



PROSTATITIS

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CONFLICTS OF INTEREST

- NO CONFLICTS WITH THIS TALK

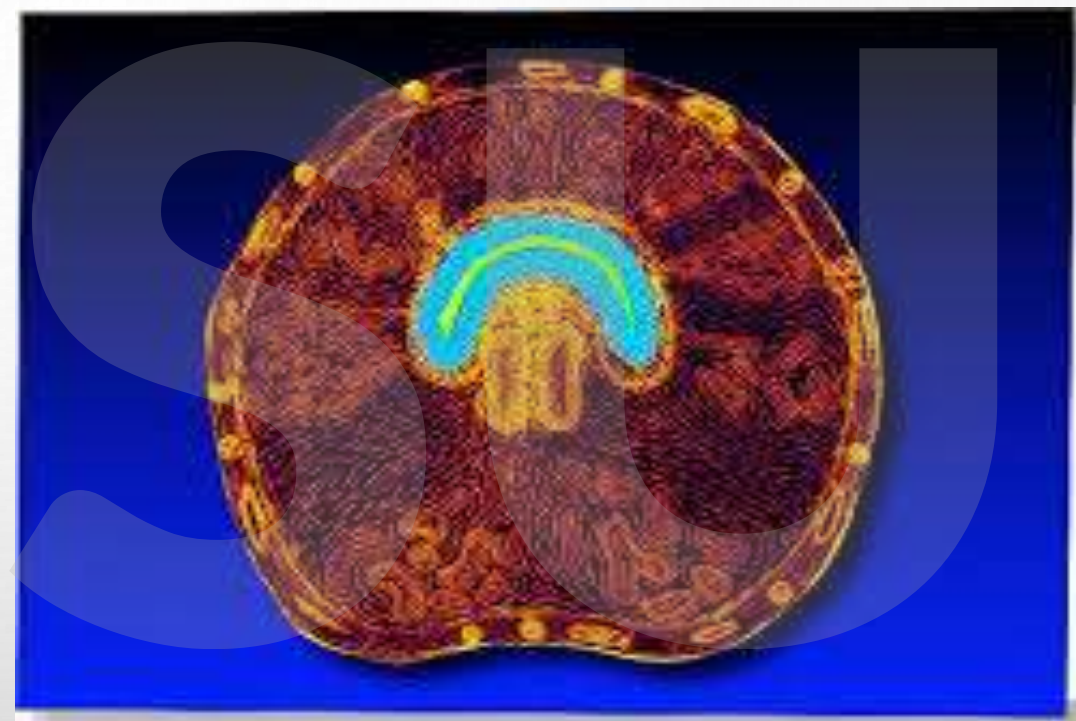
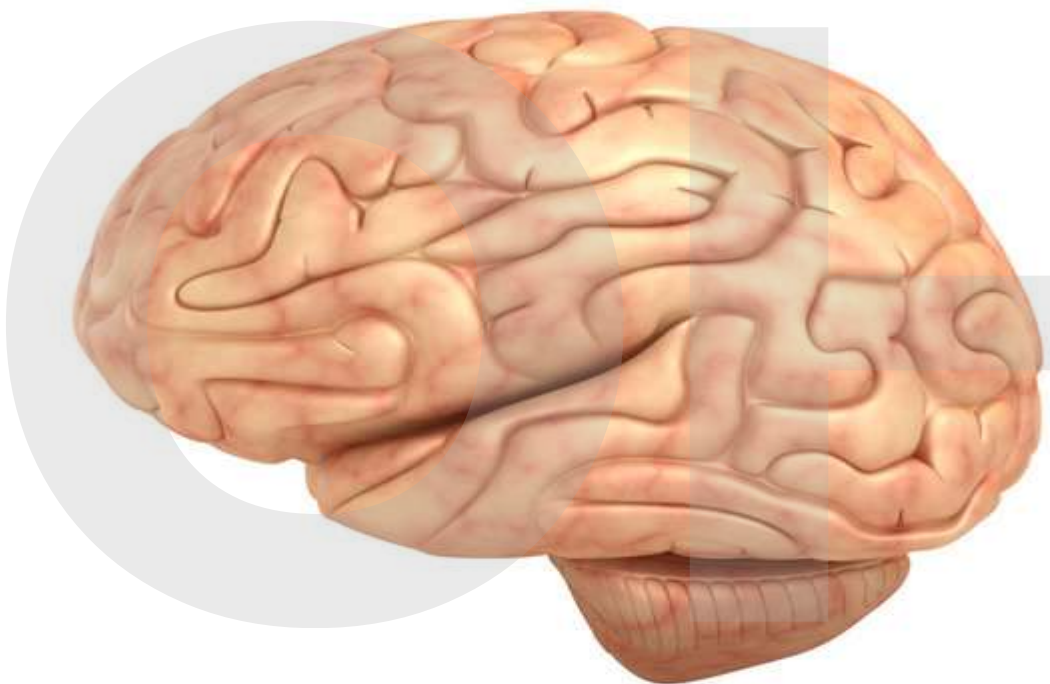
OHSU



