

## Purpose of this manual

This brochure is for the trainees and residents to clarify the indications and techniques of treatment of various diseases in Urology. All of residents should carefully read this and understand the aim of it.

The first version was published in 2002, and this is the second version in 2004.

This manual is also to be revised at every time when the staffs of our department need.

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## **RENAL CANCER**

### Therapeutic indications by TNM

- 1) cT1aN0M0 and appropriate location of tumor (without technical problems)  
 Partial nephrectomy  
 Technique;
  - Retroperitoneal approach
  - Non-ischemic if possible
  - Intra-operative ultrasonography
  - Argon beam coagulator or Sonosurge (ultrasonic scalpel)
  - No LN dissection
- 2) cT1aN0M0 with technical problem in the location of tumor, cT1bN0M0, and cT1N0M1  
 Hand-assisted laparoscopic nephrectomy (HALN)  
 Technique; Use Lap-Disc and no LN dissection
- 3) cT2  
 Radical nephrectomy  
 Technique; Transperitoneal approach and L-shape skin incision  
 LN dissection; until aortocaval
- 4) No candidate for nephrectomy  
 Immunotherapy (see below)

#### Additional:

- Patients with functional solitary kidney or synchronous bilateral cancer  
 Partial nephrectomy should be done as possible, and tumor size is not limited.

### **Adjuvant therapy for renal cancer**

#### Indications

- Patients with LN or distant metastasis (clinically or pathologically)
- Stage; pT3
- pV1 and/or pL1, or INF  $\gamma$ , or G3
- Performance status should be 0 or 1

#### Method

- Continuous subcutaneous infusion of IFN  $\alpha$  ( $300 \times 10^4$  units/day) for 1 month (5 days/week  $\times$  4 weeks).

### **Immunotherapy**

- 1) Continuous subcutaneous infusion of IFN $\alpha$  ( $300 \times 10^4$  units/day) for 3 month (5 days/week  $\times$  12 weeks).  
 After 3 months, NC continue IFN $\alpha$  up to 6 months, and if PD go to IL-2.  
 If NC after 6 months, continue IFN $\alpha$  or go to IL-2, and if PD go to IL-2.
- 2) IL-2 intravenous infusion ( $70 \times 10^4$  units/ 3 days,  $105 \times 10^4$  units/3 days, and  $140 \times 10^4$  units/ up to 60 days).  
 If NC after 60 days, go to continue or chemotherapy, and PD go to chemotherapy.

### **Chemotherapy**

## ***RENAL PELVIC CANCER***

### Therapeutic indications by TNM

#### 1) cT1-2 N0 M0

Hand-assisted retroperitoneoscopic nephroureterectomy

- LN dissection; from upper pole of the kidney to aortic bifurcation
- UV-J; cuff resection

#### 2) cT3 N0 M0

Radical nephroureterectomy

- Transperitoneal approach and median skin incision
- LN dissection; upper pole of the kidney to aortic bifurcation
- UV-J; cuff resection

#### 3) cT4, or any T cN1-3 and/or cM1

Chemotherapy

CCr ≥ 50	MVAC	3 courses	Second line (PG therapy)
CCr < 50	PG therapy	6 courses	
	Paclitaxel 200mg/m <sup>2</sup>		Day 1(1 hour i.v. infusion)
	Gemcitabine 1000mg/m <sup>2</sup>		Day 1, 8, 15(30 min i.v. infusion) / every 21 days

### **Adjuvant chemotherapy**

Indication

pT3, or pN1, or pV1

Technique

MVAC; 2 courses

## ***URETERAL CANCER***

### Therapeutic indications by TNM

#### 1) Ta or T1 N0 M0, G 1, solitary, <2.0cm, and papillary tumor with negative cytology

Transurethral ureteroscopic resection

Transurethral resection of tumor

Holmium-YAG Laser ablation by flexible ureterorenoscope

#### 2) Multiple cT1 and cT1-2 N0 M0

Hand-assisted retroperitoneoscopic nephroureterectomy (same as renal pelvic cancer)

LN dissection;

- U1; upper pole of the kidney to aortic bifurcation
- U2; lower pole of the kidney to common iliac
- U3; aortic bifurcation to internal iliac

UV-J; cuff resection

#### 3) cT3 N0 M0

Radical nephroureterectomy

Transperitoneal approach and median skin incision

LN dissection

- U1; upper pole of the kidney to aortic bifurcation
- U2; lower pole of the kidney to common iliac
- U3; aortic bifurcation to internal iliac

UV-J;

- U1, U2; cuff resection
- U3; partial cystectomy

## 4) cT4, or any T cN1-3 and/or cM1

## Chemotherapy

CCr ≥ 50	MVAC	3 courses	Second line (PG therapy)
CCr < 50	PG therapy	6 courses	
	Paclitaxel 200mg/m <sup>2</sup>		Day 1(1 hour i.v. infusion)
	Gemcitabine 1000mg/m <sup>2</sup>		Day 1, 8, 15(30 min i.v. infusion) / every 21 days

## Additional operation:

- U3 and solitary, and able to perform ureterovesicostomy  
Partial ureterectomy with ureterovesicostomy

**Adjuvant chemotherapy**

Indication: pT3, or pN1, or pV1

Regimen: MVAC; 2 courses

**Adjuvant bladder instillation chemotherapy**

Indication: Simultaneous bladder tumor (Included G2, and pT1)

Technique; MMC+cylocide (per week) for 10 times

**CIS in the upper urinary tract**

Diagnosis: by positive cytology or biopsy (under ureterorenoscopy)

## Technique

BCG Instillation (40mg/saline 40ml for 8 times) with D-J catheter; 2courses

Head down (10-15°) during instillation of BCG

After BCG therapy, re-ureterorenoscopic evaluation is scheduled.

## ONCOLOGICAL CHEMOTHERAPY

### Principles of therapy

- All the chemotherapeutic agents should be given to the patients as same as the amount of original regimens.
- If  $WBC < 2.5 \times 10^3$  or  $Plt < 75 \times 10^3$  (Side effect; Grade II) before i.v. injection of any chemotherapeutic agents, scheduled agents should be skipped.

### Grading of the major side effects (by Japan Society of Clinical Oncology)

Grade	0	1	2	3	4
Blood					
Hgb	$\geq 11.0$	10.9-10.0	<b>9.9-8.0</b>	<b>&lt;8.0</b>	-
WBC ( $\times 10^3$ )	$\geq 4.0$	3.9-3.0	<b>2.9-2.0</b>	<b>1.9-1.0</b>	<b>&lt;1.0</b>
Neutro ( $\times 10^3$ )	$\geq 2.0$	1.99-1.5	<b>1.49-1.0</b>	<b>0.99-0.5</b>	<b>&lt;0.5</b>
Plt ( $\times 10^3$ )	$\geq 100.0$	99-75	<b>74-50</b>	<b>49-25</b>	<b>&lt;25</b>
Liver					
T-bil	WNL	-	<b>&lt;2.0 <math>\times</math> Nu</b>	<b>2.1-10.0 <math>\times</math> Nu</b>	<b>&gt;10.0 <math>\times</math> Nu</b>
AST/ALT	WNL	$\leq 2.5 \times$ Nu	<b>2.6-5.0 <math>\times</math> Nu</b>	<b>5.1-30.0 <math>\times</math> Nu</b>	<b>&gt;30.0 <math>\times</math> Nu</b>
ALP	WNL	$\leq 2.5 \times$ Nu	<b>2.6-5.0 <math>\times</math> Nu</b>	<b>5.1-10.0 <math>\times</math> Nu</b>	<b>&gt;10.0 <math>\times</math> Nu</b>
Kidney					
Cr	WNL	$<1.5 \times$ Nu	<b>1.5-3.0 <math>\times</math> Nu</b>	<b>3.1-6.0 <math>\times</math> Nu</b>	<b>&gt;6.0 <math>\times</math> Nu</b>
Proteinuria (mg/l)	-	1+ $\leq 300$ mg	++ +++ <b>&gt;300mg, &lt;1000mg</b>	++++ <b>&gt;1000mg &lt;3000mg</b>	<b>Nephritic syndrome</b>

## **BLADDER CANCER**

### Therapeutic indications by TNM

1) cT1 N0 M0 for therapy, and all Stages of cancers for T staging.

#### TUR-Bt

Resect the tumor superficially at first, then deeper.

If pre-operative urine cytology is positive and multiple tumors, randomized biopsy (CPB) should be done.

#### Adjuvant intravesical chemotherapy

	Numbers of tumor	pT stage	Grade I	Grade II	Grade III
Primary	Solitary	Ta	-		
		T1			
	Multiple	Ta or T1			
Recurrent	Solitary	Ta			
		T1			Cystectomy*
	Multiple	Ta			
		T1			Cystectomy*

: BCG instillation ; BCG (40mg) intravesical therapy (once a week / 8 times)

: Randomised Study: Intravesical FARM therapy

Single instillation just after TUR versus once a week / 10 times.

\*: Cystectomy is recommended for the “reccurent G3 and pT1” patients.

2) cT2 or cT3 N0 M0, and G3 pT1 with resistant to BCG therapy.

#### Radical cystectomy

Indication: PS 0 or 1, and if T3, neoadjuvant MVAC 2 course should be done.

- Male patients; Cysto-prostato-urethrectomy
- Female; Cysto-urethrectomy with anterior vaginal wall resection
- Urinary diversion

Ileal conduit (Bricker’s ope + turnble stoma) with urethrectomy

Ileal Neobladder (Studer) when no cancer in trigonum and urethra

3) any T N0 M0 with refusal of cystectomy, or poor candidate

Arterial Infusion Chemoradiotherapy after alteration of intra-pelvic blood flow (AIC therapy)

Using a subcutaneous reservoir system in lower abdominal wall.

