

Supplementary

Table S2 Basic features of the included studies

First author	Year	Country	Type strain	Infection Carrier	Infection Medium	Interventions	Bladder model (main components)
Iain J. Abbott (13)	2020	Australia	E. coli, E. cloacae, K. pneumoniae	MHA plate	Cation-adjusted MHB supplemented with glucose-6-phosphate (25 mg/L)	drug-free MHA vs. fosfomycin containing MHA (64 mg/L, 512 mg/L)	An adaptation of a previously described <i>in vitro</i> model (21): a 1:16 scale to <i>in vivo</i> , to sixteen independent bladder compartments, compartment volumes and flow rates were modified in order to simulate different urinary exposures
Nylev Vargas-Cruz (14)	2019	USA	multidrug resistant P. aeruginosa, carbapenem-resistant E. coli and K. pneumoniae, C. albicans, P. mirabilis, E. faecalis	silicone Foley catheter	a viscous disinfecting solution (1% PG + 0.4% CAP + 1.5% HEC) +MHB	1% PG + 0.4% CAP + 1.5% HEC irrigation solution vs. no irrigation solution	An <i>in vitro</i> CAUTI prevention model: consisted of a soft 6 cm long silicone urethral tract through which the catheter could be threaded with cuffs deflated, the urethral tract consisted of a 4mm annular opening at the center of a 25mm diameter soft silicone cylinder; the irrigation solution was allowed to slowly drain by gravity
Iain J. Abbott (15)	2019	Australia	E. coli, K. pneumoniae	agar plates	CAMHB supplemented with 25mg/L glucose-6-phosphate (G6P)	colony counts on drug-free MHA and MHA with 64 and 512mg/L fosfomycin (with 25mg/L G6P)	A dynamic bladder infection <i>in vitro</i> model was adapted from previous studies (21): constructed on a 1:16 scale, consists of autoclavable 1.01mm PVC tubing run through sequentially arranged peristaltic pumps delivering matching flow rates from the fresh medium reservoir (a) into the 16 bladder compartments (d) run in parallel, a fourth peristaltic pump facilitated automated and timed intermittent bladder-compartment voiding to the waste container (e), with a urine output of 1mL/min, 6 voids/day and a post-void residual volume <50mL

Jonathan Nzakizwanayo (16)	2019	UK	P. mirabilis	silicone Foley catheter	artificial urine	crystalline biofilm or encrustation formed on catheters can be evaluated using flame photometry	An <i>in vitro</i> bladder model system, according to specifications originally described by Stickler et al. (49): bladder model, closed drainage system, and media supply: (1) double walled glass vessel representing the bladder. (2) foley catheter inserted into the model and connected to drainage bag to form sterile closed drainage system. (3) sterile urine/artificial urine supplied to “bladder” via a peristaltic pump at a constant flow rate of ~0.7 mL/min
Hamed Imani Rad (17)	2019	Iran	P. mirabilis, E.coli	all-silicone Foley catheter	synthetic urine (SU)	SU medium, SU medium with P. mirabilis, SU medium with E. coli, SU medium with purified allicin vs SU medium with P. mirabilis with 2 µg/ml IAA (a known urease inhibitor)	A synthetic bladder has been described previously (49): consists of a glass chamber, a Size-16 Ch all-silicone Foley catheter was inserted aseptically into the chamber through an outlet at the base, a sterile drainage container attached to the catheter, sterile SU was pumped into the chambers at 0.5 ml/min
L. Wang (18)	2019	UK	E.coli, P. mirabilis	silicone catheter	artificial urine	comparisons of Ag-PTFE nanocomposite coated and uncoated catheters, two concentrations of E. coli suspension (106 and 102 cells/mL)	The model consisted of a glass vessel (‘bladder’), an acrylic tube with a length of 13 cm and an inner diameter of 6 mm (‘urethra’, based on the average lengths of male and female urethra) and two peristaltic pumps (artificial urine was pumped into the ‘bladder’ at a rate of 0.5 mL/min). The branch at the bottom of the acrylic tube could allow the source of infection to be injected, thus representing the urethral meatus.
Yuchen Xu (19)	2019	China	E. coli, S. aureus, P. mirabilis	waterborne polyurethane (WBPU) polymers	artificial urine	WBPU emulsions were mixed with ciprofloxacin (0.1 mg) or streptomycin (1 mg) and prepared into films	The model of the bladder was generated as previously described (49), and the latter has been described previously (58): It

