

### Master Lecture No. 8

# **Post-Orgasmic Illness Syndrome**

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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 <u>1 in 1,500</u> 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 <u>1 in 2,000</u> people
  - Diseases that are statistically rare, chronically debilitating, or inadequately treated but not life-threatening are excluded from their definition





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#### About ORDR

ORDR is part of the National Center for Advancing Translational Sciences (NCATS)

The goals of ORDR are to identify, stimulate, coordinate and support research to respond to the needs of patients who have any one of the approximately 6,800 rare diseases known today. Read more about ORDR.

#### **Upcoming Conferences**

#### 2014 International Pathogenic Neisseria Conference

Sunday, October 12, 2014 - Friday, October 17, 2014 Asheville, NC

#### Research

### ORDR

#### **ORDR Programs**

ORDR coordinates the following collaborative research efforts

- Bench-to-Bedside Awards
- The Rare Diseases Clinical Research Network
- . Global Rare Diseases Patient Registry and Data Repository (GRDR)
- Rare Diseases Human Biospecimens/Biorepositories (RD-HuB)
- <u>Undiagnosed Diseases Program</u>



#### **Research Funding Resources**

Funding opportunities from the NIH and other sources



#### Tools for Researchers

Resources to aid in research

#### Resources

#### Featured Guide

How to Find a Disease Specialist





#### Rare Diseases Resources

A collection of resources for the rare disease community



#### Genetics Resources

A collection of resources that provide information on genes, genomics, and genetic



#### Genetic Testing and Treatment

Learn about genetic testing and finding healthcare services



#### Support for Patients and **Families**

Organizations that can help you find support and assistance

MORE CONFERENCES )

#### Other Names for this Disease

- Post orgasmic sick syndrome

See <u>Disclaimer</u> regarding information on this site. Some links on this page may take you to organizations outside of the National Institutes of Health.

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.

#### On this page

In Depth 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.

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#### orphanet

The portal for rare diseases and orphan drugs





#### Rare diseases are rare, but rare disease patients are numerous

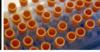
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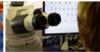














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#### Other documents

Council Recommendation on an action in the field of rare diseases

State of Art of rare diseases.

#### Other rare diseases websites

Rare Diseases - European Commission

**EUCERD Joint Action** 

European Medicines Agency

IRDIRC

Office of rare diseases research (US)

EC Expert Group on Rare Diseases (EU)

#### **Events**

See all

22

XVème forum des associations - internet des objets, applications mobiles : des révolutions NTIC pour les maladies rares

22 September, 2014, Paris, France

SEPT 25

9th International Research Symposium on Marfan Syndrome and related disorders

25-27 September, 2014, Paris, France

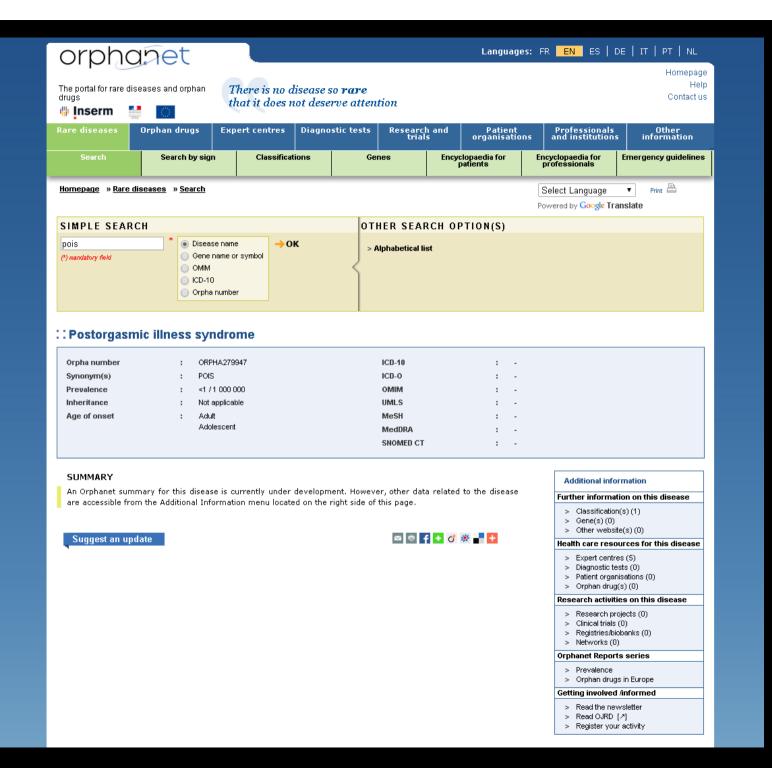
OCT ICORD 2014 Annual Meeting: Societal value of Prevention, Diagnosis and Treatment of Rare Diseases

