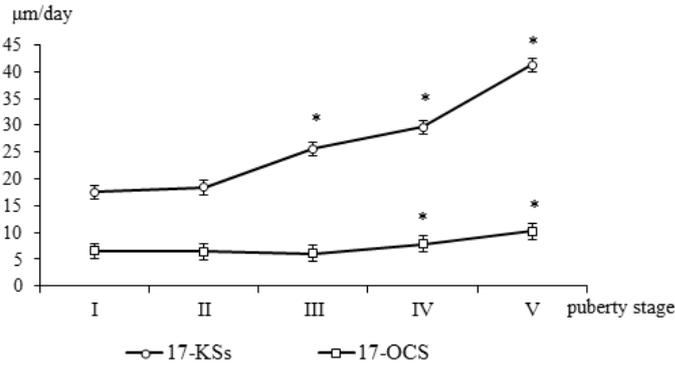
At the initial stage of the study, it was found that the stages of puberty in children have features [Fig. 1]. 70% of 11-year-old boys are at the SoP I, while the same stage group of girls' accounts for 20%, and 80% of girls corresponds to SoP II. The most striking gender differences were found at 13 years old, when the majority of the girls examined (60%) were already at SoP IV and moreover 30% of them proceed to SoP V. 80% of boys aged 13 years are only at the SoP III. 80% of adolescent girls reach the SoP V at the age of 14 and finally at the age of 15 (100%), while 30% of 15-year-old boys are still at the SoP IV. That is, puberty of girls is observed in an earlier age period and ends at 13-14 years, while 30% of 15-year-old boys are at the SoP IV. Features of the sexual development of girls can be associated with features of regulation of the female genital glands [2]. The fundamental difference between the reproductive system of women and that of the male body is its rhythm. The function of the female reproductive system is a clear biological rhythm. This is what determines its reliability and ensures the continuation of the species.



**Fig. 1:** Distribution of boys and girls of 11-15 years old by stages of puberty (%).

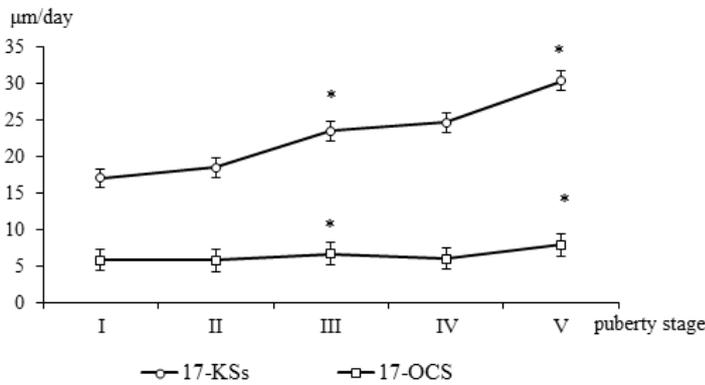
According to our data, the content of 17-KS in the daily urine in boys of the SoP I is  $17.54 \pm 1.43 \mu\text{m/day}$  [Fig. 2]. The level of 17-KS in boys of the SoP V is steadily increasing. The total increase in excretion of 17-KS reaches 135.11%. During the transition to SoP II in boys, the excretion level of 17-KS with daily urine changes insignificantly by 4.84%. SoP III is the period of gonad activation [11,12]. Androgen metabolites increase by 40.50%, and in 13-year-olds - by 21.00%. Considering the indicators of androgen excretion in boys of the SoP IV, we also revealed their significant increase compared to stage III in boys, which is 15.72% ( $p < 0.05$ ). SoP V as a stage of the final formation of reproductive function is characterized by the greatest hormonal changes. In adolescents at the final stage, the release of 17-KS increases by 40.65% ( $p < 0.05$ ). It is known that testosterone accounts for 90% of all androgens formed, during metabolism 17-KS are formed, which are excreted in the urine in the form of compounds [2,7]. Half of all 17-KS are decay products of AC, not of sex hormones. The AC androgens stimulate the appearance of secondary sexual characteristics, the development of bone and muscle tissue [5], anabolic effects on protein metabolism, increase muscle strength in adolescents.

