Retrograde ejaculation and male infertility

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Incompetence of the internal urethral sphincter causes semen to pass into the bladder. Infertility can be successfully treated by restoring normal ejaculation or by sperm retrieval techniques.

Retrograde ejaculation (RE) involves semen passing into the bladder through a patent bladder neck at the time of ejaculation, rather than down the urethra and into the vagina. First described by De Albuquerque in 1939, RE has become increasingly well recognized. Despite this it remains an uncommon cause of infertility, affecting fewer than 1% of couples undergoing infertility investigations (Okada et al, 1998).

NORMAL EJACULATION

The internal sphincter (sphincter vesicae) surrounds the preprostatic part of the male urethra and consists of circular smooth muscle fibres. The external sphincter (or sphincter urethrae, responsible for urinary continence) is found surrounding the membranous urethra (*Figure 1*). Both sphincters are closed in the resting state and both open to allow urination (*Figures 2a* and *b*).

Ejaculation is a complex process and so is divided into three phases. The first phase is emission, the passage of seminal fluid into the posterior urethra aided by contraction of the vasa deferentia. The second phase involves closure of the bladder neck (the internal sphincter), forming a pressure chamber between the two sphincters (*Figure 2c*). The third phase, expulsion, is caused by opening of the external sphincter accompanied by rhythmical contractions of the bulbocavernosus and ischiocavernosus muscles. This acts to propel seminal fluid down the urethra (*Figure 2d*) while the internal sphincter remains contracted to prevent retrograde flow into the bladder.

RE occurs if the seminal fluid passes from the posterior part of the urethra into the bladder

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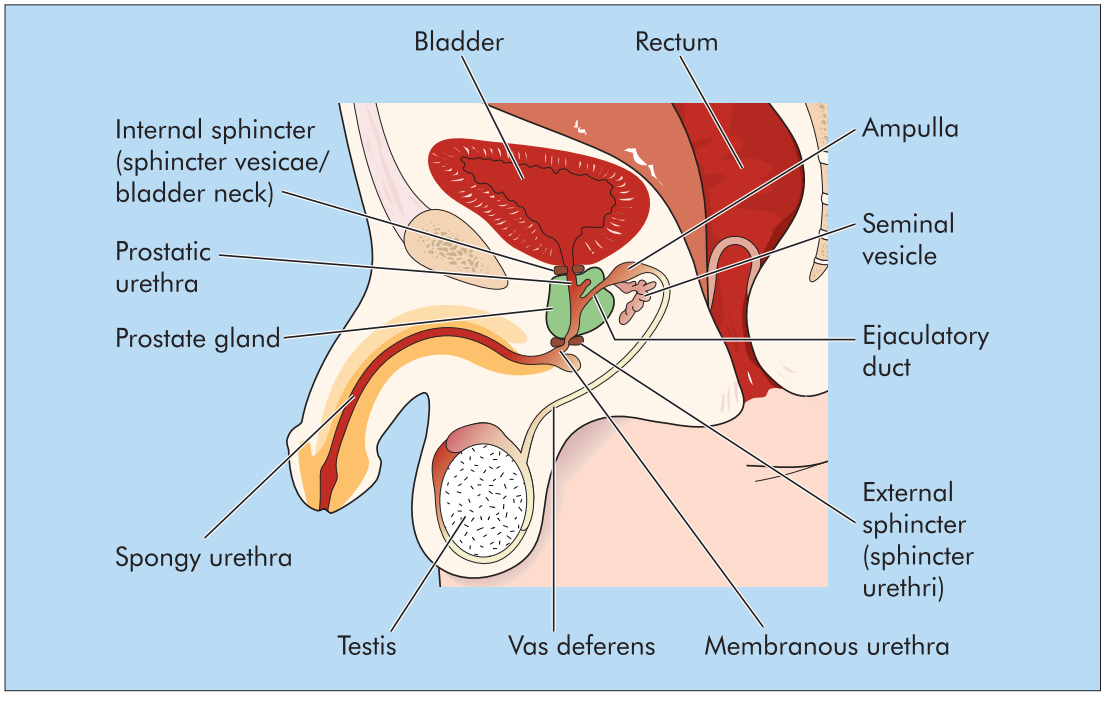

Figure 1. The positions of the internal and external urethral sphincters.