7-9 October, 2014, Ede, The Netherlands

OCT

64th Annual Meeting of the American Society of Human Genetics: ASHG 2014

18-22 October, 2014, San Diego, US





Alone we are rare. Together we are strong.™







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**News & Events** 



#### News

#### Events



New Rare Disease Education for Healthcare Professionals Partnership

NORD and Frontline Medical Communications have announced a strategic alliance to increase awareness and understanding of rare diseases. Read the press release >



Read a letter from Peter L. Saltonstall regarding a recent article on a family's incredible journey seeking a diagnosis. More >



Tell Senate to Pass Newborn Screening Reauthorization Act

Join NORD in supporting this important March of Dimes campaign. More >

#### NORD Publishes Physician Guide to HoFH

The latest in NORD's collection of guides for physicians is on rare disease that can lead to heart attack in children and young adults. More >

More news >

#### WHAT IS NORD?

The National Organization for Rare Disorders (NORD) provides advocacy, education and other services to improve the lives of all people affected by rare diseases. More >

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#### RECENT GRANT RECIPIENTS

Research Grants

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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:

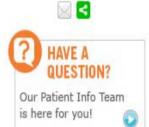
#### Post-Orgasmic Illness Syndrome (POIS)

(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
  - 1. Meston CM, Buss DM. Why humans have sex. Arch Sex Behav 2007;36:477–507.
  - 2. Leigh BC. Reasons for having and avoiding sex: Gender, sexual orientation, and relationship to sexual behaviour. J Sex Res 1989;26:199–209.
  - 3. Hawton K. Sex therapy a practical guide. Oxford: Oxford Medical Publications; 1985:14–5.
  - 4. Masters W, Johnson V, Kolodny R. Heterosexuality. New York: Harper Collins; 1994:41–72
  - 5. Waldinger MD, Schweitzer DH. Postorgasmic illness syndrome: Two cases. J Sex Marital Ther 2002;28:251–5.

# 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
- 1. Waldinger MD, Schweitzer DH. Postorgasmic illness syndrome: Two cases. J Sex Marital Ther 2002;28:251–5.

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# 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

### The New York Times

# Sex and Depression: In the Brain, if Not the Mind

By RICHARD A. FRIEDMAN, M.D. Published: January 19, 2009

As everyone knows, sex feels good.

⊕ Enlarge This Image



Or does it? In recent years, I've come across several patients for whom sex is not just unpleasurable; it actually seems to cause harm.

One patient, a young man in his mid-20s, described it this way: "After sex, I feel literally achy and depressed for about a day."

Otherwise, he had a clean bill of health, both medical and psychiatric: well adjusted, hardworking, lots of friends and a close-knit family.

da

David Sute

Related

# 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<sup>¶</sup>

- 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

Table 2	Characteristics	of	postorgasmic illness
syndrome	(POIS)		

	Mean ± SD
POIS	
Age of onset	$26 \pm 13$ years
Duration of complaints	4.6 ± 2.8 davs
Time of onset POIS after ejaculation	64 ± 219 minutes
Time of onset POIS after ejaculation	N (%)
<30 minutes	39 (87)
30-60 minutes	1 (2)
60–180 minutes	1 (2)
180–240 minutes	3 (7)
1,440 minutes	1 (2)
·	·

Waldinger, M.D., et al., Postorgasmic Illness Syndrome (POIS) in 45 Dutch caucasian males: clinical characteristics and evidence for an immunogenic pathogenesis (Part 1). J Sex Med, 2011. 8(4): p. 1164-70.

# Complaints Of POIS Were Categorized in Seven Clusters Of Symptoms

Table 4	Categorization of POIS complaints		
Clusters	Complaints	Freq.	%
General	Extreme fatigue/exhausted	36	80
	Problems finding words/incoherent	10 8	22 18
	Concentration difficulties	39	87
	Can not stand noise/light/photophobia  Depressed mood	35 4 7	78 9 15
Flu-like	Feverish/extreme warmth/perspiration/	35	78
Head	Ill with flu/feeling sick/feeling cold Headache/pressure/heavy/woolly/swollen/ cotton wool/full feeling/foggy feeling in	21 25	47 55
Eyes	Burning/red injected eyes	20	44
	Watery/irritating/running/itching eyes Dry/sensitive/painful eyes/pressure on	12 9	27 20
Nose	Congestion nose	14	31
Throat	Watery/snotty/runny nose/sneezing Dirty taste in mouth/dry mouth Tickling cough/hoarse voice/sore throat	15 5 5	33 11 11
Muscles	Muscle tension in back/neck  Muscle weakness/feeling tired muscles/	11 8	24 18
	Leg pain/muscle pain/heavy legs	14	31
	rension/neavy reeling/sumness muscles	10	22

