Primary urinary tract infection: the role of undetected hematogenous seeding of the urinary tract

I. G. Baraboutis, E. P. Tsagalou, J. L. Lepinski, I. Papakonstantinou, V. Papastamopoulos, A. T. Skoutelis, S. Johnson

► To cite this version:

I. G. Baraboutis, E. P. Tsagalou, J. L. Lepinski, I. Papakonstantinou, V. Papastamopoulos, et al.. Primary urinary tract infection: the role of undetected hematogenous seeding of the urinary tract. *European Journal of Clinical Microbiology and Infectious Diseases*, 2010, 29 (9), pp.1095-1101. 10.1007/s10096-010-0967-2 . hal-00596736

HAL Id: hal-00596736

<https://hal.science/hal-00596736>

Submitted on 30 May 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Manuscript Number: EJCMIID-D-10-00026R1

Title: PRIMARY STAPHYLOCOCCUS AUREUS URINARY TRACT INFECTION : THE ROLE OF
UNDETECTED HEMATOGENOUS SEEDING OF THE URINARY TRACT

Article Type: Article

Keywords: Staphylococcus aureus; urinary tract infection; primary
staphylococcus aureus urinary tract infection; Escherichia coli urinary tract infection; urinary tract
catheterization

Corresponding Author: Dr Ioannis G Baraboutis, M.D.

Corresponding Author's Institution: Evangelismos General Hospital

First Author: Ioannis G Baraboutis, M.D.

Order of Authors: Ioannis G Baraboutis, M.D.; Eleftheria P Tsagalou, M.D.; Jeanette L Lepinski, R.N.; Ilias
Papakonstantinou, M.D.; Vassilios Papastamopoulos, M.D.; Athanasios T Skoutelis, M.D.; Stuart Johnson,
M.D.

Abstract: Purpose. Staphylococcus aureus (SA) bacteriuria may accompany SA bacteremia but primary
SA urinary tract infection (UTI) may also occur. Our clinical observation of SA UTIs following
intravenous catheter-related phlebitis lead us to review hematogenous and ascending route-related
risk factors in patients with primary SA UTIs.

Methods. Charts from all patients with SA UTIS over 11/2 year period were reviewed for concurrent or
recent hospitalization, intravenous catheterization and for known UTI risk factors. Patients with
concurrent SA bacteremia were excluded. Patients with E.coli UTIs during the same period were
included as controls.

Results. Twenty cases of primary SA UTI were compared with 43 E.coli UTI cases and did not differ in
age, diabetes mellitus, prostatic hypertrophy, previous UTI and other urinary tract (UT) abnormality.
However, cases were more likely than controls to have had recent or concurrent hospitalization, UT
catheterization and history of recent phlebitis. In multivariate analysis, UT catheterization and recent
hospitalization retained significant association with SA UTI. Similar results were shown for the
methicillin-resistant SA UTI subgroup.

Conclusions. Even though UT catheterization is the main predisposing factor for primary SA UTI, some
cases may be mediated through unrecognized preceding bacteremia related to intravascular device
exposure or other healthcare-related factor.

Response to Reviewers: EJCMIID - D 10 - 00026

Answers to Reviewers' comments:

Reviewer #2: This is a retrospective analysis of 20 cases of staph aureus bacteriuria without a
concurrent SA bacteremia. The authors conclude that, despite the main predisposing role of UTI

catheterization, unrecognized transient bacteremia due to recent hospitalization and intravascular device exposure in these patients, may play an important role for SA UTI. The study has some interesting hints and, although retrospective, may give some important messages for this not well defined entity.

However, the information given cannot support a full paper submission, but rather a brief report.

ANSWER. The manuscript is being resubmitted using the "concise article" format, as requested by the Editorial Office.

The authors should clarify the number of patients with upper or lower UTI, as it is interesting to identify whether SA bacteriuria is related to pyelonephritis or not.