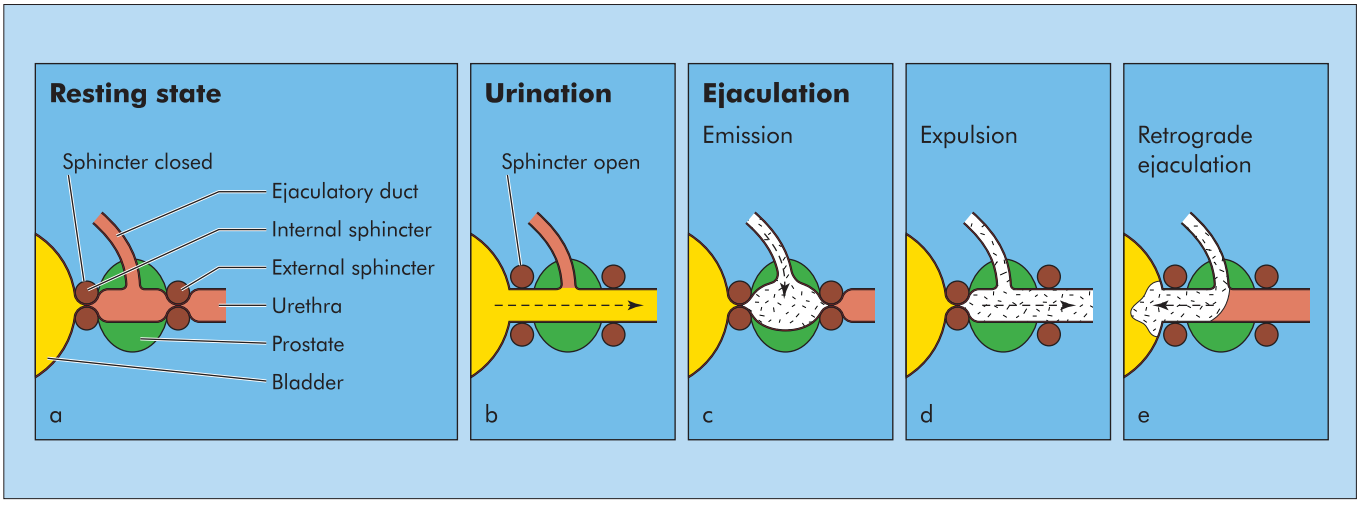

Figure 2. The function of the urethral sphincters during urination and ejaculation.

through a patent bladder neck along the path of least resistance (*Figure 2e*).

AETIOLOGY

RE may be congenital or acquired (*Table 1*). If acquired it may be secondary to a medical condition, surgery or traumatic insult. Additionally the causes of RE should be thought of as either mechanical damage to the internal sphincter or a condition that somehow compromises its innervation.

Bladder neck and prostate surgery

Surgery to the prostate for obstructive urinary symptoms is probably the commonest cause of RE but the men who require surgery tend to be elderly and are not usually worried about their reproductive potential. Reassurance should be all that is required.

Operative nerve damage

Any operation occuring in close proximity to the lumbar spine may cause RE as a result of damage to the sympathetic chain or the hypogastric nerves. The incidence of RE varies and depends on the degree of dissection of the retroperitoneal space. These operations include spinal fixation for kyphoscoliosis, aortic aneurysm repair, abdominoperineal resection for rectal cancer and para-aortic lymph node dissection for testicular cancer.

Diabetes mellitus

RE in diabetic men is well recognized as a result of disturbance of the sympathetic nerves secondary to diabetic neuropathy (Greene and Kelalis, 1967). Patients may complain of a gradual reduction in seminal volume leading to anejaculation at the time of orgasm as a result of disease progression as the neuropathy worsens.

TABLE 1.
Aetiology of retrograde ejaculation

Congenital	Sphincteric	Ectopic ejaculatory ducts or ureters
	Innervation	Spina bifida
Acquired	Sphincteric	Prostate resection
		Bladder neck surgery
	Innervation	Operative nerve damage
		Aortic aneurysm repair
		Lymph node dissection
		Abdominoperineal resection of rectum
	Diabetes mellitus	
	Spinal injury	
	Drugs	α-blockers
		Antidepressants
Idiopathic		

Spinal injury

Spinal injury often affects young and previously healthy men and can have a devastating effect on fertility through many causes. While the majority of patients can achieve full or partial erection, only 3–15% can demonstrate ejaculatory capability. External vibratory massage and electrical stimulation have been used to achieve ejaculation. However, whether spontaneous or stimulated, ejaculation in these patients will often be retrograde.

Drugs

Alpha-receptor blocking agents used in patients with benign prostatic hypertrophy have RE as a well-recognized side effect as they work to relax the prostatic smooth muscle (Debruyne, 2000).

Antidepressant medications reported to have caused RE include clozapine and risperidone.

Whatever the drug cause of RE, the effect seems to be reversible on cessation of medication. It is therefore vital to warn patients that they may experience this side effect while on the drug and that it is not harmful and potentially only temporary.

Congenital causes

Ectopic placement of structures near the internal sphincter (such as ureters or ejaculatory ducts) may interfere with its mechanical function (Lee et al, 2000) and spina bifida, with its variable effects on the spinal nerves, may also cause RE.

