

1 Microorganisms attached to the lumens and balloons of indwelling urinary catheters and
2 correlation with symptoms, antibiotic use, and catheter specimen of urine results

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31 Abstract:

32 *Purpose:* To quantify and identify microorganisms attached to the lumens and balloons
33 of removed urethral urinary catheters and relate this to patient-specific information.

34

35 *Methodology:* Indwelling urethral urinary catheters were collected from patients at a
36 large teaching hospital in the UK. The balloon and lumen were separated, sonicated, and
37 microorganisms were enumerated from the sonicate. Catheter specimen urine results
38 were retrospectively reviewed.

39

40 *Results:* Sixty-one catheters were analysed. The most commonly isolated organisms
41 were *Escherichia coli* and *Enterococcus faecalis*. 19.7% of patients received antibiotics
42 while catheterised and 25% of those had a multi-drug resistant (MDR) organism
43 attached to the lumen. Conversely, only 2.04% of catheters from patients not known to
44 be receiving antibiotics had a MDR organism present. All lumens were colonised
45 irrespective of antibiotic use. Symptom presentation did not correlate with numbers of
46 colonising organisms or species. Despite heavy colonisation, only 8/61 patients were
47 symptomatic.

48

49 *Conclusion:* This study demonstrated that indwelling urinary catheters in place for 10
50 days or greater were universally colonised and there was no correlation of colonisation
51 with symptom presentation. Symptomatic presentation remains for the most important
52 factor for defining CAUTI.

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58 Introduction:

59 Infection is a well-recognised and costly complication of use of indwelling urinary
60 catheters and is associated with increased mortality and increased length of hospital

61 stay(1, 2). The common causative agents of CAUTI reported in the USA include
62 *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus* spp., *Proteus mirabilis*,
63 *Pseudomonas aeruginosa*, *Candida* spp., and staphylococci(3) with approximately 20%
64 of organisms isolated being multidrug-resistant (MDR)(4).

65 However, there has been considerable confusion between symptomatic UTI
66 (CAUTI) requiring antibiotic treatment and asymptomatic bacteriuria (CAASB) found
67 commonly in catheterised patients but not requiring treatment. This has led to over-use
68 of antibiotics with concomitant concern regarding resistance and adverse events (5).
69 Most of the data on causative bacteria of both CAUTI and CAASB are derived from urine
70 samples taken from the catheter (despite these being discouraged in catheterised
71 patients) and little is known about the bacteria that colonise catheters(6). Though some
72 authors have examined catheters, there has not, to our knowledge, been a systematic,
73 quantitative study of the contents of removed urinary catheters. Therefore, this
74 pragmatic study aims to quantify organisms attached the lumens and balloons of
75 indwelling urethral urinary catheters and correlate this with patient data on antibiotic
76 usage, symptom presentation, and catheter specimen urine (CSU) results.

77

78 Methods:

79 *Setting and sample collection*

80 Between June 2015 and July 2016, indwelling urethral urinary catheters that
81 remained in situ for ten days or greater from male and female patients over 16 years of
82 age were collected from patients at Nottingham University Hospitals NHS Trust,
83 Nottingham, UK. Catheters were collected from urology theatres, male urology ward,
84 neurosurgery wards, and a neurorehabilitation centre by clinical staff when removed
85 according to clinical need. Clinical staff were instructed to remove the catheter according
86 to standard local protocols and if possible drain, but not flush, the lumen of any residual
87 urine. Clinical staff were provided with an audit form to complete with patient details
88 including the date the catheter was inserted, if the patient was prescribed antibiotics to
89 their knowledge, and if they were symptomatic for CAUTI. Catheters were collected from

90 areas where experienced ward staff were familiar with CAUTI and its diagnosis. Local
91 guidelines state antibiotics for CAUTI should be started immediately and the catheter
92 changed during the treatment course, which is 7 days. The catheters were then placed in
93 a resealable bag and stored in the specimen fridge (approx. +4°C) with information
94 about antibiotics received and current symptoms of CAUTI. The catheters were analysed
95 within 24 hours of removal.