ANSWER. We tried to avoid studying just bacteriuria by using quite strict criteria to define "urinary tract infection" (ending up this way with 20 patients only). Those are described in the "materials and methods" section. Besides a positive urinalysis and urine culture, we required at least 4 pertinent symptoms (out of the following: dysuria, frequency, hematuria, fever more than 38°C, suprapubic tenderness, costovertebral area tenderness to percussion) AND documentation in the chart of a clinical impression of urinary tract infection by the responsible physicians. Since 1. there is significant symptom overlap between cystitis, prostatitis and pyelonephritis and 2. the diagnosis written in the patient charts was, in the majority of cases, just "urinary tract infection" without further specification, we feel we do not have data accurate enough to discriminate between upper and lower UTI in the 2 groups. So, we think that "symptomatic urinary tract infection" is the best description we can come up with (we have made appropriate corrections in the "materials and methods" section). Also, we have put a pertinent comment in the "limitations of the study" section.

We thank the Editorial Office and the reviewers for their time and effort

On behalf of the authors

Ioannis G. Baraboutis

Electronic Supplementary Material

[Click here to download Electronic Supplementary Material: SA UTI COVER LETTER REVISED.doc](#)

PRIMARY *STAPHYLOCOCCUS AUREUS* URINARY TRACT

INFECTION : THE ROLE OF UNDETECTED HEMATOGENOUS

SEEDING OF THE URINARY TRACT

INTRODUCTION

Staphylococcus aureus (*S. aureus*, SA) is the causative factor of a great variety of infections in outpatients as well as in hospitalized patients. It is considered one of the commonest causes of nosocomial infection in US hospitals and in many European countries [1]. On the other hand, urinary tract infections (UTI) are one of the commonest types of infections encountered in clinical practice, while they constitute the most common type of nosocomial infection in the US [1]. Up to 95% of nosocomial UTIs may be associated with indwelling urinary catheters [1].

Despite the above, *S. aureus* has been known for years to be a relatively rare urinary isolate [2]. Older studies, involving outpatients or inpatients or mixed populations, report a percentage of 0.5% to 6% of all positive urine cultures [3,4,5,6]. Newer reports mention a 13.1% contribution of *S. aureus* in a bacteremic UTI case-series involving mostly elderly people in a large community hospital [7].

1 The clinical significance of a positive urine culture for SA has been long
2 debated. Traditionally *S. aureus* has been considered to invade the kidney
3 from the hematogenous route, resulting in intrarenal or perinephric
4 abscesses [6,8]. *S. aureus* bacteriuria may occur in 7% of patients with *S.*
5 *aureus* bacteremia and in 13% of cases of *S. aureus* endocarditis
6 according to an older study [9], although more recent data doubt this
7 association [10].

8 On the other hand, some investigators of *S. aureus* bacteremia include the
9 urinary tract as the portal of entry, although infrequently [2]. In vitro, *S.*
10 *aureus* is able to attach to and aggregate onto uroepithelial cells through
11 glycoproteins found in bladder mucin, like GP51, which is significantly
12 increased in the presence of urinary tract infection [11]. This retrograde
13 pattern of *S. aureus* UTI (or *primary SA UTI*) has been mostly
14 documented in elderly men with presence of important predisposing
15 factors in the urinary tract. These include presence of indwelling
16 catheters, obstruction or other abnormalities, instrumentation or surgery
17 [2,4]. Rates of secondary bacteremia in these groups of patients have
18 been reported to range from 2.3% to 8.3% [2,4,6,12].

19 Even more puzzling and also much less studied is the clinical significance
20 of SA bacteriuria without documented bacteremia before or after the
21 positive *S. aureus* urine culture date. A study of SA bacteriuria without
22 documented bacteremia from 1997 speculates a transient unidentified

1 bacteremic state, at least for some of these patients [13]. The above
2 speculation of a transient bacteremic state leading to *S. aureus* urine
3 colonization or even UTI (which, if existed, would possibly be another
4 candidate for the definition of “primary SA UTI” besides the already
5 known UTI via the ascending route) could potentially apply to some
6 clinical observations we made in our clinical practice.
7
8
9
10
11
12
13
14
15
16