## **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<sup>¶</sup>

- 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**

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

# **Age Distribution**

Age	N	
20-29 year	8	
30-39 year	9	
40-49 year	11	
50-59 year	13	
60-69 year	4	
Onset POIS		
since puberty	22 (49%)	
In the twenties	24 (51%)	

# **Features of Complaints POIS**

	Mean ± SD
Age of onset of complaints	$26 \pm 13 \text{ yr}$
Duration of complaints	$4.6 \pm 2.8 \text{ yr}$
Start of Complaints after Ejaculation	N (%)
< 30 min	39 (87)
30- 60 min	1 (2)
60-180 min	1 (2)
180-240 min	3 (7)
1440 min	1 (2)

# **Co-morbid Allergy**

	N (%)
atopic males	26 (58)
hay fever	10 (22)
animals	9 (20)
house-dust mite	8 (18)
food	3 (7)
grass	3 (7)
eczema	3 (7)
asthma	3 (7)
medication	2 (4)
insects	1 (2)
detergent	1 (2)

### Classification & Freq. POIS Complaints (I)

Clusters	Complaints	Freq.	%
General	extreme fatigue, exhausted		80
	palpitations	10	22
	problems finding words	8	18
	concentration difficulties	39	87
	quickly irritated	35	78
	can not stand noise or light	4	9
	depressed mood	7	15
Flu-like	feverish, perspiration, shivery	35	78
	Ill-with flu, feeling sick, feeling cold	21	47
Head	pressure head, woolly, foggy feeling,	25	55

## Classification & Freq. POIS Complaints (II)

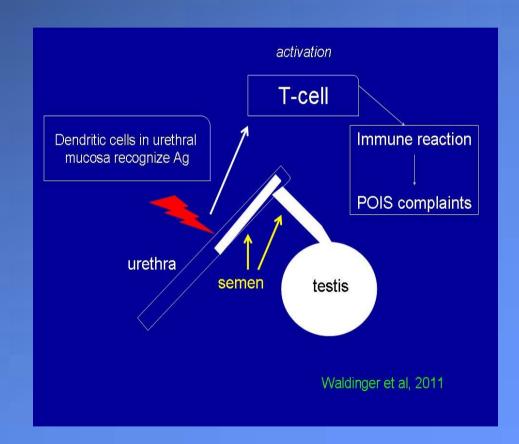
Clusters	Complaints	Freq.	%
Eyes	burning, red injected eyes	20	44
	blurred vision	10	22
	watery itching eyes	12	27
	dry, painful, pressure on eyes	9	20
Nose	congestion nose	14	31
	watery nose, sneezin	15	33
Throat	dry mouth, dirty taste		11
	sore throat		11
Muscles muscle tension in back/neck		11	24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

# **Comparison of Hypersensitivity Types**

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

## **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 Tcell 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

- 1. Ohman JL Jr, Malkiel S, Lewis S, Lorusso JR. Allergy to human seminal fluid: Characterization of the allergen and experience with immunotherapy. J Allergy Clin Immunol 1990;85:103-7
- 2. Lee J, Kim S, Kim M, Chung YB, Huh JS, Park CM, Lee KH, Kim JH. Anaphylaxis to husband's seminal plasma and treatment by local desensitization. Clin Mol Allergy 2008;6:13

# 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
  - 1. Waldinger MD, Quinn P, Dilleen M, Mundayat R, Schweitzer DH, Boolell M. A multi-national population survey of intravaginal ejaculation latency time. J Sex Med 2005;2:492–7
  - 2. Waldinger MD, McIntosh J, Schweitzer DH. A five-nation survey to assess the distribution of the intravaginal ejaculatory latency time among the general male population. J Sex Med 2009;6:2888–95.

# 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

Waldinger, M.D., M.M. Meinardi, and D.H. Schweitzer, Hyposensitization therapy with autologous semen in two Dutch caucasian males: beneficial effects in Postorgasmic Illness Syndrome (POIS; Part 2). J Sex Med, 2011. 8(4): p. 1171-6.

### Hyposensitization with autologous semen

- Risks includes erythema, general POIS complaints, anaphylactic shock
- At skin reaction ≤ grade 2+ increase semen dilution
- At skin reaction ≥ grade 3+ decrease semen dilution
- Semen dilution
  - Subject 1 1: 40,000 → 1:20
  - Subject 2 1 : 20,000 → 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 <u>not</u> the manifestation of an <u>allergy</u> for autologous semen, but POIS is the systemic manifestation of an <u>auto-immune</u> 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**