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The Androgen Control of Sebum Production. Studies of Subjects With Dihydrotestosterone Deficiency and Complete Androgen Insensitivity*

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ABSTRACT

To evaluate the androgen control of sebum, subjects with complete androgen insensitivity and male pseudohermaphrodites with inherited 5α-reductase deficiency and decreased dihydrotestosterone (DHT) production had sebum production studied. A hydrophobic polymeric film applied to the forehead was used to measure sebum production through the use of air filled micropores. Sebum scores of normal preadrenarchal children (ages 2–6), and normal age-matched adult males and females, were studied as well as males treated with the 5α-reductase inhibitor, finasteride, for benign prostatic hyperplasia who were studied at baseline and after drug therapy.

Androgen insensitive subjects had no sebum production by this methodology, and the results were identical to preadrenarchal children. In contrast, adult male pseudohermaphrodites with 5α-reductase deficiency and a selective decrease in DHT production had sebum production scores identical to normal age-matched males. Males with benign prostatic hyperplasia treated with the 5α-reductase inhibitor, finasteride, to lower DHT levels did not decrease the sebum score from baseline values.

The lack of demonstrable sebum in androgen-insensitive subjects clearly demonstrates the absolute androgen control of sebum production. The DHT dependency of the sebaceous gland, however, could not be demonstrated in this study. Two 5α-reductase isoenzymes 1 and 2, have been described. 5α-reductase-2 is the gene responsible for inherited 5α-reductase deficiency. Although the degree of inhibition of DHT *in utero* and in adulthood in male pseudohermaphrodites with a defect in 5α-reductase-2 enzyme activity caused severe impairment of external genital and prostate differentiation and decreased facial and body hair, it had no demonstrable effect on sebaceous gland development or function. Furthermore, lowering DHT levels in adulthood had no effect on sebum production. If the gland is rich in the enzyme 5α-reductase-2, it is proposed that the sebaceous gland is either exquisitely sensitive to DHT, requiring only small amounts for normal development and function, or that male levels of testosterone compensate for DHT and maintain normal sebaceous gland activity throughout life. It is also possible that 5α-reductase-1 is the enzyme of the sebaceous gland and is unaffected in the inherited condition and by finasteride. (*J Clin Endocrinol Metab* **76:** 524–528, 1993)

SEBACEOUS glands are under sex steroid regulation and undergo changes in activity during life which correlate with the changing hormonal milieu (1, 2). In humans, the glands are large at birth, involute during childhood, and enlarge again with puberty. In adulthood, sebum is produced by both sexes, but the amount produced is greater in men. Once maturity is attained, there is little change in sebum production. Sebaceous gland activity declines in both sexes in old age (3).

The androgen control of sebum production and its role in the pathogenesis of acne is suggested by the following data. Male castrates produce less sebum than normal males (4) and they do not have acne (5), a situation which reverses when treatment with testosterone (T) is initiated. Androgen administration also results in a significant increase in sebum production in women (1, 6). Topical application of T has also been shown to induce sebaceous gland enlargement, demonstrating a direct action at the target site (1, 2). Whereas androgens can increase sebum production, estrogens have been found to have the opposite effect (1, 2).

Animal experiments have demonstrated the presence of 5α-reductase activity in sebaceous gland tissues (7–10). Moreover, inhibitors of 5α-reductase activity, and consequently dihydrotestosterone (DHT) production, have been found to reduce sebaceous gland function in the hamster costovertebral spot, suggesting that T acts through conversion to DHT in the gland (11). Additionally, in hypophysectomized rats T is inactive whereas DHT is active in inducing sebaceous gland secretion (7).

Since sebaceous glands in man are also rich in 5α-reductase activity (12, 13), it has been assumed that DHT is the essential androgen for sebaceous gland maturation and lipid synthesis (14). However, uncertainty remains as to whether DHT has a prime regulatory function for sebaceous glandular activity *in vivo* (15, 16).

