



Therapeutics Today

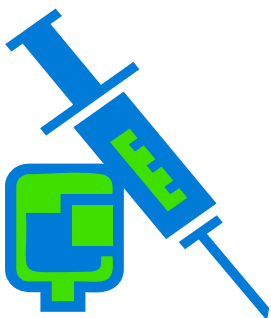
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How to manage hirsutism. Hirsutism is defined as the presence of excess hair growth (in an androgen-dependent distribution) in women. Although regarded as a purely cosmetic problem by some, studies have shown that it can have a similar effect on quality of life scores as chronic illnesses such as asthma, epilepsy or diabetes. A recent paper (*BMJ 2009; 338: 823-6*) outlined current management strategies. Hirsutism may appear at the time of menarche, menopause, during pregnancy or with the onset of obesity. **Causes:** Most women have either idiopathic hirsutism or polycystic ovary syndrome (PCOS). Rarer causes (frequently associated with more severe and/or more rapid onset hirsutism) include congenital adrenal hyperplasia, ovarian or adrenal androgen-secreting tumours, Cushing's syndrome, acromegaly or **certain drugs** (hormones with androgenic activity,

corticosteroids especially high dose, drugs acting on the pituitary gland and anti-epileptic agents such as valproate, phenytoin or phenobarbital). **Diagnosis** is usually clinical, based on the presence of a male distribution of hair growth. Important points in the history include the speed of hair appearance, menstrual pattern, recent weight gain, family history of diabetes, drug history (including use of COCs) and presence of other features of androgen excess such as acne or male alopecia. Since testosterone assay levels perform poorly in the female range, testosterone levels should be reserved for cases of hirsutism with rapid onset, for women with other symptoms and signs of PCOS or in cases that are severe or resistant to treatment. **Management:** most cases can be treated in primary care with non-systemic methods. **Women should be advised that the routine methods of hair removal such as shaving, waxing, threading and depilatory creams do not exacerbate hair growth in any way.** More permanent methods which aim to destroy the hair follicle include electrolysis, laser and pulsed light therapy; the longterm efficacy of the latter two methods have not been well established to date. Women should be encouraged to lose weight if obese and to exercise, both of which are associated with improvement and promote response to drug treatment. **Pharmacotherapy:** As hair grows in cycles, it can take months for an individual hair follicle to proceed through the different phases, including the anagen phase (stimulated by testosterone); therefore patients should be told that it may take weeks/months for treatment benefit to be seen. **Eflornithine**, a topical cream, is licensed for the treatment of hirsutism (face and chin) in women. Studies showed some improvement in 70% of treated patients, usually within 8 weeks. Treatment should be discontinued after 4 months if no improvement is seen. Systemic treatments include **COCs** such as Dianette® and Yasmin® which contain antiandrogenic progestogens and are effective for hirsutism (unlicensed indication). Levonorgestrel / norethisterone-containing COCs potentially exacerbate hirsutism while "third generation" COCs have neutral androgenic effects. **Androgen receptor antagonists** such as spironolactone, cyproterone acetate and flutamide have been used for resistant cases (unlicensed indication). **Specialist referral** is recommended for severe cases, those with rapid onset, those resistant to 12 months' therapy, if serum testosterone levels are twice the upper limit of normal, or if hirsutism is part of the metabolic syndrome, which requires a multidisciplinary approach to treatment. Management should be individualised in order to ensure compliance with the longterm regimen required.



Update on mumps outbreak in Ireland. Over 1,470 cases of mumps have been notified in Ireland in the first 3 months of this year. This represents a 16-fold increase compared with the same period in 2008 and is the largest number reported since mumps became a notifiable disease in 1988. The April edition of *Epi-Insight* (www.hpsc.ie) reported that **86% of cases were in 15-34 year-olds and >66% in 15-24 year-olds.** Where clinical data are available, the following complications have been recorded: hospitalisation (31/499), orchitis (50/265), pancreatitis (12/453) and reports of deafness (n=5) meningitis (n=2), mastitis (n=2) and one case of encephalitis. The National Immunisation Advisory Committee has recommended that everyone <25 years of age should have received 2 doses of the MMR vaccine, which is the only way to prevent mumps and its associated complications. **If vaccination status is unknown,**

the vaccine should be administered since an additional dose of MMR won't cause harm. Further information for prescribers and patients is available at the user-friendly website: www.mumps.ie



