Sexual health and dysfunction in men and women with diabetes

David Edwards and Nicholas Forgione

Sexual dysfunction is common in people with diabetes and, although much research has focused on erectile dysfunction, there is a paucity of knowledge regarding sexual dysfunction in women. Despite the evidence, sexual dysfunction is poorly evaluated and managed in patients with diabetes. Taking a basic sexual history is therefore an important skill for a primary care clinician, as an individual's sexual background will help to provide the appropriate treatment, be it pharmacological or psychological. This article discusses the identification and treatment of male and female sexual dysfunction in people with diabetes and explores how to take a sexual history.

Sexual dysfunction is common in people with diabetes. Much medical research has focused on male sexual dysfunction, particularly erectile dysfunction (ED). In general, male sexual dysfunction is more obvious and measurable than female sexual dysfunction. There is also more research into ED because effective treatments have been developed. This gender imbalance is being addressed as more research on female sexual dysfunction is published. This article looks first at the identification and treatment of male and female sexual dysfunction and then at how best to conduct a consultation about sexual dysfunction.

Sexual health in men with diabetes Erectile dysfunction

An Australian survey showed that at least one in five men over the age of 40 years has erectile problems and about one in 10 men is completely unable to have an erection (Andrology Australia, 2014). About 50% of men with diabetes will suffer from ED within 10 years of the diagnosis and this may be a manifestation of more generalised vascular disease. ED can be defined as the persistent inability to attain or maintain an erection that lasts long enough for satisfactory sexual activity (Hatzimouratidis et al, 2010). ED affects over half of men with diabetes, (Diabetes UK, 2013) and around 5% of men with ED have undiagnosed diabetes (Nieschlag et al, 2006). It is three times more common and occurs 10–15 years earlier in life in men with diabetes than those without (Feldman et al, 1994).

An erection is initiated by sexual stimulation and is a vascular process controlled by the autonomic nervous system. The blood vessels in the corpora cavernosa dilate, leading to increased arterial inflow and reduced venous outflow. Smooth muscle relaxation is crucial, and nitric oxide (NO) has been identified as the agent largely responsible for smooth muscle relaxation in the corpora cavernosum. NO stimulates guanylate cyclase, which leads to increased production of cyclic guanosine monophosphate, and it is thought that this induces smooth muscle relaxation through the opening of calcium channels (Price, 2010). In men with diabetes, evidence suggests that autonomic neuropathy and endothelial dysfunction contribute to the failure of NO-induced smooth muscle relaxation, resulting in ED (Sáenz de Tejada et al, 1989; 2004). The pathophysiology in diabetes is complex, however, and knowledge has been gradually increasing since the 1990s (Cellek et al, 2013).

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Article points

- Men with diabetes are more likely to develop erectile dysfunction, have androgen deficiency, premature ejaculation, balanitis, phimosis, Peyronie's disease and penile fibrosis than men without diabetes.
- 2. Women with diabetes may present with sexual dysfunction, fungal and bacterial infections, polycystic ovarian syndrome and fertility problems.
- Clinicians can encourage patients to provide a full sexual history by listening, looking interested, maintaining eye contact and providing encouraging verbal and non-verbal cues.

Key words

- Androgen deficiency
- Contraception
- Sexual dysfunction

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Page points

- Erectile dysfunction (ED) in men with diabetes is often multifactorial in aetiology and can be more severe and resistant to treatment than in men without ED.
- 2. There is evidence that ED may be an early marker for endothelial dysfunction, and that cardiovascular health should be assessed in men presenting with ED.
- 3. The individual presenting with ED must be medically assessed. Assessment should involve a sexual, medical, psychosocial and cultural evaluation.
- 4. Three phosphodiesterase-5 (PDE5) inhibitors are currently available in Australia – sildenafil, tadalafil and vardenafil

Box 1. Factors involved in erectile dysfunction in diabetes.