To study the influence of T and DHT in sebum production

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in man, male pseudohermaphrodites with 5α-reductase deficiency and a selective decrease in dihydrotestosterone production, and subjects with complete androgen insensitivity who are unresponsive to both T and DHT were evaluated and compared. Their results were also compared to age-matched adult males and females and prepubertal boys and girls. In another part of the study, adult males had sebum studies performed before and after treatment with the 5α-reductase inhibitor, finasteride (MK906), as part of a double-blind placebo-controlled study for treatment of benign prostatic hypertrophy (BPH).

Subjects and Methods

Subjects

Study A. Sebum production was evaluated in 12 subjects with inherited male pseudohermaphroditism due to 5α-reductase deficiency (MPH); 9 subjects were part of a large Dominican kindred, and 3 were from New Guinea. The mean age was 27 yr (age range, 19–40). Eight androgen insensitive (AI) subjects were evaluated with a mean age of 45 (age range, 15–78). Six AI subjects had their gonads intact when studied, and 2 subjects were on cyclic estrogen and progesterone replacement therapy after gonadectomy at the time of evaluation. Twenty-two normal adult Dominican males with a mean age of 28 yr (age range, 17–39), and 21 normal adult Dominican females with a mean age of 29.0 yr (age range, 18–37), normal menses, and no history of hirsutism or acne, were evaluated. Preadrenarchal boys and girls were also evaluated. This study group was comprised of 10 normal healthy Dominican boys ranging in age from 2–5 yr (average age was 3.7 yr), and 12 healthy Dominican girls ranging in age from 2–6 yr (average age was 4.3 yr). None of the children had clinical signs of secondary sexual development.

Study B. Ten men with an average age of 66 yr (age range, 58–74) were part of a multicenter double-blind placebo-controlled study to evaluate the efficacy of the 5α-reductase inhibitor finasteride in the treatment of BPH. Patients entering the double-blind clinical trial were treated with either placebo, 1 mg, or 5 mg Finasteride daily for 1 yr. After this they entered into open extension on 5 mg of drug. Sebum studies were performed at baseline and 6 months. They were studied again in the open extension when they were on drug for a total of 15–18 months. Those patients who were on placebo were studied in the open extension after 6 months on drug.

Procedures

Measurement of sebum production was performed with Sebutape (Hermal Pharmaceutical Laboratories, Oak Hill, NY), a hydrophobic, polymeric film that measures sebum activity through the use of air-filled micropores (17, 18). When sebum from the skin surface comes in contact with the tape, numerous tiny air cavities previously filled with air become filled with sebum. Consequently, sebum-filled pockets become transparent cavities forming a pattern of sebum droplet deposition.

The test was performed in the following manner. The forehead of each subject was thoroughly cleansed with alcohol swabs. A Sebutape patch was placed on the forehead for 1 hr. The patch was removed and the amount of sebum measured on a scale of 0–5 using reference patterns provided in the kit. A zero (0) pattern was equal to no sebum production, whereas a five (5) pattern signified highest sebum output. The patches were read by the investigator (LC) who was blinded to the identity of the subjects.

To test the reproducibility and reliability of the Sebutape testing procedure, 13 subjects, 9 normal males, 2 5α-reductase-deficient subjects, and 2 androgen-insensitive subjects with gonads intact, had the test performed on 2 separate days at random times. In the AI subjects and the 5α-reductase deficient, the test was repeated 1–2 yr later. The results were the same for all subjects, with the exception of 1 subject who had a difference of 0.5.

Plasma androgens from randomly obtained samples were determined in subjects with inherited 5α-reductase deficiency, AI subjects with intact gonads and nine subjects treated with the 5α-reductase inhibitor, finasteride.

Serum androgens were measured by RIA after separation by paper chromatography by a previously published method (19). The antibodies for T and DHT were obtained from Pantex (Santa Monica, CA).