Studying the dynamics of 17-KS excretion in girls [Fig. 3], we found that their level changes similarly to boys. In girls of the SoP I, the level of 17-KS is  $17.02 \pm 0.55 \mu\text{m/day}$ , and the content of 17-KS at the SoP II significantly increases by 8.63%. At SoP III, this indicator increases by 30.65%, compared with girls of the SoP II, and reaches reliable values ( $p < 0.05$ ). Girls at the SoP IV show a slight increase in the number of 17-KS in daily urine - by  $1.13 \mu\text{m/day}$ . Girls at the SoP V have the hormone level by 23.41% higher than the level at the SoP IV ( $p < 0.05$ ). However, this increase is not as significant as in boys.



**Fig. 2:** Change in the excretion of 17-ketosteroids and 17-oxycorticosteroids in boys at SoP I-V.

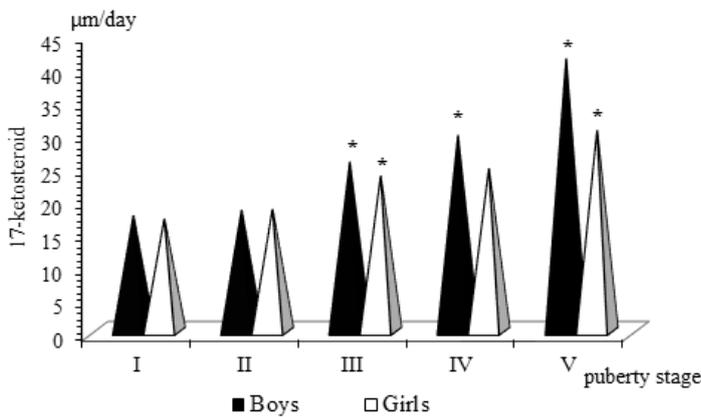
Note: a significant difference between the stages of puberty is "\*" p <0.05



**Fig. 3:** Change in the excretion of 17-ketosteroids and 17-oxycorticosteroids in girls at SoP I-V.

Note: a significant difference between the stages of puberty (p <0.05)

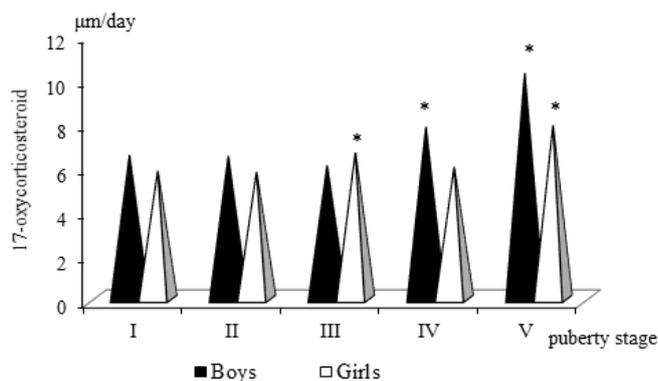
The analysis of the sexual characteristics of the androgenic function of the adrenal cortex indicates that up to the SoP V, no significant gender differences in the excretion of 17-KS between boys and girls were found. Whereas boys of SoP V had their level by 35.61% higher than girls in this period (p <0.05).



**Fig. 4:** Comparative data on the dynamics of excretion of 17-ketosteroids in boys and girls at different stages of puberty.

Note: a significant difference between the stages of puberty is "\*" p <0.05

The level of 17-OCS has features [Fig. 4]. In boys of SoP I, the initial level of 17-OCS is  $6.52 \pm 0.23 \mu\text{m/day}$ . From SoP I to V, the excretion level of 17-OCS with daily urine increases by  $3.71 \mu\text{m/day}$  or 56.90%. By SoP III, there was no significant change in this metabolite. At the final SoP, 17-OCS continues to increase by 30.97%. This jump indicates a change in the adaptive capacity of adolescents.



**Fig. 5:** Comparative data on the dynamics of excretion of 17-oxy corticosteroids in boys and girls at SoP I-V.

Note: a significant difference between the stages of puberty is "\*"  $p < 0.05$

During girls' sexual development, the release of cortisol changes in a wave-like fashion - it decreases at the SoP II, and at the SoP III it increases by 14.97% ( $p < 0.05$ ). However, a jump in the excretion of 17-OCS is noted only at the SoP V, which is also characteristic of boys.