QUESTION: WHAT PERCENTAGE OF PATIENTS WITH PROSTATITIS HAVE A BACTERIAL CAUSE?

- A) 10%
- B) 25%
- C) 50%
- D) 65%
- E) 80%

OHSU



COMMONALITIES

- BOTH BRAIN AND PROSTATE HAVE A BLOOD-ORGAN BARRIER
- IMPACTS ANTIBIOTIC PENETRATION IN UNINFLAMED ORGAN
- DURATION OF THERAPY IS OFTEN LONGER
- DIAGNOSING INFECTION IS DIFFICULT IN BOTH
- RARE INFECTIONS CAN HIDE IN THEM
 - CRYPTOCOCCUS, TUBERCULOSIS
- BIOPSY OFTEN NEEDED FOR DIAGNOSIS

CASE 1

- 25 YO MAN, MULTIPLE SEXUAL PARTNERS
- PRESENTS WITH DYSURIA, BURNING PAIN, URGENCY AND FREQUENCY AND PERINEAL PAIN
- HAS FEVER TO 101F
- SUPRAPUBIC TENDERNESS, PROSTATE BOGGINESS
- WCC 12K
- UA 3+ WBC, 1+ RBC, 1+ LE
- URINE CULTURES NEGATIVE

CASE 2

- 65 YO MAN, MARRIED, NO ACTIVITIES. DIABETES AND HTN
- HAVING URINARY SYMPTOMS LAST 3 MONTHS. 3 VISITS NOW
- TREATED WITH 7 DAYS OF BACTRIM, OR LEVOFLOXACIN EACH VISIT
- PAIN ON ERECTIONS AND EJACULATION, SOME BLOOD SEEN
- NO FEVERS
- PROSTATE EXAM SOME BOGGINESS
- UA – 10 WBC, 1+ LE
- URINE CULTURE – *KLEBSIELLA PNEUMONIA* > 10⁵, PAN SUSCEPTIBLE

CASE 3

- 43 YO PORTLAND BICYCLE ENTHUSIAST. MARRIED, NO OTHER PARTNERS
- RIDES 40 MILES EVERY SUNDAY
- NOW HAS FULLNESS IN PERINEUM, PENILE PAIN, ERECTILE DYSFUNCTION
- AFEBRILE
- PROSTATE NORMAL ON EXAM
- UA – 5 WBC, NO LE OR RBC
- URINE CULTURE NEGATIVE, GC AND CHLAMYDIA NEGATIVE

HISTORY

- FIRST DESCRIBED IN 1815 BY LEGNEAU.
- MAIN TREATMENT WAS REPEATED PROSTATE MASSAGE.
- IN 1930'S ANTIBIOTICS CAME INTO REGULAR USE.
- EVIDENT THAT MOST FORMS OF PROSTATITIS DID NOT RESPOND TO AB'S.

PROSTATITIS: A MAJOR CLINICAL PROBLEM

INCIDENCE/PREVALENCE: 4% -11%

8-12% OF UROLOGIST OFFICE VISITS

LIFE TIME PREVALENCE 14.8%

MOST COMMON UROLOGICAL DIAGNOSIS IN MEN > 50

QUALITY OF LIFE IS DISMAL (DEPRESSING) !