						(1x1 cm; thickness, 0.5 cm) vs WBPU film	consisted of a glass fermentation flask, a 14F catheter was inserted into the flask through a section of silicone tubing (a 'urethra') attached to a glass outlet at the base of the flask. Sterile urine was then supplied to the bladder at 0.5mL/min such that a residual volume of 30mL collected in the bladder below the level of the catheter eyelet.
M. Frant (20)	2018	Germany	E. coli, S. aureus, S. epidermidis, En. Faecalis, P. aeruginosa, P. mirabilis	standard polyurethane (PUR) ureteral stent, PUR and silicone tube	patients' urine, artificial urine	uncoated and coated PUR and silicone tubes (equipped with TANP coating embedded in a degradable polymer matrix PLGA) (in vitro BioEncrustation model) vs explanted ureteral stents (in vivo situation) and under sterile conditions (Encrurator®)	The samples were incubated in the BioEncrustation model under gentle stirring, test medium was replaced from the bioreactor at a flow rate of 3 ml/min. The scheme of the employed in vitro-BioEncrustation test design is presented later.
Iain J. Abbott (21)	2017	Australia	E. coli, E. cloacae, K. pneumoniae	in vitro Fosfomycin susceptibility testing	MHB supplemented with glucose-6-phosphate (G6P, 25mg/L)	MHB+G6P vs incorporated with Fosfomycin	The in vitro model was constructed to reflect normal human urodynamics on a 1:15 scale. Autoclavable PVC tubing and glassware were connected by peristaltic pumps, which enabled eight bladder compartments were run in parallel and placed on magnetic stirring and heating element. Simulated urination was performed four times each day, leaving a post-void residual volume of 1.5–3.0mL.
Joel Rosenblatt (22)	2017	USA	MRSA, E. coli, C. albicansi	a Foley catheter	trypticasesoy agar, disinfectant solutions	Single agent or double or triple combinations of 1% polygalacturonic acid, 0.4% caprylic acid and 0.3% hydrogen peroxide	The novel double cuff Foley and disinfectant solutions were evaluated in an established in vitro CAUTI model (43): A double cuff flushable Foley catheter with a novel irrigation cuff indwelled in a simulated urethra.

Trace Hobbs (23)	2017	Canada	<i>P. mirabilis</i>	silicone tubing, sponge, glass capillary	artificial urine	a laboratory model to represent the urinary tract and enable the control of biofilm induced stone formation	The in vitro system consisted of reservoirs, a KA, a ureter analog, a BA and a waste reservoir (350 ml in the KA and 100 ml in the BA). The CDC Biofilm Reactor, which simulates kidney and bladder reservoirs. Peristaltic pumps were used to control all fluid flow through the system. AU flow was started immediately after inoculation and maintained throughout the experiment at 1.0 and 0.4 ml per minute into the KA and the BA, respectively. The BA was emptied every 4 hours between 8:00 am and 8:00 pm, leaving a residual volume of approximately 25 ml.
R.Y.R. Chua (24)	2017	Singapore	<i>E. coli</i> UTI89	silicone urinary catheter	human urine (a single male donor)	100% silicone urinary catheter vs silver-hydrogel catheter vs AMP-coated catheter	The peristaltic pumps ensured a continuous supply of urine at 0.7 mL/min or 1 L/day from the reservoir into each of the two 250-mL polypropylene receptacles that simulated the bladders. Each urinary catheter was connected to an effluent collection vessel that simulated the drainage bag.
Mario Maierl (25)	2017	Austria	<i>P. mirabilis</i> HI4320	silicone tubing	artificial or human urine	The in vitro dynamic model of a catheterized bladder enabled reproducible monitoring of biofilm formation.	The urine is pumped from the reservoir using a peristaltic pump (use a channel for each model, 30ml/h). 10 L polycarbonate carboy for urine reservoir. Borosilicate Glass bladder models.
Scarlet Milo (26)	2016	UK	<i>P. mirabilis</i> RS1, <i>E. coli</i> NSM59	Foley silicone catheter	artificial urine	hydrophilization of catheter surfaces via silanisation of the silicone surface, coated with the gel/dye solution	The model consisted of 200ml double-walled glass vessel. The coated catheters were inserted aseptically into the vessel via silicone tubing attached to a glass outlet at the base, and attached to a sterile drainage bag. Sterile artificial