CDDP 30mg/m<sup>2</sup>

ADM 20mg/m<sup>2</sup>

Day 1 on the 1<sup>st</sup>, 2<sup>nd</sup>, 5<sup>th</sup> and 6<sup>th</sup> week

Radiation therapy

from Day 1: total 60 Gy

Chemoradiation (poor candidate for AIC)

CDDP 5mg/m<sup>2</sup>

Everyday before radiation

Radiation therapy

Total 60 Gy

4) cT4, any T cN1-3 and/or cM1, and refused cystectomy

#### Chemotherapy

CCr 50 MVAC 3 courses Second line (PG therapy)

CCr < 50 PG therapy 6 courses

Paclitaxel 200mg/m<sup>2</sup> Day 1(1 hour i.v. infusion)

Gemcitabine 1000mg/m<sup>2</sup> Day 1, 8, 15(30 min i.v. infusion)

/ every 21 days

#### Adjuvant chemotherapy

Indication: pT3, or pN1, or pV1

Regimen: MVAC; 2 courses

# PROSTATE CANCER

## Biopsy of prostate

### Indication:

1. At least one of PSA >4.0ng/ml, and abnormal findings on DRE or TRUS-P
2. If PSA 2.5~4.0 ng/ml; PSA-V 0.75/year after annual PSA follow
3. Re-biopsy for *Gray zone* PSA after 6months;
  - If age 75 years, stable or rising of PSA (Check every 3 months)
  - If age 76 years: PSA-V 0.75

### Technique:

1. Sextant biopsy {If prostate volume 30g, 8 cores (add each anterior horn)}
2. Re-biopsy: 10 cores (each TZ and anterior horn)

## Examination for TNM Staging:

- TRUS-P, pelvic MRI, and systemic bone scan for Standard evaluation.
- Abdominal CT scan: If PSA>50ng/ml, or PSA  $\geq$  20ng/ml and GS  $\geq$  8 for the detection of para-aortic LN metastasis.

## Therapeutic indications by TNM

1) cT1a N0 M0: active monitoring (watchful waiting)

2) cT1b, cT1c-T2 N0 M0:

- 75 years old and PS 0-1

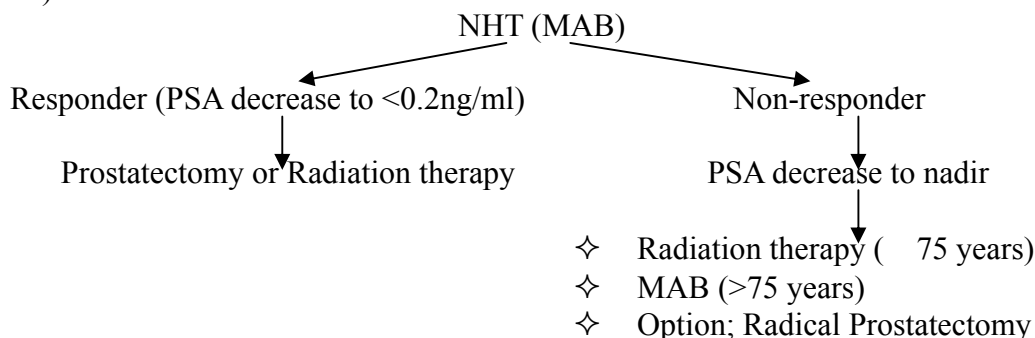
### Radical prostatectomy

50% Organ confined→Operation

< 50% Organ confined→Neoadjuvant hormone therapy (NHT) with MAB more than 6 months or until PSA nadir (PSA nadir: lowest level of PSA after initial treatment)

- From 76 to 80 years old, reject or high risk for prostatectomy, Radiation therapy (prostate+SV) after NHT: Total dose of 70Gy
- No candidate for prostatectomy or radiation therapy  
Hormone therapy: intermittent androgen suppression (ISA) with MAB

3) cT3 NO MO:



4) Any T N1 and/or M1

### MAB

- If Gleason scores 8, 75 years, and PS 0-1 V-TEC therapy
  - Paclitaxel: 135mg/m<sup>2</sup> (Day 2)
  - Carboplatin: AUC 5 (Day 2)
  - Estramustine Phosphate (EMP): 2cap (every day)
  - VP-16 :50mg (Day 1-10)
  - Every 3 weeks, and total 3 cycles

➤ If 80 years old

1) IAS (Intermittent androgen suppression)

Undetectable PSA more than 12 months      withdraw MAB

↓ (check PSA and testosterone every 3 mos.)  
PSA 1.5ng/ml

↓  
IAS

2) Surgical castration with anti-androgen up to PSA nadir.

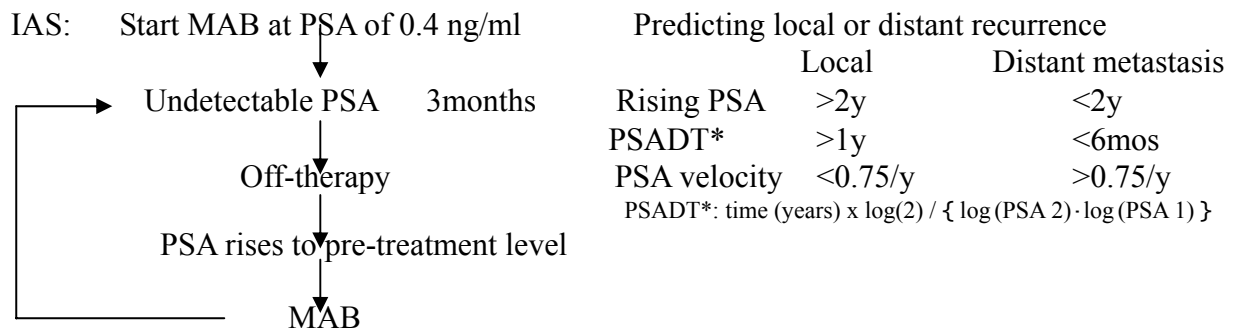
### Rising PSA after radical treatment

1) After Prostatectomy: Start after PSA>0.4 ng/ml

- *Local recurrence*      Salvage radiation therapy ( 64Gy) after biopsy.
- *Distant metastasis*      intermittent androgen suppression (IAS)

2) After radiation therapy

- Consecutive PSA rise      Start IAS at PSA of 1.5 ng/ml



### Hormone refractory prostate cancer (HRPC)

Check the serum testosterone level < castration level

1. Withdraw anti-androgen (flutamide 4 weeks, bicalutamide 8 weeks)
2. Alter anti-androgen
3. Chemotherapy
  - 1) 75 years old, PS 0-1  
3 cycles of Paclitaxel+Carboplatin+EMP+VP-16 (V-TEC therapy)  
maintain with EMP(4 cap) + cyclophosphamide(100mg)
  - 2) >75 years old EMP (4 cap) + cyclophosphamide (100mg)
4. Dexamethasone: initial dose; 1.5 mg/day 1.0mg/day 0.5 mg/day (maintain)
5. Incadronate disodium (Biphonal®): 10mg div / every 2 weeks

**Partin's Nomogram 2001**

Gleason score Pathological findings		PSA 0 ~ 2.5				PSA 2.6 ~ 4.0				PSA 4.1 ~ 6.0				PSA 6.1 ~ 10.0				PSA 10.1 ~			
		Clinical Stage				Clinical Stage				Clinical Stage				Clinical Stage				Clinical Stage			
		T1 c	T2a	T2b	T2c	T1 c	T2a	T2b	T2c	T1 c	T2a	T2b	T2c	T1 c	T2a	T2b	T2c	T1 c	T2a	T2b	T2c
2 ~ 4	OC	95	91	88	86	92	85	80	78	90	81	75	73	87	76	69	67	80	65	57	54
	CP	5	9	12	14	8	15	20	22	10	19	25	27	13	24	31	33	20	35	43	46
	SV+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	LN+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5 ~ 6	OC	90	81	75	73	84	71	63	61	80	66	57	55	75	58	49	46	62	42	33	30
	CP	9	17	22	24	15	27	34	36	19	32	39	40	23	37	44	46	33	47	52	51
	SV+	0	1	2	1	1	2	2	2	1	1	2	2	2	4	5	5	4	6	8	6
	LN+	0	0	1	1	0	0	1	1	0	1	2	3	0	1	2	3	2	4	8	13
3+4=7	OC	79	64	54	51	68	50	41	38	63	44	35	31	54	35	26	24	37	20	14	11
	CP	17	29	35	36	27	41	47	48	32	46	51	50	36	49	52	52	43	49	47	42
	SV+	2	5	6	5	4	7	9	8	3	5	7	6	8	13	16	13	12	16	17	13
	LN+	1	2	4	6	1	2	3	5	2	4	7	12	2	3	6	10	8	14	22	33
4+3=7	OC	71	53	43	39	58	39	30	27	52	33	25	21	43	25	19	16	27	14	9	7
	CP	25	40	45	45	37	52	57	57	42	56	60	57	47	58	60	58	51	55	50	43
	SV+	2	4	5	5	4	6	7	6	3	5	5	4	8	11	13	11	11	13	13	10
	LN+	1	3	6	9	1	2	4	7	3	6	10	16	2	5	8	13	10	18	27	38
8 ~ 10	OC	66	47	37	34	52	33	25	23	46	28	21	18	37	21	15	13	22	11	7	6
	CP	28	42	46	47	40	53	57	57	45	58	59	57	48	57	57	56	50	52	46	41
	SV+	4	7	9	8	6	10	12	10	5	8	9	7	13	17	19	16	17	19	19	15
	LN+	1	3	6	10	1	3	5	8	3	6	10	16	3	5	8	13	11	17	27	38

# PENILE CANCER

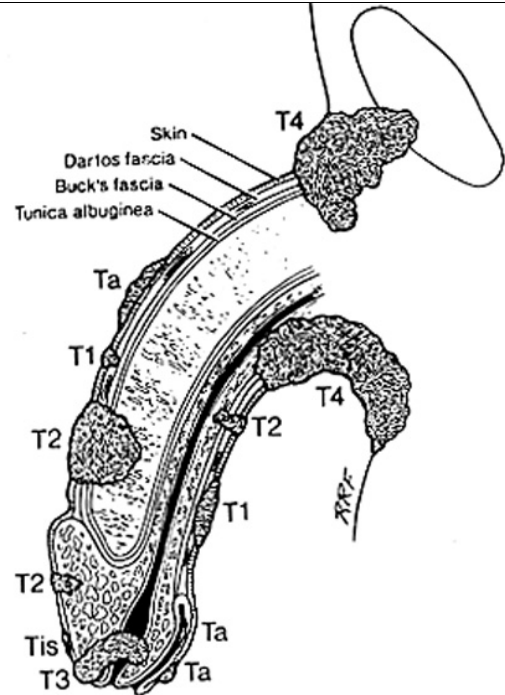
## Classification of Penile Cancer

Stage I (A)	Tumors confined to glans, prepuce, or both.
Stage II (B)	Tumors extending onto shaft of penis
Stage III (C)	Tumors with inguinal metastasis that are operable
Stage IV (D)	Tumors involving adjacent structure; tumors associated with inoperable inguinal metastasis or distant metastasis

### TNM CLASSIFICATION OF PENILE CARCINOMA

Primary Tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma-in-situ
Ta	Noninvasive verrucous carcinoma
T1	Tumor invades subepithelial connective tissue
T2	Tumor invades corpus spongiosum or cavernosum
T3	Tumor invades urethra or prostate
T4	Tumor invades other adjacent structures
Regional Lymph Nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single, superficial, inguinal lymph node
N2	Metastasis in multiple or bilateral superficial inguinal lymph nodes
N3	Metastasis in deep inguinal or pelvic lymph node(s), unilateral or bilateral
Distant Metastases (M)	
MX	Presence of distant metastasis cannot be assessed
M0	No distant metastases
M1	Distant metastases

Adapted from Union Internationale Contre le Cancer (UICC): TNM Atlas: Illustrated Guide to the TNM/TNM Classification of Malignant Tumours, 3rd ed. New York, Springer-Verlag, 1989, pp. 237-244; and American Joint Committee on Cancer: Manual Staging for Cancer, 3rd ed. Philadelphia, J. B. Lippincott, 1988, pp. 189-191.