- Autonomic neuropathy
- Peripheral neuropathy
- Hypertension
- Peripheral vascular disease
- Hyperlipidaemia
- Drug-related side effects
- Hypogonadism with reduced sexual desire (double risk)
- Psychological factors including depression
- Ejaculatory disorders
- Retrograde ejaculation or anejaculation
- Reduced sensation (e.g. Peyronie's disease, balanitis, phimosis, fibrosis)

Assessment, management and treatment of erectile dysfunction

The MALES (Men's Attitudes to Life Events and Sexuality) study demonstrated that 64% of men with ED reported at least one comorbidity (Rosen et al, 2004). ED in men with diabetes is often multifactorial in aetiology (Box 1) and is more severe and resistant to treatment than in men without diabetes. ED may be a marker for diabetes, depression, lower urinary tract symptoms and cardiovascular disease, and has an adverse impact on quality of life. It is vital that when individuals attend for an appointment related to their diabetes, every consideration and opportunity is given by the primary care team to optimise their lifestyle, including smoking cessation and encouraging exercise. Smoking can increase the risk of ED (Feldman et al, 1994) and quitting smoking may improve erectile function, though the degree of improvement is dependent on factors such as the severity of the ED prior to quitting and the presence of other significant health problems.

Evidence suggests that ED may be an early marker for endothelial dysfunction (Pegge et al, 2006), and that cardiovascular health should be assessed in men presenting with ED. Furthermore, the risk of developing coronary heart disease is doubled for men with ED and type 2 diabetes compared with men without ED (Ma et al, 2008). With this in mind, "getting fit for sex" can be the gateway to improving overall health.

It is important that the individual presenting with ED (whether or not he has diabetes) is medically assessed. Assessment involves a sexual, medical, psychosocial and cultural evaluation. Physical examination should include a full cardiovascular, neurological and genito-urinary assessment. Initial blood tests that should be considered when assessing a man with ED are lipids, glucose, HbA_{1c} and androgens. Full blood count, liver function and thyroid function tests can be useful additional measures. Testing for prostate-specific antigen, creatinine and electrolytes should also be considered. Clinicians should adopt a "treat to target" approach to issues such as hypertension and hypercholesterolaemia.

Drug therapy

Three phosphodiesterase-5 (PDE5) inhibitors are currently available in Australia – sildenafil, tadalafil and vardenafil. These are usually prescribed as "on demand" dosing, though tadalafil 5 mg can be used as daily dosing. The treatment success rate with sildenafil in men with diabetes has been reported as 56–59% (Price et al, 1998; Rendell et al, 1999). The choice between these treatments usually depends on the preference of the individual. Many men with diabetes require the maximum dose of PDE-5 inhibitor and it should also be made clear that the drugs are only effective in combination with sexual stimulation.

It has been suggested that men who have not responded to treatment with a PDE-5 inhibitor may be successful with further education and attempts at intercourse. One study reported that intercourse success rates in men treated with sildenafil reached a plateau after eight attempts. It can be concluded that men should attempt intercourse eight times using the maximum recommended dose of PDE-5 inhibitor before being considered a non-responder (McCullough et al, 2002). There is some evidence that PDE5 inhibitor use in men with type 2 diabetes may be associated with a reduction in all-cause mortality (Anderson et al, 2016).

Other treatments

It may be helpful to prescribe a vacuum erection device (VED) for use on a daily basis as a penile trainer to encourage blood flow into the penis and as a confidence builder, as many people with ED have been without erections for several years. The VED is a suitable alternative for men who do not want to take or have contraindications to other pharmacological therapies. A consensus statement that draws together recommendations for post-surgical ED has confirmed that using a VED either alone or in combination with other treatments can be helpful (Kirby et al, 2013). It is not unusual for men to require more than one therapy for their ED, which may include testosterone replacement.

Other forms of ED treatment include injections into the corpora cavernosum, or penile implant surgery. In men with neuropathy, alprostadil injection therapy has been shown to be an effective treatment for ED (Porst, 1996).

Other novel treatments for ED include lowintensity extracorporeal shock wave therapy (Vardi et al, 2012). This procedure has been demonstrated to work on humans and may add another dimension to treating ED. Stem-cell therapy when related to "restoration of normal penile vasculature and neuronal homeostasis" is also of interest (Albersen et al, 2013). Similarly, NO-releasing microspheres have been shown to improve ED in diabetic rats (Soni et al, 2013). Time will tell whether these studies become part of routine ED management.