Results

Sebum studies

Ten normal boys and 12 normal girls between the ages of 2–6 yr had no detectable sebum production by this methodology (Fig. 1), and had a sebum score of 0. Similarly, the sebum score of all adult subjects (with or without intact gonads) with complete androgen insensitivity was zero (Table 1) (Fig. 1). One subject with incomplete AI had a low score of 1 (data not shown).

The mean sebum score for 21 control adult males was 4.4 ± 0.6 which was significantly higher than the mean sebum score of 3.3 ± 1.2, for 21 control adult females ($P < 0.05$) (Fig. 1).

The mean sebum score of adult male pseudohermaphrodites with 5α-reductase deficiency (4.5 ± 0.6) was not significantly different from the mean sebum score of normal adult males (4.35 ± 0.6) ($P > 0.05$), but was significantly greater than the mean sebum score of normal adult females (3.32 ± 1.2) ($P < 0.05$) (Fig. 1).

Males treated with the 5α-reductase inhibitor, finasteride, had no significant change in mean sebum score at 6 months and 1 yr (Table 1). The placebo-treated men had no change in sebum score when tested at 6 months and after they were placed on Finasteride (5 mg) for 6 months.

Androgen levels

The mean plasma T level was increased in patients with male pseudohermaphroditism due to 5α-reductase deficiency, and the mean plasma DHT level was low with an elevated mean T/DHT ratio (Table 2). The plasma T levels ranged from normal to high and the plasma DHT levels ranged from low normal to low.

Subjects with complete androgen insensitivity and intact testes had elevated serum T levels with normal to low DHT levels and mildly elevated T/DHT ratios (Table 2). These findings in AI subjects have been previously described (20, 21), and were not significantly different from the subjects with 5α-reductase deficiency ($P > 0.05$).

Subjects who were administered the 5α-reductase inhibitor, finasteride, had plasma DHT levels that were significantly reduced from baseline levels with markedly elevated T/DHT ratios, whereas subjects treated with a placebo for 6 months had T/DHT ratios that remained within the normal range (Table 3).

Discussion

Our results demonstrate that preadrenarchal children of both sexes (ages 2–6) have undetectable sebum production by the method used. It has been previously demonstrated

