BLADDER DYSFUNCTIONS AND INTERRELATION WITH PAIN

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Bladder Function

• Storage and evacuation of urine

• Bladder wall must be compliant
  • Bladder pressure remains relatively constant

• Urothelium: barrier between urine and plasma
  • Glycoaminoglycan layer (GAG)
Bladder Function

- Cellules en ombrelle
- Couche de cellules intermédiaires
- Cellules basales
  - Turn over: 150 js
  - Fibres nerveuses afférentes

- Plaques d’uroplakine
- Jonctions serrées

- Glyco-amino-glycans
- Vésicules discoïdes
Innervation
Bladder Capacity
ml

150 - 200
I’ve a First Sensation
It’s a yet passive desire
First Desire B1

250 - 300
At home, I would go to toilet
Here I can wait
Normal Desire B2

350 - 400
I’ve to go but, I contract
my sphincter to finish what
I’m doing
Strong Desire B3

> 500
I go to toilet immediately
before the leakage
Urgency URG
Micturition

- **Normal Miction**
  - Frequency < 8/day
  - Volume 200 – 300 ml

  - No miction during night
  - No pain
  - No urgency
Bladder dysfunctions

- Overlapping symptoms ++
  - Frequency
  - Urgency

- Urinary tract infection
- Overactive bladder
- Bladder pain syndrome
Overactive Bladder (OAB)

• Definition
  • Urgency
  • Frequency (night and day time)
  • With or without Urgency incontinence
  • No pain

• Associated with overactivity of the Detrusor observed during urodynamics

• The etiology of OAB is unclear
Bladder Pain Syndrome (BPS)

- **Definition (ESSIC)**
  - Pain, pressure or discomfort associated with the urinary bladder
  - Sometimes radiating to the groins, vagina, rectum or sacrum
  - With at least one other symptom, such as
    - Daytime and/or night-time increased urinary frequency
    - Persistent urge
  - With or without cystoscopic abnormalities

- The etiology of BPS is unclear
Pain

• In the first definition of BPS (NIDDK), « pain » is relieved by voiding but soon returns

• In the new definition of BPS (ESSIC) is not only a « pain » but also a « discomfort »

• In BPS, urgency is associated with pain

• In OAB, there is no notion of pain
Urgency

• Is urgency discriminative?  No
  • 91% of patients with OAB
  • 81% of patients with BPS  
  
Clemens et al/ Neurourol Urodyn 2011

• Is urgency different?
  • Urgency is associated with the fear of incontinence in OAB
  • Urgency is associated with the fear of pain in BPS
Frequency

• The sensation of urge (void)
  • Stretch receptors
  • Functional bladder capacity ≠ anatomical capacity

• Frequency
  • Bladder sensation (pain)
  • Bladder capacity (fibrosis, decreased with age)
Physiopathology OAB and BPS

• Urothelium
  • Alteration of GAG layer
  • Activation of afferents fibers C
  • A short number of randomized controlled studies confirm efficacy of intravesical GAG layer replenishment therapy in BPS but also in OAB.
    
    *Madersbacher H, . GAG layer replenishment therapy for chronic forms of cystitis with intravesical glycosaminoglycans--a review. Neurourol Urodyn. 2013;32:9-18*

• Inflammation
  • Neurogenic inflammation
In practice

• BPS is like OAB with pain??
• Can OAB move toward BPS??

• What is the difference between OAB and BPS?
Can OAB move toward BPS?

• 15% of BPS patients have detrusor overactivity

• At what time, do we have to think about that?
  • When anticholinergic treatment is ineffective
  • If associated pelvic pains exists
  • If urgency without urinary leak

Bladder Pain / Interstitial Cystitis Symptom Score (BPIC-SS)

- Develop a patient-reported symptom score
- 3 axes with 8 items
  - Urgency
  - Frequency
  - Pain
- Validation (cut of ≥ 19/38)
  - Sensitivity 72%
  - Specificity 86%
- BPIC-SS
  - Differentiated BPS from OAB
  - Selection for Clinical trials

Humphrey et al Eur Urol 2012
RELATION BETWEEN SYMPTOM SCORES QUESTIONNAIRES AND BPS?
Correlation PUF - Cystoscopy

Brewer E et al. Urology 2007

- Validation PUF score
  - 97 patients
  - **No correlation** between PUF score and cystoscopy
Ulcerative / Non-Ulcerative

- 214 patientes (36 Ulcerative / 178 Non-Ulcerative)
  - Two groups were comparable
    - Numbers of painful areas
    - Abdominal/pelvic pain
    - Back pain

- **Pain scores** (ICSI-PI, MPQ-SF, and BPI)
  - No difference

*Killinger et al. Int Urogynecol J 2012*
Symptom scores

- Questionnaires
  - O’Leary-Sant Symptom Index (ICSI)
  - Pelvic Pain and Urgency/Frequency (PUF)
  - …