- 17 • *Case-report A:* Young woman with eosinophilic meningitis and
18 prolonged hospital stay was seen in f/up with a superficial phlebitis
19 at the site of a previous intravenous catheter in her wrist/forearm.
20 The site was not warm or fluctuant and she had no systemic
21 symptoms so she was treated conservatively with warm
22 compresses. The following visit she mentioned symptoms of a UTI
23 so a urinalysis (UA) and a urine culture (UC) were sent and she
24 was started on trimethoprim-sulfamethoxazole empirically. The
25 UC yielded $>10^5$ colonies/ml of *S. aureus* (pure growth).
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43 • *Case report B:* 42 year-old patient with advanced AIDS and HIV-
44 related dementia was hospitalized briefly for mental status changes.
45 During his hospital stay, he received a brief course of intravenous
46 anti-CMV therapy. The hospital course was uneventful, he
47 improved and was discharged home after 8 days. There was no
48 urinary tract (UT) manipulation during his hospital stay or later and
49 there was no history of UTI or UT abnormality. Four weeks later,
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

1 he was evaluated as outpatient. He had no systemic symptoms but
2
3 reported new-onset urinary frequency, dysuria and suprapubic pain.
4
5 UA showed significant pyuria and UC revealed pure growth of
6
7
8 $>10^5$ colonies/ml of *S. aureus*.
9

10
11 We hypothesized that the ``primary *S. aureus* UTI`` identified in those
12
13 two patients was blood-borne in origin. In the first case, it could be
14
15 related to transient bacteremia related to intravenous site
16
17 thrombophlebitis, while in the second case there was no obvious primary
18
19 focus but the patient had been recently hospitalized, received intravenous
20
21 therapy and was significantly immunocompromised. Several reports of
22
23 increased rates of *S. aureus* bacteremia in the HIV/AIDS population are
24
25 now available [14,15].
26
27
28
29
30
31
32
33
34
35
36
37
38
39

40 MATERIALS AND METHODS

41
42 To put our hypothesis in perspective we wanted to further evaluate the
43
44 occurrence of this phenomenon/syndrome, should it exist. Our study was
45
46 approved by the Institutional Review Board (IRB) of Northwestern
47
48 University and Lakeside Veterans Affairs (VA) Hospital.
49
50
51 We used the Infection Control records of the VA hospital for the purposes
52
53 of our research. We reviewed the infection control line listing of patients
54
55 with *S. aureus* infections of the time period between March 2000 and
56
57
58
59
60
61
62
63
64
65

1 September 2001 and we identified patients with positive urine cultures for
2
3 *S. aureus* without documented concurrent *S. aureus* bacteremia. Then,
4
5 we used the computerized medical record system of our hospital to search
6
7 the charts of those patients for clinical and microbiological data to
8
9 support the diagnosis of “SA symptomatic UTI without concurrent
10
11 bacteremia”.
12
13
14
15

16 The diagnosis of “symptomatic UTI” was present when all the following
17
18 criteria were present: 1. positive urine culture for *S. aureus* in pure
19
20 growth and $>10^5$ CFU/mL, 2. more than 10 white blood cells per high-
21
22 power field on urinalysis, 3. positive test for nitrates or leucocyte
23
24
25
26
27
28 esterase, 4. at least 4 out of the following 6 symptoms/signs: dysuria,
29
30
31 frequency, hematuria, fever more than 38°C, suprapubic tenderness,
32
33
34 costovertebral area tenderness to percussion and 5. diagnosis of urinary
35
36
37 tract infection by the responsible physicians.
38

39 “Concurrent bacteremia” was defined as at least one blood culture
40
41
42 positive for *S. aureus* in the 2 weeks preceding or the 72 hours after the
43
44
45 first urine culture yielding *S. aureus*.
46

47 By using the above-described definitions, we finally came across with a
48
49
50
51 list of 20 patients eligible for further study.
52

53 For those 20 patients, we collected demographic and medical history data
54
55
56 about pre-existing illnesses (with attention to conditions predisposing to
57
58
59 UTI). We recorded data about prior hospitalization within the last six
60
61
62
63
64
65

1 months and inpatient or outpatient status when the urine culture (UC) was
2
3 obtained. Paper chart notes were also reviewed looking for history of
4
5 recent hospitalization at another facility possibly not recorded on
6
7 electronic VA chart.
8
9

10
11 Dates of prior vascular procedures (peripheral line and/or central venous
12
13 catheter placement) that took place during the last month before the
14
15 positive UC date were also recorded. Subsequently, we carefully
16
17 reviewed all the medical and nursing notes up to 1 month prior to the
18
19 positive UC date looking for any sign of local inflammation at the site of
20
21 the peripheral or central catheter entry. We included recordings about
22
23 local redness, swelling, induration and presence of pus.
24
25
26
27
28
29

