Post-Orgasmic Illness Syndrome

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Disclosures

• No relevant disclosures ...
People Engage in Sexual Activity for a Number of Reasons

- Feelings of *calmness, contentment, and sedation* after orgasm, particularly in men, have been described as inducements for intercourse [1-4]

- In 2002, Waldinger et al. [5] described a collection of symptoms following orgasm in two males that were qualitatively similar but more extreme and prolonged than the expected state of relaxation and somnolence that would normally occur

Post-orgasmic Illness Syndrome (POIS)

- Symptoms consisted of severe myalgia and fatigue associated with a flu-like state following orgasm.
- Symptoms last for 2-7 days and had been present since puberty.
- The symptoms were severe enough that the individuals avoided ejaculating to try to prevent the symptoms.
- To date, POIS is a rarely described syndrome, and despite having a significant impact on quality of life for individual sufferers, little is known about its epidemiology and etiology.

Approximately 50 cases in literature...

- Approximately 50 cases in the literature [1-5]
- ? Similar or related conditions
  - Sexual headache
  - Dhat syndrome
  - Postcoital dysphoria (PCD)

• 45 males with suspected POIS
• Symptoms did not occur during sexual contact without ejaculation
• In 87% of men, POIS symptoms started within 30 minutes after ejaculation
• All men reported a gradual intensity peak of symptoms, most of which were experienced on day 2

5 Preliminary Criteria for POIS

1. One or more of the following symptoms: sensation of a flu-like state, extreme fatigue or exhaustion, weakness of musculature, experiences of feverishness or perspiration, mood disturbances and/or irritability, memory difficulties, concentration problems, incoherent speech, congestion of nose or watery nose, itching eyes

2. All symptoms occur immediately (e.g., seconds), soon (e.g., minutes), or within a few hours after ejaculation that is initiated by coitus, and/or masturbation, and/or spontaneously (e.g., during sleep)

3. Symptoms occur always or nearly always, e.g., in more than 90% of ejaculation events

4. Most of these symptoms last for about 2 to 7 days

5. Disappear spontaneously.
Postorgasmic Illness Syndrome (POIS) in 45 Dutch Caucasian Males: Clinical Characteristics and Evidence for an Immunogenic Pathogenesis (Part 1)

Marcel D. Waldinger, MD, PhD,*† Marcus M.H.M. Meinardi, MD, PhD,‡ Aeilko H. Zwinderman, PhD,§ and Dave H. Schweitzer, MD, PhD†

- Proposed an **immunogenic mechanism**
- Local allergic reactions of eyes and nose were reported in 44% and 33% of subjects
- 58% had an atopic constitution
- 88% men had a positive skin-prick test with their own semen

Skin-Prick Test

- Defrost of frozen semen / diluted with 0.9% NaCl (saline) to a concentration of 1 : 40,000
- Intradermal injection of 0.05 ml of the diluted auto-semen in left forearm
- Response was compared to intradermal injection of 0.05 ml of 0.9% NaCl in left forearm
- Skin reaction interpretation at 15 minutes
- Skin reaction measured according to a standardised weal and erythema protocol (neg ... 4+)
# Age Distribution & Onset of Symptoms

<table>
<thead>
<tr>
<th>Age</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29 year</td>
<td>8</td>
</tr>
<tr>
<td>30-39 year</td>
<td>9</td>
</tr>
<tr>
<td><strong>40-49 year</strong></td>
<td><strong>11</strong></td>
</tr>
<tr>
<td>50-59 year</td>
<td>13</td>
</tr>
<tr>
<td>60-69 year</td>
<td>4</td>
</tr>
</tbody>
</table>