Thus, gender differences in the dynamics of excretion of 17-OCS begin to appear at the SoP IV, when the boys show the first significant increase in their content. The difference is 30.26% ( $p < 0.05$ ). At stage V, gender differences persist, and the level of 17-OCS in boys is 5% higher than in girls ( $p < 0.05$ ). A comparison of the level of excretion of androgens and glucocorticoids with the level of somatic development of children at different SoP complements the neuroendocrine characterization of the stages of puberty in boys and girls [2,5,9]. According to our data, the SoP I is characterized by the absence of signs of an increase in the functional activity of glucocorticoid and androgenic functions of AC in both sex groups; SoP II - the appearance of minor changes in the excretion level of 17-KS and 17-OCS in both boys and girls, within 10-15% with respect to SoP I; SoP III - a significant increase in the number of androgen metabolites compared to SoP II: in boys - by 40%, and in girls - by 30%; SoP IV - a progressive increase in the number of 17-KS, most pronounced in boys; SoP V - a jump in the excretion of 17-KS and 17-OCS in both sex groups. The augmented classification of SoP taking into account the AC activity allows us to judge not only about the features of hormonal regulation of puberty but also the formation of the neuroendocrine mechanism of adaptation reactions of adolescents during puberty.

## SUMMARY

- The analysis of the sexual characteristics of the androgenic function of AC showed that before the SoP III there were no significant differences between boys and girls. At SoP IV, excretion of 17-KS in girls is 35.6% higher ( $p < 0.05$ ), and at SoP V the release of androgen metabolites predominates in boys.
- Sexual differences in the excretion of glucocorticoid metabolites are clear at the SoP IV, when the boys show the first significant increase in 17-OCS by 30.24%, superior to girls ( $p < 0.05$ ). At the SoP V, sexual characteristics are preserved and the level of 17-OCS in boys is 30.15% higher than in the group of girls.

## CONCLUSION

Analyzing the data obtained, we conclude that the excretion of androgen and glucocorticoid metabolites in boys and girls of SoP I-V is unidirectional, characterized by a maximum increase at the SoP I and V.

### CONFLICT OF INTEREST

There is no conflict of interest.

### ACKNOWLEDGEMENTS

The work is performed according to the Russian Government Program of Competitive Growth of Kazan Federal University.

### FINANCIAL DISCLOSURE

None.

## REFERENCES

- [1] Sudakov KV. [2000] Physiological basis and functional systems. The course of lectures, Sudakov KV, M.: Medicine, 120.
- [2] Drzhevetskaia IA. [1987] Endocrine system of a growing organism. Drzhevetskaia IA, M.: Vysshaya Shkola, 177.
- [3] Kuznetsova EA, Adamchik AS, Goncharov NP, Katsia GV. [2016] Diagnostic value of diurnal fluctuations of free forms

- of testosterone and cortisol in obesity and metabolic syndrome in men under 50, *Andrology and genital surgery*, DOI: 10.17650/2070-9781-2016-17-1-28-33
- [4] Lebenthal Y, Gat-Yablonski G, Shtai B. [2006] Effect of sex hormone administration on circulating ghrelin levels in peripubertal children *J Clinic. Endocrinol. Metabolism*, 91(1):328-331.
- [5] Selverova NB. [2009] The binary nature of hormonal influences in ensuring physical and mental development, *Materials of the scientific conference, Physiology of Human Development*, 165-166.
- [6] Ostrander MM, Ulrich-Lai YM., Choi DC. [2006] Hypo activity of the hypo thalamo pituitary adrenocortical axis during recovery from chronic variable stress *Ibid.* DOI: 10.1210/en.2005-1041
- [7] Sapronov NS, Bairamov AA. [2013] Cholinergic mechanisms of regulation of male sexual function. *St Petersburg: Art Express*, 272.
- [8] Erik M, Omer M, Anthony C, et al. [2016] Stress reactivity and personality in extreme sport athletes: Thepsychobiology of BASE jumpers, *Physiology & Behavior*, 167:289-297. DOI: 10.1016/j.physbeh.2016.09.025.
- [9] Tanner J, *Human Biology M.* [1968]
- [10] Kolb VG, Kamyshnikov VS. [1976] *Clinical biochemistry*, Minsk.
- [11] Lozano-Berges G, Matute-Llorente Á, González-Agüero A, Vicente-Rodríguez G, Casajús JA. [2018] Soccer helps build strong bones during growth: a systematic review and meta-analysis, *European Journal of Pediatrics*, 177(3):295-310. DOI: 10.1007/s00431-017-3060-3.
- [12] Drain JR, Groeller H, Burley SD, Nindl BC. [2017] Hormonal response patterns are differentially influenced by physical conditioning programs during basic military training, *Journal of Science and Medicine in Sport*. 98-103. -DOI: 10.1016/j.jsams.2017.08.020