Because treatment decisions for inguinal node dissections are currently based on the characteristics of the primary lesion (see Treatment of Inguinal Nodes), a careful assessment of the depth of invasion of the primary is required. This diagram illustrates the importance of depth of invasion in assigning tumor (T) stage.

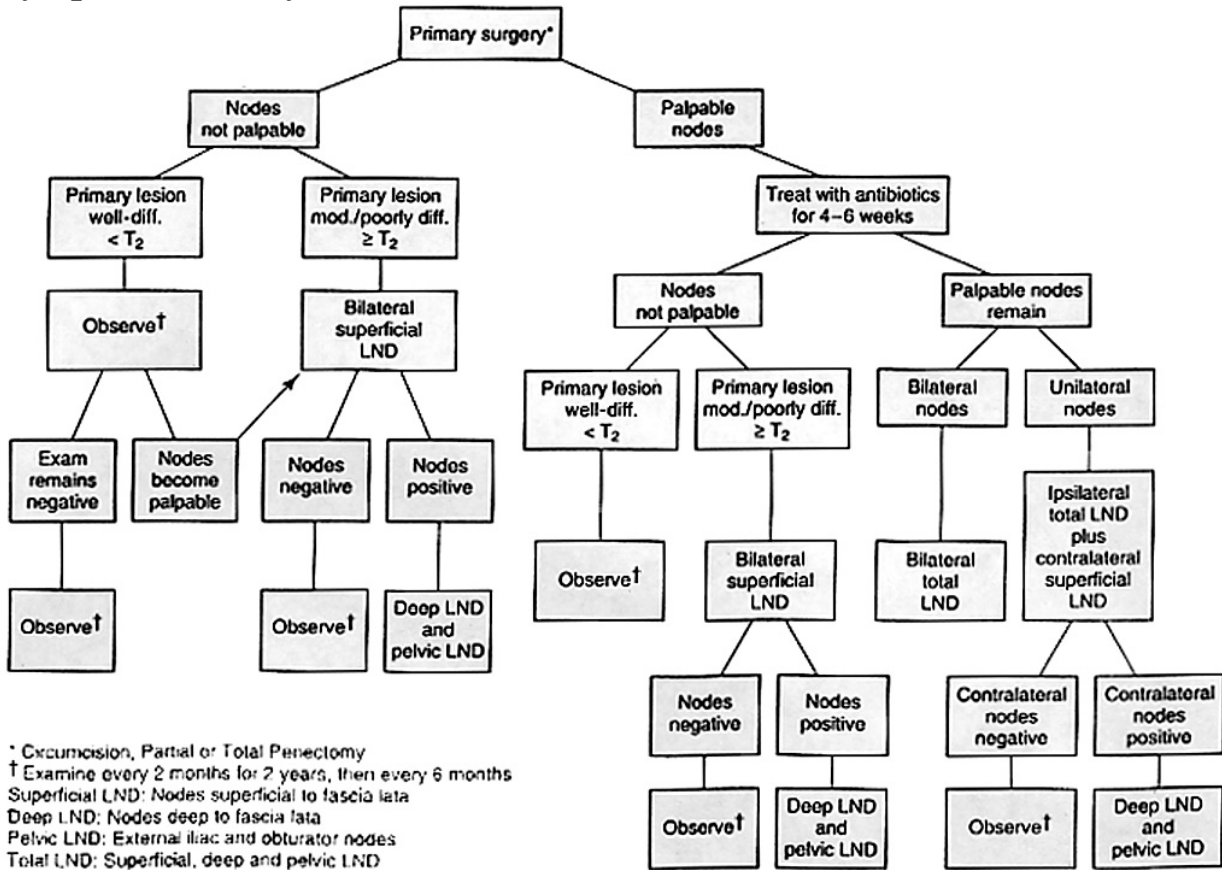
## Treatment of primary lesion (according to T Stage)

- 1) cTis, cTa: Conservative surgical treatment
  - Local excision
  - Laser therapy (neodymium-YAG, Carbon dioxide)
- 2) cT1-2 (within distal two-thirds of penis):
  - Partial amputation of penis (2cm from the proximal margin of the tumor)
- 3) cT2 in the proximal third of the penis and cT3 (not prostate involvement):
  - Total penectomy with perineal urethrotomy
- 4) cT3 (prostatic involvement) and cT4
  - Emasculatation with prostatectomy (Mitrofanoff) or cystectomy (urinary diversion)
- 5) Inoperable cases
  - Conservative radiochemotherapy
    - Chemoradiation (poor candidate for AIC)
 

CDDP	5mg/m <sup>2</sup>	Everyday before radiation
Radiation therapy		Total 60 Gy.

Lymphadenectomy and distant metastasis: see next page

# Lymphadenectomy



palpable: clinically detectable

## Metastatic disease

POMP combined chemotherapy (3 course)

- PEP 5mg/day (Day 1-6),
- VCR 1g (Day 6)
- MMC 8mg/m<sup>2</sup> (Day 6)
- CDDP 50mg/m<sup>2</sup> (Day 6)

## **URETHRAL CANCER**

To distinguish between Ta and T1, Staging TUR-biopsy should be performed.

### Therapeutic indications by TNM

#### **Male**

1) cTa N0 M0

Transurethral resection

2) cT1 N0 M0: If inguinal LN is clinically detectable, LN dissection should be performed.

➤ *Fossa navicularis*

Partial penectomy

➤ *Penile urethra*

Partial (2.0cm surgical margin) or total penectomy

➤ *Bulbomembranous urethra*

Total penectomy, urethrectomy and scrotoectomy with LN dissection.

✧ Radical cysto-prostatectomy and total penectomy, superficial and deep inguinal, pelvic lymphadenectomy are required.

✧ In advanced disease, surgery with excision of the pubic ramus is useful.

✧ If the lesion involves scrotum, a scrotoectomy should be performed.

✧ If SCC, penectomy and urethro-prostatectomy together with bladder preservation with appendix (Mitrofanoff) or ileum stoma.

➤ *Prostatic urethra*

cT1: Transurethral resection

cT2 (storomal invasion): Cysto-prostatectomy and urethrectomy.

3) Any T any N M0 and poor candidate for operation

➤ TCC or SCC: Chemoradiation

Technique: CDDP + radiation 60Gy (see Bladder cancer)

➤ Adenocarcinoma: Chemotherapy (see below)

4) Any T any N M1

Chemotherapy (see next page)

#### **Female**

1) cTa: Transurethral resection

2) cT1: Total cystectomy, urethrectomy with pelvic LN dissection

➤ If tumor is localized on distal urethra, bladder preservation should be considered (using appendix or ileum stoma).

3) Any T any N M0 and poor candidate for operation

➤ TCC or SCC: Chemoradiation

Technique: CDDP 5mg/m<sup>2</sup> + radiation 60Gy (see Bladder cancer)

➤ Adenocarcinoma: Chemotherapy (see below)

4) Any T, any N, M1

Chemotherapy (see next page)

## Chemotherapy

- **Transitional cell carcinoma :**  
MVAC 3 courses (Second line is similar to chemotherapeutic regimens for bladder cancer).
- **Squamous cell carcinoma :**  
POMP therapy (3 course)
  - PEP                5mg/day (Day 1~6),
  - VCR                1.0g                (Day 6)
  - MMC                8mg/m<sup>2</sup> (Day 6)
  - CDDP                50mg/m<sup>2</sup> (Day 6)
- **Adenocarcinoma :**  
Paclitaxel based chemotherapy (3 course)
  - Taxol 135mg/m<sup>2</sup> :        Day2
  - Paraplatin AUC 5 :        Day2
  - Vepsid 50mg/body, oral : Day1-10

pT2, positive margin, lymph node metastases should be regarded as indications for adjuvant chemotherapy (2 courses). See above for regimens according to pathological findings.

## TESTICULAR TUMOR

Inguinal orchiectomy should be performed to confirm the pathological diagnosis immediately, then staging.

