Catheter-Associated Urinary Tract Infection and principle of antibiotics

導尿管相關泌尿道感染與抗生素使用原則

高雄榮總感染科

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2017/12/03

Content

- Introduction
- Epidemiology microbiology
- Pathogenesis
- Clinical Manifestations
- Diagnosis
- Treatment

Healthcare Associated Urinary Tract Infection

- 70% healthcare associated UTI are catheters related
- 20% pts had been indwelled at admisison
- In ICUs, 95% UTI are urinary catheter related
- HAIs with UTI related Blood Stream Infection: case-fatality rate 32.8%

Bennett & Brachman's , Hospital Infection 6th Edition, P476

Comparison of device-associated infection densities in adult ICUs from developed and developing countries, 1995–2008

	Number of ICUs	CR-BSI (95% CI)	Catheter-days	CR-UTI (95% CI)	Urinary catheter-days	VAP (95% CI)	Ventilator-days
Developed countries							
NNIS (1995–2003), USA*[98]	85–133†	5·0‡	1356490	5·3‡	1356490	5·8‡	115900
NHSN (2006–2008), USA*[99]	89–182†	2·1‡	699300	3·4‡	546824	2·9‡	383068
KISS (1997–2003), Germany[100]	309	1·8‡	1993541	..	..	8·0‡	1177137
KISS (2004–2009), Germany[101]	514–583†	1·3‡	4002108	2·0‡	4757133	5·1‡	2391381
Developing countries							
INICC (2002–2007), 18 developing countries*§[73]	60	8·9‡	132061	6·6‡	1030	19·8‡	1802
Argentina (1998–2004; current systematic review)[60–63]	15	24·7 (7·4–42·0)	9458	17·2 (13·4–21·1)	19013	48·0 (42·0–54·0)	5777
Turkey (1999–2005; current systematic review)[86,87,89,90]	16	11·0 (2·2–24·3)	23503	10·8 (4·2–17·4)	36343	26·0 (20·0–32·0)	39504
Current systematic review (1995–2008)[60–63,65,66,68,72–74,78,79,81,83,86,87,89,90]	226	11·3 (9·0–13·6)	373848	9·8 (7·7–11·8)	427831	22·9 (19·1–26·6)	263027

發展中國家的感染密度是已發展國家的5~10倍

***Lancet* 2011; 377: 228–41**

美國CDC National Healthcare Safety Network

- The incidence of catheter-associated UTIs in 2012 was 1.4 to 1.7 per 1,000 catheter days in inpatient adult and pediatric medical/surgical floors

American Journal of Infection Control 41 (2013) 1148-66

2015台灣醫療照護相關感染監視資訊系統(TNIS)

表四：2015 年醫學中心及區域醫院加護病房感染部位別醫療照護相關感染密度統計結果

醫院層級	感染部位	病房數	感染人次數	住院人日數	感染密度(‰)	MIN	百分位					MAX
							10	25	50	75	90	
醫學中心	血流	205 (198)	2,197	829,519	2.6	0	0.6	1.3	2.3	3.5	5.2	15.6
	肺炎	205 (198)	550	829,519	0.7	0	0	0	0.4	0.8	2.1	10.4
	泌尿道	205 (198)	1,920	829,519	2.3	0	0	0.9	1.9	3.5	4.8	9.1
	其他	205 (198)	707	829,519	0.9	0	0	0.2	0.7	1.3	2.1	23.8
區域醫院	血流	270 (252)	1,407	863,479	1.6	0	0	0	1.2	2.1	3.0	11.0
	肺炎	270 (252)	838	863,479	1.0	0	0	0	0.4	1.3	2.3	4.9
	泌尿道	270 (253)	1,602	863,479	1.9	0	0	0	1.2	2.2	3.1	8.1
	其他	270 (254)	428	863,479	0.5	0	0	0	0.2	0.7	1.3	3.7

備註：住院人日數<50 的病房不納入百分位排序，括弧內數值為符合條件納入百分位排序的病房數。

2015台灣醫療照護相關感染監視資訊系統(TNIS)

