

Chapter 1 : Disorders of orgasm and ejaculation in men | Read by QxMD

Corresponding author. Australian Centre for Sexual Health, Sydney, Australia; Search for more papers by this author. Conflicts of Interest. Chris McMahon, Paid consultant and clinical trial investigator to Pfizer, Icos Lilly, Bayer, GlaxoSmithKline, American Medical Systems, Johnson & Johnson.

Ejaculatory dysfunctionâ€”the evolution of a new understanding Chris G. After thousands of years, millions of words and pictures, and billions of attempts, he still often finds the goal largely unobtainable. Until recently, our understanding of premature ejaculation PE was an eclectic mix and homogenization of ancient historical and culturally diverse influences. However, recent basic and clinical research has resulted in a new understanding and a paradigm shift in the way we classify, define, evaluate, diagnose and treat PE. Premature ejaculation PE ; ejaculatory dysfunction Submitted Jan 31, Accepted for publication Mar 07, The Bible states that semen was intended to be deposited only in vaginas and mainly for the purpose of procreation. Onan discovered that during coitus he could not ejaculate into Tamar: The Indian god Shiva, who has the power to destroy and create, is often represented with an erect phallus, a symbol of power and fertility. Semen is considered to be a precious substance in Indian cultures and many myths have been created around it 2. Atharva-ved, one of the ancient Indian religious books mentions that drops of blood are required to make one drop of semen. Loss of semen was considered then and still is as a loss of strength. The Kama Sutra was written between the first and fourth centuries AD by Mallanaga, a bachelor belonging to the Vatsyayana sect. It is best described as the lifestyle book of its era which was devoted to personal discipline and offered a range of knowledge that the reader may acquire, to find and keep a partner. Although initially published in Britain in , it was considered by Victorian England to be far too lewd and was not officially available until Part two of the Kama Sutra deals exclusively with sexual intercourse and considers different lengths of time to ejaculation as having various merits. This is a clear reference to the fact that PE causes bother, frustration and relationship friction. Chinese sexology can be traced back many dynasties. The Tang Dynasty â€” AD was considered to be sexually free, and during this period sex was positively encouraged as the means to good health. Early Taoist philosophers saw frequent and long-lasting sex as promoting balance between the Yin negative, dark, feminine and Yang positive, bright, masculine. Sex was considered the very essence of nature and harmony. Delaying or suppressing ejaculation was felt to be beneficial, and a disciplined approach to delaying ejaculation became popular. In the Ming Dynasty [â€”], attitudes to sex became more restricted, and by the Qing Dynasty [â€”], sexuality was repressed and regulated 5. He makes specific reference to PE, but offers no remedy for the problem. Man in the pride of his strength, works like a pestle, and the woman, with lascivious undulations, comes artfully to his aid. Soon all too soon the ejaculation comes! Life, the afterlife, fertility and creation are important parts of Egyptian history, and representations of such can be seen on many temple carvings and paintings. Of particular interest were the remedies that the ancient Egyptians considered useful for various sexual ailments and problems. The lotus flower was an important icon in ancient Egypt 7. Magical properties have been associated with the lotus flower since it arose at the beginning of time from the waters of Nun the original waters 1. It was immortalized in modern times when lotus and corn flowers were discovered in the coffin of Tut-Ankh-Amon. At the first ray of the sun, the lotus flower opens up and releases a hyacinth like scent. When an Egyptian buried his nose in a lotus flower and kept it there for a while, the effect on him may have been considerable, and the scent may have been sufficient to achieve an alteration in consciousness 8. This may have had the effect of reducing anxiety and possibly delaying ejaculation, although there is no specific mention of PE. The evolution of the current understanding and treatment of PE In Gross described what is presumably the first case of rapid ejaculation in the medical literature 9. In , Karl Abraham described rapid ejaculation, which he called ejaculatio praecox During the 20th century our understanding of PE evolved through several distinct periods. Between and the consensus was that PE was a neurosis and psychosomatic disorder linked to unconscious conflicts, and was best treated with classical psychoanalysis Schapiro described two types of PE: Several authors suggested that high levels of anxiety and excessive and controlling concerns about sexual performance and potential sexual failure might distract a man from