96 An audit to retrospectively review catheter specimen urine (CSU) results during
97 the period of catheterisation of the patients who had catheters included in this study was
98 approved by Nottingham University Hospitals NHS Trust (Audit ID: 17-309Q) in
99 December 2017. The period of catheterisation was available in the notes and according
100 to the audit form provided by the clinical staff. All CSU results from each patient's period
101 of catheterisation with the collected catheter were obtained retrospectively from
102 microbiology reports available on a hospital-wide information system, NotIS (Nottingham
103 Information System).

104

105 *Analysis of catheters*

106 The catheter was removed from the specimen bag using sterile forceps and
107 placed onto a sheet of sterile autoclaved aluminium foil. Stainless steel, straight-jawed
108 surgical clamps clamped the catheter on the lumen downstream of the balloon and on
109 the lumen upstream of the drainage and balloon inflation ports. The balloon was then
110 detached from the catheter body using a sterile scalpel and placed into a sterile universal
111 container. Phosphate buffered saline (PBS, Oxoid, Basingstoke, UK) was added to the
112 Universal container so that it covered the entire surface of the balloon section. The
113 drainage and balloon inflation ports were separated from the catheter body and
114 discarded. This left the lumen section with its ends clamped. Opening both ends of the
115 clamps briefly, 1-2 mL PBS were introduced to fill the lumen depending on the size of the
116 catheter. The ends were quickly resealed and the catheter placed into a resealable
117 freezer bag.

118 The balloon section and catheter lumen were sonicated for five minutes at 30 kHz
119 to detach microorganisms. After sonication, both ends of the catheter body section were
120 cleaned with an alcohol pre-injection swab (Mölnlycke Healthcare, Göteborg, Sweden).
121 The lumen sonicate was drained into a sterile Bijou bottle (Sterilin, Newport, UK). 200µL
122 of the balloon and lumen sonicates and appropriate dilutions were spread onto cysteine-
123 lactose electrolyte deficient (CLED) agar (Oxoid, Basingstoke, UK) and incubated
124 overnight in air at 37°C. Colonies were enumerated and general microbiological
125 identification performed, including use of the API identification system (bioMérieux,
126 Marcy-l'Étoile, France) and MALDI-ToF (Microflex LT Mass Spectrometer, Bruker
127 Daltronics). All isolates were tested for resistance according to EUCAST guidelines(7, 8).
128 If culture negative, the plates were incubated for a further 24 hours.

129

130 *Statistics*

131 Data were analysed in GraphPad Prism 7.01 (La Jolla, California, USA). Normality was
132 assessed by histogram, and some data not normally distributed were log-transformed.
133 Correlation was assessed using the Pearson correlation. Significance was defined as
134 $p < 0.05$ and was calculated by unpaired t-test and one-way ANOVA depending on the
135 number of comparisons.

136

137 Results:

138 *Catheter Collection Demographics*

139 Sixty-one urethral urinary catheters were analysed. The mean age of patients
140 from who the catheters were collected from was 68 years and 10/61 were female. The
141 reasons for catheterisation were predominantly for management of urinary retention
142 (64.62%), management of neurological or neurosurgical issues (21.31%), and
143 transurethral resection of the prostate (16.39%), which correspond with specialties of
144 the departments from which they originated. The types of catheters also varied with the
145 majority being all-silicone for long-term use (50.8%), PTFE-coated (23.33%), all-silicone
146 for short-term use (15.00%), latex (3.33%), hydrogel-coated latex (3.3.3%), and

147 hydrogel-coated silicone (3.33%). There was no significant difference in the quantity
148 ($p=0.4803$, one-way ANOVA) of organisms attached to lumens of the different catheter
149 types. However, there were more species of microorganisms per catheter attached to
150 PTFE catheters than to all-silicone catheters ($p=0.0073$). The lumen sizes ranged from
151 12Ch to 20Ch.

