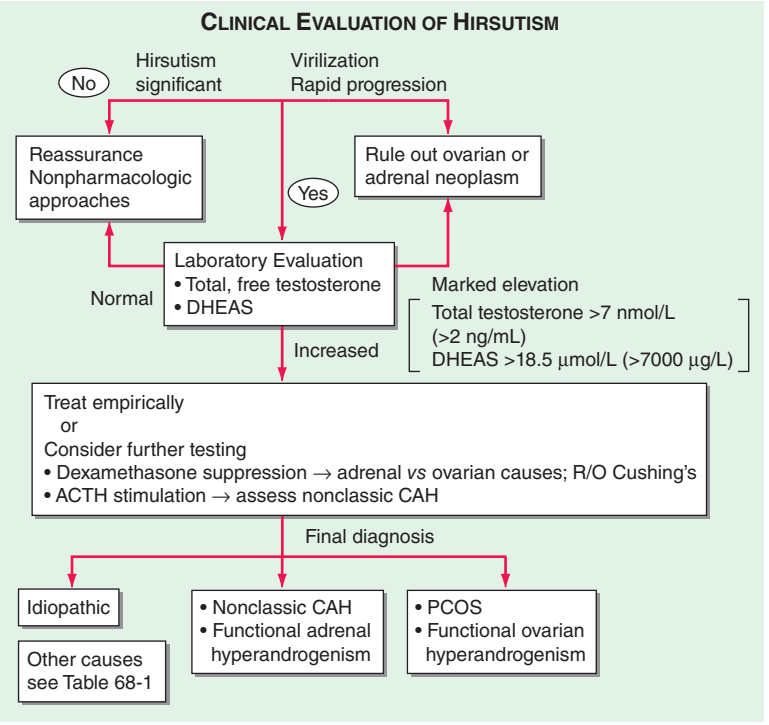

FIGURE 68-2 Algorithm for the evaluation and differential diagnosis of hirsutism. ACTH, adrenocorticotropic hormone; CAH, congenital adrenal hyperplasia; DHEAS, sulfated form of dehydroepiandrosterone; PCOS, polycystic ovarian syndrome.

Nonpharmacologic treatments include (1) bleaching; (2) depilatory (removal from the skin surface), such as shaving and chemical treatments; and (3) epilatory (removal of the hair including the root), such as plucking, waxing, electrolysis, and laser therapy. Despite perceptions to the contrary, shaving does not increase the rate or density of hair growth. Chemical depilatory treatments may be useful for mild hirsutism that affects only limited skin areas, though they can cause skin irritation. Wax treatment removes hair temporarily but is uncomfortable. Electrolysis is effective for more permanent hair removal, particularly in the hands of a skilled electrologist. Laser phototherapy appears to be efficacious for hair removal. It delays hair regrowth and causes permanent hair removal in most patients. The long-term effects and complications associated with laser treatment are being evaluated.

Pharmacologic therapy is directed at interrupting one or more of the steps in the pathway of androgen synthesis and action: (1) suppression of adrenal and/or ovarian androgen production; (2) enhancement of androgen-binding to plasma-binding proteins, particularly SHBG; (3) impairment of the peripheral conversion of androgen precursors to active androgen; and (4) inhibition of androgen action at the target tissue level. Attenuation of hair growth is typically not evident until 4–6 months after initiation of medical treatment and in most cases leads to only a modest reduction in hair growth.

Combination estrogen-progestin therapy in the form of an oral contraceptive is usually the first-line endocrine treatment for hirsutism and acne, after cosmetic and dermatologic management. The estrogenic component of most oral contraceptives currently in use is either ethinyl estradiol or mestranol. The suppression of LH leads to reduced production of ovarian androgens. The reduced androgen levels also result in a dose-related increase in SHBG, thus lowering the fraction of unbound plasma testosterone. Combination therapy also has been demonstrated to decrease DHEAS, perhaps by reducing ACTH levels. Estrogens also have a direct, dose-dependent suppressive effect on sebaceous cell function.

The choice of a specific oral contraceptive should be predicated on the progestational component, as progestins vary in their suppressive effect on SHBG levels and in their androgenic potential. Ethynodiol diacetate has relatively low androgenic potential, whereas progestins such as norgestrel and levonorgestrel are particularly androgenic, as judged from their attenuation of the estrogen-induced increase in SHBG. Norgestimate exemplifies the newer generation of progestins that are virtually nonandrogenic. Drospirenone, an analogue of spironolactone that has both antimineralocorticoid and antiandrogenic activities, has been approved for use as a progestational agent in combination with ethinyl estradiol.

Oral contraceptives are contraindicated in women with a history of thromboembolic disease and women with increased risk of breast or other estrogen-dependent cancers **(Chap. 413)**. There is a relative contraindication to the use of oral contraceptives in smokers and those with hypertension or a history of migraine headaches. In most trials, estrogen-progestin therapy alone improves the extent of acne by a maximum of 50–70%. The effect on hair growth may not be evident for 6 months, and the maximum effect may require 9–12 months owing to the length of the hair growth cycle. Improvements in hirsutism are typically in the range of 20%, but there may be an arrest of further progression of hair growth.

Adrenal androgens are more sensitive than cortisol to the suppressive effects of glucocorticoids. Therefore, glucocorticoids are the mainstay of treatment in patients with CAH. Although glucocorticoids have been reported to restore ovulatory function in some women with PCOS, this effect is highly variable. Because of side effects from excessive glucocorticoids, low doses should be used. Dexamethasone (0.2–0.5 mg) or prednisone (5–10 mg) should be taken at bedtime to achieve maximal suppression by inhibiting the nocturnal surge of ACTH.

Cyproterone acetate is the prototypic antiandrogen. It acts mainly by competitive inhibition of the binding of testosterone and DHT to the androgen receptor. In addition, it may enhance the metabolic clearance of testosterone by inducing hepatic enzymes. Although not available for use in the United States, cyproterone acetate is widely used in Canada, Mexico, and Europe. Cyproterone (50–100 mg) is given on days 1–15 and ethinyl estradiol (50 μg) is given on days 5–26 of the menstrual cycle. Side effects include irregular uterine bleeding, nausea, headache, fatigue, weight gain, and decreased libido.