Once the condition is recognised, the patient is best referred to a specialist vulval clinic. Different local arrangements pertain in the United Kingdom, some clinics being multidisciplinary and some led by dermatologists, gynaecologists, or genitourinary physicians. Since the cause of the condition is poorly understood, management is largely pragmatic and several models of care exist. The evidence base for treatment is poor.

Establishing the diagnosis and offering the patients a sympathetic hearing is an important first step. Patients are reassured by the fact that the condition is not psychosomatic in origin and that anxiety, low mood, and reduced pleasurable sensations with sexual arousal are common byproducts of chronic pain that has become associated with sex. No consistent evidence exists to date to show that women with vulval vestibulitis have an increased background rate of psychological disorders. The chronicity and severity of the symptoms often leads to secondary effects on psychological wellbeing and self esteem. This may lead to secondary sexual dysfunction in the patient or her partner, which in turn can exacerbate psychological distress, emotional disequilibrium, low self esteem, and reduced sexual and social functioning.⁴ All of these can become maintaining factors in the condition.

Advice about vulval hygiene practices is required, and patients should be advised to avoid soaps, shower gels, and similar products, and to wash with aqueous cream or emulsifying ointment.⁵ Topical local anaesthetics such as lignocaine ointment are often helpful.⁶ Topical steroid ointments and creams, oestrogen creams, and topical ketoconazole have been used in some centres,⁷ and anecdotal data support their use in some patients. A popular treatment in North America is the use of a diet low in oxalates. This was described in a single case report,⁸ but, in the absence of better evidence, it may perhaps be offered to some patients who prefer a non-medicalised approach to treatment.⁹ Many patients turn to complementary therapies.

Glazer et al have proposed that the condition is caused by a dysfunction of the pelvic floor muscles and have published impressive results for a biofeedback technique.¹⁰ Many patients do have pelvic floor dysfunction, but in some cases this seems to be secondary to the pain. Low dose amitriptyline is the treatment of choice for dysaesthetic vulvodynia and may be useful in some patients, particularly when the pain is not

restricted to attempted vaginal penetration.¹¹ In North America, vestibulectomy, a procedure that involves excision of all or part of the vestibule, has been a popular treatment. Bergeron et al have reviewed 20 published case series and note that impressive results have been obtained, but the lack of controlled studies or long term follow up throws considerable doubt on the validity of the conclusions.¹² In the United Kingdom, this procedure is rarely used.

Whatever therapeutic approach is adopted, the psychological, interpersonal, sexual, and social consequences of the condition need to be assessed. Every clinician managing patients with the condition should have access to a psychologist or psychotherapist with experience of managing sexual dysfunctions in individuals and couples. Many patients find that support from other patients may be helpful. In the United Kingdom, the Vulval Pain Society (www.vul-pain.dircon.co.uk) provides a useful handbook for patients, as does the US National Vulvodynia Association (www.nva.com).

Pat Munday *consultant genitourinary physician*

(pat.munday@whht.nhs.uk)

Ann Buchan *psychotherapist*

Watford Sexual Health Centre, Watford General Hospital, Watford, Hertfordshire WD18 0HB

Competing interests: None declared.

- 1 Friedrich EG Jr. Vulvar vestibulitis syndrome. *J Reprod Med* 1987;32:110-4.
- 2 Boardman LA, Peipert JF. Vulvar vestibulitis: Is it a defined and treatable entity? *Clin Obstet Gynecol* 1999;42:945-56.
- 3 Paavonen J. Vulvodynia—a complex syndrome of vulvar pain. *Acta Obstet Gynecol Scand* 1995;74:243-7.
- 4 Van Lankveld JJD, Philomeen TH, Weijnenborg M, Ter Kuile MM. Psychological profiles of and sexual function in women with vulval vestibulitis and their partners. *Obstet Gynecol* 1996;88:65-70.
- 5 Ridley CM. Vulvodynia: theory and management. *Dermatol Clin* 1998;16:775-8.
- 6 Zolnoun DA, Hartmann KE, Steege JF. Overnight 5% lidocaine ointment for treatment of vulvar vestibulitis. *Obstet Gynecol* 2003;102:84-7.
- 7 Eva LJ, Reid MN, Maclean AB, Morrison GD. Assessment of response to treatment in vulvar vestibulitis syndrome by means of the vulvar algesimeter. *Am J Obstet Gynecol* 1999;181:99-102.
- 8 Solomons CC, Melmed MH, Heitler SM. Calcium citrate for vulvar vestibulitis. *J Reprod Med* 1991;36:879-82.
- 9 Poole S, Ravenhill G, Munday PE. A pilot study of the use of a low oxalate diet in the treatment of vulval vestibulitis. *J Obstet Gynaecol* 1999;19:271-2.
- 10 Glazer HI, Rodke G, Swencionis C, Hertz R, Young AW. Treatment of vulvar vestibulitis syndrome with electromyographic biofeedback of pelvic floor musculature. *J Reprod Med* 1995;40:283-90.
- 11 Munday PE. Response to treatment in dysaesthetic vulvodynia. *J Obstet Gynaecol* 2001;21:610-3.
- 12 Bergeron S, Binik YM, Khalife S, Pagidas K. Vulvar vestibulitis syndrome: a critical review. *Clin J Pain* 1997;13:27-42.