monitoring his level of arousal and recognizing the prodromal sensations that precede ejaculatory inevitability has been suggested as a possible cause of premature ejaculation by several authors 14 - However, the causal link between anxiety and premature ejaculation is speculative, is not evidence-based and is in fact contrary to empirical evidence from other researchers. During this period, it was thought that a small number of cases of PE were due to a range of urological disorders including hyperesthesia of the glans penis, a short frenulum of the foreskin or changes in the posterior urethra. Treatment for this subset of sufferers included anaesthetizing ointment, incision of the frenulum, application of solutions of silver nitrate, or total destruction of the prostatic urethral verumontanum by electro-cautery. Although the behaviour therapy treatment model was the treatment paradigm, towards the end of this period an increasing number of publications on treatment with psychoactive drugs, such as off-label clomipramine, appeared in the literature. In the years 1970s, attention was directed towards the development of an understanding of the pathogenesis of lifelong PE. He suggested that lifelong PE was related to a diminished central serotonergic neurotransmission and activation or inhibition of specific 5-HT receptors. This position was supported by the outcome data of a number of animal and psychopharmacological treatment studies on PE. The notion that PE may have a genetic basis was, however, not new and was initially suggested in by Bernard Shapiro who noticed that men with PE seemed to have family members with similar ejaculatory complaints. In the last 10 years [1990s] DNA research in men with lifelong PE and male twin genetic research has supported this genetic hypothesis by providing evidence of genetic polymorphisms of the central serotonergic and dopaminergic system, which is associated with the duration of the IELT 23. During this period an increasing number of publications have reported the pharmacological treatment of PE with a variety of different medications which act either centrally or locally to retard the neuropsychological control of ejaculation and subsequent orgasm. Multiple well-controlled evidence-based studies have demonstrated the efficacy and safety of daily or on-demand administration of SSRIs in delaying ejaculation, confirming their role as first-line agents for the treatment of lifelong and acquired PE 25 - The PE treatment paradigm, previously limited to behavioural psychotherapy, progressively expanded to include drug treatment 13. The pharmaceutical industry finally developed an interest in the identification of potential therapeutic targets and the development of PE pharmacotherapy. In RCTs, dapoxetine 30 or 60 mg taken 1-2 hr before intercourse is more effective than placebo from the first dose, resulting in a 2. Dapoxetine was comparably effective both in men with lifelong and acquired PE 31 and was similarly effective and well tolerated in men with PE and co-morbid ED treated with phosphodiesterase type 5 inhibitor drugs. Dapoxetine has received approval for the treatment of PE in over 50 countries worldwide. The medical literature contains several univariate and multivariate operational definitions of PE 13, 33 - Each of these definitions characterise men with PE using all or most of the accepted dimensions of this condition: The absence of a clear IELT cut-off point in the DSM definitions has resulted in the use of a broad range of latencies for the diagnosis of PE in clinical trials ranging from 1-7 minutes 18, 48 - These ejaculation latencies cut-off points were subjectively chosen by the various authors and were not based on objective measurements of ejaculation latency in men with PE. The failure of DSM definitions to specify an IELT cut-off point means that a patient in the control group of one study may very well be in the PE group of a second study, making comparison of studies difficult and generalization of their data to the general PE population impossible. Although there have been several large evidence-based observational studies, many were methodologically flawed due to a failure to adequately define their study population, and report a prevalence in excess of that suggested by community based normative stopwatch IELT studies 56 - Conclusions regarding the epidemiology of PE and the relationship between PRO measures and IELT based on data from studies with inadequately defined and selected trial groups must be regarded with some caution and cannot be reliably generalized to subjects with this condition. This lack of an evidence based definition and general agreement as to what constitutes PE has hampered clinical research into the etiology and management of this condition, the development of PRO measures to diagnose and assess treatment intervention strategies and is a likely obstacle for regulatory agencies to interpret and assess data from clinical trials of PE investigational drugs. Evidence-based definitions seek to limit errors of diagnosis and thereby increase the likelihood that existing and newly developed therapeutic strategies are truly effective in carefully

selected dysfunctional populations. In addition, a multivariate definition containing several diagnostic criteria will decrease diagnostic errors. In the study of PE, rapidity of ejaculation, perceived ejaculatory self-efficacy or control, and negative personal and interpersonal consequences e. Operationalization is the process of defining a construct or variable by the development of a measure, procedure, or operation, for identification of instances of that construct or variable. Operationalization and the careful determination of cut-offs for each variable will minimize but never completely eliminate inclusion false positive or exclusion errors false negative of PE classification of those who have PE vs. A multivariate definition of PE provides the clinician a more discriminating diagnostic tool. The first contemporary multivariate evidence-based definition of lifelong PE was developed in by a panel of international experts 60 and subsequently revised in into a unified definition with the inclusion of acquired PE. It causes clinically significant distress in the individual. In addition, the DSM-5 definition of PE distinguishes between mild PE ejaculation occurring within approximately 30 seconds to 1 minute of vaginal penetration, moderate PE ejaculation occurring within approximately 15–30 seconds of vaginal penetration and severe PE ejaculation occurring prior to sexual activity, at the start of sexual activity, or within approximately 15 seconds of vaginal penetration. Interested parties including industry observers have, over the past 20 years, witnessed an evolution in our understanding of PE from the initial premise that PE was a psychosexual disorder to a new understanding that some men are born with a genetic propensity to ejaculate rapidly. In parallel with this new understanding, the way we classify, define, evaluate, diagnose and treat PE has undergone a paradigm change. This special focused edition of *Translational Andrology and Urology* explores the conundrum of PE and is doing so attempts to demystify the epidemiology, pathogenesis and etiology, dimensions, diagnosis and management of this common sexual complaint. Footnote Conflicts of Interest: The phallus in art and culture. Historical Committee of the European Association of Urology, An alternative, combined approach to the treatment of premature ejaculation in Asian men. Dhat syndrome--a useful diagnostic entity in Indian culture. *Br J Psychiatry*; Berkley Publishing Group, Stanford University Press, The urology of Pharaonic Egypt. Sacred luxuries, fragrance, aromatherapy and cosmetics in ancient Egypt. Cornell University Press, Practical Treatise on Impotence and Sterility. Publishing House Enke, *Zeitschr Aerztl Psychoanal* ;4: A review of cases. Group treatment of premature ejaculation. *Arch Sex Behav* ;3: How to Overcome Premature Ejaculation. *The New Male Sexuality*, Toronto: The role of anxiety in premature ejaculation: *Arch Sex Behav* ; The management of premature ejaculation. *J Int Med Res* ;5:

Chapter 2 : Standard operating procedures in the disorders of orgasm and ejaculation | Read by QxMD

McMahon, C. G., Waldinger, M., Rowland, D., Assalian, P., Kim, Y. C., Bechara, A. and Riley, A. () *Ejaculatory Disorders, in Standard Practice in Sexual Medicine.*

For the complete report please refer to *Sexual Medicine: Sexual Dysfunctions in Men and Women*, edited by T. Montorsi, Health Publications, Paris. An International Consultation in collaboration with the major urology and sexual medicine associations assembled over multidisciplinary experts from 60 countries into 17 committees. Committee members established specific objectives and scopes for various male and female sexual medicine topics. The recommendations concerning state-of-the-art knowledge in the respective sexual medicine topic represent the opinion of experts from five continents developed in a process over a 2-year period. Expert opinion was based on grading of evidence-based medical literature, widespread internal committee discussion, public presentation and debate. Premature ejaculation management is dependent upon etiology. When secondary to ED, etiology-specific treatment is employed. Retrograde ejaculation, diagnosed with spermatozoa and fructose in centrifuged post-ejaculatory voided urine, is managed by education, patient reassurance, pharmacotherapy or bladder neck reconstruction. Men with age-related penile hypoesthesia should be educated, reassured and be instructed in revised sexual techniques which maximize arousal. However, in these studies it is not obvious whether 5-HT_{2C} and 5-HT_{1A} receptors are also involved in human ejaculation since SSRI treatment activates many different post-synaptic subtype receptors. HT1A agonist and antagonists are required to further unravel the neuropharmacological mechanisms of the sexual response cycle. There are three phases of ejaculation. Premature Ejaculation PE Ejaculatory dysfunction can result from disruption at any point in this cascade of events. Medical literature contains several one-dimensional and multidimensional operational definitions of premature ejaculation. The lack of sensory areas, cerebral motor centers, spinal agreement as to what constitutes premature ejaculatory reflex is predominantly controlled by a complex interplay between central serotonergic and dopaminergic neurons with secondary the intravaginal ejaculatory latency time IELT, involvement of cholinergic, adrenergic, nitric oxide, the number of thrusts between penetration and oxytocinergic and GABAergic neurons. Each forebrain structures including the medial preoptic of the three criteria above has been operationalized, although not always with consistency [7]. Descending serotonergic pathways Operationalization of PE using the quantifiable from the nPGI to the lumbosacral motor nuclei and objective number of intravaginal thrusts tonically inhibit ejaculation. Several reported by several authors [8-11], however these brain areas are activated after ejaculation by definitions were subjective, and not supported by ascending fibers from the spinal cord and may have a possible role in satiety and the post-ejaculatory refractory time. There is considerable variance of process. Stimulation of 5-HT_{2C} receptors with the definitions offer any supportive rationale for non-selective 5-HT_{2C} agonists delays ejaculation their proposed cut-off time or normative data in male rats whereas stimulation of post-synaptic [12-15]. The inability to control and defer ejaculation until the female partner was sexually satisfied [2]. The hypothesis that PE has severely limited clinical research into the activation of post-synaptic 5-HT receptors delays understanding of PE as studies that fail to define ejaculation is supported by numerous studies in PE offer meaningless or difficult to interpret. The lack of a universally accepted operationalized definition makes comparison of different causes few if any problems. In others, the couple studies difficult or impossible as experimental may reach an accommodation of the problem group subjects in one study may very well have been placed in the control group of a second study. Frequently,

