Instructional course 4: Premature Ejaculation: Update on management

Etiology & Diagnosis of PE

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Etiology & Diagnosis of PE

Definition & Characteristics

Etiology

Diagnosis
Definition of PE

- **1980**: APA – DSM-III: Ejaculation that occurs before the individual wishes it, because of recurrent and persistent absence of reasonable voluntary control of ejaculation and orgasm during sexual activity.

- **1987**: DSM-IIIR: Persistent or recurrent ejaculation with minimal sexual stimulation before, on, or shortly after penetration and before the person wishes it.

- **1993**: ICD-10: the inability to control ejaculation sufficiently for both partners to enjoy sexual interaction + an inability to delay ejaculation sufficiently to enjoy lovemaking, and manifest as either of the following:
  - (i) occurrence of ejaculation before or very soon after the beginning of intercourse
  - (ii) ejaculation occurs in the absence of sufficient erection to make intercourse possible

- **2000**: DSM-IV-TR: …that causes marked distress or interpersonal difficulty.

Old Definitions

1. Short ejaculation time
   - Before, on, or “shortly” after penetration (DSM-IV)
   - ICD-10: <15 s

2. Reduced control and sexual satisfaction
   - Before the person wishes it (DSM-IV)

3. Negative personal consequences
   - Distress
   - Interpersonal difficulty

Old Definitions

- Authority-based (not evidence-based)
- No support from clinical / epidemiological studies
- Primarily conceptual
- Vague in terms of operational specificity
- Rely on subjective interpretations of the concepts by the clinician

McMahon CG, et al. BJU 2008
Premature ejaculation is a male sexual dysfunction characterized by:

1. Ejaculation which always or nearly always occurs before or within about one minute of vaginal penetration, and;

2. Inability to delay ejaculation on all or nearly all vaginal penetrations, and;

3. Negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy.

McMahon CG, et al. BJU 2008
The panel concluded that there are insufficient published objective data to propose an evidence-based definition of acquired PE.
Definition of PE

- April 2013, the ISSM convened a 2nd Ad Hoc Committee for the Definition of PE in Bangalore, India.
  - The same evidence-based systematic approach was adopted.
The committee unanimously agreed that men with lifelong and acquired PE are SIMILAR:
- short ejaculatory latency
- reduced or absent perceived ejaculatory control
- the presence of negative personal consequences

Men with acquired PE are DIFFERENT:
- are older,
- have higher incidences of ED, comorbid disease, CV risk factors
- have higher IELT
- self-estimated or stop-watch IELT of 3 minutes was identified as a valid IELT cut-off for diagnosing acquired PE.

Definition of PE

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ISSM definition of lifelong and acquired PE

Premature ejaculation is a male sexual dysfunction characterized by:

1. ejaculation which always or nearly always occurs before or within about 1 minute of vaginal penetration from the first sexual experiences (lifelong PE), or,

   a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE), and;

2. inability to delay ejaculation on all or nearly all vaginal penetrations, and;

3. negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy

The ISSM unified definition of lifelong and acquired PE represents the first evidence-based definitions for these conditions.

No recommendations could be made for PE patients who do not meet the ISSM criteria.

ejaculation occurs after 3 min of vaginal penetration sometimes ejaculate prematurely
The Four PE Syndromes

- PE as a “complaint” must be distinguished from PE as a “syndrome”
- PE Syndromes
  1. Lifelong PE
  2. Acquired PE
  3. Variable PE
  4. Subjective PE

The Four PE Syndromes

- **Lifelong**
  - Very short IELT
  - Neurobiological
  - Genetic
  - Medication
  - Low prevalence

- **Acquired**

- **Variable**

- **Subjective**
The Four PE Syndromes

- **Lifelong**
  - Very short IELT
  - Neurobiological genetic
  - Medication
  - Low prevalence

- **Acquired**
  - (Very) short IELT
  - Medical/Psychological
  - Medication
  - Psychotherapy
  - Low prevalence