Guidelines for the management of ED can be accessed on the Andrology Australia website (www.andrologyaustralia.org).

Therapies that may cause or worsen erectile dysfunction

Men with diabetes are commonly prescribed medications that may include ED as a side effect, and some people will stop taking these medications as a result, often without telling their doctor. Such drugs include statins, antihypertensive and antidepressant medications (e.g. non-selective beta-blockers and diuretics). However, withdrawal of a drug could compromise the treatment of another important condition and it is important to remember that the problem being treated, as well as the drugs prescribed to treat it, can be associated with ED. It may be possible to change or modify an individual's treatment to drugs that are less likely to impact erectile function.

Androgen deficiency

Androgen deficiency affects about 1 in 200 men under the age of 60 and can present with symptoms of reduced libido or ED (Nieschlag et al, 2004). In a study by Kapoor et al (2007), 20% of men with diabetes had a total testosterone level of <8 nmol/L and 31% had a testosterone level between 8 and 12 nmol/L. To prescribe testosterone under the Australian Pharmaceutical Benefits Scheme, the patient must have a testosterone level of <6 nmol/L or a testosterone level between 8 and 15 nmol/L with a high luteinizing hormone, confirmed by at least two blood samples taken on different mornings, and the patient must be treated by or in consultation with a specialist urologist, endocrinologist or sexual health specialist. GPs should refer to the Pharmaceutical Benefits Scheme for full details.

It is important that healthcare professionals screen people for hypogonadism, as there is a strong association between low testosterone and mortality and morbidity. The 10-year mortality is almost twice as high in men with low testosterone when compared with men in the highest percentile (Shores et al, 2006). Men with type 2 diabetes have double the rate of hypogonadism (Mulligan et al, 2006).

There are various preparations that are available for testosterone replacement therapy, including topical gels and 3-monthly injections. The individual needs to be monitored after 3–6 months, at 12 months and at least annually thereafter. This includes a digital rectal examination and blood tests, total testosterone, full blood count and liver function test. Guidelines concerning the management of androgen deficiency are available from Andrology Australia.

Other common diabetes-related sexual problems in men

There is a range of other conditions that occur more commonly in men with diabetes, such as premature ejaculation (PE), balanitis and

Page points

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- 2. Men with diabetes are commonly prescribed medications that may include erectile dysfunction as a side effect; some will stop taking these medications as a result.
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Page points

- 1. Men with poor metabolic control are more likely to report premature ejaculation.
- 2. The prevalence of female sexual dysfunction in women with diabetes is between 14% and 71%.
- Low desire and reduced lubrication are the most commonly reported female sexual dysfunctions.
- Simple but effective treatment for female sexual dysfunction includes topical hormone replacement therapy and/or lubricants.

phimosis, which can make sexual activity uncomfortable or painful. It is therefore important that full enquiry is made regarding these conditions.

PE is common in men with diabetes. One study reported a prevalence of 32.4% in men with type 2 diabetes aged under 50 years and 67.6% in such individuals above 50 years. Men with poor metabolic control were 9.6 times more likely to report PE compared with those who had good metabolic control (El-Sakka, 2003). Dapoxetine is available for prescribing to men aged between 18 and 64 years who experience PE. It is a short-acting, quick-onset selective serotonin reuptake inhibitor. It is taken orally and can be used as needed (approximately 1–3 hours prior to sexual activity). Other longer-acting selective serotonin reuptake inhibitors such as fluoxetine, paroxetine and sertraline are also commonly used.

Balanitis (inflammation of the glans penis) can have both physical and psychological effects on ED and intercourse owing to irritation, pain, discharge and anxiety associated with transmitting a fungal infection to a partner. The prevalence of balanitis in men with diabetes was found to be 16% compared with 5.8% in men without diabetes (Fakjian et al, 1990). Furthermore, Drivsholm et al (2005) found that 12% of men had suffered from balanitis in the 2 years prior to them being diagnosed with diabetes.

Phimosis (a condition where the foreskin cannot be retracted) and Peyronie's disease (growth of connective scar tissue in the penis) can also affect the ability to have intercourse, and both are more common in men with diabetes.