30
31 Additionally, we looked for data on any kind of UT manipulation during
32
33 the same time-period. Those included placement and presence of Foley
34
35 catheter up to 48 hours before the positive UC date and also other
36
37 urologic procedures.
38
39
40
41

42
43 To compare that patient group (“SA group” or “cases”) with other
44
45 primary UTI cases in which retrograde infection is usually the norm, we
46
47 looked for a control group of *E. coli* UTI cases without concomitant
48
49 bacteremia. The exclusion of bacteremic *E. coli* UTI cases may not have
50
51 been critical as most *E. coli* bacteremias are thought to be secondary to
52
53
54
55
56
57 *E. coli* UTI and much less likely due to other primary foci of infection.
58
59
60
61
62
63
64
65

1 We reviewed our microbiology laboratory records for *E. coli* urinary
2 isolates and identified cases of positive UCs for *E. coli* without
3 documented concurrent bacteremia for the same time period (March 2000
4 through September 2001). We went through the exact same procedure as
5 for the SA group (review of computerized medical charts to support the
6 diagnosis of “*E. coli* symptomatic UTI without concurrent bacteremia”
7 based on identical definitions to the ones for SA UTI). After eliminating
8 from our list patients not fitting the pre-specified criteria, we created our
9 control group (almost double in number than the SA cases) by selecting
10 every third eligible case from the modified microbiology list. Finally, we
11 went back to computerized and paper medical charts and collected similar
12 data for our control group as for the SA patients.

13
14 *Statistical analysis.* Collected data were entered into a Microsoft Excel
15 spreadsheet and version 13 of SPSS software was used for data
16 processing. We used Student’s t-test for independent samples for
17 comparison of continuous variables and Pearson’s chi-square test for
18 categorical variables [or Fisher’s exact test in cases of low (<5) cell
19 numbers]. Factors of statistical significance on univariate analysis were
20 used for logistic regression analysis [backward stepwise (Wald)]. A p
21 value of 0.05 or less was used for clinical significance.

RESULTS AND DISCUSSION

We were finally able to compare 20 cases of *S. aureus* symptomatic UTI with a control group of 43 *E. coli* symptomatic UTI cases. Characteristics of the *S. aureus* group and the *E. coli* control group are included in table 1.

Cases (n= 20) and controls (n= 43) were similar in respect to age (71.15 ± 11.6 vs. 67.9 ± 13.5 yrs, mean $\pm$ SD), diabetes mellitus (35% vs. 31%), prostatic hypertrophy (50% vs. 48%), previous UTI (25% vs. 26%), and other UT abnormality (15% vs. 21%). However, cases were more likely than controls to have had recent hospitalization (within the last 6 months) and recent urinary catheterization (p values of 0.012 and 0.0001 respectively). Additionally, cases exhibited a trend, as a group, for having had central line placement the month before the positive UC date (p 0.075) and also more likely to have exhibited signs of inflamed peripheral intravenous line within the same time period (p 0.008). In multivariate analysis, recent urinary catheterization and history of admission during the last 6 months for outpatients remained significant predictors of SA UTI (p 0.000 and 0.006 respectively).

We then attempted to compare each of the 2 subgroups of the SA UTI cases (MRSA and MSSA) with the control cases in a similar manner (table 1).

1 *MRSA cases.* Cases of MRSA UTI (n= 15) did not differ from controls in
2
3 terms of age, diabetes mellitus, prostatic hypertrophy, previous UTI and
4
5 other UT abnormality (15% vs. 21%). Strong differences again arose
6
7 between MRSA cases and controls when assessed for hospitalization
8
9 within the last 6 months (p 0.013) and recent urinary catheterization (p
10
11 0.000). Additionally, MRSA cases were more likely to have been
12
13 inpatients on the date of the positive culture collection (p 0.05) and to
14
15 have exhibited signs of inflamed peripheral intravenous line within the
16
17 last month before the positive culture dates as opposed to *E.coli* controls
18
19 (p 0.049). Both differences in recent urinary catheterization and recent
20
21 hospitalization for outpatients were predictors of MRSA UTI in
22
23 regression analysis (p 0.001 and 0.027, respectively).
24
25
26
27
28
29
30
31
32