ETIOLOGY

- GRAM NEGATIVE ENTEROBACTERIA ACCOUNT FOR 90% OF ACUTE BACTERIAL PROSTATITIS. (*E. COLI*, *KLEBSIELLA*, *SERRATIA*, *PSEUDOMONAS*)
- *ENTEROCOCCUS* (GRAM +VE) 5 – 10%, AND *S. AUREUS* 1%
- ROLE OF ANAEROBES ARE UNKNOWN.
- ANTI-CHLAMYDIAL ANTIBODIES IN 30% OF CHRONIC PROSTATITIS, BUT < 1% CULTURE ORGANISM.
- UNDER-REPORTED OR UNKNOWN – *UREOPLASMA UROLYTICUM*, *MYCOPLASMA GENITALIUM*

INVESTIGATION

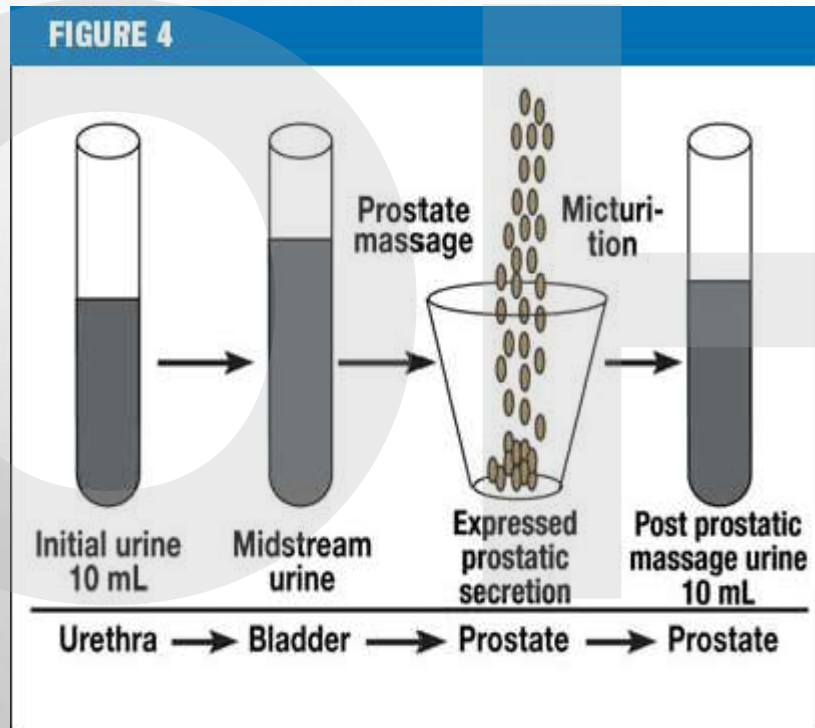
- PHYSICAL – SIGNS OF INFECTION, LOWER ABDOMINAL TENDERNESS, DRE (ANAL TONE, PROSTATE, PAIN).
 - PROSTATE BOGGINESS VERY INSENSITIVE
- EXAMINATION OF URINE.
- URODYNAMICS (VIDEO)
 - RULE OUT OTHER CAUSE – OBSTRUCTION, OAB, DYSSYNERGIA.
- CYSTOSCOPY?
- TRANSRECTAL ULTRA-SOUND (TRUS)
 - ABSCESS, MEDIAL CYSTS, SV OBSTRUCTION.
 - NOT DIAGNOSTIC FOR CHRONIC PROSTATITIS.
 - BIOPSY OF NO CLINICAL BENEFIT TO MANAGEMENT.

EXAMINATION OF URINE

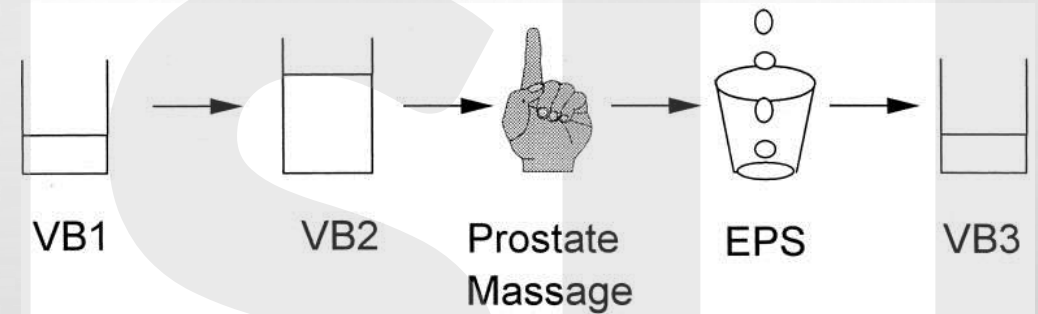
- 1968 MEARES AND STAMEY - 4 GLASS TEST.
- FOR CHRONIC PROSTATITIS ONLY.
- SIMPLIFIED 2 GLASS TEST SIMILAR SENSITIVITY AND SPECIFICITY TO 4 GLASS TEST.
- 10 WBC'S PER HPF IS CUT OFF FOR INFLAMMATORY AND NON-INFLAMMATORY CATEGORY III PROSTATITIS.