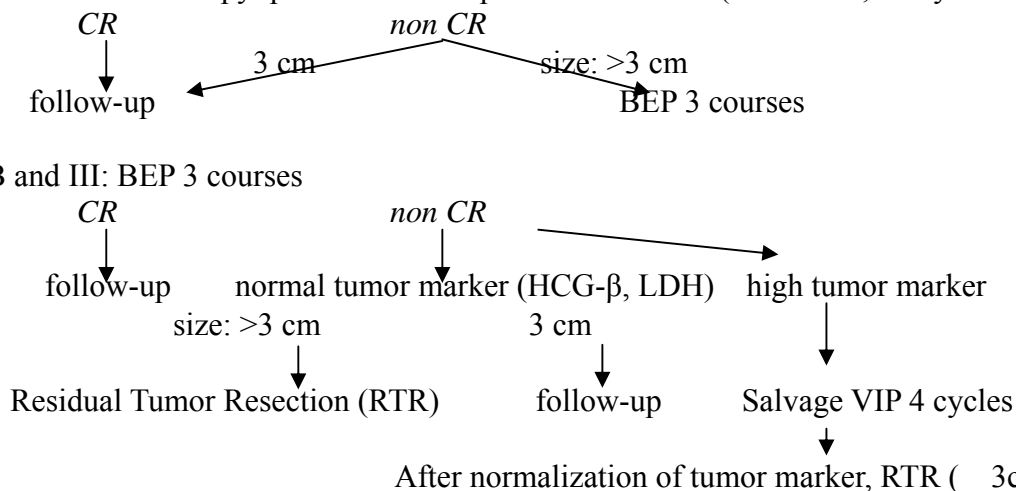
### Classification by International Germ Cell Collaborative Group

Prognosis	Non-Seminoma	Seminoma
Good	<p>Testis/retroperitoneal primary and No non-plumunary visceral metastases and Good markers-all of AFP &lt; 1,000ng/ml hCG &lt; 5,000 IU/l(1,000ng/ml) LDH &lt; 1.5 × upper limit of normal</p> <p>56% of seminomas 5-year PFS 89% 5-year survival 92%</p>	<p>Any primary site and No non-plumunary visceral metastases and Normal AFP, any hCG, any LDH</p> <p>90% of seminomas 5-year PFS 82% 5-year survival 86%</p>
Intermediate	<p>Testis/retroperitoneal primary and No non-plumunary visceral metastases and Intermediate markers-any of AFP ≥ 1,000 and ≤10,000 ng/ml hCG ≥ 5,000 and ≤50,000 IU/l LDH ≥ 1.5 × N and ≤ 10 × N</p> <p>28% of seminomas 5-year PFS 75% 5-year survival 80%</p>	<p>Any primary site and No non-plumunary visceral metastases and Normal AFP, any hCG, any LDH</p> <p>10% of seminomas 5-year PFS 67% 5-year survival 72%</p>
Poor	<p>Mediastinal primary or Non-plumunary visceral metastases or Poor markers-any of AFP &gt; 10,000ng/ml or hCG &gt; 50,000 IU/l or LDH &gt; 10 × upper limit of normal</p> <p>16% of seminomas 5-year PFS 41% 5-year survival 4811%</p>	<p>No patients</p>

### Therapeutic indications by pathological diagnosis and clinical Stage Seminoma

Stage I: Surveillance

Stage IIA: Radiation therapy: para-aortic and ipsilateral iliac LN (CT follow; every 3 months)



**Non seminoma (NSGCT)**

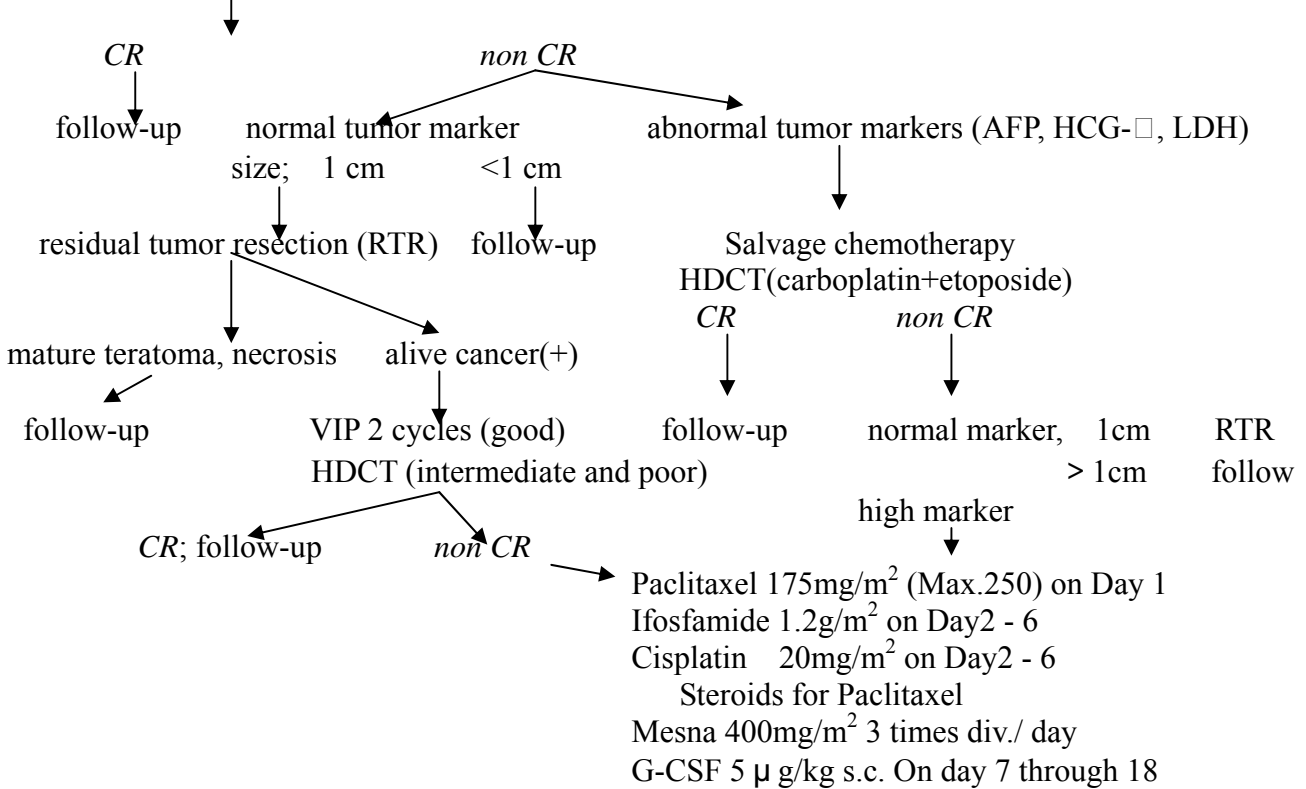
Stage I: surveillance

Stage II and III: Chemotherapy according to International germ cell consensus classification by International Germ Cell Collaborative Group (IGCCG; see next page)

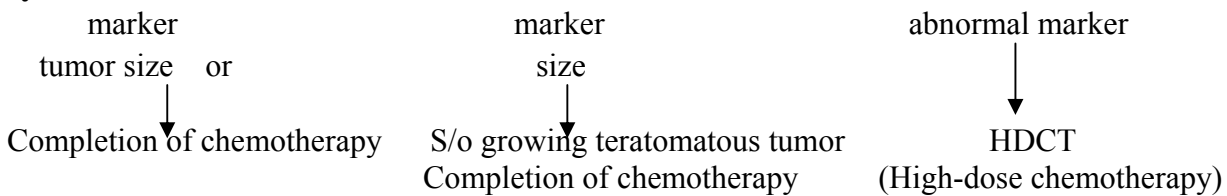
**Initial Chemotherapy**

BEP (**3 cycles for good ~intermediate prognosis, 4 cycles for poor prognosis**)

(rising tumor markers after 2 cycles High Dose Chemotherapy; HDCT)



**#1: Check tumor markers at every cycles of chemotherapy, and perform imaging study after 2 cycles**



**#2: Poor prognosis: prepare for PBSCT during induction chemotherapy (Harvest on 2<sup>nd</sup> cycle)**

**Follow-up schedule after therapy and during surveillance**

Physical examination, chest Xp, CT, tumor marker

- 1 years; every 3 months
- 2-5 years; every 6 months
- 6 years ~ ; annually
- Bone scan annually

## ADRENAL TUMOR

### Examination

Abdominal US, CT, MRI, Adrenal Scintigram ( $^{131}\text{I}$ -adosterol,  $^{131}\text{I}$ -MIBG)

#### Hormonal examination

Diagnosis	Blood sample	Urine sample
<b>Primary Aldosteronism</b>	Plasma Renin Activity, aldosterone	aldosterone
<b>Cushing syndrome</b>	ACTH, circadian rhythm of cortisol	17-OHCS, 17-KS
<b>Adrenocortical cancer</b>	ACTH, testosterone, progesterone, estrogen, progesterone, aldosterone, cortisol, 17-OH progesterone	17-OHCS, 17-KS, pregnanediol, pregnantriol
<b>Pheochromocytoma</b>	dopamine, adrenalin, noradrenalin	dopamine, adrenalin, noradrenalin, MN, NMN, VMA, HVA
<b>Neuroblastoma</b>		VMA, HVA, ratio of VMA/HVA

### Adrenal cancer

#### Staging System (Sullivan et al)

- Stage I: confined to the adrenal gland, 5.0cm.  
 Stage II: confined to the adrenal gland, >5.0cm.  
 Stage III: local invasion that involve adjacent organs or regional lymph nodes.  
 Stage IV: distant metastasis, invasion into adjacent organs plus regional lymph nodes.

#### Therapy by Clinical Stage

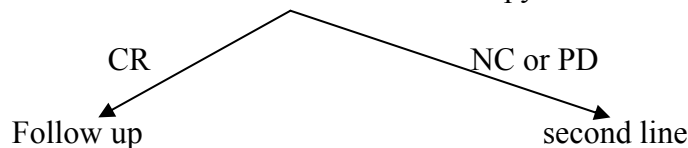
- Stage I, II: Adrenalectomy  
 Stage III: Adrenalectomy with LN dissection and resection of adjacent organ (kidney and spleen)  
 Stage IV: Biopsy or resection of the tumor, and Chemotherapy

#### Chemotherapy

1<sup>st</sup> line: EP therapy; CDDP and etoposide

Method: VP-16 100mg/m<sup>2</sup> on day1 ~ 3, CDDP 100mg/m<sup>2</sup> on day 1; every 4weeks

After 3 sessions of chemotherapy



2<sup>nd</sup> line: Mitotane (o, p'-DDD)

Method: Initial therapy; 2-3g/day, then doses up to 6-12g/day (6 months)

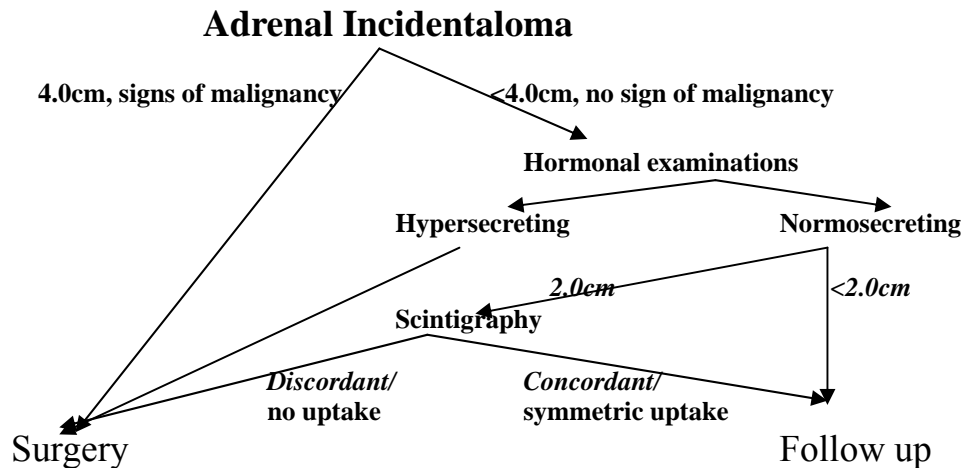
Monitoring; o, p'-DDD level 14 to 20 mg/l

Pharmacology: Dose of >3g/day causes adrenolytic effect. Plateau of blood level at 8 weeks, and hormonal replacement is needed up to 2 – 4 weeks

#### Postoperative follow up

- If hormone-secreting carcinoma, the hormone should be checked as a tumor marker.
- Every 6 months, Chest X-p and CT scan (optional adrenoscintigram) should be done.