表八：2015 年醫學中心及區域醫院加護病房種類別導尿管相關泌尿道感染密度及導尿管使用比率

導尿管相關泌尿道感染密度

醫院層級	ICU 種類	病房數 [2]	裝置相關感染人數	導管使用人日數	感染密度(‰)	MIN	百分位 [1]					MAX
							10	25	50	75	90	
醫學中心	內科 ICU	54 (53)	775	175,441	4.4	0.4	1.7	3.2	4.2	5.7	8.5	10.6
	外科 ICU	63 (62)	655	211,414	3.1	0	0.9	1.6	2.9	3.9	5.4	10.5
	心臟科 ICU	16 (15)	126	32,691	3.9	0	-	1.9	3.2	4.4	-	8.4
	兒科 ICU	43 (34)	27	10,155	2.7	0	0	0	0	4.1	7.8	19.6
	綜合科 ICU	28 (26)	140	52,018	2.7	0	0	0.9	2.1	4.2	5.6	8.9
	合計	204(190)	1,723	481,719	3.6	0	0	1.3	3.1	4.7	6.8	19.6
區域醫院	內科 ICU	60 (56)	405	167,778	2.4	0	0.4	1.2	2.2	3.3	4.7	7.0
	外科 ICU	46 (43)	385	133,842	2.9	0	1.2	1.7	2.4	3.2	4.8	7.9
	心臟科 ICU	13 (12)	47	24,493	1.9	0	-	1.1	1.6	2.1	-	3.1
	兒科 ICU	62 (7)	1	1,454	0.7	0	0	0	0	0	6.0	14.9
	綜合科 ICU	89 (80)	612	238,532	2.6	0	0.4	1.1	2.1	3.6	5.2	10.1
	合計	270 (198)	1,450	566,099	2.6	0.4	0.4	1.2	2.1	3.2	4.9	14.9

Study for Monitoring Antimicrobial Resistance Trends (SMART)
常見泌尿道感染菌種與排名

UTIs in 2009 and 2010, from 8 medical centers in Taiwan, No mention of CAUTI, 475 isolates

	Pathogen	
1	*Escherichia coli*	47.2%
2	*Klebsiella pneumoniae*	14.3%
3	*Pseudomonas aeruginosa*	8.8%
4	*Proteus mirabilis*	8.0%
	Total	77.5%

International Journal of Antimicrobial Agents 40S1(2012)S37-S43

2007-2016 醫學中心加護病房泌尿道感染常見菌種排名

UTI	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
菌種	排名	排名	排名	排名	排名	排名	排名	排名	排名	排名
Escherichia coli	1	2	2	2	1	1	1	1	1	1
Yeast-like	3	3	3	3	3	2	3	3	3	2
Candida albicans	2	1	1	1	2	3	2	2	2	3
Enterococcus faecium	9	8	8	7	8	7	6	5	4	4
Pseudomonas aeruginosa	4	5	5	5	5	5	5	6	6	5
Klebsiella pneumoniae	5	7	6	6	6	6	7	7	6	6
Other *Candida* spp. or NOS	7	4	4	4	4	4	4	4	5	7
Enterococcus faecalis	10	10	10	10	9	9	8	8	8	8
Acinetobacter baumannii	6	6	7	8	7	8	9	9	9	9
Enterobacter species	8	9	9	9	10	10	10	10	10	10

2007-2016 區域醫院加護病房泌尿道感染常見菌種排名

UTI	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
菌種	排名	排名	排名	排名	排名	排名	排名	排名	排名	排名
Escherichia coli	1	1	1	1	1	1	1	1	1	1
Candida albicans	2	2	2	2	2	2	2	1	2	2
Klebsiella pneumoniae	4	3	4	3	3	4	4	4	4	3
Enterococcus faecium	11	10	9	9	8	8	6	6	6	4
Pseudomonas aeruginosa	3	4	3	4	4	3	3	3	3	5
Other *Candida* spp. or NOS	7	7	7	6	5	5	5	5	5	6
Enterococcus faecalis	12	11	11	11	10	9	11	9	9	7
Yeast-like	5	5	5	7	6	6	7	8	7	8
Acinetobacter baumannii	6	6	6	5	7	7	7	7	8	9
Proteus species	8	8	8	8	9	9	9	10	11	10