EXAMINATION OF URINE

CLASSIC STAMEY 4 GLASS TEST



Sketch of the 4-glass test for the diagnosis of chronic bacterial prostatitis and chronic pelvic pain syndrome (9)



4-Glass Test (Meares-Stamey Test)

Classification	Specimen	VB ₁	VB ₂	EPS	VB ₃
CAT II	WBC	-	+/-*	+	+
	Culture	-	+/-*	+	+
CAT IIIA	WBC	-	-	+	+
	Culture	-	-	-	-
CAT IIIB	WBC	-	-	-	-
	Culture	-	-	-	-

PROSTATITIS DIAGNOSIS

DONNA R. COFFMAN, MD

COMPARISON OF FOUR-GLASS AND TWO-GLASS PREMASSAGE AND POSTMASSAGE TEST

Nickel JC, Shoskes D, Wang Y, et al: How does the pre-massage and post-massage 2-glass test compare to the Meares-Stamey 4-glass test in men with chronic prostatitis/chronic pelvic pain syndrome? J Urol 176(1):119-124, 2006 .

The Premassage postmassage test (PPMT) may offer an adequate screening test as an alternative that is simpler, faster, and less expensive than the four-glass test .

CLASSIFICATION

Table 15–1. CLASSIFICATION SYSTEM FOR THE PROSTATITIS SYNDROMES

Traditional	National Institutes of Health	Description
Acute bacterial prostatitis	Category I	Acute infection of the prostate gland
Chronic bacterial prostatitis	Category II	Chronic infection of the prostate gland
N/A	Category III chronic pelvic pain syndrome (CPPS)	Chronic genitourinary pain in the absence of uropathogenic bacteria localized to the prostate gland with standard methodology
Nonbacterial prostatitis	Category IIIA (inflammatory CPPS)	Significant number of white blood cells in expressed prostatic secretions, postprostatic massage urine sediment (VB3), or semen
Prostatodynia	Category IIIB (noninflammatory CPPS)	Insignificant number of white blood cells in expressed prostatic secretions, postprostatic massage urine sediment (VB3), or semen
N/A	Category IV asymptomatic inflammatory prostatitis (AIP)	White blood cells (and/or bacteria) in expressed prostatic secretions, postprostatic massage urine sediment (VB3), semen, or histologic specimens of prostate gland

N/A, not applicable.

Table 1. Classification of Prostatitis According to Classical and Newer National Institutes of Health (NIH) Categories Based on Prostatic Localization Studies for White Blood Cells (WBC) and Bacteria

Classical classification (NIH category)	Prostatitis cases, %	Mid-stream urine specimen (VB2)		Prostatic specimen (EPS or VB3)	
		WBC	Culture	WBC	Culture
ABP (I)	<1	++	+	++	+
CBP (II)	5-10	+	+	+	+
CP/CPPS (III)	80-90				
Inflammatory (IIIA)		-	-	+	-
Noninflammatory (IIIB)		-	-	-	-
AIP (IV)	10	+	-	-	-

NOTE. Adapted from Doble [4]. +, present or positive; ++, present in large numbers or strongly positive; -, negative; ABP, acute bacterial prostatitis; AIP, asymptomatic inflammatory prostatitis; CBP, chronic bacterial prostatitis; CP/CPPS, chronic prostatitis/chronic pelvic pain syndrome; EPS, expressed prostatic secretions; VB2, voided bladder second specimen (a clean-catch mid-stream urine specimen); VB3, voided bladder third specimen (a post-prostatic massage urine specimen).