Inhaled insulin

May prove to be a panacea

For over 80 years exogenous insulin has been given by injection. The injection devices have improved—disposable syringes and pen injection devices are more convenient and less traumatic than the boil to sterilise, use until too blunt devices of yesteryear—but patients and healthcare professionals remain uneasy about the concept of injections. Yet the evidence based drive for increasingly tight glycaemic control means that more patients should be offered more injections. A recent attempt to circumvent the need for injection that may soon hit a clinic near you is the use of the

lung as an absorption pathway, with the development of insulins to be taken by inhalation. Two versions, a powder and an aerosol, may be nearing launch.

Insulin can be effective given by inhalation. This was first shown in 1971, although the early work was not pursued, and it was not until 2000 that the modern era of inhaled insulin began.^{1 2} The bioavailability is 10-15% and the dose equivalent about three times that of injected insulin. The pharmacodynamics of inhaled insulin offer an action profile with a fast onset (although slightly longer run-off) akin to that of rapid

acting insulin analogues given subcutaneously, which in studies have shown better postprandial glucose control and less tendency to nocturnal hypoglycaemia.²⁻³ A Cochrane review of randomised controlled trials comparing inhaled with injected short acting unmodified human insulin used for prandial insulin replacement, in conjunction with a basal injected insulin, concluded that inhaled insulin provided equivalent control to fully injected regimens.⁴ However, the injected regimens were not always optimised: analogue insulins were not included, and control groups often simply continued their pre-trial regimens of injection twice daily. An opportunity to improve control with injected insulin was missed. With either regimen, fewer than 25% patients achieved optimal control. The included trials were short and conducted in patients with type 1 or 2 diabetes already on insulin. The review did not examine trials of inhaled insulin added to oral agents, but the data would again imply bioequivalence. In patients with type 2 diabetes, adding inhaled insulin to oral hypoglycaemic regimens does improve control more than doing nothing.⁵

The advantages of inhaled over injected insulins to date relate to patients' preferences. This is important—apart from patients' comfort, an expensive new insulin could have huge potential advantage if it encouraged adherence and resulted in more patients with diabetes achieving treatment targets. Sadly, the published data on patients' satisfaction, superficially encouraging, are difficult to interpret, as invariably patients have been comparing a new treatment with an old one. When a specially designed questionnaire was used, treatment satisfaction improved significantly in patients with type 1 and type 2 diabetes on taking part in the trials, irrespective of whether the mealtime insulins they took were injected or inhaled.⁶⁻⁸ Although the improvement was greater with inhaled insulin the injected insulin treatment was identical to pre-trial treatment limiting the potential for improvement. Notably, improvement in treatment satisfaction correlated with improved glycaemic control. Might greater satisfaction have been obtained with injected regimens if these had been optimised effectively? Were the studies just too short to show the biomedical gains one might anticipate from a treatment expressly designed to support compliance, or do the problems of insulin therapy extend beyond a dislike of needles?

Inhaled insulin has potential problems. The bioavailability is affected by asthma (decreased) and smoking (increased).⁹⁻¹⁰ Of course, if patients really dislike injections so much inhaled insulin might make its biggest impact on complications of diabetes if it were to be available only to proved non-smokers. Formation of anti-insulin antibodies is higher with inhaled insulin, and although this is dismissed as not affecting insulin requirement over time, older diabetologists will remember the drive to reduce insulin antibody formation, with the fears that antibodies delay and render unpredictable insulin absorption and even that antibody-antigen complexes may increase risk of microvascular disease.¹¹ Finally, there have been concerns about possible long term effects of insulin on lung structure and function, although current published trials report no deleterious effects over the short-term.

