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Citation	Campbell, Benjamin C., Peter B. Gray, Dan T. A. Eisenberg, Peter Ellison, and Michael D. Sorenson. Forthcoming. Androgen receptor CAG repeats and body composition among Ariaal men. <i>International Journal of Andrology</i> .
Published Version	doi:10.1111/j.1365-2605.2007.00825.x
Accessed	February 17, 2015 2:00:36 PM EST
Citable Link	http://nrs.harvard.edu/urn-3:HUL.InstRepos:2580545
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(Article begins on next page)

Androgen Receptor CAG Repeats and Body Composition among Ariaal Men

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Key words: testosterone, androgen receptor, population variation, Africa, pastoral nomads

Abstract

To determine population variation in the androgen receptor (AR) and its association with body composition in a subsistence population we sampled 87 settled and 65 nomadic males ages 20+ among the Ariaal of northern Kenya. Anthropometric measures included height, body mass index (BMI), fat free mass (FFM), upper arm muscle plus bone area (AMPBA), % body fat (%BF), suprailliac skinfold (SISF), and waist to hip ratio (WHR). Salivary testosterone (T) was determined from both morning (Am T) and afternoon (Pm T) samples. Hair roots were obtained for genotyping AR CAG repeat length. AR CAG repeat length did not vary between the two sub-groups (overall value = 22.6 ± 3.1). Multiple regression models, controlling for age and residence, indicate that Pm T was positively associated with all measures of body composition. AR CAG repeat length was a significant positive predictor of height, FFM % BF, SISF and waist circumference. There was a significant negative Pm T by AR CAG repeat length interaction in predicting all measures but AMPBA. These findings provide evidence for population variation in AR CAG repeat length and suggest that both T and androgen receptor CAG length play a role in body composition in this extremely lean population.

Introduction

Testosterone levels among men vary across populations, with subsistence populations showing lower levels relative to industrialized populations (Ellison et al. 2002). Lower testosterone levels among men in subsistence populations are thought to reflect energetic limitations (Panter-Brick and Ellison 1996, Campbell et al. 2005, Ellison et al. 2001). Bribiescas (2001, 2005, 2006) has suggested that lower testosterone levels under conditions of poor nutrition would allow the allocation of energy away from muscle toward other somatic functions, including the immune system (Muehlenbein and Bribiescas 2005).

Current findings support an impact of chronic undernutrition on testosterone levels among men in subsistence populations. Testosterone has been positively associated with markers of energetic status including weight, biceps skinfold and midarm circumference among the Tamang of Nepal (Panter-Brick and Ellison 1996), body fat among the Turkana and Ariaal of Kenya (Campbell et al 2003, 2006a, 2006b) and fat free mass among men in Harare, Zimbabwe (Lukas et al. 2005). Furthermore, Lukas et al. (2005) found a relationship between height and afternoon testosterone values in men under 60, which they interpret to indicate that the effects of testosterone may be primarily associated with the development of overall body size (and potential muscle mass) at puberty, rather than the maintenance of muscle during adulthood per se.

However, previous analyses have not taken into the account the potential effects of the androgen receptor (AR). Increasing number of CAG repeats in the AR reduces the efficiency with which the AR receptor transduces the cellular effects of testosterone (Berlin et al. 2000), modulating the effect of testosterone on androgenic tissue, including

spermatogenesis and bone mass (Zitzmann and Nieschlag 2003). The number of AR CAG repeats has been associated with age-related changes in testosterone (Krithivas et al. 1999, Walsh et al. 2005). In addition, the number of CAG repeats have been positively associated with BMI (Alevizaki et al. 2003), body fat, Zitzman et al. 2003) and fat free mass (Walsh et al. 2005), but not the effects of testosterone on muscle mass (Woodhouse et al. 2003).

Thus we chose to investigate the potential role of AR CAG repeat length on body composition among the Ariaal, pastoralists of northern Kenya. Studies demonstrating shorter CAG repeats among both Africans (Kittles et al. 2001, Esteben et al. 2006) and African-Americans (Kittles et al. 2001) suggest that the Ariaal may also exhibit shorter CAG repeats, increasing the impact of testosterone on body composition in this population. Previous research has demonstrated both chronic undernutrition and low testosterone levels among the Ariaal, along with a lack of age-related decline in testosterone (Campbell et al. 2003, 2006), accentuating the role of energetic limitation. In addition, the existence of settled and nomadic sub-populations that are culturally and genetically similar but vary in terms of ecology allow for the investigation of gene by environment interactions. Thus, the Ariaal are an apt population for investigating the role of the AR in modulating the effects of testosterone on body composition.

Based on earlier results, we expect to find shorter CAG repeats on average among the Ariaal compared to non-African populations. Furthermore, because the AR mediates the androgenic effects of testosterone on target tissues we predict that individuals with fewer AR CAG repeats will show a stronger effect of testosterone on body size and body composition.

