Master Lecture No. 8

Post-Orgasmic Illness Syndrome

Chris G McMahon MBBS FACHSHM
Australian Centre for Sexual Health
Prof Marcel Waldinger
Division Pharmacology
Depart. Pharmaceutical Sciences
University of Utrecht, The Netherlands

Practice of Neurosexology
Amstelveen, The Netherlands
**Post-Orgasm Illness Syndrome**

or **POIS** is a post-ejaculation complex of local and systemic symptoms, which occur within sec/min/hours after ejaculation.
POIS is a Rare Disease ...

- A **rare disease**, also referred to as an **orphan disease**, is any disease that affects a small percentage of the population.
- Most rare diseases are genetic, and thus are present throughout the person's entire life, even if symptoms do not immediately appear.
- Many rare diseases appear early in life, and about 30 percent of children with rare diseases will die before reaching their fifth birthday.
- No consensus regarding what prevalence defines a disease as rare.
Defining a rare disease ...

- The **US Rare Diseases Act of 2002** defines rare disease strictly according to prevalence
  - "any disease or condition that affects < 200,000 people in the United States," or about **1 in 1,500** people

- In **Japan**, the legal definition of a rare disease is one that affects <50,000 patients in Japan, or about **1 in 2,500** people

- However, the **European Commission on Public Health** defines rare diseases as "life-threatening, chronically debilitating diseases which are of such low prevalence that special combined efforts are needed to address them"
  - The term low prevalence is later defined as generally meaning fewer than **1 in 2,000** people
  - Diseases that are statistically rare, chronically debilitating, or inadequately treated but not life-threatening are excluded from their definition
Post orgasmic illness syndrome

OVERVIEW

These Web pages are updated as the Genetic and Rare Diseases Information Center receives questions and as new information becomes available. If you don't see many information resources on this page, it may be because the information Center hasn't yet received a question about this condition.

Your Questions Answered
by the Genetic and Rare Diseases Information Center

Please contact us with your questions about Post orgasmic illness syndrome. We will answer your question and update these pages with new resources and information.

In Depth Information

- Orphanet is a European reference portal for information on rare diseases and orphan drugs. Access to this database is free of charge.
- PubMed is a searchable database of medical literature and lists journal articles that discuss Post orgasmic illness syndrome. Click on the link to view a sample search on this topic.
**Postorgasmic illness syndrome**

**Orpha number**: ORPHA279547

**Synonym(s)**:  
- FOS

**Precedence**:  
- Not applicable

**Inheritance**:  
- Not applicable

**Age of onset**:  
- Adult
- Adolescent

**ICD-10**: E70

**ICD-9**:  
- Not applicable

**OMIM**:  
- Not applicable

**MeSH**:  
- Not applicable

**HUGG**:  
- Not applicable

**OMIMCAT**:  
- Not applicable

**SUMMARY**

An Orphanet summary for this disease is currently under development. However, other data related to the disease are accessible from the Additional Information menu located on the right side of this page.

**Suggest an update**

---

**Additional information**

- **Further information on this disease**
  - Classification (1)
  - Genes (2)
  - Other websites (0)

- **Healthcare resources for this disease**
  - Expert centres (5)
  - Diagnostic tests (9)
  - Patient organisations (2)
  - Orphan drugs (6)

- **Research activities on this disease**
  - Research projects (6)
  - Guidelines (6)
  - Registrars (6)
  - Networks (9)

- **Orphanet Reports series**
  - Frequency
  - Orphan drugs in Europe

- **Getting involved**
  - Read the newsletter
  - Read OrphID (1)
  - Register your activity
RECENT GRANT RECIPIENTS

Recipients of research grants from NORD

Rare disease research is rarely a priority, and the NORD Research Grant Program exists to encourage the study of diseases for which there may be few or no other sources of funding. Recent recipients of NORD research grants are listed below.

Two previous award recipients have recently had the manuscripts of the NORD-funded studies published. Read the studies from the European Journal of Haematology and Nature Medicine.