**Adrenal tumor (benign)  
Incidentaloma**



**Surgery for adrenal tumor (benign)**

- <5cm Transabdominal Laparoscopic Adrenalectomy  
Retroperitoneoscopic adrenalectomy (history of upper abdominal surgery)
- 5cm Hand-assisted laparoscopic Adrenalectomy  
Open adrenalectomy (malignant tumors could not be ruled out)

**Postoperative replacement of glucocorticoid**

	Ope	Day 1	2	3	4	5	6	7	8	9-14	15-17	18-
Removal of tumor	200											
6 AM		100	100	70	50	25						
7 AM							37.5	25	20	20	20	15
5 PM	50	50	25	25	25	125	12.5	12.5	10	5	5	5

Hydrocortisone (mg)

**Diagnostic criteria for Pre-clinical Cushing Syndrome**

- Existence of adrenocortical incidentaloma
- Without pathognomonic symptoms observed in Cushing Syndrome
- Laboratory data
  - 1) Basal cortisol; WNL
  - 2) Spontaneous secretion of cortisol
    - Serum cortisol  $\geq 3$ mg/dl after Dexamethasone 1mg
    - Serum cortisol  $> 1$ mg/dl after Dexamethasone 8mg
  - 3) ACTH < normal range
  - 4) <sup>131</sup>I-adsterol scintigram; positive
  - 5) No circadian rhythm
  - 6) Decrease in serum DHEA-S
  - 7) Postoperative Addison’s syndrome or atrophy in the removed adrenal gland.

1) and 2) major factor, and necessary for added one of 3) - 6) or 7)

# CONGENITAL HYDRONEPHROSIS

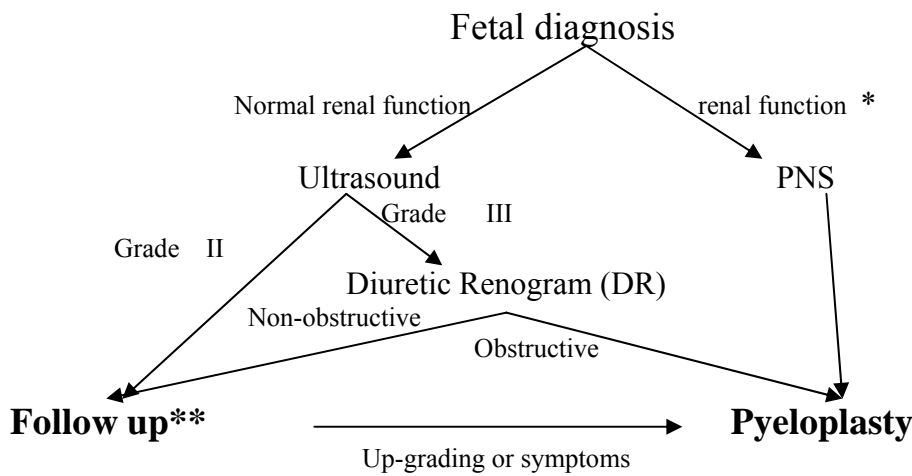
## Examination

- ◇ US, IVP, RP, Diuretic Renogram
- ◇ BUN, Cr, CCr

## Ultrasound Grading of hydronephrosis

- Grade 0 no hydronephrotic change
- Grade I dilation of renal pelvis and normal renal calyces
- Grade II dilation of renal pelvis and several dilated renal calyces
- Grade III all of renal calyces are dilated.
- Grade IV Added to Grade III, calyceal deformation and thinned renal cortex.

## Chart of the treatment for Congenital hydronephrosis



## Normal ranges of serum-Cr levels in Japanese children\* (97.5% tile)

Age	Girl	Boy
1 - 2	0.6	0.6
3 - 4	0.7	0.7
5 - 8	0.8	0.7
9 - 11	0.8	0.8
12	0.9	0.8
13 - 14	0.9	0.9
15 - 16	1.0	1.0
17 -	1.1	1.1

➤  $CCr (\mu\text{mol/l}) = Cr (\text{mg/dl}) \times 88.4$

## Follow up\*\* methods and intervals

Methods and intervals		Ipsilat. renal uptake by renoscintigram
IVP; Twice a year	US at every 3 months	40%
	US at every 2 months	30 to 40%
	US at every 1 months	20 to 30%
	US at every 2 weeks	<20%

## Surgical Procedures for ureteropelvic junction obstruction

### Indication for surgery

- Symptoms for obstruction.
- Impairment of renal function.
- Development of renal stones.
- Recurrent pyelonephritis

Intrinsic: Adults ( ≥ 18years old or stature ≥ 160cm)

Endopyelotomy (Transurethral preferable than Percutaneous)

Indications: length of stenosis ≤ 2.0cm, able to insert guide wire through the lesion, without deterioration of ipsilateral renal function.

Relative indications: high insertion of ureter, large redundant pelvis.

Pyeloplasty\* (open or retroperitoneoscopic)

Child: Open Pyeloplasty

Extrinsic: Pyeloplasty\* (open or retroperitoneoscopic) \*Anderson-Hynes method

### Postoperative Follow Up

- 1) Removal of ureteral stent is scheduled 6 weeks after operation.
- 2) IVP and US; every 3 months, and diuretic renogram; 3, 6 and 12 months in first year.
- 3) No improvement after 6 to 12 months, re-operation should be considered.
- 4) One year after operation, IVP; every 6months, and Diuretic renogram; every year.

## VUR

### Examinations:

- VCUg, IVP, US, and Renoscintigram (check of renal scarring)

### Classification:

Grade	Description
I	Into the non-dilated Ureter
II	Into the pelvis and calyces without dilatation
III	Mild to moderate dilatation of the Ureter, renal pelvis, and calyces with minimal blunting of the fornices.
IV	Moderate ureteral tortuosity and dilatation of the pelvis and calyces.
V	Gross dilatation of the ureter, pelvis, and calyces; loss of papillary impressions; and ureteral tortuosity.

### Primary VUR in children

Reflux grade	Age	Scarring	Initial therapy*	Follow up treatment
<b>I – II</b>	<b>Any</b>	<b>Yes/No</b>	<b>Antibiotic Prophylaxis</b>	<b>Surgery</b>
<b>III-IV (unilat.)</b>	<b>Any</b>	<b>Yes/No</b>	<b>Antibiotic Prophylaxis</b>	<b>Surgery</b>
<b>III-IV (bilat.)</b>	<b>0 to 5</b>	<b>Yes/No</b>	<b>Antibiotic Prophylaxis</b>	<b>Surgery</b>
<b>III-IV (bilat.)</b>	<b>6 to 10</b>	<b>Yes/No</b>	<b>Surgery</b>	
<b>V (unilat.)</b>	<b>0 to 5</b>	<b>Yes/No</b>	<b>Antibiotic Prophylaxis</b>	<b>Surgery</b>
<b>V (unilat.)</b>	<b>6 to 10</b>	<b>Yes/No</b>	<b>Surgery</b>	
<b>V (bilat.)</b>	<b>Less than 1</b>	<b>Yes/No</b>	<b>Antibiotic Prophylaxis</b>	<b>Surgery</b>
<b>V (bilat.)</b>	<b>1 to 5</b>	<b>No</b>	<b>Antibiotic Prophylaxis</b>	<b>Surgery</b>
<b>V (bilat.)</b>	<b>1 to 5</b>	<b>Yes</b>	<b>Surgery</b>	
<b>V (bilat.)</b>	<b>6 to 10</b>	<b>Yes/No</b>	<b>Surgery</b>	

### VUR in adults

Incidence: 7% in UTI patients in adults

After treatment of recurrent UTI, operation should be done because spontaneous resolution of VUR after puberty is less than in children.

### Secondary VUR

Children: posterior urethral valves, Neurogenic bladder (spina bifida, DSD)

Control of these basal disorders should be done at first, then keep follow up.

### Initial therapy

Antibiotic Prophylaxis:

Low dose prophylactic antibiotic therapy by ABPC, AMPC or oral cepharosporins

Periods of administration: 3 years (until the expected resolution of reflux occurs)

Periodic urine culture at every 3 month

Annual radiographic study: VCUg and US (IVP is added if necessary)

### Surgery

First choice: Cohen Cross-Trigonal Technique

*(If ureter is dilatated, plication, infolding or exsitional tapering is considered.)*

Second choice : Glenn-Anderson Technique

*(Especially for possible necessity of retrograde catheterization in the future and persistent postreimplantation reflux.)*

Endoscopically injection:(*applied to poor candidate for operation and grade III or IV*)

### Follow up schedule after surgery

US on 1, 3, 6 and 12 months followed by annual check-up for 3 years

VCUG on 6 or 12 months after surgery.

## ***BENIGN PROSTATIC HYPERPLASIA***

### Examination

IPSS, DRE, Abdominal US for screening of renal disorders

TRUS-P (Volume, T-zone volume, evaluation of P-zone)

Uroflowmetry (Voided volume, residual urine, Qmax, Qave)

**PSA: If in Gray zone, Sextant biopsy is need under following condition!**

PSA density: PSAD > 0.15 ng/ml/cm<sup>3</sup>, PSAD-TZ > 0.35 ng/ml/cm<sup>3</sup>

PSA verocity > 0.75ng/ml/year, F / T ratio of PSA < 0.15

Patient	Symptom I-PSS	QOL QOL index	Function Qmax and Residual urine	Prostate volume
good	0 – 7	0 or 1	15ml/s and 50ml	< 20ml
moderate	8 – 19	2 – 4	5ml/s and <100ml	< 50ml
severe	20 - 35	5 or 6	< 5ml/s and 100ml	50ml

	Severity Index		
	good	moderate	severe
<b>Excellent</b>	4 3	0 1	0 0
<b>Moderate</b>	- -	2 -	0 1
<b>Severe</b>	-	-	2

### Choice of Treatment

If severity index “Excellent”; watchful waiting

If severity index “Moderate or Severe”; medical treatment

**1-blocker treatment more than 3 months**

- If irritable symptoms are dominant, naftopidil is more preferable than tamsulosin.
- If normal PSA, over 30ml of prostate, erectile dysfunction, over 80 years old and without past history of cerebral and myocardial infarction, combination with anti-androgen is recommended.