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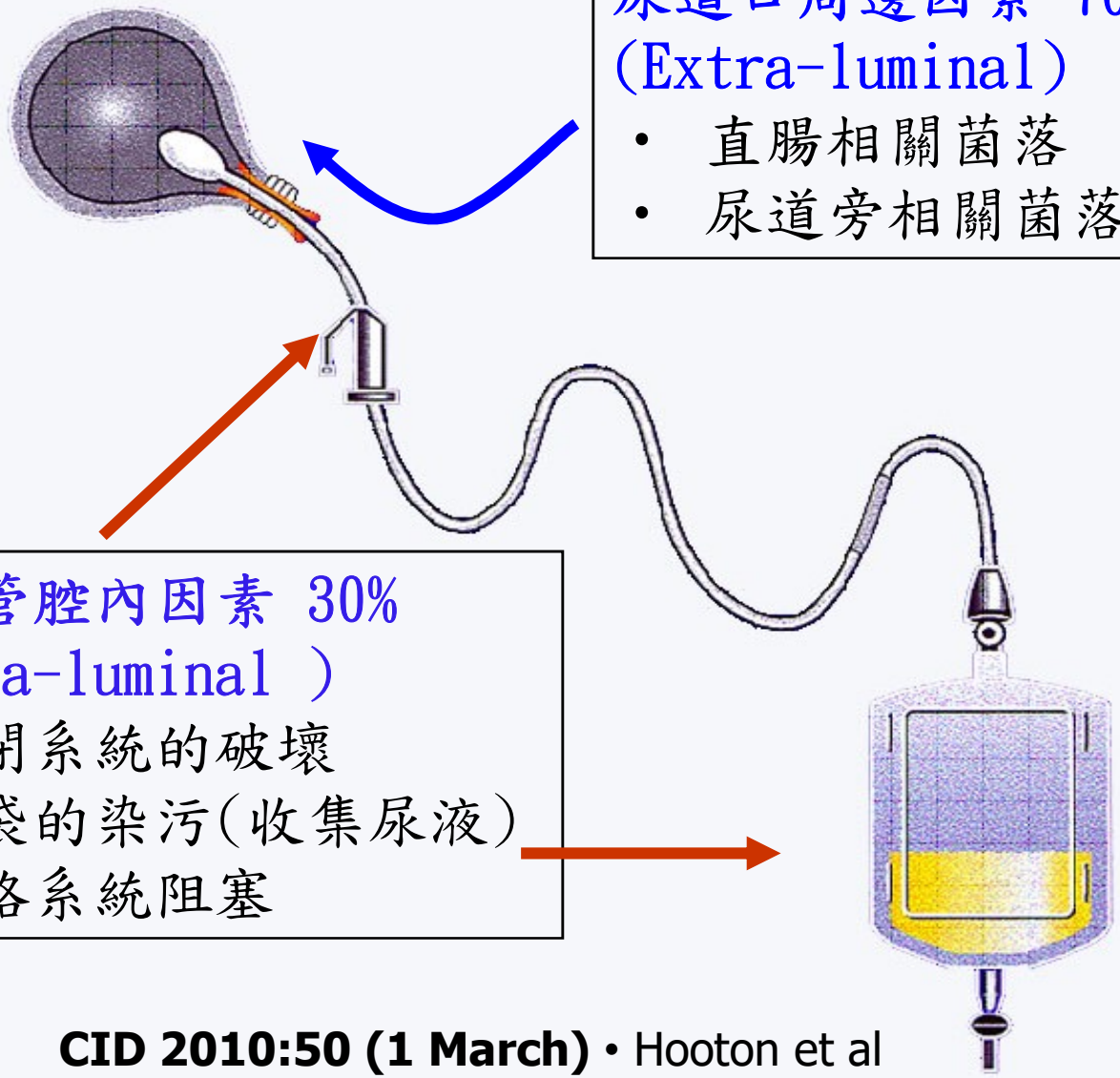
導尿管相關泌尿道感染的致病機轉