152

153 *Identification of microorganisms attached to the lumens and balloons*

154 107 and 103 organisms were isolated from the lumens and balloons, respectively,
155 of 58 urinary catheters. Three lumens (4.9%) and three balloons (4.9%), not from the
156 same catheter, were culture - negative. The same microorganisms were isolated from
157 the lumen and the balloon of the same catheter in 65.6% of collected catheters. The
158 most commonly isolated organisms in both the balloons and lumens were *E. coli* and *E.*
159 *faecalis* (Table I).

160

161 *Drug Resistance and Antibiotic Exposure*

162 Sixteen urinary catheters (26.2%) were from patients known to be receiving
163 antibiotics and 12 of these were known to be receiving antibiotics for treatment of
164 CAUTI, the other four receiving antibiotics prophylactically for other conditions and for
165 treatment of other infections. Antibiotics prescribed for treatment of CAUTI included iv
166 piperacillin-tazobactam, amoxicillin clavulanic acid, trimethoprim and pivmecillinam.
167 Antibiotics for the four receiving antibiotics prophylactically and for other infections
168 include iv piperacillin-tazobactam, amoxicillin clavulanic acid, vancomycin and
169 meropenem. Of the 16 catheters from patients known to be receiving antibiotics, all
170 lumens were colonised by at least one microorganism and 15/16 of the balloons were
171 colonised. Antibiotics did not significantly reduce colonisation of catheter lumens
172 ($p=0.7153$) or balloons ($p=0.4516$).

173 Four multi-drug resistant organisms were isolated, including two extended-
174 spectrum beta-lactamases (ESBL)-producing *E. coli* and two meticillin-resistant *S.*
175 *epidermidis*. MDR organisms were isolated from 25% of catheters from patients known

176 to be receiving antibiotics and from 2.04% of catheters from patients not known to be
177 receiving antibiotics ($p=0.0216$, Fisher's exact test).

178

179 *Length of catheterisation and colonisation of catheter lumens*

180 Information regarding the exact duration of catheterisation was available for
181 48/61 catheters. There was no correlation between the duration of catheterisation and
182 the number of microorganism species (Figure 1a) or the quantity of each microorganism
183 (Figure 1b) in the lumen for catheters from patients symptomatic for CAUTI and
184 asymptomatic. 8/61 patients were symptomatic for CAUTI (despite 12 being treated for
185 CAUTI, only 8 had symptoms recorded) and length of catheterisation was available for
186 7/8. There was no significant difference between the number of isolates ($p=0.7741$) or
187 the quantity (CFU/mL) ($p=0.0976$) of microorganisms isolated from the lumens of
188 catheters from symptomatic and asymptomatic patients underlining the importance of
189 symptoms, not microbiological culture, in the diagnosis of CAUTI.

190

191 *CSU and Catheter Colonisation*

192 Three of the 61 patient notes were unavailable and were not included in this
193 analysis. 28 CSU samples from 22 patients were taken during the period of
194 catheterisation from which the catheter was collected and processed as standard by the
195 microbiology department. Generally, there was a poor consensus between the laboratory
196 CSU results and the organisms attached to the catheter lumens and balloons in that
197 additional organisms (the majority of which were *E. faecalis*) were excluded from the
198 reports despite catheter colonisation in significant numbers. Only 28.6% of the
199 laboratory CSU reports matched the contents of the lumen and balloon. This suggests
200 that CSU results do not reflect what is present on the catheter.

201 Antibiotic choice does not appear to be influenced by CSU results. Two of the 12
202 patients prescribed antibiotics for CAUTI never had a CSU sent, and an additional 2/12
203 had a CSU sent but the results were 'no growth'. An additional patient was prescribed

204 cephalixin for an ESBL *E. coli* and another patient was prescribed pivmecillinam despite
205 the results of a pivmecillinam resistant *Proteus spp.* in the report.