Materials and Methods

Study Site The Ariaal are pastoral nomads inhabiting both upland and lowland regions around the Ndoto mountains in Marsabit District, Kenya. First appearing in oral history in the 1880s, they are derived from groups of poor Rendille and Samburu who banded together to build up their herds in the mountains. Culturally, they still exhibit features of both Rendille and Samburu, including Samburu age-set rituals and Rendille annual camel blessings (Fratkin 1998).

In terms of subsistence, the lowland Ariaal herd camels which tolerate the arid conditions well, but are bothered by ticks at higher elevations. The Ariaal depend on their animals for nutrition in the form of milk, blood and meat. Milk is the staple, providing as much as 75% of the calories and 90% of the protein intake during the wet season for the nomads (Fratkin 1998). Lowogosa, the nomadic encampment we sampled for this study is located approximately 45 minutes from the settlement of Korr and 3 hours from the town of Logologo, by vehicle. The nearest clinic is in Ngrunit about 40 minutes away. Children do not attend elementary school.

In contrast, upland Ariaal herd cattle, which need more water and are not bothered by ticks. In addition, the upland Ariaal also tend crops, primary maize. In Songa, the village we sampled, the existence of irrigation supports the production of crops including oranges that are sold in the nearby town of Marsabit, approximately 45 minutes away. Songa also includes an elementary school and a nurse's station.

All procedures were approved by the Institutional Review Boards at Boston University. The study was explained to all participants and consent obtained prior to data collection.

Sample

We sampled 102 settled men from Songa and 103 nomadic men from Lowogoso in August of 2005. The sample was stratified by 10 years age groups; 20-29, 30-39, 40-49, 50-59, 60+. We obtained hair samples from 156 of these men, including 87 settled men and 69 nomadic men. The other 50 men lacked sufficient hair to obtain a sample, either because of baldness or the fact that they had shaved their heads.

Measures

Anthropometrics Anthropometric measures included height, weight, arm, waist and hip circumference and 4 skinfolds; triceps, subscapular, midaxillary, and periumbilical. Derived measures include % body fat, calculated from skinfolds based on the D-W equations (Durnin & Womersley 1972). Because the D-W equations are based on a Caucasian sample, they may provide somewhat missing leading absolute values of % body fat for comparison with other populations. However, they should provide a relatively consistent measure of % body fat within the population. We also calculated arm muscle plus bone area (AMPBA), calculated as $[\text{MUAC} - (\pi \times \text{TCSF}/10)]^2/4$ where MUAC is mid upper arm circumference and TCSF is the triceps skinfold (Gurney and Jelliffe 1973). Fat free mass (FFM) was calculated as $\text{weight (kg)} * (100 - \% \text{body fat})$. Waist to hip ratio (WHR) was calculated as $\text{waist circumference} / \text{hip circumference}$. We chose to use waist circumference rather than waist to hip ratio (WHR) in our regression analyses because several studies have concluded it is a better measure of abdominal obesity (Clasey et al. 1999, Ponliot et al. 1994).

Age. During interviews, ages were estimated with reference to an event calendar and age set membership, and further ambiguities checked with local assistants (see Gray and Campbell 2005 for further details).

Salivary Testosterone Saliva samples were collected using standard methods (Ellison 1988) including stimulation of saliva with Original flavored Carefree gum. Morning samples were collected within 15 minutes of 09:00 hours, while afternoon saliva samples were collected within 15 minutes of 16:00 hours. Sodium azide was added as a preservative. Samples were stored at ambient temperature for approximately one month, then frozen until assayed in the Reproductive Ecology Laboratory at Harvard University. Assay procedures relied on standard RIA techniques based on modifications of a commercially available kit obtained from Diagnostic Systems Laboratories (see methods in Campbell et al. 2003). The interassay coefficient of variation was 15%. The intraassay coefficient of variation was 7%. One hundred fifty-three am testosterone values were obtained for the individuals genotyped. Four of those values were 3 S.D.s from the mean and removed. One hundred fifty-two pm testosterone values were obtained. Two values differed more than three S.Ds and were removed. This left a sample size of 149 and 150 for subsequent analyses including hormonal values.

Androgen Receptor Genotyping Hair samples with roots were obtained by plucking, and immediately placed in zip lock bags for transportation to Mike Sorenson's lab at Boston University. Samples were stored in their zip lock bags in a -20°C freezer until analysis. Bulbs were removed from hairs under a dissecting microscope, and DNA was extracted with DNeasy kits (Qiagen) with the addition of 30 µl of 100 mg/ml DTT (dithiothreitol) and finally eluted in 200 µl of water.