CATEGORY I – ACUTE BACTERIAL

THE PATIENT TYPICALLY COMPLAINS OF :

- URINARY FREQUENCY, URGENCY, AND DYSURIA.
- OBSTRUCTIVE VOIDING COMPLAINTS INCLUDING HESITANCY, POOR INTERRUPTED STREAM, STRANGURY, AND EVEN ACUTE URINARY RETENTION ARE COMMON. TENESMUS.
- PERINEAL AND SUPRAPUBIC PAIN
- ASSOCIATED PAIN OR DISCOMFORT OF THE EXTERNAL GENITALIA.
- SIGNIFICANT SYSTEMIC SYMPTOMS INCLUDING FEVER, CHILLS, MALAISE, NAUSEA AND VOMITING, AND EVEN FRANK SEPTICEMIA WITH HYPOTENSION

NOT COMMON

APPROXIMATELY 5% OF PATIENTS WITH ACUTE BACTERIAL PROSTATITIS MAY PROGRESS TO CHRONIC BACTERIAL PROSTATITIS) CHO ET AL., 2005

CATEGORY I – ACUTE BACTERIAL

- SEND MSSU (MID STREAM SPECIMEN OF URINE) / BLOOD CULTURES.
- CT PELVIS
 - MAY SHOW PROSTATIC ABSCESS
- ANTIBIOTICS
 - I.V. IF EVIDENCE OF SEPSIS
 - CEPHALOSPORINS, OR FLUOROQUINOLONES.
 - 4 WEEKS TREATMENT.
- SURGERY
 - SP CATHETER
 - TRUSS OR CT TO EXCLUDE ABSCESS.
 - ABSCESS BEST DRAINED BY TUR.

CATEGORY II – CHRONIC BACTERIAL PROSTATITIS.

- 10% OF ALL PROSTATITIS
- RECURRENT UTI'S IN 25 – 40%
- MAY BE ASYMPTOMATIC BETWEEN EPISODES OR HAVE A LONG HISTORY OF CPPS.
- TREAT WITH ANTIBIOTICS
 - FLUOROQUINOLONES (CIPRO AND LEVOFLOXACIN) MOST EFFECTIVE, BACTRIM NEXT ALTERNATIVE.
 - 6-12 WEEKS OF TREATMENT.
 - 60 – 85% BACTERIOLOGICAL CURE.
 - 40% SYMPTOM CURE.

PREVENTATIVE ISSUES?



Table 2. Antibiotics with Pharmacological Data, Clinical Case Report(s), or a License to Support Their Use for Treatment of Bacterial Prostatitis

Drug(s) ^a	Prostate tissue or fluid concentration	FDA approval	Reference(s)
Amoxicillin-clavulanate	Tissue, 3.8–7.2 $\mu\text{g/g}$ amoxicillin	UTI	[55, 56]
Ampicillin-sulbactam	Tissue, 0.42–548.33 $\mu\text{g/g}$ ampicillin	No	[57]
Piperacillin	Tissue, 70.7 $\mu\text{g/g}$	UTI	[42, 58]
Piperacillin-tazobactam		No	
Cephalexin	Tissue, 0.5–10 $\mu\text{g/g}$	UTI, ABP	[42, 59, 60]
Cefazolin	Fluid, <10 $\mu\text{g/mL}$	UTI, BP	[42, 60]
Cefaclor	Tissue, 0.74 $\mu\text{g/g}$	C-UTI, UC-UTI	[42, 61]
Cefuroxime	Tissue, 7.6–29.2 $\mu\text{g/g}$	UTI	[62–64]
Cefotetan	Tissue, 36 $\mu\text{g/g}$; Fluid, 0.8 $\mu\text{g/mL}$	UTI	[42, 65]
Cefotaxime	Tissue, 6.8–22.5 $\mu\text{g/g}$	UTI	[42, 66–68]
Ceftriaxone	Tissue, 12.9–73.7 $\mu\text{g/g}$	UTI	[42, 69]
Ceftazidime	Tissue, 23.4 $\mu\text{g/g}$	UTI	[70]
Cefepime		C-UTI, UC-UTI	
Cefixime	Tissue, 1.08 $\mu\text{g/g}$	UC-UTI	[71]
Cefpodoxime	Tissue, 0.5 $\mu\text{g/g}$	UC-UTI	[72]
Aztreonam	Tissue, 6–10 $\mu\text{g/g}$	C-UTI, UC-UTI	[73, 74]
Imipenem ^b	Tissue, 5.3 $\mu\text{g/g}$	C-UTI, UC-UTI	[21, 42]
Doripenem		C-UTI	
Ertapenem ^b		C-UTI	[75]
Vancomycin ^b		No	[76, 77]
Trimethoprim-sulfamethoxazole	Tissue, 7.1 $\mu\text{g/g}$ for trimethoprim, 24 $\mu\text{g/g}$ for sulfamethoxazole	UTI	[78]
Nitrofurantoin		UTI	
Ciprofloxacin	Tissue, 0.6–4.18 $\mu\text{g/g}$	UTI, CBP	[79]
Gatifloxacin	Fluid, 1.72–3.1 $\mu\text{g/mL}$	UTI	[80]
Levofloxacin	Tissue level greater than corresponding plasma level	C-UTI, UC-UTI	[81]
Moxifloxacin	Fluid, 3.8–8.5 $\mu\text{g/mL}$	No	[82, 83]
Ofloxacin	Tissue, 4.1 $\mu\text{g/g}$; fluid, 4.0 $\mu\text{g/mL}$	C-UTI, UC-UTI, BP	[84]
Prulifloxacin	Tissue, 1.9–5.5 $\mu\text{g/g}$	No	[85]
Clindamycin	Tissue level greater than corresponding plasma level	No	[42]