206

207 Discussion:

208 A novel method was developed for analysing the attached bacteria in the lumens
209 and balloons separately without sampling the catheter external surface. The most
210 commonly isolated organisms from the lumens and balloons of indwelling urinary
211 catheters were Enterobacteriaceae and enterococci. Of interest, *Proteus mirabilis* is
212 frequently cited (9) as a major problem in catheter users, but was isolated from only
213 3/61 catheters collected, of which only two were blocked by mineral encrustations. In
214 total, five catheters were blocked and *E. coli* and *E. faecalis* were the most common
215 organisms isolated from the blocked catheter lumens, which is interesting as neither
216 produces urease, which is cited as the cause of catheter blockage(10).

217 60.7% of lumens and 57.4% of balloons were colonised by two or more
218 organisms. This proportion is slightly lower than that found by Warren et al, who
219 reported that 77% of their catheter urine specimens were polymicrobial, though they did
220 not examine the catheters(11). 34.4% of the bladder contents as represented by the
221 balloon isolates were different from those in the lumen. Additional organisms may be
222 detected in catheter urine culture as these can be released into the passing urine, and
223 culture results may adversely influence treatment. This can be seen from the lack of
224 correlation between the catheter contents and the CSU results. This is in agreement with
225 a study by Montgomerie et al who investigated the colonisation of the urethral meatus
226 and urine cultures in those that perform intermittent catheterisation, and found that
227 there was no correlation between urethral colonisation and urine samples (12). Quite
228 often the lack of consistency comes from an additional organism not being recorded. For
229 example, one catheter grew 10^7 and 10^6 CFU/mL *E. coli* and *E. faecalis* respectively from
230 the catheter lumen and balloon, whereas only *E. coli* was recorded in the CSU report
231 despite both present in large quantities. The patient was treated with iv piperacillin-
232 tazobactam when both isolates were sensitive to nitrofurantoin. Therefore, the

233 usefulness of CSUs is debatable given that they do not necessarily represent the
234 microenvironment in the catheter lumen and more importantly, the catheter balloon, and
235 do not appear to guide antibiotic prescribing. This then revisits the importance of
236 symptom presentation as being the guiding factor for diagnosis and treatment of CAUTI.

237 These data, which show no effect of antibiotics on the reduction of attached
238 bacteria in the catheter, support the Scottish Intercollegiate Guidelines Network (13) and
239 the Infectious Disease Society of America (14) recommendations for changing the
240 catheter before starting antibiotic treatment for CAUTI. Antibiotics do not reduce
241 attached biofilm bacteria and are likely to be a driver of antibiotic resistance. The higher
242 proportion in this study of MDR isolates from catheters of patients receiving antibiotics
243 may due to the influence of antibiotics, or it may be that MDR organisms more often
244 cause symptoms and therefore require antibiotic treatment.

245 The relationship between the time the catheter remains in situ and increased rate
246 of bacteriuria, incurring an increased risk of 5% per day, is well-established in the
247 literature (15). From 10 days onwards, 96.7% of the catheter lumens and balloons were
248 colonised in our study. There was no evidence of the number or quantity of species
249 increasing from 10 days to 119 days, which was the longest duration of catheterisation
250 in this study. It appears that by day 10, colonisation of the catheter may be established
251 and thus there may not be capacity within the catheter to support additional
252 microorganisms. In a study by Ganderton et al (16), there was no relationship between
253 duration of catheterisation and amount of biofilm. In our study, there was also no
254 difference between the number of species or the quantity of each isolate in those
255 patients who were symptomatic and those who were asymptomatic. This again
256 reinforces the emphasis for diagnosis to be placed on symptom presentation and not
257 solely on the microbiological results, which may not accurately reflect the bladder
258 contents as seen from the CSU results.