The Androgen receptor (AR) CAG tri-nucleotide repeat was typed with a PCR mix containing 1.25 μ M forward primer (TCCAGAATCTGTTCCAGAGCGTGC) and 1.25 μ M reverse primer (GCTGTGAAGGTTGCTGTTCCCTCAT), 2.5 mM dNTP, 2.5 mM MgCl₂, 0.625 units AmpliTaq Gold (ABI), 1X Buffer (ABI), 3 μ l DNA template in a total volume of 25 μ l. One of the primers for AR was fluorescently labeled. Cycle conditions were: 8 min denaturation at 95°C, 40 cycles of 30 s denaturation at 95°, 30 s annealing at 55°, 1 min extension at 72° and one final extension of 7 minutes at 72°. PCR products were analyzed on an ABI 3100 genetic analyzer using GeneMapper 3.7 (ABI). Four random samples were sequenced for length confirmation. The number of trinucleotide repeats was calculated by subtracting 214 bp from the product then dividing by three. The number of repeats ranged from 15-34.

Statistical Analysis

AR CAG repeat length showed no significant main effect on body composition or age as a continuous variable, so we split AR CAG repeat length into high and low groups. We first tried a median split (≤ 22 vs. > 22), as used previously (Walsh et al. 2005), but a split at 20 (≤ 20 vs. > 20) as used by Harkonen et al. (2003) produced stronger results so we chose to use it for the remaining analyses.

Next to determine if CAG repeat length had an impact on age related patterns of testosterone we ran separate linear regression models with Am and Pm salivary testosterone as the outcome variable and AR CAG repeat length as the predictor. Age and residence were included as controls. Given our cross-sectional data we expected the impact of AR CAG repeat length, if any, to show up as an interaction between CAG

repeat length and age. We modeled the interaction of CAG repeat length and testosterone as linear, as done previously (Krithivas et al. 1999).

Then to determine the relationship of AR CAG repeat length and testosterone on body composition, we ran separate regression analyses for height, BMI, FFM, AMPBA, %BF, and WHR. Age and residence were included as controls, and Pm T, AR CAG repeat length and their interaction were included as predictors. Again, the interaction of testosterone and AR CAG length was modeled as linear based on previous findings demonstrating a significant effect (Walsh et al. 2005). We checked for interactions between all of the predictive variables and where there was a significant interaction it was kept in the model when additional variables were added. Models using Am T yielded similar results, but were highly dependent on individuals with the 3 highest Am testosterone values and are not shown here.

Results

Table 1 shows measures of body composition for the entire sample as well as by residence. The overall average BMI of $17.8 \pm 1.9 \text{ kg/m}^2$ is less than the cut-off of 18.5 kg/m^2 indicative of chronic energy deficiency (Ferro-Luzzi et al. 1992); the overall average body fat of 9.9% characterizes a lean population. When comparing the two sub-populations, waist circumference as well as suprailliac and periumbilical skin folds are significantly greater among settled males suggesting greater abdominal fat reserves compared to the nomadic males despite the lack of difference in overall % body fat.

----- Table 1 about here -----

Figure 1 shows the frequencies of AR CAG repeats by residence. Overall, the number of CAG repeats ranges from 15 to 34, with a median of 22.5 and an overall average of 22.6 ± 3.1 . Settled and nomadic males show no difference in either the median (22.5 for both groups) or average length of CAG repeats (22.6 ± 2.9 vs. 22.7 ± 3.4 ; $p = 0.70$ by T test).

----- Figure 1 about here -----

Table 2 shows anthropometric values by AR CAG repeat length ≤ 20 and > 20 . Men with shorter AR CAG repeat length exhibit a significantly greater waist circumference and WHR ratio. None of the other anthropometric measures differ between the two groups.

----- Table 2 about here -----

Table 3 shows the result of analyses of the relationship of AR CAG repeat and age-related testosterone. Neither Am nor Pm testosterone shows a significant association with AR GAG length (split at CAG = 20), or a significant interaction between AR GAG length and age.

----- Table 3 about here -----

Table 4 shows the results of multivariate analyses of body composition testing for the predicted interaction between Pm testosterone and AR CAG repeat length. Pm testosterone is a significant positive predictor for all the variables but height and AMPBA for both of which it shows a trend. AR CAG repeat length is a significant positive predictor of height, FFM, % BF, waist circumference and SISK, and shows a trend for BMI. The interaction term Pm testosterone X AR CAG repeat length is a negative significant predictor for all of the variables tested, with the exception of AMPBA. The negative sign of the β -coefficient means that men with shorter CAG repeats show a stronger relationship between Pm testosterone and body composition.

----- Table 4 about here -----

Discussion

The results presented here are of interest in three ways. First, they indicate a greater number of AR CAG repeats among the Ariaal compared to those previously reported for other African populations (Kittles et al. 2001), suggesting greater variation in the length of CAG repeats marker among African populations than previously recognized. Second, they provide evidence that AR CAG repeat length modulates the impact of testosterone on overall body size and body composition, particularly adipose tissue. Third, they point to a close association between central adiposity and testosterone as previously reported in western populations (Svartberg et al. 2004). Together these

results suggest that the androgen receptor plays an important role in modulating energetic allocation among men under conditions of energetic limitation.