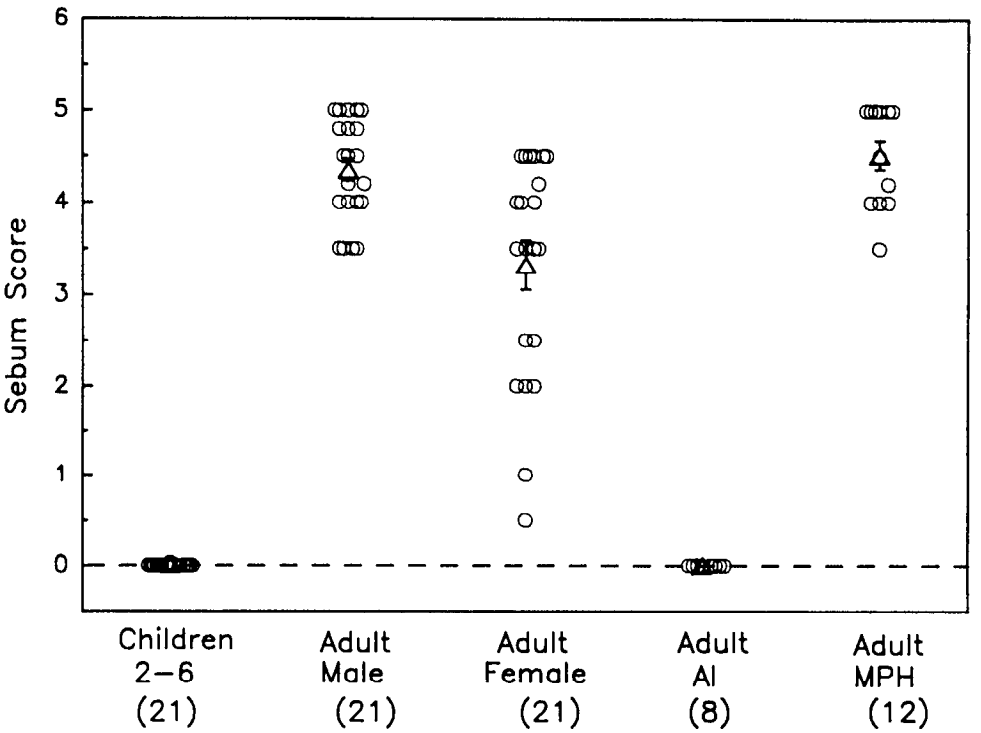

FIG. 1. AI = complete androgen insensitivity; MPH = male pseudohermaphrodites with 5α-reductase deficiency.

TABLE 1. Sebum scores (mean ± SD) in study subjects

Complete AI subjects (n = 8)			Male pseudohermaphrodites with 5-reductase deficiency (n = 12)	
Age	Sebum score		Age	Sebum score
45 ± 26	0.0		27 ± 8	4.5 ± 0.6
Finasteride-treated subjects (n = 10)				
Age	Sebum score before drug	Sebum score on placebo (6 months)	Sebum score after drug (6 months)	Sebum score after drug (>1 y)
66 ± 4.7	4.4 ± 0.4 (n = 10)	3.9 ± 0.5 (n = 4)	4.2 ± 0.6 (n = 9)	4.6 ± 0.4 (n = 5)

(n, number of patients studied).

that sebum levels decrease during the first year of life and the sebaceous gland remains small until approximately 6–7 yr of age when there is an increase in sebum output (22–24).

This study also demonstrates greater sebum production in normal males and normal females as compared to preadrenarchal children, suggesting that the hormonal changes at puberty are responsible for enhanced sebum production in both sexes. The greater production of sebum in males is no doubt due to greater androgen, as well as lower estrogen production.

Adult subjects with complete AI have undetectable sebum production and their results are identical to those of preadrenarchal children. These findings confirm the absolute androgen dependency of sebum production of the sebaceous glands, and correlate with clinical observations that subjects with complete AI, like children, have a clear complexion without acne.

Sebum production is generally higher in subjects with acne (25). Also, skin taken from the face and back of acne patients has been found to have increased 5α-reductase activity when compared to skin from control subjects (26).

Male pseudohermaphrodites with 5α-reductase deficiency and decreased DHT production have sebum production scores equal to those of normal males. It is noteworthy that, despite a severe defect in external genital and prostate development *in utero* and decreased facial and body hair at puberty, sebum production is similar to that of normal males. These results demonstrate that the decreased DHT levels due to decreased 5α-reductase activity which are sufficiently low to cause severe genital ambiguity and decreased facial and body hair, have no effect on sebaceous gland development and function in adulthood.

It is interesting that moderate to severe acne has not been described in males with this syndrome. Recently, however, three adult New Guinean male pseudohermaphrodites reported mild acneiform eruption at puberty (27). Since the original reports stating an absence of acne in affected subjects from the Dominican kindred with 5α-reductase deficiency (27–31), two affected males from this kindred have also given a history of acne during puberty, and one still has the condition in adulthood (McGinley, J. I., personal communication).

Men treated with the 5α-reductase inhibitor, finasteride, did not demonstrate a decrease in sebum production when studied at 6 months and 1 yr. Finasteride is effective in inhibiting 5α-reduction in target tissue *in vivo*, as has been demonstrated by its ability to produce a male pseudohermaphroditic rat when administered during gestation at the time of male sexual differentiation (32). 5α-Reductase azasteroid inhibitors have been shown to reduce prostate size in dogs (33–34). In humans, Finasteride has been shown to