**Onset POIS**
- since puberty: 22 (49%)
- In the twenties: 24 (51%)

<table>
<thead>
<tr>
<th>Onset of symptoms</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30 min</td>
<td>39 (87)</td>
</tr>
<tr>
<td>30-60 min</td>
<td>1 (2)</td>
</tr>
<tr>
<td>60-180 min</td>
<td>1 (2)</td>
</tr>
<tr>
<td>180-240 min</td>
<td>3 (7)</td>
</tr>
<tr>
<td>1440 min</td>
<td>1 (2)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean ± SD</th>
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<tbody>
<tr>
<td>Age of onset of complaints</td>
</tr>
<tr>
<td>Duration of complaints</td>
</tr>
</tbody>
</table>
### Freq. POIS Complaints & CoMorbid Atopy

<table>
<thead>
<tr>
<th>Clusters</th>
<th>Complaints</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>extreme fatigue, exhausted</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>palpitations</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>problems finding words</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>concentration difficulties</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>quickly irritated</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>can not stand noise or light</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>depressed mood</td>
<td>15</td>
</tr>
<tr>
<td>Flu-like</td>
<td>feverish, perspiration, shivery</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>Ill-with flu, feeling sick, feeling cold</td>
<td>47</td>
</tr>
<tr>
<td>Head</td>
<td>pressure head, woolly, foggy feeling</td>
<td>55</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Atopy</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>atopic males</td>
<td>26 (58)</td>
</tr>
<tr>
<td>hay fever</td>
<td>10 (22)</td>
</tr>
<tr>
<td>animals</td>
<td>9 (20)</td>
</tr>
<tr>
<td>house-dust mite</td>
<td>8 (18)</td>
</tr>
<tr>
<td>food</td>
<td>3 (7)</td>
</tr>
<tr>
<td>grass</td>
<td>3 (7)</td>
</tr>
<tr>
<td>eczema</td>
<td>3 (7)</td>
</tr>
<tr>
<td>asthma</td>
<td>3 (7)</td>
</tr>
<tr>
<td>medication</td>
<td>2 (4)</td>
</tr>
<tr>
<td>insects</td>
<td>1 (2)</td>
</tr>
<tr>
<td>detergent</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>
## Comparison of Hypersensitivity Types

<table>
<thead>
<tr>
<th>Type</th>
<th>Alternative names</th>
<th>Often mentioned disorders</th>
<th>Mediators</th>
</tr>
</thead>
</table>
| I    | Allergy (immediate) | ▪ Atopy  
▪ Anaphylaxis  
▪ Asthma | ▪ IgE or IgG4 |
| II   | Cytotoxic, antibody-dependent | ▪ Autoimmune hemolytic anemia  
▪ Thrombocytopenia  
▪ Goodpasture's syndrome  
▪ Membranous nephropathy  
▪ Graves' disease  
▪ Myasthenia Gravis | ▪ IgG or IgM  
▪ (Complement)  
▪ MAC |
| III  | Immune complex disease | ▪ Serum sickness  
▪ Rheumatoid arthritis  
▪ Post streptococcal glomerulonephritis  
▪ Systemic lupus erythematosus(SLE)  
▪ Extrinsic allergic alveolitis | ▪ IgG  
▪ (Complement)  
▪ Neutrophils |
| IV   | Delayed-type hypersensitivity, cell-mediated immune memory response, antibody-independent | ▪ Contact dermatitis  
▪ Mantoux test  
▪ Metal joint replacement  
▪ Chronic transplant rejection  
▪ Multiple sclerosis | ▪ T-cells |
| V    | Autoimmune disease, receptor mediated (see below) | ▪ Graves' disease  
▪ Myasthenia Gravis | ▪ IgM, IgG  
▪ (Complement) |
Proposed Mechanism

- Autologous seminal peptides or peptides released from the disrupted urethral lining cells, contact the inner mucosal epithelium of the urethra.
- During this contact, antigen(s) of semen and/or seminal fluid is recognized and taken up by dendritic cells in the epithelium.
- These cells then migrate to the T-cell zones of lymph nodes, where they present the seminal fluid antigen(s) to naïve T-cells and initiate the cascade of events of a hypersensitivity reaction.
Allo-allergic Reaction To Specific Protein Fractions Of Seminal Plasma Has Been Reported In Female Partners Of Males [1,2]