ANTIBIOTIC SUMMARY

- QUINOLONES AND TRIMETHOPRIM/SULFA ARE BEST ORAL ANTIBIOTICS
 - WATCH DRUG INTERACTIONS AND TOXICITIES
- DOXYCYCLINE GETS 40% INTO PROSTATE
- INTRAVENOUS CEPHALOSPORINS ARE SUPERIOR THAN ORAL AS THEY ACHIEVE HIGH LEVELS AND OVERCOME ALKALIZATION WITHIN THE PROSTATE
- IV ERTAPENEM AND PIP/TAZO ARE ALSO EFFECTIVE
- AVOID NITROFURANTOIN, FOSFOMYCIN AND MACROLIDES
 - HOWEVER MAY NEED A MACROLIDE FOR NGU
- USE YOUR CULTURE DATA AND RESISTANCE PATTERNS

CATEGORY IIIA – CHRONIC PELVIC PAIN SYNDROM (CPPS INFLAMMATORY)

- PAIN – PERINEUM, SUPRAPUBIC AND PENILE BUT CAN BE TESTES, GROIN AND LOWER BACK.
- PAIN DURING OR AFTER EJACULATION.
- LUTS (STORAGE AND VOIDING SYMPTOMS)
- ERECTILE DYSFUNCTION IS INCREASED.
- SYMPTOMS PRESENT FOR > 3 MONTHS.
- FREQUENTLY NON-BACTERIAL
- SICKNESS IMPACT PROFILE – QL SCORES SIMILAR TO MI, ANGINA AND CROHN'S.

CATEGORY IIIB – CHRONIC PELVIC PAIN SYNDROME (CPPS NON-BACTERIAL)

- SAME PRESENTING FEATURES AS IIIA, BUT < 10 WBC'S PER HIGH POWER FIELD ON EXPRESSED PROSTATIC SECRETION AND VB3.
- MAY HAVE ELEVATED PSA
 - REFLECTS CHRONIC INFLAMMATION
- NIH – CHRONIC PROSTATITIS SYMPTOM INDEX.

CATEGORY IV – ASYMPTOMATIC INFLAMMATORY PROSTATITIS

- AS NAME SUGGESTS!!
- WBC'S OR BACTERIA IN EPS OR VB3 OR HISTOLOGICAL EXAMINATION OF GLAND.
- PRESENT WITH OBSTRUCTION, RAISED PSA, INFERTILITY.

CPPS TREATMENT

- **α -BLOCKERS**

- MEHIK ET AL UROLOGY. 2003 SEP;62(3):425-9. RCT OF XATRAL (ALFUZOSIN) V PLACEBO FOR 6 MONTHS. MODEST BUT SIGNIFICANT REDUCTION IN PAIN AND SYMPTOM SCORE.
- WANG ET AL. INT UROL NEPH 2016 48: 8-13. RCT LEVOFLOXACIN +/- TERAZOSIN. 115 PATIENTS, THE ADDITION INCREASED RESPONSE BY 5%. NO ROLE FOR TERAZOSIN ALONE
- COHEN ET AL. PLOS ONE 2012 :7 META-ANALYSIS OF MULTIMODALITY TREATMENTS IN CPPS. NO CLEAR EVIDENCE THAT ANY WORK.