259

260 Author Contributions:

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262 writing- original draft, writing – review and editing
263 SK: Investigation, writing – review and editing
264 KA: Investigation, writing – review and editing
265 RP: conceptualisation, methodology, resources, writing – review and editing
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267 and editing, supervision

268

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275

276 References:

277 1. Bishara J, Leibovici L, Huminer D, Drucker M, Samra Z, Konisberger H, et al. Five-year
278 prospective study of bacteraemic urinary tract infection in a single institution. *Eur J Clin*
279 *Microbiol Infect Dis.* 1997;16(8):563-7.

280 2. Tambyah P, Maki D. The relationship between pyuria and infection in patients with
281 indwelling urinary catheters: a prospective study with 761 patients. *JAMA Intern Med.*
282 2000;160(5):673-7. doi:10.1086/501964

283 3. Elvy J, Colville A. Catheter associated urinary tract infection: what is it, what causes
284 it, and how can we prevent it? *J Infect Prev.* 2009;10(2):36-41.
285 doi:10.1177/1757177408094852

286

287 4. Sievert D, Ricks P, Edwards J, Schneider A, Patel J, Srinivasan A, et al. Antimicrobial-
288 resistant pathogens associated with healthcare-associated infections: summary of data
289 reported to the National Healthcare Safety Network at the Centers for Disease Control
290 and Prevention, 2009–2010. *Infect Control Hosp Epidemiol.* 2013;34(1):1-14.

291 doi:10.1086/668770

- 292 5. Gross PA, Patel B. Reducing antibiotic overuse: a call for a national performance
293 measure for not treating asymptomatic bacteriuria. *Clin Infect Dis.* 2007;45(10):1335-7.
294 doi:10.1086/522183
- 295 6. Bergqvist D, Bronnestam R, Hedelin H, Stahl A. The relevance of urinary sampling
296 methods in patients with indwelling Foley catheters. *Br J Urol.* 1980;52(2):92-5.
- 297 7. Giske C, Martinez-Martinez L, Canton R, Stefani S, Skov R, Glupczynski Y, et al.
298 EUCAST guidelines for detection of resistance mechanisms and specific resistances of
299 clinical and/or epidemiological importance. European Committee on Antimicrobial
300 Susceptibility Testing; 2013.
- 301 8. European Committee on Antimicrobial Susceptibility Testing. Antimicrobial
302 susceptibility testing: EUCAST disc diffusion method v5.0. January, 2015.
- 303 9. Stickler D. Clinical complications of urinary catheters caused by crystalline biofilms:
304 something needs to be done. *J Intern Med.* 2014;276(2):120-9.
305 doi:10.1111/joim.12220.
- 306 10. Hedelin H, Bratt CG, Eckerdal G, Lincoln K. Relationship between urease-producing
307 bacteria, urinary pH and encrustation on indwelling urinary catheters. *Br J Urol.*
308 1991;67(5):527-31.
- 309 11. Warren J, Tenney J, Hoopes J, Muncie H, Anthony W. A prospective microbiologic
310 study of bacteriuria in patients with chronic indwelling urethral catheters. *J Infect Dis.*
311 1982;146(6):719-23.
- 312 12. Montgomerie JZ, McCary A, Bennett CJ, Young M, Matias B, Diaz F, et al. Urethral
313 cultures in female patients with a spinal cord injury. *Spinal Cord.* 1997;35(5):282-5.
314
- 315 13. Scottish Intercollegiate Guidelines Network (SIGN). Management of suspected
316 bacterial urinary tract infection in adults (SIGN publication no. 88). Edinburgh:
317 Healthcare Improvement Scotland; 2012.
- 318 14. Hooton T, Bradley S, Cardenas D, Colgan R, Geerlings S, Rice J, et al. Diagnosis,
319 prevention, and treatment of catheter-associated urinary tract infection in adults: 2009
320 International Clinical Practice Guidelines from the Infectious Diseases Society of America.
321 *Clin Infect Dis.* 2010;50:625-63. doi:10.1086/650482..
- 322 15. Nicolle LE. Catheter associated urinary tract infections. *Antimicrob Resist Infect*
323 *Control.* 2014;3:23. doi:10.1186/2047-2994-3-23.