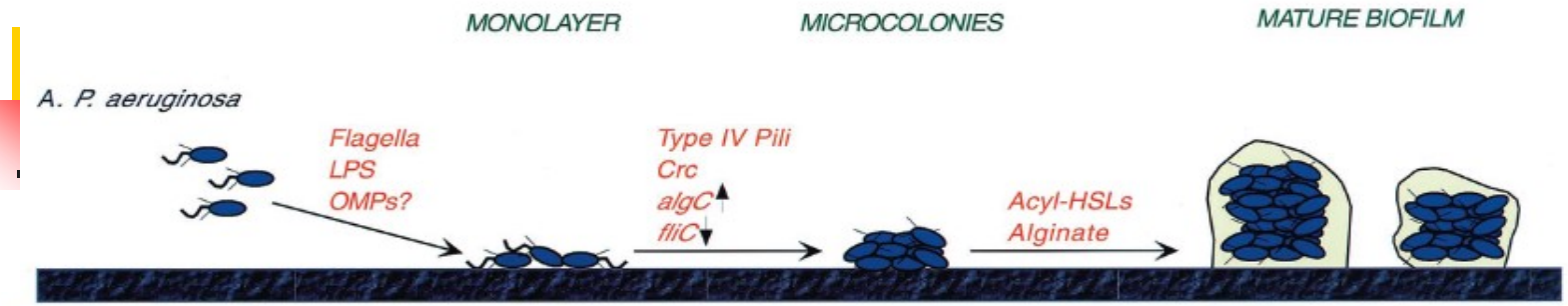


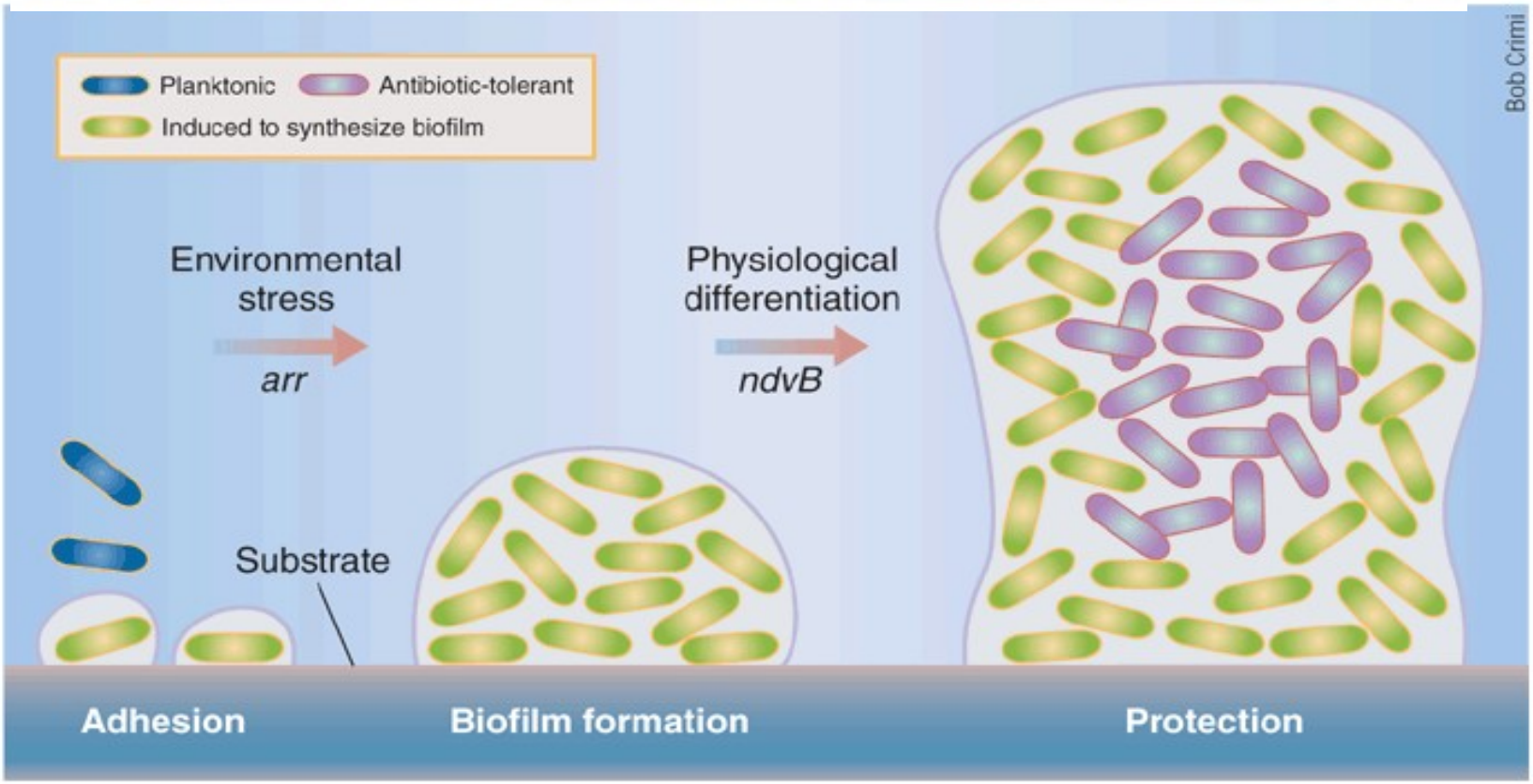
尿道口周邊因素 70%
(Extra-luminal)
- 直腸相關菌落
- 尿道旁相關菌落

