

Erectile dysfunction in diabetes



Professor
Robert Tattersall

Today's diabetes world is fast moving and exciting; knowledge is accumulating at an astonishing rate. To help understand the present, however, it sometimes helps to examine the past.

In this installment of *Tattersall's Tales*, Robert Tattersall describes the rise in knowledge, and methods for the treatment, of erectile dysfunction (or impotence) from the 19th century to the present day.

In the 19th century, impotence (as it was called in those days), seems to have been a common complication of diabetes. In his 1839 *Principles and Practice of Medicine*, John Elliotson wrote, "There is also one very remarkable symptom: the loss of sexual power and desire. I have never found this symptom absent; and sometimes it has been the very first symptom noticed by the patient." In his 1862 monograph, Frederick Pavy agreed that "loss of virility" was common and suggested vaguely that might be because the condition of the blood was "unsuited for the maintenance of functional activity in the organs in question". Interestingly, Pavy's prize patient, Joseph North, recovered his potency during his 4 months in Guy's Hospital in 1861, which was probably a good advertisement for Pavy's large private practice.

Little new about impotence was published during the first half of the 20th century, and as late as 1950 one could have found extraordinarily divergent views on its frequency. Before giving a lecture to the London Medical Society, Leonard Simpson canvassed the views of a number of experts. Elliott Joslin replied that, "impotence was very rarely complained of or observed [sic!]" in his very large clinic, while his fellow diabetes experts, Russell Wilder of the Mayo Clinic and Franklin Peck of Indianapolis, were struck by how common it was, and how often it represented a presenting symptom of diabetes. Simpson's experience was that it was uncommon in those whose diabetes had always been well controlled. Nevertheless, he added, "the incidence of impotence, elicited by specific questioning in contrast to spontaneous statements by patients, is by no means negligible."

Apart from the fact that there was considerable reticence about discussing sexual matters in the 1940s and '50s, definitions of impotence were not standardised. Simpson defined male sexual potency as "the ability to initiate, sustain and successfully conclude the act of sexual intercourse to the satisfaction of the male" (Simpson, 1950) – he pointed out that if the words "and to the satisfaction of the female" were added, then half the potent men might have to be reclassified! Putting aside clinical impressions, one of the first quantitative surveys was that of Rubin and Babbot (1958) from the department of obstetrics and gynaecology at the University of Pennsylvania, who found what they described as "a strikingly high incidence of impotence". Their interest arose because most impotent husbands of their female patients turned out to have diabetes. They interviewed 198 unselected men from the local diabetes clinic, and used Alfred Kinsey's 1948 figures as a comparator. From age 30 onwards, impotence was two to five times commoner than in the so-called "normal" men studied by Kinsey; in men with diabetes, its prevalence increased from 25% in those aged 30–39, to 54% for men in their 50s, and 100% in the over 80s. Among the younger men there was no loss of libido, at least at first. As an aside, it seems extraordinary that all studies published up to 1981 used Kinsey's

figures as their standards of comparison, since they were highly selected and sexual mores had changed markedly since the 1940s.

Most experts in the 1960s and 1970s attributed impotence to neuropathy, and, as with other forms of neuropathy, vitamins were used in treatment – presumably with some success since the placebo response in double-blind trials is 20% or higher. In 1959 Harry Keen did a randomised study of carbachol, a cholinergic agonist which stimulates bladder emptying. While the study was not published, Harry's memory is that, despite the specious pharmacological basis, it had some effect, but the gastrointestinal side effects were awful. Endocrinological and psychological factors were also considered as possible aetiological agents. In a 1963 German study of 314 men with diabetes, the (distinguished) authors (Schoffling et al) concluded that many had hypogonadotropic hypogonadism. In younger individuals, treatment for 6 months with 1000 units of chorionic gonadotrophin and 25mg testosterone propionate once- or twice-weekly, was often successful, but some needed treatment for a year or more. These findings were surprising because testosterone had been tried by many others and found only to increase desire and not performance. The alkaloid yohimbine had long had a reputation as an aphrodisiac, and in the 1960s it was marketed as a treatment for impotence in the USA as Afrodex, a mixture of yohimbine, methyltestosterone and nuxvomica. It was never clear to me how effective yohimbine was, and in the early 1970s my bosses disapproved of it for unspecified reasons.

