Norman R Zinner Debate:
“The ICS Standardisation of OA B 10 Years on: Are We Barking up the Wrong Tree?”
Thursday, 18th October 2012, 11:00-12:00

Moderators: Ted Arnold, Chris Chapple & Richard Millard

- Norman Zinner Tribute Jerry Blaivas
- OAB: The good, the bad, the ugly Alan Wein 15 mins
- OAB: Whom does the definition serve best? Kari Tikkinen 10 mins
- OAB: A urodynamic view Werner Schaefer 10 mins
- Do we need to have a brain to get OAB? Marcus Drake 10 mins
- Rebuttal, Discussion and Questions All 15 mins

OAB. Are We Barking up the Wrong Tree? A Lesson From My Dog, Norman Zinner, *Neuurology and Urodynamics* 30:1410–1411 (2011)
OAB: Whom does the definition serve best?

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Norman R Zinner Debate. The ICS Standardisation of OAB 10 Years on: Are We Barking up the Wrong Tree?
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I have no conflicts of interest.
Special acknowledgments

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McMaster University, Hamilton, ON, Canada

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Imperial College London, London, UK

Ted Johnson
Emory University, Atlanta, GA, USA
Overactive bladder syndrome (OAB) is “urgency, with or without urgency incontinence usually with increased daytime frequency and nocturia.”

- “These symptom combinations are suggestive of urodynamically demonstrable detrusor overactivity, but can be due to other forms of urethro-vesical dysfunction.”
- “These terms can be used if there is no proven infection or other obvious pathology.”
- 2002 document describes also as “urge syndrome or urgency-frequency syndrome”

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- “These symptom combinations are suggestive of urodynamically demonstrable detrusor overactivity, but can be due to other forms of urethro-vesical dysfunction.”
- “These terms can be used if there is no proven infection or other obvious pathology.”

- “urgency is the complaint of a sudden compelling desire to pass urine which is difficult to defer.”

OVERACTIVE BLADDER: SYMPTOM OR SYNDROME? J.G. BLAIVAS

– Joan and Sanford Weil Medical College, Cornell University, USA

Blaivas. BJU Int 2003:92:521

Editorial

Overactive Bladder: A Clinical Entity or a Marketing Hype?

Helmut Madersbacher

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OAB. Are We Barking Up the Wrong Tree? A Lesson From My Dog

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European Association of Urology

Editorial

Does the Imprecise Definition of Overactive Bladder Serve Commercial Rather than Patient Interests?

Kari A.O. Tikkinen a,b,*, Anssi Auvinen c

aDepartment of Urology, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland; bDepartment of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada; cSchool of Health Sciences, University of Tampere, Tampere, Finland
Publications across all journals indexed in Scopus, including the term “overactive bladder” 1998-2010

What about the patients - do OAB concept and treatments work for them?

- Antimuscarinics are the first-line drug treatment for OAB
  - However, benefits are small

- Median symptom changes with antimuscarinics in RCTs
  - Urgency: - 0.9 episodes/24 hours
  - Urgency incontinence: - 0.5 episodes/24 hours
  - Frequency: - 0.8 episodes/24 hours
  - Nocturia: - 0.1 episodes/night, NS

Adherence to OAB medications (anticholinergics) is low

**FIGURE 4** Time to Discontinuation\(^a\) of 6 Chronic Therapy Classes, Allowing for 90-Day Treatment Gap

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**Percent persistent**

- Oral antidiabetics
- ARBs
- Statins
- Bisphosphonates
- Prostaglandins
- OAB medications

**Days**

- 0
- 30
- 60
- 90
- 120
- 150
- 180
- 210
- 240
- 270
- 300
- 330
- 360
- 390
- 420
- 450
- 480
- 510
- 540
- 570
- 600
- 630
- 660
- 690
- 720

\(^a\)Discontinuation was defined as the end of days supplied for an index medication pharmacy claim immediately preceding a 90-day gap in therapy. A minimum of 12 months (maximum 24 months) continuous eligibility following the index date (day 0) was required. Beginning at day 390, the denominator for the calculation consisted of all remaining eligible patients with continuous enrollment through the end of the 30-day interval. Patients with continuous enrollment ending between day 360 and day 720 were censored at the point of their cessation of benefits.

\(^b\)Using the 90-day gap, 6-month persistence rates were prostaglandin analogs 57%, statins 62%, bisphosphonates 62%, oral antidiabetics 72%, ARBs 69%, and OAB medications 32%.

ARB = angiotensin II receptor blocker; OAB = overactive bladder.
<table>
<thead>
<tr>
<th>Reason</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not work as expected</td>
<td>611 (46.2)</td>
</tr>
<tr>
<td>Switched to a new medication</td>
<td>332 (25.1)</td>
</tr>
<tr>
<td>Learned to get by without medication</td>
<td>308 (23.3)</td>
</tr>
<tr>
<td>I had side effects</td>
<td>279 (21.1)</td>
</tr>
</tbody>
</table>
Age-standardized prevalence of overactive bladder symptoms

“OAB is misleading because it makes it too easy for clinicians to feel they have made a diagnosis when they have not. In so doing, it curtails further thinking and does not promote the scientific pursuit of fact.”