Potential Interaction between Clopidogrel and PPIs. The NMIC has received many queries regarding a potential interaction between clopidogrel and various proton pump inhibitors (PPIs). The Irish Medicines Board (IMB) has recently posted a safety advisory statement on this issue (www.imb.ie). Clopidogrel is a pro-drug which must be activated in the body and research has suggested that genetic differences in the way this activation occurs may be responsible for reducing the antiplatelet effect leading to an increased risk of heart attack and stroke. Several studies (both epidemiological and mechanism of action studies) have suggested that PPIs may

interfere with the efficacy of clopidogrel by inhibiting this activation process. However, these studies have given conflicting results with respect to the different PPIs. **No therapeutic controlled clinical trials evaluating concomitant use of clopidogrel and the various PPIs have been published, therefore there is no definitive evidence on the potential risk associated with individual PPIs.** The IMB is currently evaluating all available information, in conjunction with the other EU regulatory agencies. However, pending the outcome of this review, it has issued the following recommendations to healthcare professionals (HCPs):

- **HCPs should be aware of this interaction and the potential to increase cardiovascular events**
- **Physicians should continue to prescribe clopidogrel in view of its demonstrated benefits in its approved indications**
- **Prescribers are recommended to re-evaluate the need for starting or continuing treatment with a PPI in patients taking clopidogrel**
- **All suspected ADRs with clopidogrel/PPI usage should be reported to the IMB**

[Editor's note: The NMIC will publish the final conclusions / recommendations from the IMB review as soon as they are available. The US FDA website: (www.fda.gov/cder/drug/early_comm/clopidogrel_bisulfate.htm) also provides useful background information].



Psychiatric symptoms and chronic physical disease. Chronic medical diseases are the leading causes of death and disability in most developed countries. A recent paper reviewed the association between chronic illness and psychiatric disease (*Medicine 2008; 36 (9): 471-4*). Patients with a chronic / life-long condition may have to adjust their aspirations, relationships, employment and social activities which may contribute to psychological distress and a psychiatric disorder. Rates of depression are increased by at least 2-fold in most common chronic conditions: the 12-month prevalence of major depression varies from 8-10% for cardiovascular diseases (CVD) to 15% for COPD compared with 5% prevalence in those with no chronic illness. Around 30% of patients suffer from depression following an

acute myocardial infarction (MI), with resulting increased rates of mortality compared with non-depressed post MI patients. The presence of depression with diabetes mellitus is associated with worse glycaemic control and increased rates of mortality from diabetic complications. It is estimated that up to 20% of patients with rheumatoid arthritis (RA) may suffer from either anxiety or depression and there is evidence that management of these symptoms may reduce pain and improve functioning. These findings also have implications for treatment compliance: **up to 60% of patients with chronic illness may be poorly adherent to treatment and research has shown that individuals with concomitant depression are even less likely to comply compared with patients with no psychiatric symptoms.** The authors conclude that clinicians need to be aware that psychiatric illness may occur in association with chronic medical illness in general and that early detection and treatment will help alleviate psychiatric morbidity and may improve medical outcomes through better treatment compliance. In the same journal, an article reminds prescribers that **some treatments for medical illness may precipitate psychiatric symptoms.** The association between corticosteroids and psychiatric symptoms such as mania or euphoria is well known (*Medicine 2008; 36 (9): 501-4*). Dopaminergic agents (e.g. L-dopa, bromocriptine) and antimuscarinic agents, (e.g. biperiden) often used in combination in Parkinson's Disease, are also known to cause a range of psychiatric symptoms such as confusion, depression, agitation or mania, which may be dose-limiting in patients. However, many other medicines - CVD medicines (e.g. digoxin, β -blockers, calcium channel blockers and ACE inhibitors), opioid analgesics, NSAIDs and some anti-viral and anti-malarial agents - have also been associated with the development of psychiatric symptoms. In general such effects are usually dose-related but may occur at normal therapeutic doses / as a drug interaction; elderly or ill patients are most susceptible to psychiatric effects. **Prescribers are recommended to always review a patient's drugs if psychiatric symptoms appear while he/she is receiving pharmacotherapy for an existing medical illness.**