### Follow-up Schedule for medical treatment

	Pre-treatment	1 month	3 ms	6 ms*	Every 6 ms**
IPSS					
Uroflowmetry					
DRE					
TRUS-P					
PSA					

\*\*After TUR(V)-P, follow-up these parameters within 6 months after operation.

### \*6 months after medical treatment

1. If the patient is free from clinical symptoms, refer to other urological clinics near his address for medical follow up.
2. If the patient suffers “moderate”, pressure-flow study and cystourethroscopy (as a option) should be done. Then, recommend TUV-P. If rejected, refer to other urological clinics for TUMT.
3. Placement of Urethral stent is recommended for the poor anesthetic candidates. (cardiovascular disease, bleeding tendency).

## Absolute indications for Surgery

- Acute urinary retention
- Recurrent urinary infection
- Recurrent and severe gross hematuria
- Bladder stones
- Overflow incontinence
- Decreased kidney function
- Dilated upper urinary tract.

## URETHRAL STRICTURE

### Examination

Uroflowmetry, Voiding Cystogram, Urethrocystography

Transperineal ultrasound ( 7.5MHz)

Usefull for the evaluation of spongiofibrosis in recurrent patients.

Examine after retrograde instillation of saline or lubricant jelly.

MRI (If suspected urethral carcinoma)

### Surgical Treatment

#### ➤ Posterior Urethra

1. Endourethroplasty (Internal urethrotomy and/or TUR)
2. Open perineal repair

#### ➤ Anterior Urethra

Bulbar *Short*( $<2.5\text{cm}$ )

1. Endourethroplasty (If required more than 3 times procedure, go to 2. )
2. Excision and primary anastomosis

*Long* (  $2.5\text{cm}$ ) *included bulbomembranous*

1. Buccal mucosal-free grafts
2. Penile or Scrotal flap

Penile

1. Endourethroplasty
2. Ventral longitudinal flap (Orandi)
3. Buccal mucosal-free grafts

- If the patient is elder than 75, use of metallic stent (Memocath®) is considerable after endourethroplasty.
- Metallic stent needs 1.0cm longer than the length of urethral stricture.
- Followup should be scheduled as BPH + pelvic plane X-p to check the calcification around the stent.

# CRYPTORCHIDISM

## Classification

retractile, undescended, ectopic, absent, abdominal, canalicular, high scrotal

## Timing of surgery

1~2 years of age (1 year is better than later)

## Diagnosis and Treatment

Palpable and detected by US

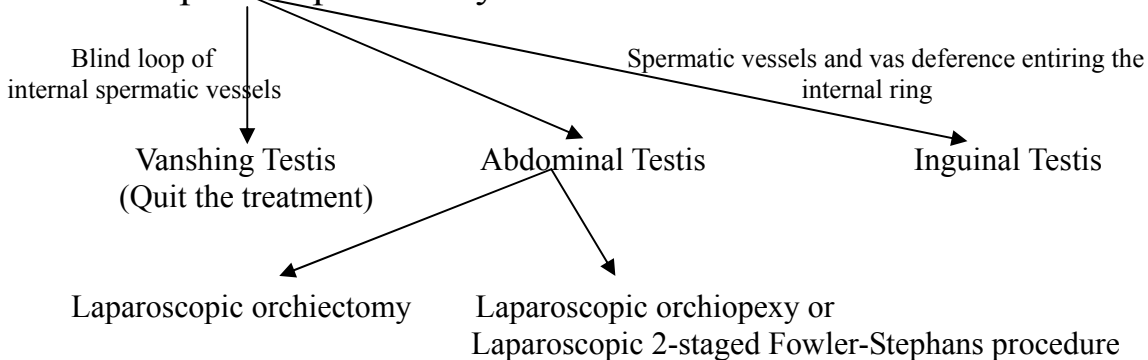
Inguinal orchidopexy

Non palpable and non-detected by US

MRI

Laparoscopic survey

### Laparoscopic Survey



## Postoperative follow up

- Re-evaluation: 1 year after surgery for location, size and viability.
- Give instructions for infertility and tumor genesis to the parents.
- In puberty, give instruction of monthly testicular self-examination to patients.

## PHIMOSIS

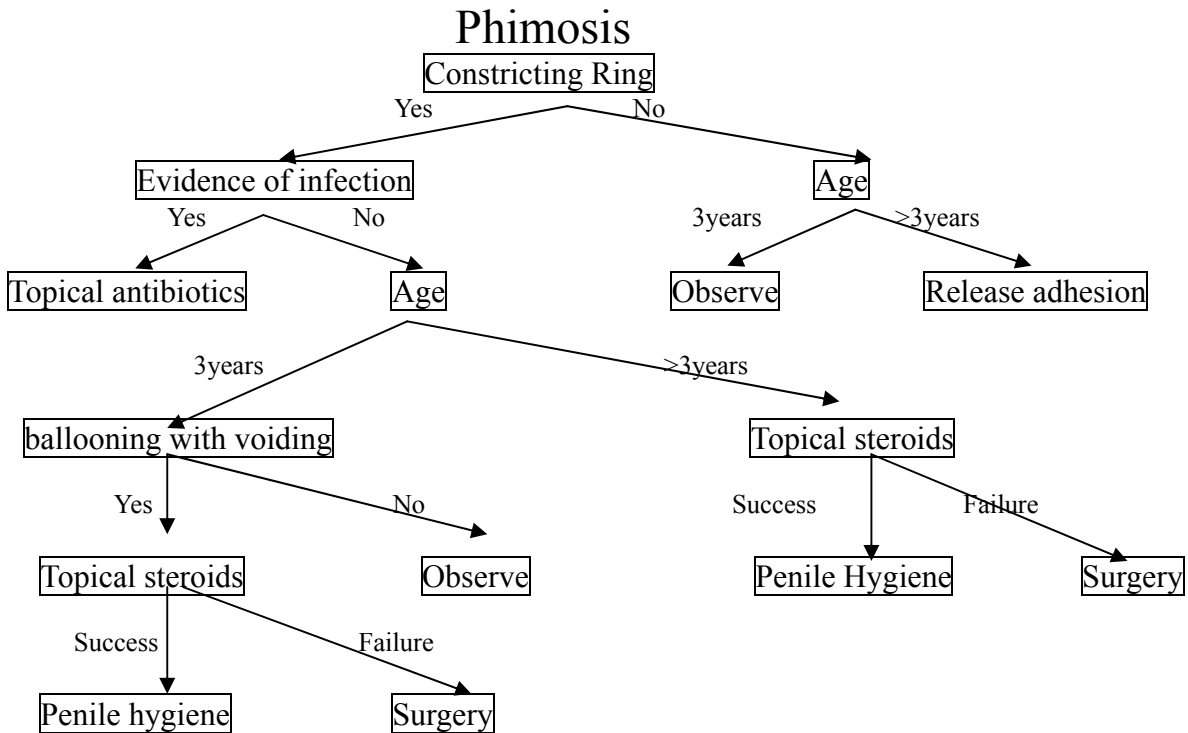
### Topical steroid therapy

Indication: parental desire to avoid surgery  
 Poor anesthetic candidates  
 History of a bleeding disorder

Method: 1 month course of 0.05% betamethasone cream twice a day (0.05% アンテベートクリーム)

### Surgical methods

<12 years old Sextant incision of prepuce  
 12 years old Circumcision



## HYDROCELE TESTIS AND SPERMATOCELE

### Preoperative management

Rule out: epididymitis, testicular torsion, testicular tumor, inguinal hernia  
 Examination: transillumination, auscultation, US

### Hydrocelectomy

Surgical indications: quite large, symptomatic, pediatric hydrocele >2-year old  
 Approach: Scrotal in adults and inguinal in child or suspected malignancy  
 Technique: Jaboulay's bottleneck or Lord's plication for adults  
 Simple excision for children

### Spermatocelectomy

Surgical indications: large, symptomatic  
 Treatment: Ligation of communication site to the epididymis

## ***CYSTOCELE***

### **Anatomical Grade**

- |     |   |
|-----|---|
| I   | descent toward the introitus            |
| II  | descent to the introitus                |
| III | descent outside the introitus on strain |
| IV  | extend outside the introitus at rest    |

### **Indications for Surgical treatment**

- Grade IV is the indication for surgical repair.
- Other grades are considered for surgery according to the patient's intention.
- If stress incontinence is coexisted, see "Stress Incontinence in Women" in the next page.

### **Surgical techniques**

For Grade IV

- Four-corner bladder suspension and vaginal wall sling using absorbable mesh.

For other grades

#### **Central defect only:**

- Anterior colporrhaphy (Kelly plication) with TVT operation.
- Posterior colporrhaphy (if rectocele exist)

#### **Lateral defect only**

- Six corner bladder suspension

### **Alternative therapy**

- Pelvic floor rehabilitation, oral or topical estrogen
- Pessary

## ***STRESS INCONTINENCE IN WOMEN***

### Classifications:

- Anatomical incontinence (AI: urethral hypermobility)
- Intrinsic sphincter deficiency (ISD)

### Examinations:

- Questionare (Impact of QOL), Uroflowmetry (RV)
- Chain CG, Pad test (60min), Stress test (Marshall-Read-Bonny test)
- Cystometry, ALPP (abdominal leak point pressure; ISD <60, hypermobility >90)

### **Blaivas classification**

<b>Type</b>	<b>Anatomical characteristics</b>
<b>0</b>	No urinary leakage during clinical and urodynamic investigation. At rest, vesical neck closed at/above the superior margin of the pubic symphysis.
<b>I</b>	At rest, vesical neck closes at/above the inferior margin of the pubic symphysis. During stress, it opened and descended less than 2cm from the inferior margin of the pubic symphysis.
<b>IIA</b>	At rest, vesical neck closed at/above the inferior margin of pubic symphysis. During stress, it opened and descended more than 2cm from the inferior margin of the pubic symphysis.
<b>IIB</b>	At rest, vesical neck closed below the inferior margin of the pubic symphysis
<b>III</b>	At rest, vesical neck and proximal urethra opened in the absence of a detrusor contraction. ( intrinsic sphincter deficiency)

### Treatment

Type 0	no candidate for operation
Type I ,II, III	<b>TVT</b> (Tension Free Vaginal Tape) Indications: No improvement after 3 months medical therapy Patients' desire to be completely dry
If cystocele is associated, concurrent repair should be done.	