導尿管腔內因素 30%
(Intra-luminal)
- 密閉系統的破壞
- 尿袋的染污(收集尿液)
- 尿路系統阻塞

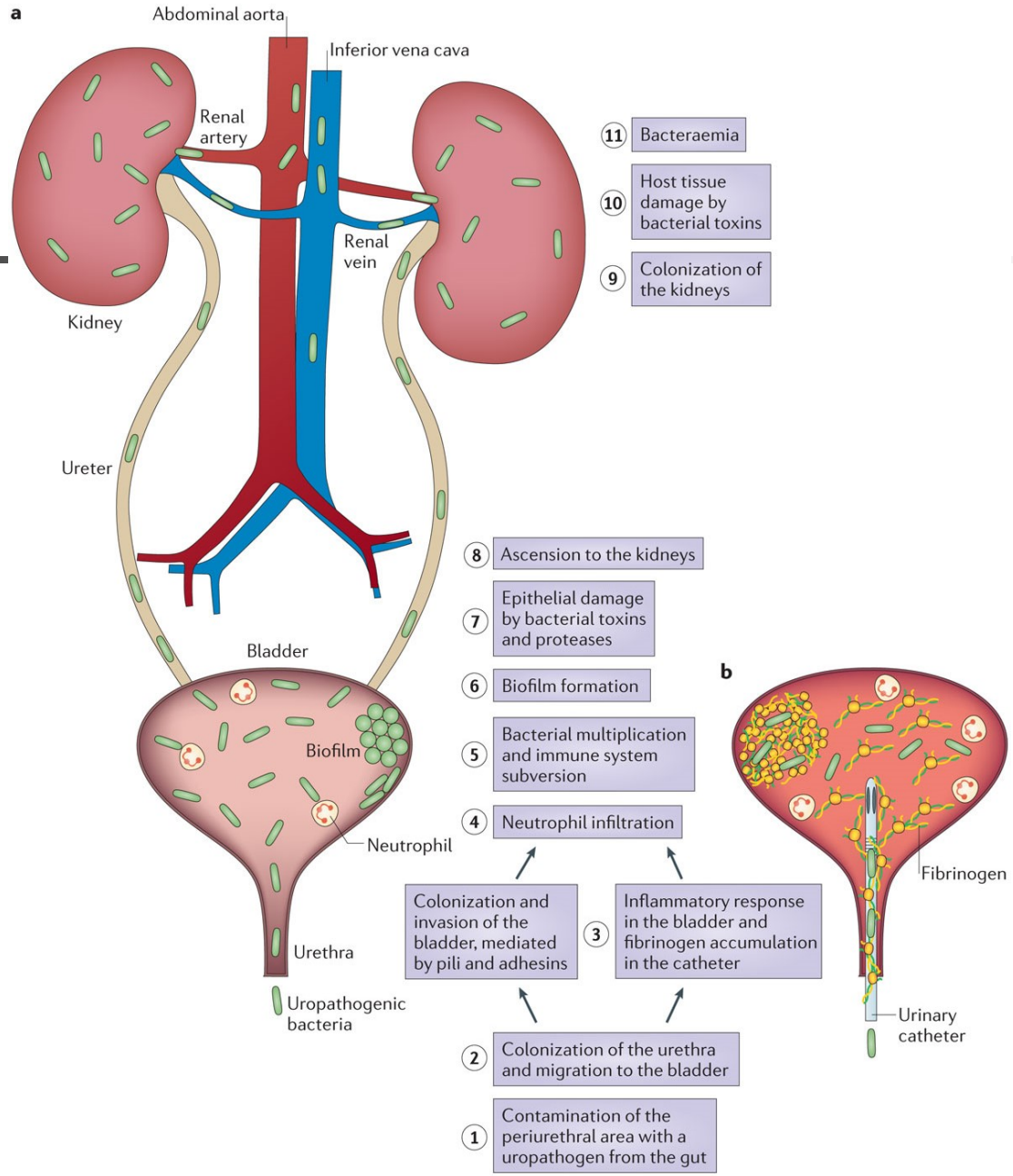
CID 2010:50 (1 March) • Hooton et al

生物膜的形成





MICROBIOLOGY AND MOLECULAR BIOLOGY REVIEWS, Dec. 2000, p. 847–867
Nature Biotechnology **23**, 1378 - 1379 (2005)


a
Abdominal aorta
Inferior vena cava
Renal artery
Renal vein
Kidney
Ureter
Bladder
Biofilm
Neutrophil
Urethra
Uropathogenic bacteria
11 Bacteraemia
10 Host tissue damage by bacterial toxins
9 Colonization of the kidneys
8 Ascension to the kidneys
7 Epithelial damage by bacterial toxins and proteases
6 Biofilm formation
5 Bacterial multiplication and immune system subversion
4 Neutrophil infiltration
3 Inflammatory response in the bladder and fibrinogen accumulation in the catheter
Colonization and invasion of the bladder, mediated by pili and adhesins
2 Colonization of the urethra and migration to the bladder
1 Contamination of the periurethral area with a uropathogen from the gut
b
Fibrinogen
Urinary catheter
Nature Reviews | Microbiology

人體對泌尿道感染的防禦機制

- Flushing action of urine
- Acidic urine inhibits pathogens
- The prostate gland in men secretes Zinc-fights bacteria
- Surface IgA
- Antibacterial substances from uro-epithelium
- Low vaginal pH-inhibits UTI causing bacteria

Mandell Bennett 6th ed

Risk factors for CAUTI

Risk factors	Odds ratio
Duration of urinary catheter	2.3 ~ 22.4
Catheter insertion after the 6th day	8.6
Catheter inserted outside of OR	5.3
rapid fatal underlying illness	2.5
Female, DM, age>50, Cr.>2mg/dl	2.0~3.0

CID 2010:50 (1 March) • Hooton et al

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CAUTI
Clinical manifestation