33 *MSSA cases.* That small subgroup again did not differ from controls in
34
35 terms of age, diabetes mellitus, prostatic hypertrophy, previous UTI and
36
37 other UT abnormality. Also, no significant differences were noted in any
38
39 parameter which differed in the previous group analyses, possibly due to
40
41 low numbers, at least in part.
42
43
44
45
46
47

48 Even though several types of infectious syndromes caused by *S. aureus*
49
50 are common in clinical practice and adequately well studied, urinary tract
51
52 involvement by this pathogen is probably not one of them. The presence
53
54 of *S. aureus* in urine cultures is not always easy either to explain or to
55
56 appreciate its significance in order to evaluate and treat accordingly. The
57
58
59
60
61
62
63
64
65

1 long-standing concept of SA bacteriuria as a common reflection of SA
2
3 bacteremia has been cast doubt, even for patients without recent
4
5 indwelling urinary catheter placement, in terms of cost-effectiveness of
6
7 extensive source investigations [10,13]. The authors of the 1997 report
8
9 do not think an extensive evaluation for an occult focus of *S. aureus*
10
11 infection is warranted for patients with SA bacteriuria, although it should
12
13 be considered with community-acquired SA bacteriuria, pure growth of
14
15 $>10^8$ organisms /L in culture and absence of urinary tract predisposing
16
17 conditions (mentioned above)[13].
18
19
20
21
22
23
24

25 On the other hand, *S. aureus* seems to be an infrequent but definite
26
27 colonizer of the urinary tract, especially in people with urinary catheters,
28
29 and, in a minority of those, a cause of symptomatic urinary tract
30
31 infection [12]. Although urinary *S. aureus* may be the source of
32
33 subsequent staphylococcal bacteremia, the proportion of patients with
34
35 chronic *S. aureus* bacteriuria who subsequently become bacteremic is
36
37 unknown [12].
38
39
40
41
42
43
44

45 Our 2 clinical cases prompted us to investigate another-probably- piece of
46
47 the puzzle: the circumstances of development of symptomatic urinary
48
49 tract infection by *S. aureus* in the absence of documented bacteremia. Our
50
51 hypothesis was that these circumstances could involve, besides prior
52
53 urinary tract manipulation leading to SA colonization, a transient
54
55 bacteremic state, at least for some of the cases, like Sheth et al speculated
56
57
58
59
60
61
62
63
64
65

1 in 1997. We carefully identified patients with the diagnosis of SA UTI
2
3 without documented preceding or concomitant bacteremia based on strict
4
5 predefined criteria and we compared them with a control group of *E.coli*
6
7
8 UTI patients in terms of predisposing factors for ascending SA UTI as
9
10 well as predisposing factors for preceding SA bacteremia, especially
11
12 focusing on exposure to healthcare system and recent presence of
13
14 intravascular devices.
15
16
17
18
19

20 The results of our study were in agreement with other reports that urinary
21
22 catheterization is probably the strongest predisposing factor for
23
24
25 colonization and/or infection of the UT by *S. aureus*. Besides that, it did
26
27 bring up-in our opinion- some interesting hints that other factors related
28
29 to exposure to the healthcare system may be participating in the process,
30
31 possibly through transient unrecognized bacteremia, at least in some
32
33 instances. The SA group had higher rates of recent hospitalization, recent
34
35 central venous catheter placement and recent line-related peripheral
36
37 thrombophlebitis. The noticed trend was largely driven by the MRSA
38
39 patients. There were significantly more inpatients included in the MRSA
40
41 subgroup than in the control group and they did have higher rates of
42
43 intravascular device placement preceding the UTI by *S. aureus*.
44
45
46
47
48
49
50
51
52
53

54 Additionally, recent hospitalization maintained its significant difference
55
56 in multivariate analysis between that subgroup and the *E.coli* control
57
58
59
60
61
62
63
64
65

group, the latter not without significant exposure to both UT

manipulations and the healthcare system.