however, pre- recurrent ejaculation with minimal stimulation mature ejaculation eventually leads to significant before, on, or shortly after penetration, and before problems in the relationship with partners regard- the person wishes it, over which the sufferer has ing the man as selfish and developing a pattern of little or no voluntary control which causes the suf- sexual avoidance. As most men with treatment as the most appropriate initial therapy. Most of these proposed etiologies are threshold represents a novel and refreshing not evidence based and are speculative at best. The approach to the treatment of premature. The lack of an operationalized definition for PE, and introduction of the selective serotonin reuptake the presence of methodological problems related inhibitors SSRI meant a revolutionary change in to the inadequate definitions used, is a common the approach to and treatment of premature ejac- flaw in the majority of these studies. Selective serotonin reuptake inhibitors encompass five compounds citalopram, fluoxe- Treatment Of Premature Ejaculation tine, fluvoxamine, paroxetine and sertraline with a similar pharmacological mechanism of action. Men with premature ejaculation should be evalu- Although the methodology of the initial drug ated with a detailed medical and sexual history, a treatment studies was rather poor, recent double physical examination and appropriate investiga- blind placebo-controlled studies demonstrated the tions to establish the true presenting complaint efficacy of SSRI and clomipramine in delaying and identify obvious biological causes such as ejaculation [20â€”24]. In spite of a development genital or lower urinary tract infection Figure 1. There are three Psychogenic Anxiety drug treatment strategies to treat premature Early sexual experience ejaculation: Psychodynamic theories Examining daily treatment with serotonergic Biological Penile hypersensitivity antidepressants paroxetine, clomipramine, sertra- Hyper-excitable ejaculatory reflex Arousal line and fluoxetine, a meta-analysis of drug treat- Endocrinopathy ment studies demonstrates that paroxetine exerts Genetic predisposition the strongest ejaculation delay [60]. Adverse effects are usually minor, [32â€”34]. It is unlikely that phosphodiesterase start in the first week after intake, gradually dis- inhibitors have a significant role in the treatment appear within 2â€”3 weeks and include fatigue, of PE with the exception of men with acquired PE yawning, mild nausea, loose stools or perspiration. Diminished libido or mild erectile dysfunction are Inhibited Ejaculation, Anejaculation infrequently reported. Any single or combination is well established. They are moderately effective of psychological or medical disease, surgical pro- in retarding ejaculation, but do so at the price of cedure or drug which interferes with either central possibly causing significant penile hypoesthesia control of ejaculation, the afferent or efferent and possible transvaginal absorption, resulting in nerve supply to the vas, bladder neck, pelvic floor vaginal numbness and resultant female anorgasmia or penis, can result in inhibited ejaculation, ane- unless a condom is use [29â€”31]. Several authors have reported their experience Inhibited ejaculation, like other sexual dysfunc- with sildenafil citrate as a treatment for PE tions, is more prevalent as men age [36]. The exact Abdominal aortic aneurysmectomy site of ejaculatory duct obstruction may be identi- Para-aortic lymphadenectomy fied by transrectal ultrasonography, vasography or Infective Urethritis Genitourinary tuberculosis by percutaneous puncture of the seminal vesicles. Schistosomiasis Four neurophysiological tests are routinely usedâ€” Endocrine Hypogonadism pudendal somatosensory evoked potentials, Hypothyroidism pudendal motor evoked potentials, sacral reflex arc Medication Alpha-methyl dopa testing and sympathetic skin responses. Treatment Thiazide diuretics Tricyclic and SSRI antidepressants should be etiology specific and address the issue of Phenothiazine infertility in men of a reproductive age. Alcohol abuse Although multiple psychodynamic and behav- ioral treatments for IE have been suggested, empirical evidence to support treatment efficacy is lacking [11,44â€”49]. Most reports are uncontrolled gressive loss of the fast conducting peripheral case reports with treatment ranging from a few sensory axons which begins to be apparent in the brief sessions of sex education to the nearly 2 years third decade of life, and the dermal atrophy, of multiple-modality treatment in more complex myelin collagen infiltration and pacinian corpus- multiple etiologic cases. The drugs facilitate the ejaculatory threshold. While medical treat- turbation over partnered sex, fear of pregnancy or ment may not always produce normal ejaculation, sexually transmissible disease [11,37â€”41]. Apfel- it may convert a patient with lack of emission into baum observed that some males achieve erections one with retrograde ejaculation. This same process is the likely cause Men with premature ejaculation secondary to of increased anecdotal clinical reports of inhibited erectile dysfunction, other sexual

Chapter 7 : Ejaculatory dysfunction

Chapter 21 / Ejaculatory Disorders 21 Ejaculatory Disorders Chris G. McMahon, MBBS,FAC hSHM From: Current Clinical Urology: Male Sexual Function: A Guide to Clinical Management, Second Edition.

Chapter 8 : Staff View: Premature ejaculation

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