TABLE 2. Serum androgen levels in male pseudohermaphrodites

Male pseudohermaphrodites with 5-reductase deficiency					Subjects with AI (nongonadectomized)				
Patient	Age	T (ng/dL)	DHT (ng/dL)	T/DHT	Patient	Age	T (ng/dL)	DHT (ng/dL)	T/DHT
1	20	520	19	27	1	16	899	44	20
2	24	866	37	23	2	20	687	26	26
3	23	1048	26	40	3	15	711	24	30
4	35	1106	32	35	4	69	487	11	44
5	40	1119	25	45	5	73	1743	44	40
6	40	1000	33	30	6	78	890	35	25
7	30	617	17	36					
8	20	1000	28	36					
9	21	1110	33	34					
10	26	790	26	30					
11	19	635	21	30					
12	29	970	32	32					
Mean ± SD		898 ± 211	27 ± 6	33 ± 6	Mean ± SD		903 ± 439	31 ± 13	31 ± 9
Normal male		(n = 31)							
Mean ± SD		582 ± 166	51 ± 21	12 ± 3					

TABLE 3. Serum androgen levels in males before and 6 months after treatment with placebo or the 5-reductase inhibitor finasteride

Patient no.	Age	Control			6 months		
		T (ng/dL)	DHT (ng/dL)	T/DHT	T (ng/dL)	DHT (ng/dL)	T/DHT
Placebo							
1	58	450	73	6	813	68	12
2	70	486	51	10	672	47	14
3	71	585	98	6	648	55	12
4	64	640	51	13	489	44	11
Finasteride 1 mg/day							
5	74	310	66	5	660	16	41
5 mg/day							
6	66	241	49	5	532	8	67
7	62	283	47	6	552	13	43
8	68	331	73	5	495	12	41
9	64	793	43	18	810[a]	6	135

[a] Done at 13 months after finasteride.

reduce prostate size in patients with BPH and to lower plasma DHT levels and increase T/DHT ratios in humans and result in the same biochemical profile as subjects with the inherited disease (35). The subjects of this study had substantial decreases in plasma DHT with lower plasma DHT levels, and in general more elevated T/DHT ratios than the male pseudohermaphrodites with inherited 5α-reductase deficiency. Yet the sebum production scores were not different from those of male pseudohermaphrodites with inherited 5α-reductase deficiency or normal adult males.

Two 5α-reductase isoenzymes have recently been cloned (36–39). 5α-Reductase-2 is the gene responsible for differentiation of the male external genitalia and prostate and is defective in male pseudohermaphrodites with 5α-reductase deficiency (39). Finasteride also has greater affinity for the enzyme 5α-reductase-2. The role of 5α-reductase-1 is presently unknown. It is present in small quantities in the prostate, but its presence in other areas rich in 5α-reductase activity is yet unknown.

If the sebaceous gland is rich in 5α-reductase-2, the normal male levels of sebum production in male pseudohermaphrodites with inherited 5α-reductase deficiency and the lack of a significant decrease in sebum production in finasteride-treated subjects, suggests that the sebaceous gland is exquisitely sensitive to low levels of DHT or that once the sebaceous gland is stimulated during puberty by DHT, as in the finasteride-treated subjects, its function can be maintained by low levels of DHT. It is also possible that T can compensate to some degree for a deficiency in DHT (31). And it is also possible that in both inherited 5α-reductase deficiency and finasteride-treated subjects, the isoenzyme 5α-reductase-1 is located in the sebaceous glands and is unaffected. Further research will clarify this.

In summary, this paper demonstrates the androgen dependency of sebum production by showing suppression of sebaceous gland secretion with total blockade to androgen action. The selective DHT dependency of sebum production, however, could not be documented in this study.

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References

1. **Pochi PE, Strauss JS.** 1974 Endocrinologic control of the development and activity of the human sebaceous gland. J Invest Dermatol.