324 16. Ganderton L, Chawla J, Winters C, Wimpenny J, Stickler D. Scanning electron
 325 microscopy of bacterial biofilms on indwelling bladder catheters. Eur J Clin Microbiol
 326 Infect Dis. 1992;11(9):789-96.

327

328 Figure legends:

329 Figure 1: Correlation of A.) The number of isolates in each catheter lumen and B.) the
 330 quantity (CFU/mL) of each isolate in each catheter plotted against length of time the
 331 catheter was in situ. The Pearson correlation coefficient was computed and indicated no
 332 correlation of variables.

333

334 Tables:

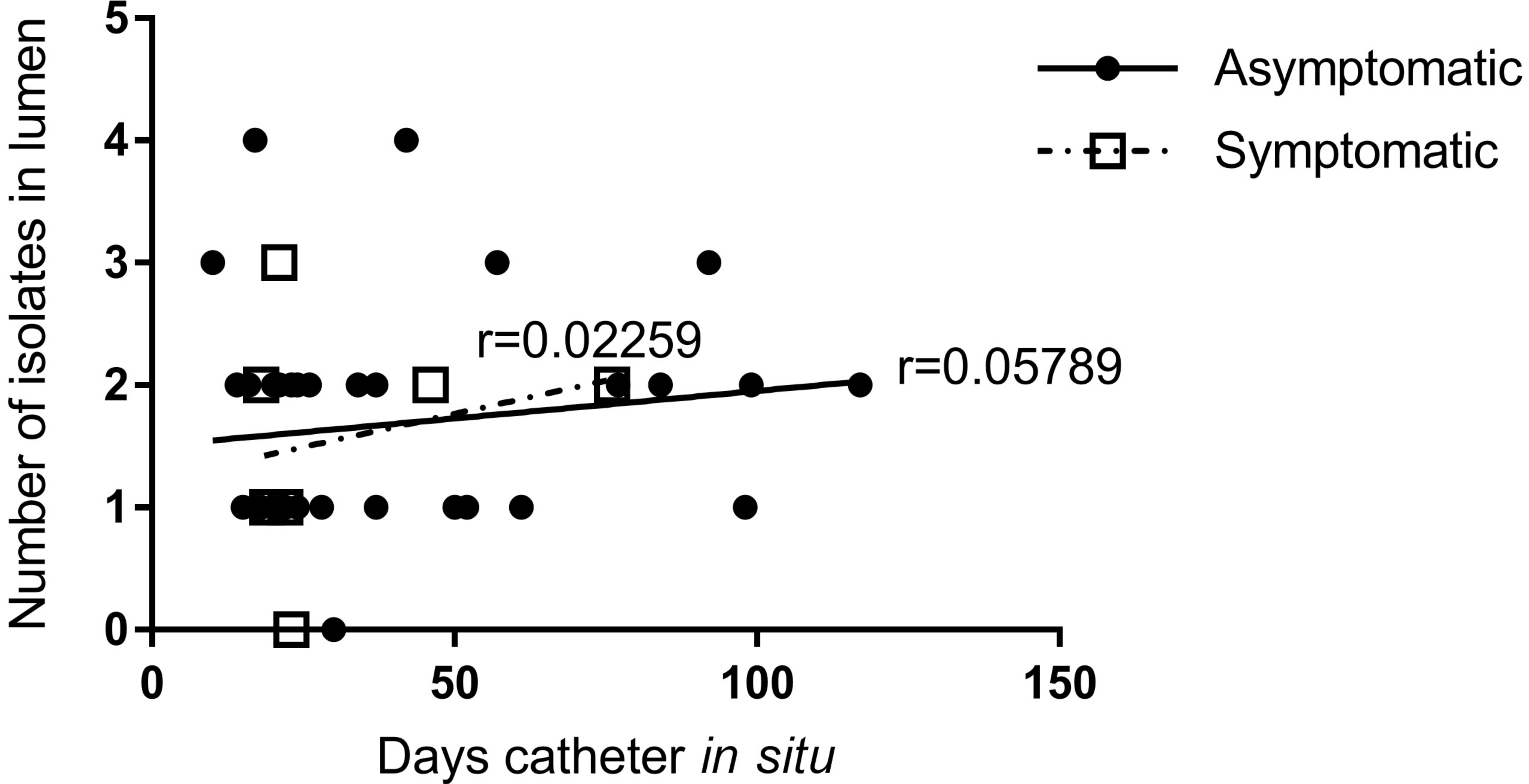
335 Table I: Inventory of microorganisms isolated from the balloons and lumens of indwelling
 336 urethral urinary catheters in situ for 10 days or greater.