ALPHA-BLOCKERS

- ALFUZOSIN, TERAZOSIN, TAMSULOSIN
- *N ENGL J MED. 2008 DEC 18;359(25):2663-73. ALFUZOSIN AND SYMPTOMS OF CHRONIC PROSTATITIS-CHRONIC PELVIC PAIN SYNDROME NICKEL JC ET AL.*
- MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF ALFUZOSIN.
- 272 MEN WERE RANDOMLY ASSIGNED TO TREATMENT FOR 12 WEEKS WITH EITHER 10 MG OF ALFUZOSIN/DAY OR PLACEBO.
- THE PRIMARY OUTCOME WAS A REDUCTION OF AT LEAST 4 POINTS IN THE CPSI SCORE.

	Placebo N=134	Alfuzosin N=138
CPSI responders	66(49%)	68(49%)

CPPS TREATMENT

- ANTI-INFLAMMATORY AGENTS

- NSAID'S IMPROVE PAIN AND SYMPTOMS.
- NICKEL ET AL J UROL. 2005 APR;173(4):1252-5. RCT OF PENTOSAN POLYSULFATE SODIUM (USED FOR INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME) VERSUS PLACEBO IN CPPS. 300MG TDS FOR 16 WEEKS. SLIGHT IMPROVEMENT OVER PLACEBO, ONLY SIGNIFICANT IN QOL SCORE.

ANTI-INFLAMMATORIES

- CELECOXIB, ROFECOXIB
- *J UROL. 2003 APR;169(4):1401-5. A RANDOMIZED, PLACEBO CONTROLLED, MULTICENTER STUDY TO EVALUATE THE SAFETY AND EFFICACY OF ROFECOXIB IN THE TREATMENT OF CHRONIC NONBACTERIAL PROSTATITIS. NICKEL JC ET AL.*
- MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF ROFECOXIB.
- 161 MEN WERE RANDOMLY ASSIGNED TO TREATMENT WITH EITHER 25-50 MG OF ROFECOXIB/DAY OR PLACEBO.
- OF THE PATIENTS, 79% ON 50 MG ROFECOXIB VERSUS 59% ON PLACEBO REPORTED NO OR MILD PAIN. BUT NOT STATISTICALLY SIGNIFICANT.

CPPS TREATMENTS???