62:191–201.
2. **Strauss JS, Pochi PE**. 1963 The hormonal control of human sebaceous glands. In: Montagna W, Ellis RA, Silver AF, eds. Biology of Skin. The Sebaceous Glands. Oxford: Pergamon Press; IV:220–254.
3. **Jacobsen E, Billings JK, Frantz R, Kinney CK, Stewart ME, Downing DT**. 1985 Age-related changes in sebaceous wax exter secretion rates in men and women. J Invest Dermatol. 85:483–485.
4. **Pochi PE, Strauss JS, Mescon H**. 1962 Sebum secretion and urinary fractional 17-ketosteroid and total 17-hydroxycorticoid excretion in male castrates. J Invest Dermatol. 39:485–489.
5. **Hamilton JB**. 1941 Male hormone substance: a prime factor in acne. J Clin Endocrinol Metab. 1:570–592.
6. **Pochi PE, Strauss JS, Downing DT**. 1979 Age-related changes in sebaceous gland activity. J Invest Dermatol. 73:108–111.
7. **Ebling EJ, Ebling E, McCaffrey V, Skinner J**. 1971 The response of the sebaceous glands of the hypophysectomized-castrated male rat to 5α-dihydrotestosterone, androstenedione, dehydroepiandrosterone and androsterone. J Endocrinol. 51:181–190.
8. **Takayasu S, Adachi K**. 1972 The *in vivo* and *in vitro* conversion of testosterone to 17β-hydroxy-5α-androstan-3-one (dihydrotestosterone) by the sebaceous glands of hamsters. Endocrinology. 90:73–80.
9. **Sansone-Bazzano G, Reisner RM**. 1974 Steroid pathways in sebaceous glands. J Invest Dermatol. 62:211–216.
10. **Gross CMAA, Wirtz P, Vermorken AJM, Mauvais-Jarvis P**. 1982 Androgenic effect of testosterone and some of its metabolites in relation to their biotransformation in the skin. Br J Dermatol. 107:549–557.
11. **Takayasu S, Adachi K**. 1970 Hormonal control of metabolism in hamster costovertebral glands. J Invest Dermatol. 55:13–19.
12. **Takayasu S, Wakimoto H, Itami S, Sano S**. 1980 Activity of testosterone 5α-reductase in various tissues of human skin. J Invest Dermatol. 74:187–191.
13. **Dijkstra AC, Goos CMAA, Cunliffe WJ, Sultan C, Vermorken AJM**. 1987 Is increased 5α-reductase activity a primary phenomenon in androgen-dependent skin disorders? J Invest Dermatol. 89:87–92.
14. **Pochi PE**. 1988 Acne: androgens and microbiology. Drug Dev Res. 13:157–168.
15. **Randall VA, Ebling FJ**. 1982 Is the metabolism of testosterone to 5α-dihydrotestosterone required for androgen action in the skin? Br J Dermatol. 107[Suppl 23]:47–53.
16. **Schroder HG, Ziegler M, Nickisch K, Kaufmann J, Etreby MFE**. 1989 Effects of topically applied antiandrogenic compounds on sebaceous glands of hamster ears and flank organs. J Invest Dermatol. 92:769–773.
17. **Kligman AM, Miller DM, McGinley KJ**. 1986 Sebutape: a device for visualizing and measuring human sebaceous secretion. J Soc Cosmet Chem. 37:369.
18. **Nordstrom KM, Schmus HG, McGinley KJ, and Leyden JJ**. 1986 Measurement of sebum output using a lipid absorbent tape. J Invest Dermatol. 87:260–263.
19. **Peterson RE, Imperato-McGinley J, Gautier T, Sturla E**. 1977 Male pseudohermaphroditism due to steroid 5α-reductase deficiency. Am J Med. 62:170–191.
20. **Imperato-McGinley J, Peterson RE, Gautier T, Cooper G, Danner R, Arthur A, et al**. 1982 Hormonal evaluation of a large kindred with complete androgen insensitivity: evidence for secondary 5α-reductase deficiency. J Clin Endocrinol Metab. 54:931–941.
21. **Jukier L, Kaufman M, Pinsky L, Petersen RE**. 1984 Partial androgen resistance associated with secondary 5α-reductase deficiency: identification of a novel qualitative androgen receptor defect and clinical implications. J Clin Endocrinol Metab. 59:679–688.