Organisms isolated from catheter lumens		Organisms isolated from catheter balloons	
Enterobacteriaceae	47	Enterobacteriaceae	40
<i>Escherichia coli</i>	24	<i>E. coli</i>	20
<i>Klebsiella pneumoniae</i>	5	<i>Klebsiella pneumoniae</i>	5
<i>Enterobacter cloacae</i>	4	<i>Enterobacter cloacae</i>	4
<i>Klebsiella oxytoca</i>	3	<i>Klebsiella oxytoca</i>	3
<i>Proteus mirabilis</i>	3	<i>Morganella morganii</i>	2
<i>Morganella morganii</i>	2	<i>Citrobacter koseri</i>	1
<i>Serratia liquefaciens</i>	2	<i>Citrobacter koseri/amalonicus</i>	1
<i>Hafnia alvei</i>	1	<i>Hafnia alvei</i>	1
<i>Pantoea</i> spp.	1	<i>Pantoea</i> spp.	1
<i>Citrobacter koseri</i>	1	<i>Proteus mirabilis</i>	1
<i>Citrobacter koseri/amalonicus</i>	1	<i>Serratia liquefaciens</i>	1
Enterococci	18	Enterococci	20
<i>Enterococcus faecalis</i>	17	<i>Enterococcus faecalis</i>	19
<i>Enterococcus faecium</i>	1	<i>Enterococcus faecium</i>	1
Pseudomonas spp.	16	Pseudomonas spp.	12
Staphylococci	14	Staphylococci	19
<i>Staphylococcus epidermidis</i>	4	<i>Staphylococcus epidermidis</i>	9
<i>Staphylococcus aureus</i>	3	<i>Staphylococcus aureus</i>	3
<i>Staphylococcus capitis</i>	2	<i>Staphylococcus caprae</i>	2
<i>Staphylococcus haemolyticus</i>	2	<i>Staphylococcus haemolyticus</i>	2
<i>Staphylococcus caprae</i>	1	<i>Staphylococcus xylosus</i>	1
<i>Staphylococcus lugdunensis</i>	1	<i>Staphylococcus hominis</i>	1
<i>Staphylococcus saprophyticus</i>	1	<i>Staphylococcus saprophyticus</i>	1
<i>Staphylococcus xylosus</i>	1		

		Yeasts	7
Yeasts	6	<i>Candida albicans</i>	4
<i>Candida albicans</i>	4	<i>Candida glabrata</i>	1
<i>Candida guilliermondii</i>	1	<i>Candida guilliermondii</i>	1
<i>Candida parapsilosis</i>	1	<i>Candida parapsilosis</i>	1
Others	6	Others	5
<i>Micrococcus spp.</i>	2	<i>Streptococcus agalactiae</i>	1
<i>Corynebacterium propinquum</i>	1	<i>Streptococcus bovis</i>	1
<i>Streptococcus agalactiae</i>	1	<i>Streptococcus gordonii</i>	1
<i>Streptococcus bovis</i>	1	<i>Streptococcus intermedius</i>	1
<i>Streptococcus intermedius</i>	1	<i>Corynebacterium propinquum</i>	1
Total:	107	Total:	103

337

a.)



b.)