Frequency of CAG repeats

The range of CAG repeats of 14 to 34 reported here is within the normal range of 11-34 established in the U.S. population where CAG repeat number > 35 is associated with Kennedy's disease (LaSpada et al. 1991). The median of 22.5 is at the high end of the value of 19 to 22 from 13 populations genotyped by Esteben et al. (2006). The average CAG repeat number of 22.6 ± 3.1 is also at the high end of average values reported for those populations, which range from 19.1 ± 5.9 (Ivory Coast) to 22.6 ± 6.0 (Turkey). The higher average reflects the relatively greater range of the Ariaal values, which include 11 individuals with more than 26 repeats, the highest number reported for the populations studied by Esteben et al. (2006). Furthermore, in comparison with results on African-Americans (17.8 ± 10.97), Sierra Leoneans (17.3 ± 7.77), and Nigerians (16.7 ± 17.3) from Kittle et al. (2001) the Ariaal value of 22.6 ± 3.1 repeats reflect both a substantially higher average and lower variability.

The basis for the greater range of CAG repeat lengths among the Ariaal is not clear at this point. Given the extreme leanness of Ariaal men, it might reflect a shift in the relative costs and benefits of androgenicity associated with chronic undernutrition. While increased androgenicity may have generally beneficial effects, including increased libido, mood and erectile function (Zitsman et al. 2006) it may also entail greater energetic costs. Chronic undernutrition would increase the consequences of those energetic costs for survival, thus relaxing selection for shorter CAG repeat length and leading to a greater range of CAG repeat values as exhibited by the the Ariaal men

sampled here. However, it is important to note that the distribution of CAG repeat length reported here is potentially biased by the exclusion of bald men from the sample who are more likely to have short CAG repeat lengths (Ellis et al. 2001), making any such speculations tentative.

Turning to the Ariaal sub-population comparison, the lack of a significant difference in CAG length between nomadic and settled Ariaal males is not unexpected. The two groups separated sometime in the middle of the 20th century (Fratkin 1998) and still maintain close ties by marriage, leaving relatively little chance for genetic differentiation. Thus, differences in average AR CAG repeat length are unlikely to play a role in sub-groups differences in body composition, though the interaction of AR CAG repeat length environmental factors, such as caloric availability could play a role.

AR CAG length and Age-Related Testosterone

The lack of an association between AR CAG repeats and testosterone levels is consistent with several earlier reports (Krithivas et al. 1999, Harkonen et al. 2003, Canale et al. 2005). In contrast, the lack of an association between AR CAG repeats and age-related testosterone is contrary to findings that shorter CAG repeat length is associated with faster age-related decline of testosterone (Walsh et al. 2005, Krithivas et al. 1999). These earlier findings have been interpreted to suggest that men with shorter CAG repeats are more sensitive to the feedback effects of testosterone. Thus our results may simply reflect the relative lack of an age-related decline in testosterone among the Ariaal.

Association of T and AR CAG Repeats with Body Composition

Pm testosterone, AR CAG repeat length and their interaction all showed significant associations with body composition. AR CAG repeat length was significantly

and positively related to height, and FFM, consistent with the suggestion that testosterone is important in determining final body size (Lukas et al. 2005). Men with more AR CAG repeats are taller, but there is only a marginal effect of Pm T. This suggests that AR CAG repeat length may mediate the effects of testosterone on pubertal growth. Longer CAG repeats may result in less effective testosterone exposure of long bones thus allowing growth to continue and resulting in greater adult height (Zachmann et al. 1976).

Our finding that CAG repeat length is a significant positive predictor of FFM and % body fat is consistent with previous results (Walsh et al. 2005, Zitzmann et al. 2003) as is the significant interaction of CAG repeat length with Pm T in predicting % BF (Lapauw et al. 2007). In addition, the fact that Pm testosterone, but not AR CAG repeat length or their interaction showed an association with AMPBA is consistent with results showing that testosterone administration in young men increases muscle mass, with no interaction with CAG repeat length (Woodhouse et al. 2003).

On the other hand, the positive association of testosterone and overall (%BF) and central (waist circumference) adiposity is in opposition to results from western samples find a negative relationship between adiposity and testosterone (Allan et al. 2006, Vermeulen et al. 1999). Thus this finding requires further consideration.

Mechanisms Linking Testosterone and Adiposity

The positive relationship between adiposity and testosterone among Ariaal men is consistent with previous reports of a positive association between testosterone and body fat among Ariaal (Campbell et al. 2003) and Turkana (Campbell et al. 2006a) nomads. Both endurance runners and individuals on a low calorie/low protein diet show lower

adiposity, insulin and bioavailable testosterone compared to sedentary controls (Fontana et al. 2006).

Furthermore, elite runners show a positive association between abdominal fat and serum testosterone levels (Hetland et al. 1998), similar to the positive association of waist circumference and testosterone reported here and in previous studies (Campbell et al. 2003, Svartberg et al. 2004). Thus both low testosterone levels and their positive association with adiposity exhibited by Arrial men may be presumed to reflect their low caloric diet, and low adiposity, as well as highlighting the importance of abdominal adiposity.