22. **Agache P, Blanc D, Barrand C, Laurent R**. 1980 Sebum levels during the first year of life. Br J Dermatol. 103:643–649.
23. **Ramasastry P, Downing DT, Pochi PE, Strauss JS**. 1970 Chemical composition of human skin surgace lipids from birth to puberty. J Invest Dermatol. 54:139–144.
24. **Pochi PE, Strauss JS, Downing DT**. 1977 Skin surface lipid composition, acne, pubertal development, and urinary excretion of testosterone and 17-ketosteroids. J Invest Dermatol. 69:485–489.
25. **Strauss JS, Pochi PE, Downing DT**. 1975 Skin lipids and acne. Annu Rev Med. 26:27–32.
26. **Sansone G, Reisner RM**. 1971 Differential rates of conversion of testosterone to dihydrotestosterone in acne and in normal human skin—a possible pathogenic factor in acne. J Invest Dermatol. 56:366–372.
27. **Imperato-McGinley J, Miller M, Wilson JD, Peterson RE, Shackleton C, Gajdusek DC**. 1991 A cluster of male pseudohermaphrodites with 5α-steroid reductase deficiency in Papua, New Guinea. Clin Endocrinol (Oxf). 34:293–298.
28. **Imperato-McGinley J, Guerrero L, Gautier T, Peterson RE**. 1974 Steroid 5α-reductase deficiency in man: an inherited form of male pseudohermaphroditism. Science. 186:1213–1215.
29. **Imperato-McGinley J, Peterson RE, Gautier T, Sturla E**. 1979 Male pseudohermaphroditism secondary to 5α-reductase: a model for the role of androgens in both the development of the male phenotype and the evolution of a male gender identity. J Steroid Biochem Mol Biol. 1:637–645.
30. **Imperato-McGinley J, Peterson RE, Gautier T**. 1981 Male pseudohermaphroditism secondary to 5α-reductase deficiency: a review. In: Novy MJ, Resko JA, eds. Fetal Endocrinology. New York: Academic Press; 359–382.
31. **Grino P, Griffin JE, Wilson JD**. 1990 Testosterone at high concentrations interacts with the human androgen receptor similarly to dihydrotestosterone. Endocrinology 126(2):1165–1172.
32. **Imperato-McGinley J, Binienda Z, Arthur A, Minenberg D, Vaughan ED, Quimby F**. 1986 The development of a male pseudohermaphroditic rat using an inhibitor of the enzyme 5α-reductase. Endocrinology 116:807–812.
33. **Wenderoth UK, George FW, Wilson JD**. 1983 The effect of a 5α-reductase inhibitor on androgen-mediated growth of the dog prostate. Endocrinology 113:569–573.
34. **Brooks JR, Berman C, Garnes D, et al**. 1986 Prostatic effects induced in dogs by chronic or acute oral administration of 5α-reduced inhibitors. Prostate. 9:65–75.
35. **Imperato-McGinley J, Shackleton C, Orlic S, Stoner E**. 1990 C19 and C21 5β/5 metabolite ratios in subjects treated with the 5α-reductase inhibitor Finasteride—comparison of male pseudohermaphrodites with inherited 5α-reductase deficiency. J Clin Endocrinol Metab. 70(3):777–782.
36. **Andersson S, Russell DW**. 1990 Structural and biochemical properties of cloned and expressed human and rat steroid 5α-reductases. Proc Natl Acad Sci USA. 87:3640–3644.
37. **Jenkins EP, Hsieh C-L, Milatovich A, et al**. 1991 Characterization and chromosomal mapping of a human steroid 5α-reductase gene and pseudogene and mapping of the mouse homoloque. Genomics. 11:1102–1112.
38. **Jenkins EP, Andersson S, Imperato-McGinley J, Wilson JD, Russell DW**. 1992 Genetic and pharmacological evidence for more than one human steroid 5α-reductase. J Clin Invest. 89:293–300.
39. **Andersson S, Berman DM, Jenkins EP, Russell DW**. 1991 Deletion of steroid 5α-reductase 2 gene in male pseudohermaphroditism. Nature. 354:159–161.