DIAGNOSIS

A history of any of the medical conditions or operations described above should raise suspicion of RE as a possible cause of subfertility. Diagnostic features of RE include intermittent emission of ejaculate, orgasm without ejaculation and the presence of sperm in post-coital specimens of urine.

RE with antegrade passage of some of the initial sperm-free portion of the ejaculate suggests that a condition called partial RE may exist and so a low semen volume (not just an absent ejaculate) should raise suspicion of RE.

TREATMENT

The treatment of infertility associated with RE aims to either restore antegrade (normal) ejaculation or to retrieve spermatozoa from the urine for use in assisted reproductive technologies (*Table 2*).

Restoration of antegrade ejaculation

This may be attempted through surgical means, using drugs or by using special manoeuvres to close the bladder neck at ejaculation.

Operative measures: Some authors have described using surgery to restore antegrade ejaculation, either by fashioning a new internal sphincter after excising old scar tissue or by inserting an artificial sphincter controlled by a pump in the scrotum.

These operations have shown success only for patients whose RE is secondary to sphincter damage and it is unlikely that these techniques would work in those patients whose bladder necks are patent as a result of impaired innervation.

Drug treatments: Many drugs have been found to reverse RE, mainly via α-adrenergic action which produces closure of the internal sphincter. Phenylpropanolamine, brompheniramine and the tricyclic antidepressant imipramine (Aizenberg et al, 1996) have all been used, with the best results seen in those patients whose RE is the result of nerve involvement of diabetes and lymph node dissection.

Thus for RE secondary to a nervous cause, a trial of drug therapy is probably worthwhile as it is non-invasive and tends to have few side effects.

TABLE 2.
Treatment of retrograde ejaculation

Restoration of antegrade ejaculation	Surgical	Refashioning of internal sphincter
		Artificial sphincter implant
	Drug treatments	Brompheniramine
		Tricyclic antidepressants
	Special manoeuvres	Post-coital voiding
		Full bladder
		Catheter balloon tamponade
Sperm retrieval from urine	Medium instillation	
	Oral adjustment of pH and osmolarity	
Surgical sperm retrieval		

Special manoeuvres: A pregnancy achieved by a couple having intercourse as usual followed by the male partner urinating into the vagina has been reported (Marmar et al, 1977), but many couples would find this distasteful.

Partial antegrade ejaculation has been achieved by ensuring the bladder is full during masturbation (Crich and Jequier, 1978), presumably by the full bladder creating an angled valve at the bladder neck.

Antegrade ejaculation has also been achieved by passing a Foley catheter and pulling the balloon against the bladder neck to create a seal (Liukko and Nikkanen, 1979). This enabled 1.5 ml of semen to be used for intracervical insemination but pain and haematuria restricted use of this method. The acceptability of masturbating with an indwelling catheter probably restricts this method to those patients who already have one in situ for urinary reasons.

Retrieving sperm from urine

Sperm retrieved from post-coital urine is often found to be of poor quality in terms of viability and motility and this is thought to be directly attributable to contact with the urine (Vijayakumar et al, 1986).

When sperm has been analysed in different urine samples (Makler et al, 1981) it was found that the majority of urine was hyperosmotic and acidic and rapidly induced complete immobility of the sperm. Adjustment of both the pH and the osmolarity of the urine, before addition of sperm, helped to prevent this harmful effect.

Adjustment of bladder conditions

The majority of publications detailing successful conceptions are case reports (Kamischke and Nieschlag, 1999).

Some authors advocate passing a urinary catheter to empty the bladder followed by instilling a liquid medium to provide a less hostile intravesical environment for the sperm once RE has occurred. For many patients, however, the procedure is unacceptable and may cause them to discontinue treatment.

Many authors instead perform adjustment of the urine conditions by ingestion of alkalinized fluids, followed by voiding of the post-coital urine and semen mixture. However, there is no consensus (or any agreed protocol) as to the best method to achieve optimum pH and osmolarity of the urine orally.

Retrieved sperm have been used in assisted conception technologies such as intracervical insemination, in-utero insemination and intracytoplasmic sperm injection. If it is not possible to retrieve viable sperm from urine then the last resort of surgical sperm retrieval directly from the testis or epididymis (followed by intracytoplasmic sperm injection) can be used (Wood et al, 2002).

CONCLUSION

RE has a number of therapeutic options to aid the chances of conception. If this diagnosis is kept in mind when considering the infertile male it can be easily diagnosed and therefore treated. HM

Conflict of interest: none.

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KEY POINTS

- Retrograde ejaculation is a rare cause of male infertility.
- Retrograde ejaculation is caused by an incompetent internal urethral sphincter.
- Initial treatment is aimed at restoring antegrade ejaculation.
- Assisted conception may be performed using sperm retrieval from urine or directly from the testis.