The prevalence of Peyronie's disease in men with diabetes and ED has been estimated as 20.3% (Arafa et al, 2007). Data on the natural history of Peyronie's disease suggest that 13% of cases will gradually resolve, 47% will remain stable and 40% will worsen (Gelbard et al, 1990). There are various treatments available, directed at those in whom the condition is getting worse, including surgery and verapamil injection.

Phimosis is common in men with diabetes. One study showed that 32% of men presenting at a urology clinic had diabetes and phimosis (Bromage et al, 2008), reinforcing the need to check fasting blood glucose levels when this condition is discovered. Physiological phimosis may just require an improvement in hygiene and observation, whereas pathological phimosis will require referral to a urologist.

Diabetes can also cause penile fibrosis due to loss of endothelium and smooth muscle cells from the corpus cavernosum (Burchardt et al, 2000).

Sexual health in women with diabetes

The paucity of knowledge regarding female diabetes and sexual health is only gradually being addressed. Research has been difficult to design and there are many methodological problems (De Veciana, 1998).

Nowosielski et al (2010) conducted an analysis of 544 Polish women, as well as reviewing a number of studies on women with diabetes. The authors found that the prevalence of female sexual dysfunction in women with diabetes was between 14% and 71% (17-71% with type 1 and 14-51% with type 2 diabetes), but they accepted it could be either underor overestimated. Low desire (17-85%) and reduced lubrication (14-76%) were the most frequently reported female sexual dysfunctions; orgasmic and pain disorders were less common (1-66% and 3-61%, respectively). The authors describe possible explanations as to the causes of this, including decreased receptivity to sexual stimulation and endothelial deregulation due to diabetic neuropathy (Nowosielski et al, 2010).

Caruso et al (2006) found that reduced sexual satisfaction and sexual activity were a result of decreased clitoral blood flow. Some authors comment that factors such as age, body mass index, duration of diabetes, glycaemic control, HbA_{1c} level, menopausal status, the use of hormonal and oral contraceptives, or even the presence of diabetes complications could be relevant, whereas others found contradictory results. An association has been found in women with type 1 diabetes between retinopathy and reduced vaginal blood flow, and in the same study women with neuropathy were also found to have reduced clitoral sensitivity (Both et al, 2012).

Simple but effective treatments for female sexual dysfunction include topical hormone replacement therapy (Rees, 2009) using topical oestrogens, vaginal lubricants or a combination of the two. Care is required when advising or prescribing vaginal moisturisers and lubricants (Edwards and Panay, 2016). Many women with type 2 diabetes are post-menopausal and the symptoms of menopause can include vaginal dryness and a lack of libido, among others. Guidelines on the management of post-menopausal women are available from the Australian Menopause Society (www.menopause.org.au).

Pre-conception care

The joint Royal Australian College of General Practitioners/Diabetes Australia (2016) guideline for diabetes in pregnancy recommends that women with diabetes should be informed about the benefits of good pre-conception glycaemic management. In a study by Pearson et al (2007), women who planned for pregnancy and waited until their glycaemia was under control before stopping contraception had lower rates of adverse outcomes. For advice on pre-pregnancy blood glucose targets, refer to www.pregnancyanddiabetes.com.au.

Contraception

Women of childbearing age should be informed about the need for effective contraception. Women with diabetes (type 1 and type 2) with no vascular disease can generally use any form of contraception. However, women with nephropathy, neuropathy, retinopathy or other vascular disease should not use progestogenonly injectable contraception because the side effects can aggravate these complications. These include a tendency to gain weight; a potential increase in coagulation factors for prothrombin (II), VII, VIII, IX and X; a risk of retinal thrombosis; potential glucose intolerance; and, rarely, abscess formation at the injection site. Likewise, combined oral contraceptives should only be used with consideration of the above risk factors. Sterilisation is an option but must be performed in a setting with healthcare professionals experienced in managing diabetes, as well as backup medical support. Contraception

Box 2. Case example.

Mr G, aged 28 years, presented to his GP with erectile dysfunction (ED). He has type 1 diabetes and is treated with a basal-bolus insulin regimen. He has read about the effect that diabetes can have on erections. He has been married for 2 years and has had ED for the past 6 months but still has early morning erections.