Interestingly, Arrial men with shorter AR CAG repeats exhibit a stronger positive relationship between adipose tissue and current testosterone levels, contrary to expectations based on the lipolytic effects of circulating T (Herbst & Bhasin 2004). Instead the impact of AR CAG repeat length on the association of testosterone and adiposity may act through the effects of energetic status on T production, perhaps by altering the impact of testosterone feedback at the level of the hypothalamus (Crabbe et al. 2007). Alevizaki et al. (2003) report higher estrogen levels among men with more CAG repeats, suggesting that estrogen feedback might also be involved.

In terms of energy signals, acute hypoglycemia, has been related to reduced LH stimulation and testosterone production in human males (Oltmanns et al. 2001), while administration of leptin to acutely fasting men stops the decline in testosterone by maintaining LH stimulation (Chan et al. 2003). Thus to the extent that greater adiposity among Arrial men is reflected in higher blood glucose and leptin levels, it may also be related to higher testosterone levels. However, contrary to expectation, Bribiescas and

Hickey (2006) report an inverse relationship between fat and leptin among Ache males, confounding the expectation of leptin as a clear signal of energy stores among chronically undernourished men.

Population Comparison

The Ariaal men sampled here are quite lean with an average body fat of 10%. The extent to which our results linking testosterone, variation in the androgen receptor and adiposity can be generalized to other energy limited populations is unclear. Lukas et al. (2006) reported a positive association between salivary testosterone and FFM among 100 Zimbabwean men with an average of 15% body fat, while Bribiescas (2005) did not find a significant relationship between testosterone and either BMI or FFM among 17 Ache foragers of Paraguay with an average body fat of 18%. Whether variation in AR CAG repeat length plays a role in population variation in the relationship of testosterone to body composition is an obvious question for future investigation.

Summary

Among Ariaal males the frequency of AR CAG repeat lengths is substantially greater and the variance less than those reported for other African populations to date. Furthermore, variation in both testosterone and AR CAG repeat length play a role in body composition among Ariaal males, suggesting the possibility of selection against androgenicity in this population. Our analyses suggest that variation in AR CAG repeat length is more strongly related to adiposity, particularly abdominal adiposity, than to muscle, consistent with earlier findings from western samples. The positive relationship between testosterone and adiposity reported here is consistent with previous findings in nutritionally stressed groups and may reflect a close association between energetic status

and testosterone production among chronically undernourished populations. More work in energetically stressed populations is called for to help understand the mechanisms by which variation in the male reproductive axis is related to energetic status.

Acknowledgements

We thank Daniel Lemoille and Jason Radak for help with data collection, Matthew McIntyre and Lee Gettler for helpful comments on the manuscript, and Brad Stankiewicz for extracting DNA. This study was funded by the Wenner-Gren Foundation.

References

- Alevizaki, M., Cimponeriu, A.T., Garofallaki, M., Sarika, H.L., Alevizaki, C.C., Papamichael, C., Philippou, G., Anastasiou, E.A., Lekakis, J.P. & Mavrikakis, M. (2003) The androgen receptor gene CAG polymorphism is associated with the severity of coronary artery disease in men. *Clinical Endocrinology (Oxford)*, 59, 749-55.
- Allan, C.A., Strauss, B.J., Burger, H.G., Forbes, E.A., & McLachlan, R.I. (2006) The association between obesity and the diagnosis of androgen deficiency in symptomatic ageing men. *Medical Journal of Australia*, 185, 424-427.
- Beilin, J., Ball, E.M., Favaloro, J.M., & Zajac, J.D. (2000) Effect of the androgen receptor CAG repeat polymorphism on transcriptional activity: Specificity in prostate and non-prostate cell lines. *Journal of Molecular Endocrinology*, 25, 85-96.
- Bribiescas, R.G. (2001) Reproductive ecology and life history of the human male. *Yearbook of Physical Anthropology*, 44, 148-176.
- Bribiescas, R.G. (2005) Age-related differences in serum gonadotropin (FSH and LH) salivary testosterone and 17-beta estradiol levels among Ache Amerindian males of Paraguay. *American Journal of Human Biology*, 27, 114-21.
- Bribiescas, R.G. & Hickey, M.S. (2006) Population variation and differences in serum leptin independent of adiposity: a comparison of Ache Amerindian men of Paraguay and lean American male distance runners. *Nutrition and Metabolism (London)*, 30, 34
- Campbell, B.C., O'Rourke, M.T. & Lipson, S.F. (2003) Salivary testosterone and body composition among Ariaal males. *American Journal of Human Biology*, 15, 697-708.
- Campbell, B.C., Leslie, P.W. & Campbell K.L. (2006a) Age-related changes in testosterone and SHBG among Turkana Males. *American Journal of Human Biology*, 18, 71-82.
- Campbell, B.C., Gray, P.B. & Ellison, P.T. (2006b) Age-related changes in body composition and salivary testosterone among Ariaal Males. *Aging: Clinical and Experimental Research*, 18, 470-476.
- Canale, D., Caglieresi, C., Moschini, C., Liberati, C.D., Macchia, E., Pinchera, A. & Martino, E. (2005) Androgen receptor polymorphism (CAG repeats) and androgenicity. *Clinical Endocrinology (Oxford)* 63:356-61.
- Chan, J.L., Heist, K., DePaoli, A.M., Veldhuis, J.D., & Mantzoros C.S. (2003) The role of falling leptin levels in the neuroendocrine and metabolic adaptation to short-term starvation in healthy men. *Journal of Clinical Investigation*, 111, 1409-1421.
- Clasey, J.L., Bouchard, C., Teates, C.D., Riblett, J.E., Thorner, M.O., Hartman, M.L., Weltman, A. (1999) The use of anthropometric and dual-energy X-ray absorptiometry