Few people like injections and some are so terrified they refuse appropriate treatment for diabetes. Many are

discouraged by previous experience of injections—none of whom will have used current insulin injection devices—and by healthcare professionals using injection therapy as a threat in a (vain) attempt to improve adherence. For patients with established type 1 diabetes lack of freedom to eat or not eat and the demand for (painful) blood glucose testing may be much more of an issue than injection therapy itself.¹² In one study only 14% of injections were missed because they were injections.¹³ In this group healthcare providers will need more robust evidence of patients' preference than is currently available. Where inhaled insulins could really have an impact (in the developed world) will be if healthcare professionals and patients start to use insulin much earlier and more aggressively in type 2 diabetes, affecting the progression of diabetic complications. In the developing world, where cultural taboos against injection treatments may be even more real than here, inhaled insulin may be expected to deliver more in terms of health benefit—but is not likely to be more affordable or available than the currently inadequate supplies of injected insulin. Meanwhile, all patients are waiting to see if the new inhalations are safe. If they are, and if they are cheap enough, at least one barrier to better diabetes treatment may fall.

Stephanie A Amiel *professor*

Department of Medicine, King's College School of Medicine, London SE5 9PJ

K George M M Alberti *professor*

Department of Endocrinology and Metabolic Medicine, Imperial College, St Mary's Hospital, London W2 1NY
(george.alberti@ncl.ac.uk)

Competing interests: KGMMA has received consultancy fees from Pfizer and non-specified research funds from NovoNordisk; SA has received consultancy fees from Aventis, Pfizer, and NovoNordisk for use in research.

- 1 Wigley FM, Londono JH, Wood SH, Shipp JC, Waldman RH. Insulin across respiratory mucosae by aerosol delivery. *Diabetes* 1991;20:552-7.
- 2 Heinemann L, Klappoth W, Rave K, Hompesch B, Linkeschow R, Heise T. Intra-individual variability of the metabolic effect of inhaled insulin together with an absorption enhancer. *Diabetes Care* 2000;23:1343-7.
- 3 Kim D, Mudaliar S, Chinnapongse S, Chu N, Boies SM, Davis T, et al. Dose-response relationships of inhaled insulin delivered via the aerodose insulin inhaler and subcutaneously injected insulin in patients with type 2 diabetes. *Diabetes Care* 2003;26:2842-7.
- 4 Royle P, Waugh N, McAuley L, McIntyre L, Thomas S. Inhaled insulin in diabetes mellitus. *Cochrane Database Syst Rev* 2003;CD003890.
- 5 Weiss SR, Cheng SL, Kourides IA, Gelfand RA, Landschulz WH. Inhaled Insulin Phase II Study Group. Inhaled insulin provides improved glycemic control in patients with type 2 diabetes mellitus inadequately controlled with oral agents: a randomized controlled trial. *Arch Intern Med* 2003;163:2277-82.
- 6 Capperelli JC, Gerber RA, Kourides IA, Gelfand RA. Development and factor analysis of a questionnaire to measure patient satisfaction with injected and inhaled insulin for type 1 diabetes. *Diabetes Care* 2000;23:1799-803.
- 7 Gerber RA, Capperelli JC, Kourides IA, Gelfand RA. Treatment satisfaction with inhaled insulin in patients with type 1 diabetes: a randomized controlled trial. *Diabetes Care* 2001;24:1556-9.
- 8 Capperelli JC, Cefalu WT, Rosenstock J, Kourides IA, Gerber RA. Treatment satisfaction in type 2 diabetes: a comparison between an inhaled insulin regimen and a subcutaneous insulin regimen. *Clin Ther* 2002;24:552-64.
- 9 Himmelman A, Jendle J, Mellen A, Petersen AH, Dahl UL, Wollmer P. The impact of smoking on inhaled insulin. *Diabetes Care* 2003;26:677-82.
- 10 Henry RR, Mudaliar SR, Howland WC 3rd, Chu N, Kim D, An B, Reinhardt RR. Inhaled insulin using the AERx Insulin Diabetes Management System in healthy and asthmatic subjects. *Diabetes Care* 2003;26:764-9.
- 11 Selam JL. Inhaled insulin for the treatment of diabetes: projects and devices. *Expert Opin Pharmacother* 2003;4:1373-7.
- 12 Bradley C, Todd C, Gorton T, Symonds E, Martin A, Plowright R. The development of an individualized questionnaire measure of perceived impact of diabetes on quality of life: the ADDQoL. *Qual Life Res* 1999;8:79-91.
- 13 Zamanini A, Newson RB, Maisey M, Feher MD. Injection related anxiety in insulin treated diabetes. *Diab Res Clin Pract* 1999;46:239-46.