After taking a fuller history it transpired that his mother-in-law is dying from cancer and there is family pressure to conceive a first grandchild before she dies. This social pressure had put psychological strain on him to perform sexually to fit in with his wife's ovulation. An explanation of the effect of psychological stress on performance, fertility education and a phosphodiesterase-5 inhibitor enabled a grandson to be conceived and born prior to his mother-in-law's death.

an Australian Clinical Practice Handbook (National Health and Medical Research Council, 2012) provides further guidance on contraceptive management.

Other diabetes-related sexual problems

Fungal and bacterial infections are common in women with diabetes, and vulvovaginal candidiasis occurs more often in this group (Bohannon, 1998). Vulvovaginal candidiasis that is chronically recurring can be a marker for diabetes (Sobel, 1997). It may also occur as a side effect of SGLT-2 inhibitor therapy in both men and women. An improvement in glycaemic control can reduce the risk of reinfection.

Polycystic ovary syndrome (PCOS) is a common problem, affecting 5–10% of all women of childbearing age. The most common features are hyperandrogenism and chronic anovulation, which can lead to infertility and sexual dysfunction (Eftekhar et al, 2014). There is a high prevalence of diabetes (16%) and hypertension (40%) in women with PCOS (Carmina and Lobo, 1999). Metformin can help improve insulin sensitivity sufficiently to induce ovulation and facilitate conception. Clomiphene citrate is the drug of choice in inducing ovulation (Balen and Rutherford, 2007a), but where there is a lack of ovarian response, other more complicated and expensive treatment regimens may be needed (Carmina and Lobo, 1999). Once pregnancy is achieved there is increased risk of spontaneous abortion because of abnormal hormonal levels, abnormal embryos due to atretic oocytes, and an abnormal endometrium (Carmina and Lobo, 1999). In the established pregnancy, there are increased rates of complications such as

Box 3. Taking a basic sexual history.

Below are a range of areas that should be covered to take a full sexual history.

- "So, what appears to be the problem?" Ideally, try to obtain both the patient's and partner's perspective.
- "How long has it been going on?" Establish the severity of the problem.
- "What actually happens?"
- Confirm the duration of relationship, and the partner's age and gender.
- If there are multiple partners, past or present, establish if the problem has occurred with all of them.
- Establish if the partner has a problem. Is it sexual (e.g. atrophic vaginitis), general medical (e.g. arthritis in the knees) or psychological (e.g. depression)?
- Determine if intercourse is possible and, if so, what sort (vaginal, oral or anal)?
- Establish if there is the same problem with masturbation.
- Enquire about sexually transmitted infections past or present (in the patient or partner) and protective measures taken.
- Ask about the need for contraception or if conception is being attempted.
- Explore the general medical and social history (past and present).
- Consider the potential impact of other medical conditions such as cardiovascular disease, depression and cancer (in the patient and partner).
- Establish if there have been any hospital admissions or surgery (especially genital), past or present, not forgetting obstetric or infertility aspects.
- Consider who else is at home (children, elderly relatives, flatmates or animals)?
- Determine if there is any work or family stress, and if there have been any changes in the patient's situation or level of stress?
- Explore if there any cultural or religious factors regarding the patient and partner.
- Obtain a drug history and ask about whether drugs used were prescribed or recreational and when they were initiated or discontinued with regard to a sexual problem.

pre-eclampsia, diabetes, premature labour and stillbirth. In a study by Legro et al (1999), almost a third of women with PCOS of reproductive age had impaired glucose tolerance and 7.5% had diabetes. Basson et al (2010) noted that overweight but not lean women with PCOS have an increased incidence of sexual dysfunctions, noting that further research in such women with PCOS was needed. The authors also commented that an "optimal balance of hormonal milieu is critical to normal sexual functioning" but that hormones were only one component.

Diabetes-related infertility in men and women

The link between diabetes and ED has already been discussed and needs to be assessed when couples present with fertility issues. Integrity of the central and peripheral neurotransmitters and autonomic nervous system are of paramount importance for erection and ejaculation (Sáenz de Tejada and Goldstein, 1988).