When I started in Nottingham in 1975, textbooks suggested that it was easy to distinguish between organic and psychogenic impotence but, except for a few blatant cases, we did not find it so easy. I remember that we devoted a couple of journal clubs to the problem. At one, Dr Martin Cole, a botanist who ran a sex institute in Birmingham, came to talk about surrogate partners. He thought they might be used as a means of differential diagnosis but we were too conservative to take this up. More promising was the work of Ismet Karacan (1978) in Texas. His patients were admitted to a sleep laboratory and had a strain gauge put round the base of the penis to record erections during REM sleep. Unfortunately, this did not distinguish between hard and flabby erections so, if memory serves me right, Karacan employed an assistant who felt the erection and photographed it with a polaroid camera. My colleague David Hosking repeated this work in our more humble surroundings. The only place where an empty bed could be found was in a ward where we parked our chronic and undischargable patients. This was not ideal since the nature of the neighbours meant that some of the study subjects never got to sleep. Also, the nurses did not regard it as part of their job description to feel and photograph erections. Nevertheless, David did recordings on 30 patients with diabetes and concluded that some had psychogenic impotence (Hosking, 1979). One subject who was totally impotent with his wife had such a large erection that he broke

the strain gauge. After being shown the results, he left his wife, and when I saw him 20 years later was still fully potent.

For those with organic impotence there was no treatment until the London physiologist Giles Brindley showed that injecting papaverine into the corpora cavernosa caused an erection. This was memorable in being the first effective medical treatment for impotence, but also for that way in which Brindley announced his discovery during a lecture at the American Urological Association in 1983. He had injected his penis 15 minutes earlier and, after showing a few slides, dropped his pants to reveal an impressive erection. Memories of those who were present differ but most think he walked among the audience and invited people to feel the quality of his chemically induced erection (Klotz et al, 2005). Most patients were aghast at the idea of sticking needles into their penis, and in the late 1980s vacuum pumps became relatively popular in England. They had actually been invented in the 19th century, but were not widely used until the American businessman, Geddings Osbon, made one in the 1970s to treat his own impotence. FDA approval was given in 1983 and it was marketed as ErecAid. Pumps were always more popular with older than younger men, and the drop out rate was high. Penile implants were another solution but – at least the sophisticated ones – were too expensive for us in Nottingham. Our urologists were also concerned that implanting them in people with diabetes would lead to infection.

The answer to some maidens' prayers, a pill to treat what was now called male erectile dysfunction, came in 1998 from an unlikely source. A phosphodiesterase type-5 inhibitor had been synthesised a few years earlier at the Pfizer laboratories in Sandwich, Kent. This compound, sildenafil, was originally tested as a treatment for angina, but was found to have the (unexpected) side effect of producing erections. Pfizer therefore changed tack and developed it for the treatment of erectile dysfunction, for which it was approved in 1998 and marketed as Viagra (Kling, 1998). It worked slightly less well in men with diabetes, and was equally as effective as Caverject and MUSE (Medicated Urethral System for Erections; Freeman and Bodansky, 1999). Where it scored over the alternative treatments was in terms of convenience and, unlike them, the little blue pill was advertised for free in the form of coverage in newspaper articles. Viagra also scored over Caverject and MUSE in that it could be started in the privacy of a GP surgery. The rest, as they say, is history, and is well known to readers of this journal.

Brindley GS (1983) Cavemosal alpha-blockade: a new technique for investigating and treating erectile impotence. *British Journal of Psychiatry* **143**: 332–7

Freeman MS, Bodansky HJ (1999) Effectiveness of treatment for impotence in diabetic men. *Diabetic Medicine* **16**: 1048–9

Hosking DJ, Bennet T, Hampton JR et al (1979) Diabetic impotence: studies of nocturnal erection during REM sleep. *BMJ* **2**: 1394–6

Karacan I, Salis PJ, Ware JC et al (1978) Nocturnal penile tumescence and diagnosis in diabetic impotence. *American Journal of Psychiatry* **135**: 191–7

*Kinsey AL, Pomeroy WB, Martin CE (1948) *Sexual behaviour in the human male*. WB Saunders, Philadelphia

Kling J (1998) From hypertension to angina to viagra. *Modern Drug Discovery* **1**: 31–8

Klotz L (2005) How (not) to communicate new scientific information: a memoir of the famous Brindley lecture. *BJU International* **96**: 956–7

Rubin A, Babbott D (1958) Impotence and diabetes mellitus. *JAMA* **168**: 498–500

Simpson L (1950) Impotence. *BMJ* **1**: 692–7

Schoffling K, Federlin K, Ditschuneit H, Pfeiffer EF (1963) Disorders of sexual function in male diabetics. *Diabetes* **12**: 519–27

*Alfred Kinsey (1894–1956) was originally an entomologist whose all-consuming interest was gall wasps. He and his associates conducted over 18,500 interviews for this, for the time, scandalous book. For further details of Kinsey's life and methods, see: Gathorne-Hardy J (1998) *Sex the Measure of All Things: A Life of Alfred C Kinsey*. Chatto and Windus, London