(DXA) measures to estimate total abdominal and abdominal visceral fat in men and women. *Obesity Research*, 7, 256-64.

- Crabbe, P., Bogaert, V., De Bacquer, D., Goemaere, S., Zmierzak, H., & Kaufman, JM. (2007) Part of the interindividual variation in serum testosterone levels in healthy men reflects differences in androgen sensitivity and feedback setpoint: contribution of the androgen receptor polyglutamine tract polymorphism. *Journal of Clinical Endocrinology and Metabolism* Jun 19; [Epub ahead of print]
- Durnin, J.V.G.A., & Womersley, J. (1974) Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16-72 years. *British Journal of Nutrition*, 1974, 32, 77-97.
- Ellis, J.A., Stebbing, M. & Harrap, S.B. (2001) Polymorphism of the androgen receptor gene is associated with male pattern baldness. *Journal of Investigative Dermatology*, 116,452-5.
- Ellison, P.T. (1988) Human salivary steroids: methodological considerations and applications in physical anthropology. *Yearbook of Physical Anthropology*, 31, 1115-42.
- Ellison, P.T. (2001) *On Fertile Ground*, Cambridge, MA, Harvard University Press.
- Ellison, P.T., Bribiescas, R.G., Bentley, G.R., Campbell, B.C., Lipson, S.F., Panter-Brick, C. & Hill, K. (2002) Population variation in age-related decline in male salivary testosterone. *Human Reproduction*, 17, 3251-3253.
- Esteban, E., Rodon, N., Via, M., Gonzalez-Perez, E., Santamaria, J., Dugoujon, J.M.,Chennawi, F.E., Melhaoui, M., Cherkaoui, M., Vona, G., Harich, N., & Moral, P. (2006) Androgen receptor CAG and GGC polymorphisms in Mediterraneans: repeat dynamics and population relationships. *Journal of Human Genetics*, 51, 129-36.
- Ferro-Luzzi, A., Sette, S., Frnaklin M., James, W.P.T. (1992) A simplified approach of assessing adult chronic energy deficiency. *European Journal of Clinical Nutrition*, 46, 173-186.
- Fontana, L., Klein, S., & Holloszy, J.O. (2006) Long-term low-protein, low-calorie diet and endurance exercise modulate metabolic factors associated with cancer risk. *American Journal of Clinic Nutrition*, 84,1456-1462.
- Fratkin, E. (1998) *Ariaal Pastoralists of Kenya: Surviving Drought and Development in Africa's Arid Lands*. Needham Heights, MA: Allyn and Bacon.
- Gray, P. & Campbell, B. (2005) Erectile dysfunction and its correlates among the Ariaal of northern Kenya. *International Journal of Impotence Research*, 17, 445-449.