Transient, sometimes asymptomatic and spontaneously resolving *S.*

aureus bacteremia, is a well known phenomenon.to experienced

clinicians but not adequately studied. Any attempt to further study that

phenomenon in a prospective way would be probably unethical,

especially when thinking of how devastating *S. aureus* bloodstream

infection can be to the point that even the finding of colonization of a

removed intravascular catheter without documented bacteremia may

warrant immediate antistaphylococcal therapy [16]. Nevertheless, some

studies have touched on that issue from different angles. In an older

prospective study of sources and outcome of MRSA bacteremia and

septicaemia (total of 82 episodes), circulation access sites were the

commonest source of the bacteremia with non-surgical wounds including

burns, varicose ulcers and bed sores as the next most common [17]. The

authors categorized 15 of those episodes of bacteremia as transient and,

even though they did not provide exact details, they mentioned that 14 of

the 82 episodes resolved without antimicrobial therapy. Patients with

transient bacteremia were relatively younger than patients with

septicaemia. The 2 groups had, although, similar rates of serious

underlying diseases and recent surgery. In 10% of cases, there was no

obvious source for bacteremia. In 3 of those, there had been recent

1 surgery, while in 4 of the remaining 5, patients had been recently
2
3 receiving intravenous fluids. *Staphylococcus aureus* can be an infrequent
4
5 cause of transient bacteremia after tooth surgery [18] and also after both
6
7 upper and lower gastrointestinal endoscopy, where it has been long
8
9 realized that bacteremia is usually transient and asymptomatic [19].
10
11 Interestingly, the small MSSA UTI group seemed also to have had its
12
13 share of healthcare and intravascular device exposure despite no detected
14
15 difference in inpatient status on the culture date. Also, no difference arose
16
17 in urinary catheterization rates when compared with the *E.coli* group.
18
19
20 More definite conclusions about that group were precluded by its small
21
22 size.
23
24
25
26
27
28
29
30
31 *Strengths of the study.* We have not found any prior studies addressing
32
33 this specific question. We tried our best to apply strict criteria for patient
34
35 enrollment in the study. The study group derived from a significantly
36
37 homogeneous population in terms of demographics and underlying
38
39 illnesses. A significant degree of homogeneity also holds true about
40
41 completeness of medical care data for the population, based on the almost
42
43 exclusive care at the VA hospital, computerized medical records and full
44
45 availability of nursing records. Additionally, we carefully created a
46
47 control group of *E.coli* UTI cases based on the same criteria for more
48
49 accurate comparison purposes. Finally, although we can only speculate
50
51 that our hypothesis may be true under certain circumstances and in
52
53
54
55
56
57
58
59
60
61
62
63
64
65

1 certain patients, we believe in our results since they seem to be making
2 physiologic sense in terms of what is known about epidemiology and
3 clinical behavior of *S. aureus*.
4
5
6

7
8 *Limitations of the study.* There was obviously no definite conclusion of a
9 new pathogenetic pathway for *S. aureus* symptomatic urinary tract
10 infection from our retrospective study. Despite our efforts for
11 completeness, we definitely had missing data about hospitalization
12 events, urinary tract instrumentation and and intravascular device use.
13
14 Still, we believe that if data were even more complete, that would have
15 augmented possible differences between the study groups. In the same
16 line, we did not assess other risk factors for *S. aureus* bacteremia (surgery
17 etc). Additionally, since a. there is significant symptom overlap between
18 cystitis, prostatitis and pyelonephritis and b. the diagnosis documented in
19 the patient charts was, in the majority of cases, just “urinary tract
20 infection” without further specification, our data were not accurate
21 enough to discriminate between upper and lower UTI in the 2 groups.
22
23 That is why we maintained the general term “symptomatic urinary tract
24 infection” throughout. Furthermore, we did not obtain outcome data of
25 our study patients. A recent well-designed study reported worse outcomes
26 in those cases of *S. aureus* bacteremia accompanied by bacteriuria [20].
27
28 Finally, patient numbers were small, especially that of the MSSA UTI
29 subgroup.
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

1 We conclude that even though urinary tract catheterization is probably
2 the strongest predisposing factor for primary *S. aureus* UTI, some cases
3 may be mediated through another pathogenetic mechanism, i.e.,
4 unrecognized preceding bacteremia related to intravascular device
5 exposure or other healthcare-related factor. We are not sure if a larger,
6 prospective study could clarify this issue. Still, we believe that clinicians
7 treating patients with *S. aureus* UTI should thoroughly inquire both about
8 recent UT instrumentation and recent hospitalization with intravascular
9 device use.