- Only 10% to 32%
- 90% are asymptomatic bacteriuria ?
- CA-ASB: catheter associated asymptomatic bacteriuria
- CA-UTI: Fever and chills are the most symptoms
  - **Systemic**: new onset or worsening of fever, rigors, altered mental status, malaise, or lethargy with no other identified cause
  - **Localized**: flank pain; costovertebral angle tenderness; acute hematuria; pelvic discomfort;
  - dysuria, urgent or frequent urination, or suprapubic pain or tenderness in those whose catheters have been removed

CID 2010:50 (1 March) • Hooton et al

無症狀菌尿症定義：Asymptomatic bacteuria

- 無症狀女性，連續兩次尿液檢體分離出同一隻菌，且>10^5 CFU/ml (B-II).
- 無症狀男性，單次尿液檢體分離出單一細菌，且>10^5 CFU/ml (BIII).
- 單次導尿尿液檢體分離出單一細菌，且>10^2 CFU/ml (A-II)

Clinical Infectious Diseases 2005; 40:643–54

Catheter associated asymptomatic bacteriuria

- The incidence of bacteriuria associated with indwelling catheterization
- 3%–8% per day

N Engl J Med **1974; 291:215–219**
N Engl J Med **1966; 274:**1155–1161
Infect Control 1981 Sep-Oct;2(5):380-6

Table 2. Prevalence of asymptomatic bacteriuria in selected populations.

Population	Prevalence, %	Reference
Healthy, premenopausal women	1.0–5.0	[31]
Pregnant women	1.9–9.5	[31]
Postmenopausal women aged 50–70 years	2.8–8.6	[31]
Diabetic patients		
Women	9.0–27	[32]
Men	0.7–11	[32]
Elderly persons in the community[a]		
Women	10.8–16	[31]
Men	3.6–19	[31]
Elderly persons in a long-term care facility		
Women	25–50	[27]
Men	15–40	[27]
Patients with spinal cord injuries		
Intermittent catheter use	23–89	[33]
Sphincterotomy and condom catheter in place	57	[34]
Patients undergoing hemodialysis	28	[28]
Patients with indwelling catheter use		
Short-term	9–23	[35]
Long-term	100	[22]

[a] Age, ⩾70 years.

Clinical Infectious Diseases 2005; 40:643–54

CA-UTI收案定義

- Patients with indwelling urethral, indwelling suprapubic, or intermittent catheterization
- Presence of symptoms or signs compatible with UTI
- No other identified source of infection along with 10^3 CFU/mL of >= 1 bacterial species
  - in a single catheter urine specimen
  - or in a midstream voided urine specimen from a patient whose urethral, suprapubic or condom catheter removed within the previous 48 h (A-III).
- In the catheterized patient, pyuria is not diagnostic of CA-bacteriuria or CA-UTI (A-II)

CID 2010:50 (1 March) • Hooton et al

CAUTI 收案新定義

- 尿液培養:
  - 不超過兩種菌種, 菌落量 > 10^5 CFU/ml
- CAUTI發生時間:
  - 導尿管置放超過兩天(置放當天為第一天)
  - CAUTI時仍置放導尿管或是CAUTI發生前已拔掉導尿管
- 症狀或徵兆(其中一項即可):
  - 發燒>38度
  - 下腹痛、側腰痛(無其他原因解釋)
  - 頻尿、尿急、解尿疼痛(有尿管時，不適用)

CDC January 2017

CAUTI 收案新定義
排除的菌種

- Mixed flora (>超過兩種菌種)
- *Candida* species or yeast not otherwise specified
- mold
- dimorphic fungi or
- parasites

CDC January 2017

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Can screen and treat CA-ASB prevent CA-UTI ?

- Screening for and treatment of CA-ASB are not recommended to reduce subsequent CA-bacteriuria or CA-UTI in patients with
  - short-term(A-II) indwelling urethral catheters.
  - long-term(A-I) indwelling urethral catheters.
  - neurogenic bladders managed with intermittent catheterization (A-II).
- except in pregnant women (A-III) and patients who undergo urologic procedures for which visible mucosal bleeding is anticipated (A-III)

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Cephalexin for susceptible bacteriuria in a febrile, long-term catheterized patients

- 對象:長期尿管放置病患
- 介入:10天cephalexin
- 17 cephalexin group pts for 545 pt-weeks, 18 control group pts for 477 pt-week
- 兩組發燒事件及抗生素使用的機會皆相似，但是cephalexin Group 分離出較多抗Cephalexin的菌種
- 結論: 不需要治療長期尿管留置病患的 CAS-UTI

JAMA 1982 Jul 23;248(4):454-8.