View the Recipients from:

2013

NORD 2013 GRANT RECIPIENTS

NORD’s Medical Advisory Committee has recommended, and the NORD Board of Directors has approved, the awarding of nine research grants in December 2013. The patient organizations that funded the grants (when applicable), investigators, their institutions, and their projects are as follows:

**Post-Orgasmic Illness Syndrome (POIS)**
(Funded by the patient group, the POIS Forum)

**Barry R. Komisaruk, Ph.D.**
Rutgers University

*Is POIS a case of Vagal Dystonia?: An fMRI Brain Activity Analysis*
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
- Waldinger et al named this cluster of symptoms following ejaculation as post-orgasmic illness syndrome (POIS)
- 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

Is POIS an Orphan Disease or may it be more common than reported in the literature?

• In the *New York Times* in January 2009, Richard Friedman, a NYC psychiatrist describes several patients who experience low mood and somatic symptoms following orgasm, whose symptoms improved with the use of SSRIs.

• Evidence of many more undiagnosed sufferers of POIS is seen in the existence of an extremely active Internet forum where more than 100 people have self-reported symptoms of POIS.
Postorgasmic Illness Syndrome (POIS) in 45 Dutch Caucasian Males: Clinical Characteristics and Evidence for an Immunogenic Pathogenesis (Part 1)


- 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
Complaints Of POIS Were Categorized in Seven Clusters Of Symptoms

<table>
<thead>
<tr>
<th>Clusters</th>
<th>Complaints</th>
<th>Freq.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Extreme fatigue/exhausted</td>
<td>36</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Palpitations</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Problems finding words/incoherent speech/dysarthria</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Concentration difficulties</td>
<td>39</td>
<td>87</td>
</tr>
<tr>
<td>Flu-like</td>
<td>Feverish/extreme warmth/perspiration/ shivery</td>
<td>35</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>Ill with flu/feeling sick/feeling cold</td>
<td>21</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>Headache/pressure/heavy/woolly/swollen/cotton wool/full feeling/foggy feeling in the head</td>
<td>25</td>
<td>55</td>
</tr>
<tr>
<td>Eyes</td>
<td>Burning/red injected eyes</td>
<td>20</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>Blurred vision</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Watery/irritating/running/itching eyes</td>
<td>12</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Dry/sensitive/painful eyes/pressure on eye</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Nose</td>
<td>Congestion nose</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>Watery/shotty/runny nose/sneezing</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td>Throat</td>
<td>Dirty taste in mouth/dry mouth</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Tickling cough/hoarse voice/sore throat</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Muscles</td>
<td>Muscle tension in back/neck</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Muscle weakness/feeling tired muscles/ flabby legs</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Leg pain/muscle pain/heavy legs</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>Tension/heavy feeling/stiffness muscles</td>
<td>10</td>
<td>22</td>
</tr>
</tbody>
</table>
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
- Intracutaneous injection of 0.05 ml of the diluted auto-semen in left forearm
- Response was compared to intracutaneous 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 protocol
Skin Reaction Grading System

neg. = wheal and erythema < 5 mm
1+ = wheal 5-10 mm and erythema of 11-20 mm
2+ = wheal and erythema of 21-30 mm
3+ = erythema of 31-40 mm
4+ = wheal > 15 mm or erythema > 40 mm
Skin Prick Test with Autologous semen

- N=45
- 33 (73%) consented in a skin-prick test with their own diluted semen
- Semen
  - Test pos. in 29/33 (88%) males – grade 2+ to grade 4+
  - Test neg. in 4/33 (12%) males
- Saline
  - Test neg. In 33/33 (100%) - wheal max 2 mm
Patients Forearm Before Skin Prick
Single Blind Skin Prick
Positive Skin Reaction 5 min After Skin Prick: Severity Mild
### Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD yr</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age patient</strong></td>
<td>43 ± 13</td>
</tr>
<tr>
<td><strong>Age partner</strong></td>
<td>42 ± 11</td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
<td>N (%)</td>
</tr>
<tr>
<td><strong>Married</strong></td>
<td>20 (44)</td>
</tr>
<tr>
<td><strong>Partner living together</strong></td>
<td>6 (13)</td>
</tr>
<tr>
<td><strong>Partner not-living together</strong></td>
<td>7 (16)</td>
</tr>
<tr>
<td><strong>Divorced</strong></td>
<td>3 (7)</td>
</tr>
<tr>
<td><strong>Single</strong></td>
<td>9 (20)</td>
</tr>
<tr>
<td><strong>Duration Relationship</strong></td>
<td>Mean ± SD yr</td>
</tr>
<tr>
<td><strong>Married</strong></td>
<td>18.8 (11.3)</td>
</tr>
<tr>
<td><strong>Partner living together</strong></td>
<td>4.2 (2.9)</td>
</tr>
<tr>
<td><strong>Partner not-living together</strong></td>
<td>6.6 (8.4)</td>
</tr>
</tbody>
</table>
# Age Distribution