10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31 **Note:** Part of this work was presented as a poster at the 42th annual IDSA
32 meeting, 30 Sep-3 Oct, Boston, MA (paper 533, page 143 of abstract
33 book).

34 REFERENCES

- 35 1. [No authors listed]: National Nosocomial Infections Surveillance
36 (NNIS) Report; Data summary from January 1992-June 2004,
37 issued Oct 2004. *Am J Infect Control* 2004 Dec; 32(8): 470-85.
- 38 2. Arpi M, Renneberg J: The clinical significance of *Staphylococcus*
39 *aureus* bacteriuria. *J Urol* 1984 Oct ; 132(4) : 697-700.

3. Blazevic DJ, Stemper JE, Matsen JM: Organisms encountered in urine cultures over a 10-year period. *Appl Microbiol* 1972 Feb; 23(2): 421-2.
4. Demuth PJ, Gerding DN, Crossley K : *Staphylococcus aureus* bacteriuria. *Arch Intern Med* 1979 Jan; 139(1): 78-80.
5. Pead L, Crump J, Maskell R: Staphylococci as urinary pathogens. *J Clin Path* 1977 May; 30(5): 427-31.
6. Jepsen OB, Larsen SO, Dankert J, et al: Urinary-tract infection and bacteremia in hospitalized medical patients- a European multicentre prevalence survey on nosocomial infection. *J Hosp Infect* 1982 Sep; 3(3): 241-52.
7. Ackermann RJ, Monroe PW: Bacteremic urinary tract infection in older people. *J Amer Geriatr Soc* 1996 Aug; 44(8): 927-33.
8. Sobel JD, Kaye D: Urinary tract infections (Chapter 66) in: Mandell GL, Bennett JE, Dolin R (editors). *Principles and Practice of Infectious Diseases*. Vol 1, Sixth Edition, Elsevier Churchill-Livingstone 2005.
9. Lee BK, Crossley K, Gerding DN: The association between *Staphylococcus aureus* bacteremia and bacteriuria. *Am J Med* 1987 Aug; 65(2): 303-6.
10. Ekkelenkamp MB, Verhoef J, Bonten MJ: Quantifying the

relationship between *Staphylococcus aureus* bacteremia and *S. aureus* bacteriuria: A retrospective analysis in a tertiary care hospital. *Clin Infect Dis* 2007 Jun 1; 44(11): 1457-9.

11. Shupp Byrne DE, Sedor JF, Soroush M, McCue PA, Mulholland SG : Interaction of bladder glycoprotein GP51 with uropathogenic bacteria. *J Urol* 2001 Apr; 165(4):1342-6.
12. Muder RR, Brenner C, Rihs JD et al: Isolation of *Staphylococcus aureus* from the urinary tract: Association of Isolation with symptomatic urinary tract infection and subsequent staphylococcal bacteremia. *Clin Infect Dis* 2006 Jan 1; 42(1): 46-50.
13. Sheth S, DiNubile MJ: Clinical significance of *Staphylococcus aureus* bacteriuria without concurrent bacteremia. *Clin Infect Dis* 1997 Jun; 24(6): 1268-9.
14. Senthilkumar A, Kumar S, Sheagren JN: Increased incidence of *Staphylococcus aureus* bacteremia in hospitalized patients with acquired immunodeficiency syndrome. *Clin Infect Dis* 2001 Oct; 33(8): 1412-6.
15. Jacobson MA, Gellermann H, Chambers H: SAB and recurrent Staphylococcal infection in patients with acquired immunodeficiency syndrome and AIDS-related complex. *Am J Med* 1988 Aug; 85(2): 172-6.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
16. Ekkelenkamp MB, van der Bruggen T, van de Vijver DA, Wolfs TF, Bonten MJ : Bacteremic complications of intravascular catheters colonized with *Staphylococcus aureus*. *Clin Infect Dis* 2008 Jan 1; 46(1): 114-8.
17. Cafferkey MT, Hone R, Kean CT: Sources and outcome for methicillin-resistant *Staphylococcus aureus* bacteraemia. *J Hosp Infect* 1988 Feb; 11(2): 136-43.
18. Tomás I, Pereira F, Llucían R, Poveda R, Diz P, Bagán JV. Prevalence of bacteraemia following third molar surgery. *Oral Dis*. 2008 Jan; 14(1): 89-94.
19. Nelson DB: Infection control during gastrointestinal endoscopy. *J Clin Lab Med* 2003 Mar; 141(3): 159-67.
20. Huggan PJ, Murdoch DR, Gallagher K, Chambers ST: Concomitant *Staphylococcus aureus* bacteriuria is associated with poor clinical outcome in adults with *S. aureus* bacteraemia. *J Hosp Inf* 2008 Aug; 69(4): 345-9.