### **Medical treatment:**

- $\alpha$  or  $\beta$ -adrenergic sympathetic agonist, and tricyclic antidepressant,
- Pelvic floor exercise
- Estrogen therapy after Gynecologic check for uterine cancer
- Bladder neck support prosthesis (Introl®) or Urethral plug for poor candidate for operation.

### **Poor candidate for transvaginal operation**

#### **Type IIA, IIB:**

- Pubovaginal sling
- Burch colposuspension

#### **Type III:**

- Periurethral injection of collagen (GAX collagen; after 12 months medical therapy)
- Artificial sphincter

## ***INTERSTITIAL CYSTITIS***

### **Criteria for the diagnosis of Primary Interstitial Cystitis by NIADDK**

#### Inclusion criteria

- Glomerulations or Hunner's ulcer on cystoscopic examination.
- Pain associated with the bladder on urinary urgency.

#### Exclusion criteria

- Bladder capacity >350ml on awake cystometry.
- Absence of intense urge to void with bladder filled to 150ml of water.
- Demonstration of phagic involuntary bladder contractions during cystometry.
- Duration of symptoms less than 9 months.
- Absence of nocturia.
- Symptoms relieved by antimicrobials, urinary antiseptics, anticholinergics, antispasmodics (muscle relaxants).
- Frequency of urination while awake < 8 times per day.
- Age < 18 years

#### Exclusion criteria for the diagnosis of primary disease

- Diagnosis of bacterial cystitis or prostatitis within 3 months period\*
- Bladder or lower uteretal calculi
- Active genital herpes\*
- Uterine, cervical, vaginal, or urethral cancer\*
- Urethral diverticulum
- Cyclophosphamide or any type of chemical cystitis\*
- Tuberculous cystitis\* (inclusion of BCG instillation)
- Radiation cystitis\*
- Benign or malignant bladder tumors\*
- Vaginitis\*

\*Causes of secondary interstitial cystitis.

### **Examinations**

- Frequency-volume Chart
- Uroflowmetry (UFM)
- Urine cytology (R/O of CIS in the bladder) and urine culture
- Interstitial Cystitis Symptom Score, and Visual Analogue Scale for the pain.
- Cystometry
- Cystoscopy\*

1. Characteristic clinical features: voiding volume < 200ml in a whole day and over 10 times of urination with urgency.
2. Check the frequency-volume chart and UFM of the incurable Chronic Pelvic Pain Syndrome patients, and you should rule out of IC.
3. \*If IC is highly suspected with severe pain in the bladder, cystoscopy should be performed under spinal anesthesia (after admission), and check the glomerulations or Hunner's ulceration. Simultaneously, biopsy of bladder mucosa (rule out of CIS in the bladder) and hydro-distension therapy should be performed (80cmH<sub>2</sub>O for 3 to 5 minutes).

## Treatment for IC

There is no effective treatment for the IC covered by health insurance. All the treatments described below are now under clinical trials.

### 1. Hydro-distension Therapy

- Under spinal or epidural anesthesia, 80cmH<sub>2</sub>O (saline) and under 500 ml for 3 to 5 minutes by cystoscopy.
- Cold cup biopsy of bladder mucosa should be performed simultaneously.
- IC Grading by cystoscopic findings provoked by Dr. Takei.

Grade	Cystoscopic findings
I	Minimal gromerulation
II	Gromerulations
III	Hunner's ulcer
IV	Crack

### 2. Oral Suplatast tosilate (IPD®) (under clinical trial)

- After hydro-distension therapy, 100mg of oral IPD® administered after every meals (300mg/day).

Option: Bladder instillation of dimethyl sulfoxide; DMSO (under clinical trial)

- Bladder instillation of 50ml of 50% DMSO for 10 to 20 min once a week, up to 4 to 8 weeks.

## Follow-up Schedule for the treatment

	Pre-treatment	1 month	3 ms	6 ms	Every 6 ms
IC symptom score					
Uroflowmetry					
Frequency-volume chart					
Urine cytology					

# UROLITHIASIS

## Diagnosis

Imaging: KUB, US, excretory urography (contraindication; allergy to contrast media, Cr>2.0)

Laboratory investigations:

- ✧ Urinarysis: pH, Leukocytes, bacteria (urine culture)
- ✧ Cystine test (if cystinuria cannot be excluded)
- ✧ Blood analysis; calcium, phosphate, albumin, creatinine, urate.

## Pretreatment care

- For UTI, antimicrobial chemotherapy should be started before stone-removing procedure.
- Anti-coagulant agents should be stopped 10days before.

## Renal stones

Indications for surgery: stone size 5mm, severe clinical symptom, and solitary kidney

Contraindication: intrarenal stone (R1)

		First choice	Second choice**
R2 and R3	From 0.5 to 2.0cm	ESWL*	PNL or TUL
	From 2.0 to 3.0cm	ESWL* with double-J stent	PNL
	3cm or staghorn	PNL monotherapy (or combined ESWL*)	Nephrolithotomy or Pyelolithotomy

\*ESWL; Contraindicated in patients with coagulation disorder or pregnant women.

\*\* For the residual stones after 3 sessions of ESWL

- Nephrectomy should be considered in case of a nonfunctioning and thinned cortex of the kidney.

## Ureteral stones

Indications for surgery: stone size 5mm, severe clinical symptom, and solitary kidney

Location	First choice	Second choice**
U1	ESWL	TUL or PNL
U2	ESWL	TUL
U3	ESWL or TUL( 1cm)	TUL

\*\* For the residual stones after 3 sessions of ESWL

## Bladder stones

Transurethral lithotripsy : Lithotrite (Young, Ryall) for < 3.0cm

: Lithoclast for 3.0cm

- Evaluation and treatment for bladder outlet obstruction should be done simultaneously.

## Preventive treatment in Calcium stone disease for the recurrent patients

- ✧ 24-hour urine volume should exceed 2,000ml.
- ✧ Mixed balanced diet given instructions by the department of nutrition in this hospital.

## Pharmacological treatments

Uric acid stones	Cystine stones
Urine volume 2500ml/day	Urine volume 3000ml/day
Oral Uralyt® (potassium and sodium citrate) 3.0g/day	Thiola (tiopronin) 250-2000mg
Oral allopurinol 200mg/day	Captopril (75-150mg/day)/day

## URINARY TRACT INFECTION

### Evaluation timing of antimicrobial agents on urinary tract infection.

- Patients should be evaluated for clinical symptoms, urinalysis, and urine culture.
- Except for uncomplicated cystitis, KUB and color Doppler US should be performed when they are diagnosed.
- In febrile patients, CBC, biochemistry, and urine (sediment and culture) are scheduled at pre-treatment, after 3 and 7 days.
- For the evaluation of the antimicrobial treatment according to Guideline for clinical trials in UTI
  - Pre- administration
  - 5 to 9 days after administration: Judge of cure
  - 4 to 6 weeks after administration: Judge of recurrence

### Uncomplicated UTI

#### Acute uncomplicated cystitis

		First choice	Second choice
Young female	Single dose	Oral fuluoroquinolones*	
	3 days	Oral fuluoroquinolones	ST
	7 days		3 <sup>rd</sup> oral cephem
Recurrent		3 days of oral fuluoroquinolones	
Postmenopausal		3 days of oral fuluoroquinolones	

If clinical symptom is strong, amynoglycoside is added initially.

\* fleroxacin

#### Acute uncomplicated pyelonephritis

	First choice	Second choice
<b>Mild</b>	7 to 14 days of oral fuluoroquinolones.	Penicillin, 3 <sup>rd</sup> cephems (p.o.) or FRPM
<b>Moderate</b>	7 to 14 days of oral fuluoroquinolones.**	Penicillin, cephems (3 <sup>rd</sup> p.o. or i.v.) or FRPM
<b>Severe</b>	Amynoglycoside or parenteral fluoroquinolones (until fever ) 7 to 14 days of oral fuluoroquinolones	Penicillin or $\beta$ -lactamase inhibitor (i.v.)
<b>Pregnant</b>	Cephems (i.v. such as CTRX)	

\*\*If clinical symptom is strong, amynoglycoside is added initially.

### Complicated UTI

- Patients with complicated UTI can not be cured unless evaluation and treatment of basal diseases!

		First choice	Second choice
<b>Complicated Cystitis</b>		14days of oral fuluoroquinolones, 3 <sup>rd</sup> cephems, FRPM	ST, Penicillin, TC
<b>Complicated Pyelonephritis</b>	<b>Moderate</b>	Amynoglycosides plus 14 days of Fuluoroquinolones, 3 <sup>rd</sup> cephems, FRPM	ST, Penicillin, TC
	<b>Severe</b>	Carbapenems, 4 <sup>th</sup> Cphem , PIPC/TAZ (until fever ) oral fuluoroquinolones, 3 <sup>rd</sup> cephems, FRPM	Amynoglycoside or parenteral fluoroquinolones (until fever ) oral fuluoroquinolones

## Symptomatic fungal infection

	<b>Candida</b>	<b>Aspergillus</b>
<b>Pneumonia</b>	FLCZ: 100~400mg/day 1~2times ITCZ: 100~200mg/day 1~2times MCZ: 400~1200mg/day 1~2times AMPH: 0.4~0.6mg/kg/day	<i>First line</i> FLCZ: 100~400mg/day 1~2times ITCZ: 100~200mg/day 1~2times MCZ: 400~1200mg/day 1~2times AMPH: 0.75~1.0mg/kg/day <i>Second line</i> AMPH+5-FC: 0.3mg/kg/day + 150mg/kg/day 4 ×
<b>Sepsis</b>	AMPH 0.5~1mg/kg	AMPH 1~1.5mg/kg

## Clinical doses of antimicrobials for UTI

## Oral Fluoroquinolones

	<b>Dose</b>			
	<b>Adult</b>	<b>Sever case</b>	<b>Pregnant</b>	<b>Pediatric</b>
<b>Levofloxacin</b>	100 mg × 3	200 mg × 3	×	×
<b>Ciprofloxacin</b>	200 mg × 2 - 3	-	×	×
<b>Gatifloxacin</b>	200 mg × 2	-	×	×
<b>Sparfloxacin</b>	200 - 300mg × 1	-	×	×
<b>Tosufloxacin</b>	150 mg × 3	-	×	×
<b>Norfloxacin</b>			×	2 - 4mg/kg × 3