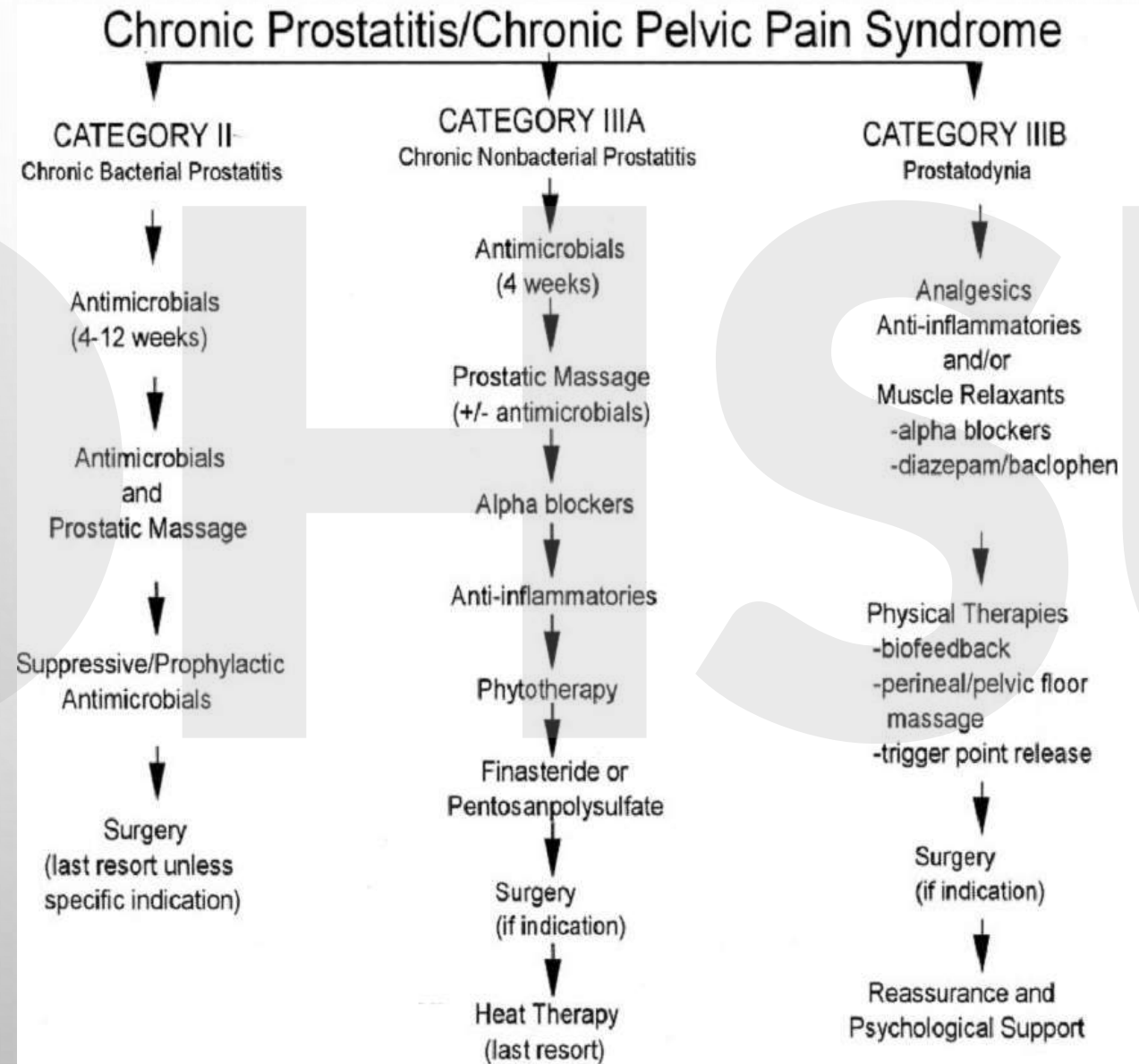
- PROSTATE MASSAGE
 - CAMPBELL'S NO GOOD EVIDENCE TO SUPPORT USE.
- PHYTOTHERAPY
 - SAW PALMETTO – NO EFFECT
 - BEE POLLEN EXTRACT (A BIOFLAVONOID) SHOWED SLIGHT IMPROVEMENTS.
- HORMONE THERAPY
 - NICKEL ET AL BJU INT. 2004 MAY;93(7):991-5. RCT OF FINASTERIDE V PLACEBO SLIGHT IMPROVEMENT BUT NOT PROPERLY POWERED.
- PERINEAL OR PELVIC FLOOR MASSAGE OR MYOFASCIAL TRIGGER POINT RELEASE
 - WHAT?
 - CORNEL ET AL EUR UROL. 2005 MAY;47(5):607-11. EPUB 2005 JAN 22. RCT OF BIOFEEDBACK SHOWED SIGNIFICANT REDUCTION IN NIH-CPSI SCORES.
 - OTHER SMALLER STUDIES GIVE SIMILAR RESULTS.

CPPS TREATMENT

• SURGERY

- TURP/BNI ONLY IF EVIDENCE OF OBSTRUCTION.
- TURP IN REFRACTORY CAT. II REPORTED.
- TURP IN CPPS – NO EVIDENCE
- RADICAL PROSTATECTOMY – ONE CASE REPORTED
'NO DEFINITIVE CLINICAL SERIES OR LONG-TERM FOLLOW-UP HAS EVER BEEN PRESENTED, AND THIS TYPE OF SURGERY SHOULD NOT BE ENCOURAGED OR RECOMMENDED AT THIS TIME'.

ALGORITHM OR TREATMENT OF CPPS



CONCLUSION

- BACTERIAL CAUSES FOR PROSTATITIS IS RESPONSIBLE FOR 10% OF CASES
- PROVEN BACTERIAL CASES SHOULD BE TREATED WITH ORAL FLUOROQUINOLONE, TRIMETHOPRIM/SULPHA OR IV ANTIBIOTIC
- NON-BACTERIAL CAUSES REQUIRE SYMPTOMATIC HELP WITH NO GOOD DATA SUPPORTING NSAID'S, ALPHA BLOCKERS OR HORMONE THERAPY, HOWEVER CAN BE TRIED ON CASE BY CASE BASIS