Table 1. Comparison of cases of *Staphylococcus aureus* Urinary tract Infections (UTIs) with *Escherichia coli* UTIs (controls) with subgroup analysis for methicillin-resistant and methicillin-sensitive isolates.

Characteristics /microorganism	<i>Escherichia coli</i> (n=43)	All cases of <i>Staphylococcus aureus</i> (n=20)	p /OR (95% CI)	<i>MRSA</i> (n=15)	p/OR (95% CI)	<i>MSSA</i> (n=5)	p/OR (95% CI)
Age	67.9±13.5	71,15±11,6	0,348/NA	73.1±9.9	0.176/NA	65.2±15.2	0.677/NA
Diabetes mellitus	14/43	7/20	0,85/1.11(0.36-3.41)	5/15	1.00/1.03(0.29-3.61)	2/5	1.00/1.38(0.21-9.22)
History of genitourinary procedure (more than 6 months ago)	6/43	4/20	0,71/1.54(0.38-6.21)	4/15	0.262/2.24(0.53-9.39)	0/5	1.00/0.88(0.78-0.98)
Benign prostatic hypertrophy	20/43	10/20	0,79/1.15(0.38-3.32)	9/15	0.37/1.72(0.52-5.69)	1/5	0.37/0.28(0.03-2.78)
History of urinary tract infection	16/43	5/20	0,67/0.77(0.23-2.56)	4/15	1.00/0.84(0.22-3.13)	1/5	1.00/0.57(0.06-5.67)
Other urinary tract abnormality	9/43	3/20	0,73/0.67(0.16-2.78)	2/15	0.71/0.58(0.11-3.06)	1/5	1.00/0.94(0.094-9.52)
Inpatient on culture date	10/43	8/20	0,17/2.2(0.70-6.88)	8/15	0.05/3.77(1.09-12.99)	0/5	0.57/0.87(0.77-0.98)
If outpatient, admission last 6 months	4/43	8/20	0,012/6.5(1.66-25.14)	6/15	0.013/6.5(1.51-27.93)	2/5	0.11/6.5(0.82-51.2)
Inpatient on culture date or recent admission	14/43	16/20	0,000/8.28(2.33-29.44)	14/15	0.000/29.0(3.46-243.22)	2/5	1.00/1..38(0.20-9.22)
Presence of indwelling urinary catheter more than 48 hours before culture date	8/43	14/20	0,0001/10.21(2.99-34.81)	13/15	0.000/28.44(5.32-151.84)	1/5	1.00/1.09(0.11-11.52)
Genitourinary procedure last 6 months	5/43	2/20	1.00/0.84(0.15-4.78)	2/15	1.00/1.17(0.20-6.77)	0/5	1.00/0.88(0.79-0.98)
Any intravenous line last 30 days	15/43	11/20	0,13/2.28(0.77-6.72)	9/15	0.089/2.8(0.84-9.37)	2/5	1.00/1.24(0.18-8.28)
Peripheral intravenous line last 30 days	15/43	7/20	0,99/1.005(0.33-3.05)	6/15	0.72/1.24(0.37-4.16)	1/5	0.65/0.46(0.05-4.55)
Central venous catheter last 30 days before positive culture date	2/43	4/20	0,075/5.12(0.85-30.78)	3/15	0.10/5.12(0.76-34.31)	1/5	0.28/5.12(0.37-69.75)
Any sign of intravenous line inflammation last 30 days before positive culture date	1/43	4/20	0,032/10.5(1.09-101.19)	3/15	0.049/10.5(0.99-110.35)	1/5	0.19/10.5(0.54-201.71)

Footnote. MRSA: methicillin-resistant *Staphylococcus aureus*, MSSA: methicillin-sensitive *Staphylococcus aureus*.OR: odds ratio, CI: confidence intervals, NA: not applicable.