The main link between women with diabetes and fertility problems appears to be obesity. Weight loss improves not only the endocrine profile but also the reproductive outcome, and 5-10% weight loss can reduce central fat by as much as 30% (Norman et al, 2004). Insulin resistance is an important pathophysiological abnormality (Balen and Rutherford, 2007b) and the greater the degree of insulin resistance, the longer the time interval between menstrual bleeds (Balen et al, 1995).

Effect of diabetes on psychological, physical and social wellbeing

The pathophysiological changes of sexual dysfunction that are associated with diabetes are mainly due to a variable combination of neuropathy, vasculopathy, hypogonadism and locally-occurring pathological factors. Although the physical effects of diabetes are well established, it should be remembered that social and psychological aspects can also play a part in sexual dysfunction. This is illustrated by the case example in *Box 2*.

The chronic nature of diabetes and its complications can lead to relationship problems, including arousal difficulties and sexual inhibition. Men with diabetes may need more physical stimulation, which may not be appreciated by the partner, who might feel unloved and less attractive. This can then lead to poor self-esteem, anxiety and depression (Bancroft and Gutierrez, 1996).

Consultation and referral Discussing sex with an individual

A number of barriers that stop healthcare professionals raising the subject of sex have been identified (Athanasiadis et al, 2006):

Lack of relevant training.

- Embarrassment.
- Time constraints.
- Conservative sexual beliefs.
- Insufficient knowledge on sexual health.
 Insufficient acceptance of the individual's sexual profile.

Respecting confidentiality at all times can be especially important in this area. Furthermore, cultural and religious attitudes need to be considered. It is also important to enquire about the partner's sexual and general health. It is always helpful to encourage the partner to attend or offer for him or her to come to the follow-up appointment to obtain this person's perspective.

Adolescents with diabetes are not excluded from having anxieties concerning sexual matters, and particular attention needs to be paid to this group; they may be having difficulty enough just coming to terms with their diagnosis of diabetes.

Finally, it is worth being aware that people may present with a "calling card" (e.g. athlete's foot) to test the clinician out. It is important to ask about sexual function so that the individual has the opportunity to voice any concerns.

Taking a basic sexual history

Every interaction between patient and clinician will be subtly different, but in broad terms the "art" of taking a sexual history is to listen, look interested, maintain good eye contact and be encouraging with both non-verbal and verbal cues (*Box 3*). It is particularly important in such conversations that the clinician adopts a non-judgemental, caring and professional consulting style to minimise embarrassment.

As part of the consultation, it is vital to ascertain what actually happens (and what does not) during sexual activity. Also, one needs to be prepared that consultations covering this topic may run into other areas. For instance, ED may be an expression of underlying psychosexual issues, and this may need to be discussed with a trained counsellor.

When to refer

Unlike many topics in general practice, sexual dysfunction seems to have a wide range of referral patterns. Some clinicians refer early to a specialist

while others will manage the majority of their patients, carrying out investigations and treating where necessary. Typical reasons to refer include:

- Pronounced psychosexual therapy needs.
- A desire to initiate therapies for ED such as intracavernosal injections, and surgery options.
- Non-response to PDE-5 inhibitors.
- Consideration of testosterone replacement therapy.
- A requirement for specialist investigations for comorbidities, such as exercise tolerance testing.
- Referrals for comorbidities found during assessment, such as prostate cancer.
- The sexual dysfunction being of a nature that is outside the competence of the clinician.

Conclusion

Sexual problems are common in both men and women with diabetes. Healthcare professionals need to be comfortable asking individuals about such problems and, where necessary, refer on to sexual dysfunction specialists. By using the individual skills of healthcare professionals, both the person's sexual difficulties and any medical or lifestyle issues can be progressively addressed, so that he or she is empowered and encouraged to holistically improve not only sexual issues but also general health.

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Page points

- Respecting confidentiality at all times can be especially important when discussing a patient's sexual history.
- It is important to ask about sexual function so an individual has the opportunity to voice any concerns.
- Health professionals need to be comfortable asking individuals about sexual problems and to refer patients to specialists when necessary.

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