## 3rd generation oral cepheems

	<b>Dose</b>			
	<b>Adult</b>	<b>Sever case</b>	<b>Pregnant</b>	<b>Pediatric</b>
<b>Cefteram</b>	100 mg × 3	-		9 - 18mg/kg/day
<b>Cefpodoxime</b>	100 mg × 2	200 mg × 2		×
<b>Cefdinir</b>	100 mg × 3	-		9 - 18mg/kg/day
<b>Cefditoren</b>	100 mg × 3	200 mg × 3		3mg/kg × 3
<b>Cefcapene</b>	100 mg × 3	150 mg × 3		3mg/kg × 3
<b>(Cefixime)</b>	100 mg × 2	200 mg × 2		1.5 - 3mg/kg × 2 ( ~ 12mg/kg/day)

## Other oral antimicrobials

	<b>Dose</b>			
	<b>Adult</b>	<b>Sever case</b>	<b>Pregnant</b>	<b>Pediatric</b>
<b>Sulfamethoxazole /Trimethoprim</b>	2g × 2	-	×	×
<b>Fosfomicin</b>	1g × 2 - 3, 0.5g × 4	-	×	40 - 120mg/kg/day
<b>Minocycline</b>	100mg × 2	-		2 - 4mg/kg/day

**Penicillin, Penicillin+ -lactamase inhibitor, Faropenem: p.o.**

	Dose			
	Adult	Sever case	Pregnant	Pediatric
<b>Amoxicillin</b>	250mg × 3 - 4	-		20 - 40mg/kg/day
<b>Ampicillin</b>	500mg × 4 - 6	-		25 - 50mg/kg/day
<b>Amoxicillin /clavulanic acid</b>	250mg/125mg × 3 - 4	-		30 - 60mg/kg/day
<b>Sultamicillin</b>	375mg × 2 - 3	-		×
<b>Faropenem</b>	300mg × 3	-		×

**Aminoglycosides**

	Dose: d.i.v. or i.m.			
	Adult	Sever case	Pregnant	Pediatric
<b>Group 1</b>				
<b>Amikacin</b>	200 - 400mg × 1	-		4 - 8mg/kg/day
<b>Isepamicin</b>	200 mg × 2 400 mg × 1 200 mg × 2	-		×
<b>Group 2</b>				
<b>Tobramycin</b>	40 mg × 2 - 3 60 mg × 2			0.8 -1.2mg/kg/day, i.m. 3mg/kg/day
<b>For MRSA</b>				
<b>Arbekacin</b>	75 -100mg × 2	-		2-3mg/kg × 2, i.m.

**2nd generation cepheims**

	Dose: i.v. or d.i.v.			
	Adult	Sever	Pregnant	Pediatric
<b>Cefotiam</b>	1g × 2	-		20 mg/kg×3 - 4( ~ 160mg/kg/day)
<b>Cefuroxime</b>	1g × 2 - 3	2g × 2 - 3		30 -100 mg/kg/day

**4th generation cepheims**

	Dose: i.v. or d.i.v.			
	Adult	Sever case	Pregnant	Pediatric
<b>Cefpirome</b>	1g × 2	2g × 2 or 4		20mg/kg × 3 - 4( ~ 160mg/kg/day)
<b>Cefepime</b>	1g × 2	2g × 2 or 4		×
<b>Cefozopran</b>	1g × 2	2g × 2 or 4		20mg/kg × 3 - 4( ~ 160mg/kg/day)
<b>Cefoselis</b>	1g × 2	-		×

**Carbapenems**

	Dose: d.i.v.			
	Adult	Sever case	Pregnant	Pediatric
<b>Imipenem</b>	0.5g × 2	0.5g × 4		~ 100mg/kg/day
<b>Meropenem</b>	0.5g × 2	0.5g × 4		×
<b>Panipenem</b>	0.5g × 2	0.5g × 4		10-20mg/kg × 3( ~ 100mg/kg/day)
<b>Biapenem</b>	0.3g × 3	0.3g × 4		×

## Other parenteral antimicrobials

	Dose: i.v. or d.i.v.			
	Adult	Sever case	Pregnant	Pediatric
<b>Piperacillin</b>	2g × 2 1g × 4	4g × 2 or 2g × 4		50-125mg/kg/day( ~ 200mg/kg/day)
<b>Piperacillin /tazobactam</b>	2.5g × 2	-		60-150mg/kg/day
<b>Ampicillin</b>	1-2g × 2	-	-	-
<b>Puzufloxacin</b>	500mg× 2	-	-	-

## Treatment of Special Bacteria

### ➤ Enterococci

Oral	First choice: Ampicillin, Amoxicillin, Faropenem Second choice: Fluoroquinolones, Sulfamethoxazole/Trimethoprim
Parenteral	First choice: Ampicillin Alternative: Piperacillin, Carbapenems

### ➤ MRSA

Oral	Minocycline, Sulfamethoxazole/Trimethoprim
Parenteral	Arbekacin, Vancomycin, Teicoplanin

### ➤ *Pseudomonas aeruginosa*

Oral	Ciprofloxacin 200mg×3, Tosufloxacin 150mg × 4, Sulfamethoxazole/Trimethoprim
Parenteral	Ceftazidime, Cefozopran, Meropenem, Imipenem, Piperacillin/tazobactam Aztreonam, Cefsulodin

### ➤ Metallo- -lactamase producing NFGNR

Parenteral	Aztreonam, Piperacillin/tazobactam
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### ➤ ESBL producing GNR

Oral*	Faropenem 900mg/day 7 days
Parenteral	Piperacillin/tazobactam, IPM/CS, MEPM

\*only against *E.coli* producing ESBL

# ***PROSTATITIS AND ACUTE BACTERIAL EPIDYDIMITIS***

## **Classification of Prostatitis by NIH**

- Category I : Acute Bacterial Prostatitis**
- Category II : Chronic Bacterial Prostatitis**
- Category III : Chronic Prostatitis(CP)  
Chronic Pelvic Pain Syndrome (CPPS)**
- Category IIIA : Inflammatory CP/CPPS**
- Category IIIB : Non-inflammatory CP/CPPS**
- Category IV : Asymptomatic inflammatory Prostatitis**

## **Examinations for Prostatitis and CPPS**

NIH-Chronic Prostate Symptom Index  
 Pre and Post Massage Test: PPMT (if possible, 4-glass test)  
 DRE  
 TRUS-P

- Pretreatment urine culture is essential, and evaluation timing is as same as UTI.
- Urine culture sample is obtained from VB1 or 2 in Category I, and EPS or VB3 in other Categories.
- Frequency-volume Chart, Uroflowmetry, and Urine cytology should be checked for the R/O of CIS in the bladder and Interstitial cystitis.
- Chlamydial infection should be ruled out in each case by PCR method.
- Treatment of infection caused by gonococci or Chlamydia should be subjected to both infections written in STD.

## **Reccomendations.**

### **Category I**

Parenteral quinolones (PZFX), 3<sup>rd</sup> or 4<sup>th</sup> cepheims (ceftazidime, cefpirome, cefepime, and cefozopran), or, carbapenems(Imipenem or Panipenem) more than 7 days followed by oral fluoroquinolones more than 7 days.

### **Category II**

Parenteral quinolones (PZFX) is preferable for the initial treatment in severe patients.  
 In mild patients, 4 weeks of oral fuluoroquinolones.

### **Category IIIA and IIIB**

- Check the frequency-volume chart and UFM of the incurable CPPS patients, and you should rule out of IC, especially in Category III. *See the page of Interstitial cystitis!*

Category IIIA	Initial antimicrobials (fluoroquinolones) 2 weeks Effective: 2 ~ 4 weeks added Ineffective: other therapies*
Category IIIB	No use of antimicrobials. other therapies*

\*  $\alpha$ 1-blockers, COX2-inhibitor, allopurinol, massage, acupuncture, counseling, etc.

## **Acute bacterial epidydimitis**

- 14 days of oral fuluoroquinolones (Ciprofloxacin, Levofloxacin, Tosufloxacin, and Gatifloxacin)
- If clinical symptom is severe, puzufloxacin, 3<sup>rd</sup> or 4<sup>th</sup> cepheims or carbapenems should be added initially.

## ***SEXUALLY TRANSMITTED DISEASES***

### **Principle**

- To cure of the STD patients,
  - 1) Make the critical diagnosis.
  - 2) Treat the patients with their sex partners simultaneously.
  - 3) Confirm the taking medicines perfect.
  - 4) Lead the patients not to infect the others, and not to be re-infected.
  - 5) Make sure of the eradication of microorganisms.

### **Gonococcal infection**

- Culture of urethral discharge or swab (pharyngeal or cervical) is necessary.
- Urethritis, cervicitis: Single therapy of cefodizime 1.0g i.v. or spectinomycin 2.0g i.m.
- Epydidymitis, PID, or systemic infection: cefodizime 1.0g i.v. × 2 or spectinomycin 2.0g i.m. /day Total 7 days.
- Pharyngitis: 3 days of intravenous cefodizime 1.0g /day

### **Chlamydial infection**

- Oral levofloxacin 200mg/day, clarithromycin 200mg/day, or tetracyclines 100mg /day Total 7 to 14 days
- Single dose of Oral azythromycin 1,000mg.

### **Syphilis**

- Asymptomatic syphilis should be treated if STS antibody elevated  $\geq 16$  times.
- Endo point of chemotherapy is “STS  $\leq 8$  times”.
- From 2002, measurement (titer) of STS is changed in UOEH (New RPR =  $0.91 \times$  old RPR).

<b>Clinical stage</b>	<b>Clinical features</b>	<b>Therapy</b>	<b>Periods</b>
Stage I	Initial induration Inguinal LN swelling	Amoxicillin or ampicillin 1500mg/day	2 to 4 weeks
Stage II	Systemic eruption Condyloma latum Syphilitic angina	If patients have allergy to penicillin, Minocycline 200mg/day	4 to 8 weeks
Stage III	Gumma	If patient is pregnant, Acetyl spiramycin 800 to 1200mg/day	8 to 12 weeks
Stage IV	Neurosyphilis Aortitis Myelophthisis	Benzylpenicillin 200-400MUnits×6 div	2 weeks

### **Trichomonas vaginitis and urethritis**

- Metronidazol 500mg/day 10 days.

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