- **Variable**

- **Subjective**

+ The Four PE Syndromes

[Diagram showing the four syndromes with associated characteristics]
The Four PE Syndromes

- **Lifelong**
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- **Variable**
  - Normal IELT
  - Normal variation
  - Reassurance
  - High prevalence

- **Subjective**
The Four PE Syndromes

Lifelong
- Very short IELT
- Neurobiological/genetic
- Medication
- Low prevalence

Acquired
- (Very) short IELT
- Medical/Psychological
- Medication
- Psychotherapy
- Normal variation
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Variable
- Normal IELT
- Normal variation
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- High prevalence

Subjective
- Normal/long IELT
- Psychological
- Psychotherapy
- High prevalence
The Four PE Syndromes

Lifelong
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- Normal IELT
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Subjective
- Normal/long IELT
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- Psychotherapy
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The distribution of PE patients according to PE syndromes

In the population (n=512/2593)

- Lifelong PE: 42%
- Acquired PE: 19%
- Variable: 26%
- Subjective: 11%
- Not classified: 2%

Etiology & Diagnosis of PE

- Definition & Characteristics
- Etiology
- Diagnosis
Etiology of PE

Psychogenic

Medication

Hormonal

Urologic

Neurologic
Etiology of PE

Psychogenic

Classically, PE was thought to be psychologically or interpersonally based. (Due to anxiety or conditioning toward rapid ejaculation based on rushed early sexual experiences)
Etiology of PE

Urologic
- ED and other sexual comorbidities
- Prostatitis
- chronic pelvic pain syndrome (CPPS)
Etiology of PE

- hypersensitivity of the glans penis
- cortical representation of the pudendal nerve ↑
- disturbances in central 5-HT neurotransmission
- genetics
Etiology of PE

Hormonal

• Thyroid disorders
Etiology of PE

Medication

• detoxification from medications
• recreational drugs
Etiology of PE

- Psychogenic
- Urologic
- Neurologic
- Medication
- Hormonal

NONE CONFIRMED IN LARGE SCALE STUDIES

Althof, S. et al. / Sex Med. 201
Psychological causes of PE

- Psychological and interpersonal factors may cause or exacerbate PE.

- These factors may be:
  - developmental (e.g., sexual abuse, attitudes toward sex internalized during childhood),
  - individual psychological factors (e.g., body image, depression, performance anxiety, alexithymia),
  - relationship factors (e.g., decreased intimacy, partner conflict)

- There has been limited research on causality (most studies only report association)

- Psychological factors may lead to PE (or vice versa)
  - E.g. performance anxiety → PE → more performance anxiety.
Etiology of PE

- Psychogenic
- Medication
- Hormonal
- Neurologic
- Urologic
Urologic causes of PE

- **Prostatitis**
  - 28% - 77% of men with CP or CPPS report early ejaculation
  - CP and CPPS are commonly detected in men with Acquired PE.
  - The mechanism linking CP and PE is unknown
  - There are some methodological limitations of the existing data (e.g. NIH-CPSI and PEDT are used)

- Routine CP screening is not recommended
  - Physical and microbiological examination in men with painful ejaculation or CP/CPPS is recommended.
Urologic causes of PE

- Erectile Dysfunction
  - Patients may mislabel or confuse the syndromes of PE and ED.
  - PE and ED may be comorbid conditions in some men (esp among men with Acquired PE)
  - ED → rush intercourse to prevent loss of erection → PE → Anxiety
  
  - Comorbid ED is associated with more severe PE symptoms.
Etiology of PE

- Psychogenic
- Medication
- Hormonal
- Urologic
- Neurologic
Neurobiology of PE

- 5-HT is the neurotransmitter of greatest interest in the control of ejaculation

- Lifelong PE may be explained by 5-HT receptor dysregulation
  - Hyposensitivity of the 5-HT2C receptors
  - Hypersensitivity of the 5-HT1A receptors