“OAB Diagnosis. The review revealed insufficient publications to address OAB diagnosis from an evidence basis”

Available at [http://www.auanet.org/content/media/OAB_guideline.pdf](http://www.auanet.org/content/media/OAB_guideline.pdf)
<table>
<thead>
<tr>
<th>Key Element of ‘Marketing Disease’</th>
<th>Suggestions for Doing Better</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Exaggerate the prevalence of disease</td>
<td></td>
</tr>
<tr>
<td>Create a broad disease definition</td>
<td>Learn exact definition and question whether it is appropriately specific.</td>
</tr>
<tr>
<td>Publicize a large prevalence estimate.</td>
<td>Ask: “Does the sample truly represent the general population?”</td>
</tr>
<tr>
<td>Blur between mild and severe.</td>
<td>Be clear about the disease spectrum.</td>
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</table>
## Key Element of ‘Marketing Disease’

<table>
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<tr>
<td>2. <strong>Encourage more diagnosis</strong></td>
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Highlight that doctors fail to recognize

Encourage people’s self-diagnosis.

Promote awareness ‘uncritically’

- Acknowledge the problems of overdiagnosis.
- Learn if awareness activities are industry sponsored.

### Key Element of ‘Marketing Disease’

<table>
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<tr>
<td><strong>3. Suggest that all disease should be treated</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Exaggerate the benefits of the drug for everyone with disease.</strong></td>
<td><strong>Objectively report benefits and study populations; Learn industry ties.</strong></td>
</tr>
<tr>
<td><strong>Understate harms of treatments</strong></td>
<td><strong>Quantify side effects</strong></td>
</tr>
<tr>
<td><strong>Imply that long-term treatment is safe and effective.</strong></td>
<td><strong>Remember that studies are typically short-term.</strong></td>
</tr>
</tbody>
</table>

Reported funding sources for overactive bladder papers by subtype

- **Industry funding (fully or partial)**
- **Non-industry funding (including charity and government) only**
- **No funding (explicitly declared)**

So, whom does the definition serve best?

1. Excellent for disease awareness campaigns but also for *disease mongering* and *selling sickness*

2. Does not optimally promote the scientific pursuit of fact
   - May be harmful for further thinking

3. Is ‘patient-friendly’ but maybe also (patient-) misleading
Be aware that

1. Overactive bladder is not a disease
   – Overactive bladder is the name given to a group of troubling urinary symptoms
     • These symptoms may (or may not) have same etiology
   – Term ‘OAB’ implies a mechanism
     • We often don’t know the mechanism of these symptoms

2. Disease-branding and drug-mongering are common promotional practices of ‘selling sickness’
   – aim is to expand markets by widening the boundaries of diagnosable conditions
Do we need a brain to get an overactive bladder?

Marcus Drake
University of Bristol & Bristol Urological Institute
Summary

- Consciousness, perception and attention
  - Intrusive urinary sensation
- Decision making- “free will”, or “volition”
  - Abnormal LUT muscle behaviour
- Personality
Perception is interpretation of sensory information to represent and understand the environment. Where subconscious sensory information becomes a conscious sensation.

Consciousness; the state of being aware of an external object or something within oneself.
Perception and attention

- In the range of competing stimuli, only one is consciously attended to (“perceived”)
- “Bottom-up” processing - Sensory transduction and afferent signalling
- Stimulus-driven attention; stimuli like sudden loud noise unavoidably attract our attention. Parietal & temporal cortex
- “Top-down“ processing - Learning & expectation alter how sensory signals are perceived
- Endogenous attention; where we choose to concentrate attention- like a conversation Frontal cortex, basal ganglia
Clinical presentations

- OAB; urgency, with or without incontinence, usually with frequency and nocturia
  - Exclude other causes of similar symptoms

- Subconscious LUT sensory information receives disproportionate attention in the competing traffic of body and environment

- Intrusive urinary sensation
Brain function; to give LUT sensory traffic due precedence amongst the overall sensory load

How the transition occurs, when subconscious (sensory) becomes conscious (sensation), determines whether a person experiences the intrusive urinary sensations called “OAB”- Endogenous versus stimulus-driven?
Volition, or free will, is the cognitive process by which an individual decides on and commits to a course of action.
Volitional control

- Actions are determined by your volition, all processes automatically adjusting to support what you decide to do
- Generally your actions require urine storage; an active maintenance of the LUT organs in the appropriate state
- When it is your will to pass urine, inhibition of the voiding reflex is switched off
Clinical presentations

- Detrusor overactivity; bladder contractions during the storage phase which may be spontaneous or provoked
- Non-volitional muscle activity counteracting the urine storage function
- Abnormal LUT muscle behaviour
Brain function; regulation of LUT smooth muscle control so it co-operates in carrying out the individual’s volitional actions

Impaired volitional control allows expression of the involuntary detrusor contractions &/or urethral relaxations called “DO”
The “gatekeepers” of urgency-frequency syndrome

- Transition of subconscious sensory traffic into conscious sensation
- Emergence of non-volitional LUT muscle activity
- Pathophysiology should be evaluated from perspective of potential influence on the gatekeepers
Do we need a brain for OAB?

- The brain is the seat of consciousness; where LUT sensory traffic takes undue precedence, a person may experience urgency.
- The brain is the seat of volition, emphasising storage roles of the LUT organs.