<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>40-49 year</td>
<td>11</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**

<table>
<thead>
<tr>
<th>Onset POIS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>since puberty</td>
<td>22 (49%)</td>
</tr>
<tr>
<td>In the twenties</td>
<td>24 (51%)</td>
</tr>
</tbody>
</table>
# Features of Complaints POIS

<table>
<thead>
<tr>
<th>Feature</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset of complaints</td>
<td>26 ± 13 yr</td>
</tr>
<tr>
<td>Duration of complaints</td>
<td>4.6 ± 2.8 yr</td>
</tr>
<tr>
<td>Start of Complaints after Ejaculation</td>
<td>N (%)</td>
</tr>
<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>
</tr>
</tbody>
</table>
## Co-morbid Allergy

<table>
<thead>
<tr>
<th>Allergy</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>
## Classification & Freq. POIS Complaints (I)

<table>
<thead>
<tr>
<th>Clusters</th>
<th>Complaints</th>
<th>Freq.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>extreme fatigue, exhausted</td>
<td>36</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>palpitations</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>problems finding words</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>concentration difficulties</td>
<td>39</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>quickly irritated</td>
<td>35</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>can not stand noise or light</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>depressed mood</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Flu-like</td>
<td>feverish, perspiration, shivery</td>
<td>35</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>Ill-with flu, feeling sick, feeling cold</td>
<td>21</td>
<td>47</td>
</tr>
<tr>
<td>Head</td>
<td>pressure head, woolly, foggy feeling,</td>
<td>25</td>
<td>55</td>
</tr>
</tbody>
</table>
## Classification & Freq. POIS Complaints (II)

<table>
<thead>
<tr>
<th>Clusters</th>
<th>Complaints</th>
<th>Freq.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>burning, red injected eyes</td>
<td>20</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>blurred vision</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>watery itching eyes</td>
<td>12</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>dry, painful, pressure on eyes</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Nose</td>
<td>congestion nose</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>watery nose, sneezing</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td>Throat</td>
<td>dry mouth, dirty taste</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>sore throat</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Muscles</td>
<td>muscle tension in back/neck</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>muscle weakness</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>muscle pain</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>stiffness muscles</td>
<td>10</td>
<td>22</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 wander 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
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

56% of the Current Group of Males Reported to Suffer From Lifelong PE with an IELT ≤ 1 Minute

- However, in the general population, prevalence of PE with an IELT ≤ 1 minute is ~2.5% [1,2]
- Relative risk of PE in POIS is 22.4-fold higher than healthy individuals
- ? induced by forced abstinence of and therefore, low frequency of sexual activity
- ? PE in these men is causally associated to immunologic factors
- However, currently, there are no data of immunologic factors relating to PE

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 include 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
- In male with lifelong PE, baseline IELT of 20 seconds increased to 10 minutes at 36/12
- The cause of this association with IELT is unknown
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?
What is POIS?

POIS is not the manifestation of an allergy for autologous semen, but POIS is the systemic manifestation of an auto-immune reaction to the man’s own semen.

Waldinger, 2011
Recently Finished Study

- Fundamental Human Study
- Immunological parameters show preliminary evidence for auto-immune reaction to autologous semen
- Publication in 2015
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 probably the manifestation of an auto-immune reaction to the man’s own semen

• More research is required ...
The more we know, the more we realize we don’t know ...
Thank You