- The main symptoms are localized e.g. vulvo-vaginal itching, occasionally generalized urticaria and sometimes even anaphylactic shock [1,2]
- The diagnosis is based on history, skin tests, and the presence of specific IgE levels for (un)fractionated seminal plasma

Seminal inflammatory cytokines

- Human seminal plasma has a variety of inflammatory cytokines and chemokines including TGF-β1, CXCL8 (ex-IL-8), GRO (CXCL1/Th17), monocyte chemotactic protein 1 (MCP-1), IL-13, and IL-17 [1]
- Some can activate basophils or mast cells and release histamine e.g. MCP-1, IL-8 and GRO proteins [2,3]
- High concentrations of spermine (2–15 mmol/L) were observed in seminal fluid [4] which may injure endothelial cells and cause wheals and erythema when injected into the skin of both patients and healthy controls

Hyposensitization Therapy with Autologous Semen in Two Dutch Caucasian Males: Beneficial Effects in Postorgasmic Illness Syndrome (POIS; Part 2)

Marcel D. Waldinger, MD, PhD,*† Marcus M.H.M. Meinardi, MD, PhD,‡ and Dave H. Schweitzer, MD, PhD§

• Two males suffering from POIS with positive autologous semen skin testing

• Hyposensitization program with multiple escalating dose subcutaneous injections of autologous semen every 2/52 for first year and then every 4/52 in the second and third year

• Progressive semen dilutions from 1:40,000 to 1:20

Hyposensitization with autologous semen

- Risks includes erythema, general POIS complaints, anaphylactic shock
- At skin reaction \( \leq \) grade 2+ - increase semen dilution
- At skin reaction \( \geq \) grade 3+ - decrease semen dilution
- Semen dilution
  - Subject 1 - 1: 40,000 \( \Rightarrow \) 1:20
  - Subject 2 - 1 : 20,000 \( \Rightarrow \) 1:280
- Gradual reduction of complaints resulted in 60% and 90% reduction of POIS complaints at 31 and 15 months
Limitations and Questions

- Skin test: no control group of IC autologous-semen injection in control group of healthy males
- Why are there so little local manifestations e.g. Urethral meatus and glans penis, and so many systemic symptoms?
Postorgasmic Illness Syndrome (POIS) in a Chinese Man: No Proof for IgE-Mediated Allergy to Semen

Nannan Jiang, MD,*1 Guangpeng Xi, MD,*1 Hongjun Li, PhD,† and Jia Yin, MD*

*Department of Allergy, Peking Union Medical College Hospital, Beijing, China; †Department of Urology Surgery, Peking Union Medical College Hospital, Beijing, China

• n=1, 3 controls
• The patient complained of lifelong premature ejaculation symptoms and allergic rhinitis
• +ve skin test but no semen-specific IgE to autologous semen
• Three healthy donors also showed positive skin tests

IgE reactivity of sera to autologous semen measured by ELISA. P, affected patient; C1, control 1; C2, control 2; Bla, blank control

Disorder of the endogenous $\mu$-opioid receptor system

- The symptoms of POIS are similar to those of opioid withdrawal syndrome.
- Opioids are involved in mediation of positive affective states generated by sexual behavior [1].
- The $\mu$-opioid receptors are thought to play a crucial role in controlling this behavior [2].
- Jiang et al. suggested that patients suffering from POIS may have a disorder of the endogenous $\mu$-opioid receptor system [3].

Conclusion

- POIS is a post-ejaculation complex of local and systemic symptoms, which occur within sec/min/hours after ejaculation
- POIS is characterized by general physical and mental complaints
- Five preliminary diagnostic criteria fulfill the manifestations of POIS quite sufficiently
- POIS is possibly a manifestation of an auto-immune reaction to the man’s own semen or a disorder of the endogenous μ-opioid receptor system
- More research is required ...
The more you learn, the more you realize how little you know...

... on Socrates by Plato
Thank You