Appropriate Management Strategies for CA-UTI

- Urine culture and Catheter Replacement before Treatment
- What's the appropriate antibiotics for empirical treatment
- Duration of treatment

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Should we replace catheter before treatment ?

- If an indwelling catheter has been in place for > 2 week at the onset of CA-UTI and is still indicated, the catheter should be replaced to hasten resolution of symptoms and to reduce the risk of subsequent CA-bacteriuria and CA-UTI (A-I)

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Should we replace catheter before antimicrobial therapy for CA-UTI in patient with long-term catheter

		3 days	7 days*	28 days*
Polymicrobial bacteriuria decreased	R(27)	24 (88%)	18 (66%)	13 (48%)
	N(27)	8 (30%)	9 (30%)	5(18.5%)
	P=	0.002	0.01	0.02
Shorter time to afebrile status	R(27)	25(92.5%)		
	N(27)	11(40%)		
	P=	<0.001		
Symptomatic clinical relapse	R(27)			3 (11.1%)
	N(27)			11 (40.7%)
	P=	0.015		0.015

R: replacement of foley group , N: no replacement of foley group

* After Complete Treatement

THE JOURNAL OF UROLOGY Vol. 164, 1254–1258, October 2000

How to get urine culture before Treatment ?

- The urine culture should be obtained from the freshly placed catheter prior to the initiation of antimicrobial therapy to help guide treatment (A-II).
- If use of the catheter can be discontinued, a culture of a voided midstream urine specimen should be obtained prior to the initiation of antimicrobial therapy to help guide treatment (A-III).

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CA-UTI Treatment

- What's the appropriate antibiotics for empirical treatment ?

SMART
UTI in Asia-Pacific region

	No of isolates	AMK	Pip/taz	CAZ	FEM	CIP	LEVO	ETP	IPM
All isolates	1762	91.7	84.9	66.0	65.3	51.4	54.4	86.9	86.6
E-coli	995	96.1	96.1	68.7	62.2	43.2	44.1	99.3	99.9
K.P	243	93.4	93.4	66.3	67.5	66.7	74.1	95.9	96.7
P.A	126	76.2	76.2	57.1	59.5	55.6	55.6	---	61.1

International Journal of Antimicrobial Agents 40S1(2012)S37-S43

E-coli susceptibility

	AMK	PIP	Pip/tazo	CAZ	FEM	CIP	LEVO	ERT	IPM
2010醫中*	96	--	--	63	--	66	64	--	--
2010區域*	96	--	--	77	--	65	67	--	--
2011醫中*	97	--	--	46	--	66	66	--	--
2011區域*	96	--	--	59	--	65	65	--	
2012高榮@	97.7	14.4	100	55.2	63.1	58.8	--	--	100
2013高榮@	99.4	14.6	85.5	61.7	69.1	58.8	--	--	100
2014高榮@	96.4	10.9	88.8	61.8	70	50.9	--	--	100

* 感染控制雜誌 101 年 12 月第二十二卷第六期
@高雄榮總 2012-2014 實驗室院內泌尿道感染菌株分析

Klebsiella pneumoniae susceptibility

	AMK	PIP	Pip/tazo	CAZ	FEM	CIP	LEVO	ERT	IPM
2010醫中*	90	--	--	68	--	74	--	96	91
2010區域*	86	--	--	72	--	70	--	97	96
2011醫中*	92	--	--	72	--	73	--	93	96
2011區域*	85	--	--	72	--	68	--	90	95
2012高榮@	81.6	22.9	--	55.2	68.4	76.3	--	--	97.3
2013高榮@	92.7	30	58.3	61	66.7	58.5	--	--	100
2014高榮@	100	41.7	65.2	70.8	83.3	70.8	--	--	100

* 感染控制雜誌 101 年 12 月第二十二卷第六期
@高雄榮總 2012-2014 實驗室院內泌尿道感染菌株分析

P.aeruginosa susceptibility

	AMK	PIP	Pip/tazo	CAZ	FEM	CIP	LEVO	IPM
2010醫中*	--	82	85	86	--	79	77	86
2010區域*	--	83	85	88	--	74	71	87
2011醫中*	--	82	84	83	--	79	77	83
2011區域*	--	82	86	87	--	73	69	87
2012高榮@	98.8	88	--	89.2	86.7	91.4	100	91.4
2013高榮@	96.8	91.8	100	91.9	96.7	93.5	--	91.7
2014高榮@	100	90.7	100	90.7	95.2	90.7	--	97.6

* 感染控制雜誌 101 年 12 月第二十二卷第六期
@高雄榮總 2012-2014 實驗室院內泌尿道感染菌株分析

Enterococcus faecalis

	AMP	PCN	PIP	Pip/tazo	GM(H)	VAN
2010醫中*	98	--	--	--	58	99
2010區域*	97	--	--	--	54	99
2011醫中*	98	--	--	--	59	99
2011區域*	93	--	--	--	52	99
2012高榮@	100	81.8	--	--	34.9	100
2013高榮@	95.5	95.5	--	--	39	100
2014高榮@	70.4	80	--	--	39	100

* 感染控制雜誌 101 年 12 月第二十二卷第六期

@高雄榮總 2012-2014 實驗室院內泌尿道感染菌株分析

Duration of Treatment

- Seven days is the recommended duration of antimicrobial treatment for patients with CA-UTI who have prompt resolution of symptoms (A-III)
- 10–14 days of treatment is recommended for those with a delayed response (A-III),
- regardless of whether the patient remains catheterized or not.