- Not for the screening or the diagnosis

- For evaluation of symptoms and/or treatments
RELATION BETWEEN FREQUENCY AND PAIN?
Voiding diaries

- Evaluation
  - Volume of micturations
  - Frequency night and day
  - Differentiate from polyuria
  - Intensity of pain before and after voiding

<table>
<thead>
<tr>
<th>Time</th>
<th>Volume</th>
<th>Pain before voiding</th>
<th>Pain after voiding</th>
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**Various clinical types**

**Frequency**

- **ABNORMALITIES ON CYSTOSCOPY**
  - Reduction of constant volumes
  - Increased frequency at night and during the day

**Volume**

- **NO SIGNIFICANT ABNORMALITY**
  - Variation of volume during the day
  - Variation of frequency at night or during the day

**Pain**

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**Nombre de mictions**

- Jour: 10 (Cystoscopie normale), 13 (Cystoscopie anormale)
- Nuit: 3 (Cystoscopie normale), 7 (Cystoscopie anormale)

**Volumes mictionnels (ml)**

- Moyens: 163 (Cystoscopie normale), 102 (Cystoscopie anormale)
- Minima: 48 (Cystoscopie normale), 29 (Cystoscopie anormale)
- Maxima: 325 (Cystoscopie normale), 205 (Cystoscopie anormale)

**ENA des douleurs avant et 15 minutes après la miction**

- Avant: 5,3
- Après: 4,4, 3,9
In practice

• BPS with abnormal cystoscopy
  – “Pathological bladder wall”
  – Voiding diaries
    – Diminution of constant volume
    – Increase of frequency night and day

• BPS with normal cystoscopy
  – “Hyper-sensibility” (Complex pelvic pain)
  – Voiding diaries
    – Variation of volume during the day
    – Variation of frequency night or day
BLADDER SENSITIZATION AND ASSOCIATED DISORDERS?
Physiopathology

- Alteration of the urothelium
- Neurogenic inflammation
- Central sensitization
- Organ cross-talk
- Visceral organ hyperalgesia/allodynia
- Pelvic sensitization
Central sensitization

Attacks of impulses:
- IL-1β
- TNF-α

Neurogenic inflammation
Local self-perpetuating reaction

Disorders:
- of cortical integration of peripheral information
- and descending control systems

Match

Fire

Stimulation X

Neurogenic inflammation and organ cross-talk

Peripheral sensitization

Orgam 1

Orgam 2

Center

Match

Orgam sensitization
BPS and associated disorders

- Allergy (and sometimes multiple allergies)
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Sjogren’s syndrome (9/10 women)
- Fibromyalgia
- Gastrointestinal disorders (IBS, IBD)
- Migraine
- Vulvodynia

Keller et al. BJU Int 2012
Overlap Dysfunction

Bullones Rodríguez et al J Urol 2013

• Reviewed 1,037 published articles

• Examined the extent of the overlap among urological and nonurological unexplained clinical conditions characterized by pain

• Up to 79% comorbidity between urological chronic pelvic pain and symptoms of irritable bowel syndrome
Central Sensitivity Syndrome

FUS: femal urethral syndrome
IC: interstitial cystitis

Central sensitivity syndrome: Yunus 2000

MPS: Myofascial pain syndrome

MPS/M yofascial pain syndrome
Painful pelvic visceral hypersensitivity

- Bladder
- Bowel

Non-painful visceral hyperactivity syndromes due to visceral hypersensitivity

Painful pelvic visceral hypersensitivity

- Bladder
- Bowel
- Vulva
- Urethra
- Prostate

Pelvic non-visceral hypersensitivity

- Musculotrigeminal (trigger points)
- Bone (bone tenderness)
- Skin, mucosa (hyperpathia, superficial allodynia)

Pelvic sensitization: clinical approach
RELATION BETWEEN PAIN AND BLADDER DYSFUNCTION?
Pudendal Nevralgia / Pelvic dysfunction

- 105 patients
- All with Nantes criterias (with positive pudendal block nerve)
- Self-questionnaires
- 87% had bladder dysfunction

Vallon, Labat 2011
Mapping of pain phenotypes / BPS

- 193 patients
- Correlation
  - Pain areas
  - QoL

Tripp et al Eur Urol 2012
Pain and Bladder dysfunction

Who is the first? Hen or egg? Pain or bladder?

- Organic bladder pathologies
  - Induced pain (infection)

- Expression of pain (bladder hyper-sensitivity)
  - Pain induced frequency and urgency

Transformation of the concept of organ pain to pain perceived in one or more organs
SAVE THE DATE

TOPICS:

- Evaluation and management strategies of chronic pelvi-perineal pain
- Meet the professor
- Workshops

More information: www.convergencespp.com