Waldinger MD. J Urol 1998
Neurobiology of PE

- DA and OXY also play important roles in ejaculation
  - the biology of these neurotransmitters in relation to ejaculation is less well studied
  - both appear to have a stimulatory effect on ejaculation
Genetics of PE

- Genetic variations cause differences in the neurobiological factors associated with PE.
  - A genetic cause for PE was first hypothesized in 1943 based on family prevalence studies.
  - Waldinger et al. confirmed this finding
    - 88% of the first-degree relatives of men with Lifelong PE have IELT < 1 min
  - Men homozygous for the L allele of a serotonin transporter protein (5-HTTLPR) have shorter ejaculation latencies
    - However, follow-up studies on this same gene locus reported conflicting results.

Schapiro B. J Urol 1943
Genetics of PE

- Other genetic studies
  - dopamine transporter gene (DAT-1)
  - polymorphism of receptors for 5-HT, OCT, and/or vasopressin

- Individual genetic polymorphisms exert a minor effect on ejaculation latency

- Men with numerous genetic variants may be predisposed to development of PE, but data remain scant and controversial

Hormonal causes of PE

- **Thyroid Hormones**
  - Anatomic and physiologic interactions between DA and 5-HT systems and the hypothalamic-pituitary thyroid axis
  - Significant correlation between Acquired PE and TSH↓ and T3↑
  - After normalizing T3 in hyperthyroid men, the prevalence of Acquired PE↓ (50% to 15%)

- However, no link has been found between T3 and PE in large cohorts of men with PE
- No routine screening is recommended
Hormonal causes of PE

Other Hormones

- Lower PRL levels are associated with Acquired PE and anxiety
- Higher T levels correlate with PE
- Both low PRL and high T levels cannot be considered etiologies of Acquired PE.
- The relationship between these hormonal abnormalities and PE is unclear.

Hormonal causes of PE

The hormonal regulation of the ejaculatory continuum

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Etiology & Diagnosis of PE

Definition & Characteristics

Etiology

Diagnosis
Diagnosis of PE

PATIENT/PARTNER HISTORY
- Establish presenting complaints
- Intravaginal ejaculatory latency time
- Perceived degree of ejaculatory control
- Degree of patient/partner distress
- Onset and duration of PE
- Psychosocial history
- Medical history
- Physical examination

SUBJECTIVE PE

VARIABLE PE

TREATMENT
- Reassurance
- Education
- Psychotherapy
- Behavioral Therapy

YES

PREMATURE EJACULATION

YES

PE SECONDARY TO ED OR OTHER SEXUAL DYSFUNCTION

YES

MANAGE PRIMARY CAUSE

NO

ACQUIRED PE

LIFELONG PE

TREATMENT
- Behavioral/Psychotherapy
- Pharmacotherapy
- Combination treatment

PATIENT PREFERENCE

TREATMENT
- Pharmacotherapy
- Behavioral/Psychotherapy
- Combination treatment

ATTEMPT GRADUATED WITHDRAWAL OF DRUG THERAPY WHEN APPROPRIATE

Althof S et al J Sex Med 2014
# Diagnosis of PE

**Table 3**  Recommended and optional questions to establish the diagnosis of PE and direct treatment

<table>
<thead>
<tr>
<th>Recommended questions for diagnosis</th>
<th>What is the time between penetration and ejaculation (cumming)? Can you delay ejaculation? Do you feel bothered, annoyed, and/or frustrated by your premature ejaculation?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optional questions:</td>
<td>When did you first experience premature ejaculation? Have you experienced premature ejaculation since your first sexual experience on every/almost every attempt and with every partner?</td>
</tr>
<tr>
<td>Differentiate lifelong and acquired PE</td>
<td>Is your erection hard enough to penetrate? Do you have difficulty in maintaining your erection until you ejaculate during intercourse? Do you ever rush intercourse to prevent loss of your erection?</td>
</tr>
<tr>
<td>Optional questions: Assess erectile function</td>
<td>How upset is your partner with your premature ejaculation? Does your partner avoid sexual intercourse? Is your premature ejaculation affecting your overall relationship?</td>
</tr>
<tr>
<td>Optional questions: Assess relationship impact</td>
<td>Have you received any treatment for your premature ejaculation previously?</td>
</tr>
<tr>
<td>Optional question: Previous treatment</td>
<td>Do you avoid sexual intercourse because of embarrassment? Do you feel anxious, depressed, or embarrassed because of your premature ejaculation?</td>
</tr>
</tbody>
</table>