Duration of Treatment

- Courses of 5–14 days have often been recommended for CA-UTI in patients with neurogenic bladders

CID 2010:50 (1 March) • Hooton et al

A Prospective, Randomized Trial of 3 or 14 Days of Ciprofloxacin Treatment for Acute Urinary Tract Infection in Patients with Spinal Cord Injury

Follow-up outcome	**3-day arm N=30**	**14-day arm N=30**	***P***
Short term			
Clinical cure	19(63)	16(53)	.60
Microbiological cure	9(30)	14(47)	.29
Relapse	10(33)	0	.001
Long term			
Clinical cure	11(37)	12(40)	1.00
Microbiological cure	1(3)	8(27)	.02
Relapse	11(37)	2(7)	.01

CID 2004:39 (1 September) • Dow et al

A Double-Blind, Randomized Comparison of Levofloxacin 750 mg Once-Daily for Five Days With Ciprofloxacin 400/500 mg Twice-Daily for 10 Days for the Treatment of Complicated Urinary Tract Infections and Acute Pyelonephritis

- CONCLUSIONS:

  A 5-day course of therapy with levofloxacin 750 mg once daily, is noninferior to a 10-day course of ciprofloxacin for the treatment of AP and cUTI.

UROLOGY 71 (1), 2008

Empirical antimicrobials suggestion

Diagnosis	Antibiotic of choice		Duration
	First choice	Alternatives	
Catheter-Associated UTI	Amikacin 15mg/Kg qd [c,I] Or Tazocin 4.5 g iv q8h [c,II] Or cefatazidime 2g iv q8h [c,II] or cefepime 2g iv q12h [c,II]	Imipenem 500 mg iv q6h or meropenem 1 g iv 8h or doripenem 500mg iv q8h [c,I] Levofloxacin 750 mg qd or ciprofloxacin 400 g iv q12h [c,II]	5-7 days (C, II) 10-14 days for patients with delayed response (C, II)

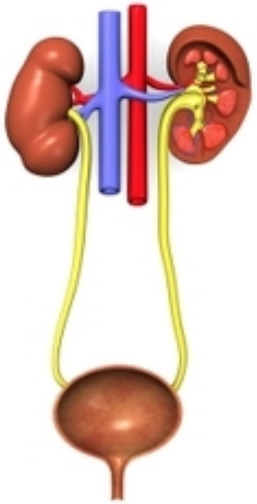
Content

- Introduction
- Epidemiology and microbiology
- Pathogenesis
- Clinical Manifestations
- Diagnosis and Surveillance
- Treatment
- Prevention

導尿管相關泌尿道感染組合式照護

Catheter-Associated
Urinary Tract Infection care bundle

高雄榮總感染科
陳瑞光



UTI bundle

- 導尿管使用適應症制定
- 提醒海報設置
- 稽核表單制定
- 資訊系統設定
- 回饋系統
- 實際運作流程

實際技術流程

- 導尿管置入技術影片(男性)
- 導尿管置入技術影片(女性)
- 導尿管照護技術影片

Comments

- Mild to moderate disease: Amikacin or Tazocin
- Severe disease: Imipenem/meropenem
- Candidiauria rarely cause true infection and enterococcus was low virulent ,we suggest clinical evaluation necessary for initial coverage
- If enterococcus coverage is considered, suggest piperacillin+amikacin or pip/tazo

Comments

- Fluoroquinolone if local drug susceptibility >70% or severe beta-lactam allergy
- Ertapenem may an empirical choice if low risk of *Pseudomonas aeruginosa* infection
- Pathogen and drug susceptibility from catheter-acquired UTIs was variable. Local microbiological data and patient individual evaluation should be taken into consideration

Take Home Message

- Catheter-associated bacteriuria is common. Don't treat asymtomatic bacteuria
- Replace urinary catheter is helpful for future de-escalation and clinical improvement.
- Empirical therapy is based on local epidemiology
- Duration of antibiotics should be emphasized to prevent further resistance
- Prevention is the best treatment


謝 謝 聆 聽
---photo by Wudy---