- Gurney, J.M. & Jelliffe, D.B. (1973) Arm anthropometry in nutritional assessment: nomogram for rapid calculation of muscle circumference and cross-sectional muscle and fat areas. *American Journal of Clinical Nutrition*, **26**, 912-915.
- Hallschmid, M., Benedict, C., Schultes, B., Fehm, H.L., Born, J. & Kern, W. (2004) Intranasal insulin reduces body fat in men but not in women. *Diabetes*, **53**,3024-3029.
- Harkonen, K., Huhtaniemi, I., Makinen, J., Hubler, D., Irjala, K., Koskenvuo, M., Oettel, M., Raitakari, O., Saad, F., Pollanen, P. (2003) The polymorphic androgen receptor gene CAG repeat, pituitary-testicular function and andropausal symptoms in ageing men. *International Journal of Andrology*, **26**, 187-94.
- Herbst, K.L., & Bhasin S. (2004) Testosterone action on skeletal muscle. *Current Opinion in Clinical Nutrition and Metabolic Care*, **7**, 271-7.
- Hetland, M.L., Haarbo, J., & Christiansen, C. (1998) Regional body composition by dual-energy X-ray absorptiometry. Relation to training, sex hormones, and serum lipids in male long-distance runners. *Scandinavian Journal of Medicine and Science in Sports*, **8**,102-108.
- Ishigaki, T., Koyama, K., Tsujita, J., Tanaka, N., Hori, S., & Oku, Y. (2005) Plasma leptin levels of elite endurance runners after heavy endurance training. *Journal of Physiological Anthropology and Applied Human Science*, **24**, 573-8.
- Kittles, R.A., Young, D., Weinrich, S., Hudson, J., Argyropoulos, G., Ukoli, F., Adams-Campbell, L., & Dunston, G.M. (2001) Extent of linkage disequilibrium between the androgen receptor gene CAG and GGC repeats in human populations: implications for prostate cancer risk. *Human Genetics*, **109**, 253-261.
- Krithivas, K., Yurgalevitch, S.M. , Mohr, B.A., Wilcox, C.J., Batter, S.J., Brown, M., Longcope, C., McKinlay, J.B., Kantoff, P.W. (1999) Evidence that the CAG repeat in the androgen receptor gene is associated with the age related decline in serum androgen levels in men. *Journal of Endocrinology*, **162**, 137-42.
- Lapauw, B., Goemaere, S., Crabbe, P., Kaufman, J.M. & Ruige, J.B. (2007) Is the effect of testosterone on body composition modulated by the androgen receptor gene CAG repeat polymorphism in elderly men? *European Journal of Endocrinology*, **156**,395-401.
- La Spada, A.R., Wilson, E.M., Lubahn, D.B., Harding, A.E. & Fischbeck, K.H. (1991) Androgen receptor gene mutations in X-linked spinal and bulbar muscular atrophy. *Nature*, **352**,77-79.
- Lukas, W., Campbell, B.C., & Ellison, P. (2005) Testosterone, aging and body composition in men from Harare, Zimbabwe. *American Journal of Human Biology*, **16**, 704-712.

- Muehlenbein, M.P. & Bribiescas, R.G. (2005) Testosterone-mediated immune functions and male life histories. *American Journal of Human Biology*, 17, 527-58.
- Nindl, B.C., Friedl, K.E., Marchitelli, L.J., Shippee, R.L., Thomas, C.D. & Patton, J.F. (1996) Regional fat placement in physically fit males and changes with weight loss. *Medicine and Science in Sports Exercise*, 28,786-93.
- Oltmanns, K.M., Fruehwald-Schultes, B., Kern, W., Born, J., Fehm, H.L. & Peters A. (2001) Hypoglycemia, but not insulin, acutely decreases LH and T secretion in men. *Journal of Clinical Endocrinology and Metabolism*, 86,4913-4919.
- Pouliot, M.C., Despres, J.P., Lemieux, S., Moorjani, S., Bouchard, C., Tremblay, A., Nadeau, A., Lupien, P.J. (1994) Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. *American Journal of Cardiology*, 73, 460-8.
- Smith, K. (1998) Farming, marketing, and changes in the authority of elders among pastoral Rendille and Ariaal. *Journal of Cross-Cultural Gerontology*, 13, 309-332.
- Smith, K. (1999) Economic transformation and changing work roles among pastoralist Rendille and Ariaal of northern Kenya. *Research in Economic Anthropology*, 20, 135-161.
- Svartberg J, von Muhlen D, Sundsfjord J, Jorde R.. (2004)Waist circumference and testosterone levels in community dwelling men. The Tromso study. *Eur J Epidemiol.* 19, 657-63.
- Vermeulen, A., Goemaere, S., Kaufman, J.M. (1999) Testosterone, body composition and aging. *Journal of Endocrinological Investigation*, 22, 110-116.
- Walsh, S., Zmuda, J.M., Cauley, J.A., Shea, P.R., Metter, E.J., Hurley, B.F., Ferrell, R.E. & Roth, S.M. (2005) Androgen receptor CAG repeat polymorphism is associated with fat-free mass in men. *Journal of Applied Physiology*, 98, 132-137.
- Woodhouse, L.J., Reisz-Porszasz, S., Javanbakht, M., Storer, T.W., Lee, M., Zerounian, H. & Bhasin, S. (2003) Development of models to predict anabolic response to testosterone administration in healthy young men. *American Journal of Physiology Endocrinology and Metabolism* 284, E1009-17.
- Zachmann, M., Ferrandez, A., Murset, G., Gnehm, H.E., Prader, A. (1976) Testosterone treatment of excessively tall boys. *Journal of Pediatrics*, 88,116-23.
- Zitzmann, M. & Nieschlag, E. (2003) The CAG repeat polymorphism within the androgen receptor gene and maleness. *International Journal of Andrology*, 26, 76-83.

Zitzmann, M., Gromoll, J., von Eckardstein, A., & Nieschlag, E. (2003) The CAG repeat polymorphism in the androgen receptor gene modulates body fat mass and serum concentrations of leptin and insulin in men. *Diabetologia*, 46,31-39.