PE = premature ejaculation
Diagnosis of PE

PATIENT/PARTNER HISTORY
- Establish presenting complaint
- Intravaginal ejaculatory latency time
- Perceived degree of ejaculatory control
- Degree of patient/partner distress
- Onset and duration of PE
- Psychosocial history
- Medical history
- Physical examination

YES

PREMATURE EJACULATION

YES

PE SECONDARY TO ED OR OTHER SEXUAL DYSFUNCTION

YES

MANAGE PRIMARY CAUSE

NO

ACQUIRED PE

TREATMENT
BEHAVIORAL/PSYCHOTHERAPY
PHARMACOTHERAPY
COMBINATION TREATMENT

NO

LIFELONG PE

TREATMENT
PHARMACOTHERAPY
BEHAVIORAL/PSYCHOTHERAPY
COMBINATION TREATMENT

ATTEMPT GRADUATED WITHDRAWAL OF DRUG THERAPY WHEN APPROPRIATE

SELECTED REFERENCES
- Althof S et al J Sex Med 2014
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SUBJECTIVE PE

TREATMENT
- Reassurance
- Education
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- Behavioral Therapy

VARIABLE PE

PREMATURE EJACULATION

PE SECONDARY TO ED OR OTHER SEXUAL DYSFUNCTION

MANAGE PRIMARY CAUSE

ACQUIRED PE

TREATMENT
- BEHAVIORAL/PSYCHOTHERAPY
- PHARMACOTHERAPY
- COMBINATION TREATMENT

LIFELONG PE

TREATMENT
- PHARMACOTHERAPY
- BEHAVIORAL/PSYCHOTHERAPY
- COMBINATION TREATMENT

PATIENT PREFERENCE

ATTEMPT GRADUATED WITHDRAWAL OF DRUG THERAPY WHEN APPROPRIATE

Althof S et al J Sex Med 2014
Thank you...
Assessment of PE

History

Patients want clinicians to inquire about their sexual health [141]. Often patients are too embarrassed, shy, and/or uncertain to initiate a discussion of their sexual complaints in the HCP’s office [142]. Inquiry by the HCP into sexual health gives patients permission to discuss sexual concerns and 1400 Althof et al.

J Sex
Physical Examination

For LPE, a physical examination is advisable but not mandatory. Some patients find it reassuring for the physician to perform a hands-on physical examination. For APE, a targeted physical examination is advisable but not mandatory. The purpose of a targeted physical examination for the patient with APE is to assess for comorbidities, risk factors, and etiologies.

Stopwatch Assessment of Ejaculatory Latency (IELT)

Stopwatch measures of IELT are widely used in clinical trials and observational studies of PE, but have not been recommended for use in routine clinical management of PE [144]. Despite the potential advantage of objective measurement, stopwatch measures have the disadvantage of...
Use of Assessment Instruments

Standardized assessment measures for PE include the use of validated questionnaires, in addition to stopwatch measures of ejaculatory latency [149]. These measures are all relatively new and were developed primarily for use as research tools. However, they may serve as valuable adjuncts for clinical screening and assessment.

Several PE questionnaires assessing lifelong and acquired subtypes have been described in the literature [150–155], although only a small number have undergone extensive psychometric testing and validation. Five validated questionnaires have been developed and published to date. Currently, there are two questionnaires that have extensive databases and meet most of the criteria for test...