Zitzmann, M., Faber, S., Nieschlag, E. (2006) Association of specific symptoms and metabolic risks with serum testosterone in older men. *Journal of Clinical Endocrinology and Metabolism*, 91, 4335-43.

Table 1 Comparison of Body Composition between Settled and Nomadic Ariaal Males

Variable	Overall	Settled	Nomadic
N	152	87	69
Age (yrs)			
Height (cm)t	172.4 ± 6.6	172.2 ± 6.7	172.6 ± 6.5
Weight (kgs)	52.9 ± 7.1	53.4 ± 7.8	52.4 ± 7.1
Body Mass Index (wt/ht ²)	17.8 ± 1.9	18.0 ± 2.1	17.5 ± 1.6
Arm Circumference (mm)	23.1 ± 2.1	23.2 ± 2.1	23.1 ± 2.1
Waist Circumference (mm)	71.0 ± 5.9	71.8 ± 6.8	70.1 ± 4.5***
Hip Circumference (mm)	86.4 ± 5.2	87.6 ± 5.3	84.9 ± 4.6+
Waist Hip Ratio (WHR)	0.82 ± 0.05	0.82 ± 0.05	0.83 ± 0.04
Subscapular Skinfold (mm)	7.5 ± 2.5	7.7 ± 3.0	7.4 ± 1.6
Midaxillary Skinfold (mm)	5.3 ± 1.7	5.5 ± 2.1	5.1 ± 0.8
Triceps (mm)	4.9 ± 1.8	4.9 ± 2.0	4.8 ± 1.4
Periumbilical Skinfold (mm)	6.0 ± 1.9	6.3 ± 2.3	5.6 ± 1.2*
Suprailliac Skinfold (mm)	4.7 ± 2.1	5.1 ± 2.7	4.3 ± 0.8*
Body Fat (%)	9.9 ± 3.8	10.2 ± 4.3	9.5 ± 2.9

+ p < 0.1; *p < 0.05; *** p < 0.001 (based on T-test)

Table 2 Body Composition by AR CAG repeat length among Ariaal Males

Variable	<=20	> 20
N	41	115
Age (yrs)		
Height (cm)t	171.4± 6.6	172.8 ± 6.6
Weight (kgs)	53.6 ± 8.0	52.7 ± 6.8
Body Mass Index (wt/ht ²)	18.2 ± 1.9	17.6 ± 1.9
Arm Circumference (mm)	23.3 ± 1.7	23.1 ± 2.2
Waist Circumference (mm)	72.9 ± 7.1	70.4 ± 5.3*
Hip Circumference (mm)	86.3± 5.5	86.4 ±5.1
Waist Hip Ratio (WHR)	0.84 ± 0.05	0.81 ± 0.04***
Subscapular Skinfold (mm)	8.0 ± 2.5	7.4 ± 2.4
Midaxillary Skinfold (mm)	5.8 ±2. 3	5.2 ±1.4
Triceps Skinfod (mm)	5.0 ± 1.8	4.8 ± 1.8
Suprailliac Skinfold (mm)	5.0 ± 2.5	4.6 ± 1.9
Periumbilical Skinfold (mm)	5.9 ± 1. 7	6.0 ± 2.0
Body Fat (%)	10.6 ± 4.3	9.6 ± 3.5

* p ,0.05; *** p = 0.001 (based on T-test)

Table 3 Androgen Receptor and Age Related Pattern of Testosterone

	Am Salivary Testosterone	Pm Salivary Testosterone
Adj. r^2	0.16	0.05
Predictor	β	β
Nomadic Residence	-.416***	-.265**
Age Group	-.105	-.048
AR CAG Repeat Length	-.038	-.070
AR X Age Group	-.018	.048

***p <0.001

Table 4 Testosterone and AR CAG length as Predictors of Body Composition.

	Height	BMI ^a	FFM ^b	AMPBA ^c	% BF ^d	Waist ^e	SISK ^f
Adj. r ²	0.01	0.10	0.09	0.01	0.17	0.21	0.15
Predictor	β	β	β	β	β	β	β
Nomadic Residence	-0.005	-0.088	-0.064	-0.044	-0.045	-0.175*	-0.174*
Age	-0.011	-1.39†	-0.252	-0.124	.314	.103	-.109
Pm T	.323†	.620***	.517***	.329†	.603***	.805***	.455**
AR	.420*	.289†	.383*	.159	.329*	.385*	.760***
Pm T X AR	-.498	-.624**	-.618**	-.333	-.641***	-.819*	-.782***

†p < 0.1; *p < 0.05; **p < 0.01; ***p < 0.001

^aBody Mass Index; ^bFat Free Mass; ^cArm Muscle Plus Bone Area; ^d% Body Fat; ^eWaist Circumference; ^fSuprailiac skinfold

Figure Captions

Figure 1 Frequency of CAG repeats among Ariaal Men. The frequency of repeats ranges from 15 to 34 within the range of 11 to 34 established as normal in a U.S. population.