							urine was supplied to the bladder model via a peristaltic pump at a flow rate of 0.75mL/min, with a reservoir (~30mL) of urine to collect in the bladder below the level of the catheter eyehole.
Andreia S. Azevedoa (27)	2016	Portugal	E. coli CECT 434, D. tsuruhatensis BM90	silicone tube	artificial urine medium	under static conditions vs. dynamic conditions	The reactor system consisted of a vertical flow cell, peristaltic (B1) and centrifugal pumps (B2), vessel containing the nutrients, recirculating silicone tubes and a waste vessel. The flow cell used is a rectangular Perspexcolumn with 10 apertures in removable rectangular pieces of Perspex where silicone coupons were placed. Pumps B1 and B2 controlled the flow rate of AUM (0.5 ml min ⁻¹) and the velocity of recirculating fluid (300 ml min ⁻¹), respectively.
Susan M. Lehman (28)	2015	USA	P. aeruginosa, P. mirabilis	hydrogel-coated silicone Foley catheters	human urine from one healthy donor, artificial urine	phage pretreatment of silicone hydrogel catheters vs untreated	The modified drip flow reactors (mDFRs) described previously (36): Four lengths of catheter were held in a custom-made square plastic tray, and each catheter was separately connected to sterile medium, bacterial inoculum, and waste flasks. The feed lines from the sterile medium flask were fitted with flow breaks to prevent upstream migration of bacteria and contamination of the sterile feed flask. Prewarmed AUM was added to the sterile medium flask (6 liters) and the bacterial inoculum flask (0.5 liters). Sterile medium was pumped through the catheters at 0.5 ml/min.
Ahmet Salvarci (29)	2015	Turkey	P. mirabilis, E. coli, P. aeruginosa	silicone catheter	healthy people urine	pure silicone vs Minocycline-Rifampin coating	For in vitro urinary system model, 5-litre sterile plastic reservoir bags representing the kidneys were used.

							The intravenous pump set was accepted as the ureter. A 500cc glass bottle was used as the bladder for the storage of the urine and the placement of sterile silicones inside. A hole for the entry of the infected urine inflowing from the metric pump and a drainage hole representing the urethra for draining the urine without any residue were perforated on the cap of the bottle. The edges of the inflow and outflow sections of the glass bottle were sealed with silicone. Jet streams were achieved via the intravenous metric pump (50ml/h). The bottle was fully emptied without leaving any residue at 4-6-hour intervals during this period.
Kristina Ivanova (30)	2015	Spain	C. violaceum CECT 5999, P. aeruginosa ATCC 10145	silicone catheter	artificial urine	acylase multilayer coatings vs uncoating, static vs dynamic conditions	A physical model of catheterized bladder, previously described by Stickler et al. (49): consisted of a glass bladder, acylase-coated silicone Foley catheter was inserted into the dynamic system and the catheter balloon inflated with 10 mL distilled H2O. Then, the bladder was filled with 60-mL sterile artificial urine containing 1 mg mL ⁻¹ TSB and inoculated with P. aeruginosa ATCC 10145. The supply of urine was started with 1 mL min ⁻¹ flow rate.
Kasper Klein (31)	2015	Denmark	E. coli	glass slides, silicone disks	artificial urine	flow chamber experiments	(1) To culture biofilms on artificial material, flow chambers were used as previously described [Andersen et al. (37)] with silicone rubber disks used as substratum surface. Bacterial seeding suspensions were passed through chambers at 100 µl/min for

							<p>20 min using a low-pulsation roller pump. A flow of urine was applied at a flow rate of 15 μl/min. The emerging biofilm was then harvested directly from the chambers by detaching the pump and elevating the medium flask to increase flow by hydrostatic pressure and manually tapping the inlet tubing to tear off bacteria by shearing force.</p> <p>(2) Flow chamber bladder cell infection was performed as previously described [Andersen et al. (34)] with some modifications. In short, glass slides containing confluent PD07i cell layers were transferred to the flow chambers and used as substratum instead of silicone disks. A 100 μl/min flow of sterile Epilife was applied for 1 h. To infect the cell layer, bacterial seeding suspension was passed through the chambers at 100 μl/min for 20min. For surface colonizations flow medium was shifted to sterile urine at 15 μl/min for different times.</p>
N. Holling (32)	2014	UK	P. mirabilis B4, E. coli	all-silicone Foley catheters	artificial urine	a constant flow rate of AU	<p>Models were run as described by Stickler et al. in 1999 (49), with minor modifications. Models consisted of a double-walled glass chamber (the bladder). Size 14 French all-silicone Foley catheters were inserted into the chamber via an outlet in the base of the glass chamber and retention balloons inflated with 10 ml sterile water. The catheter was attached to a drainage bag to form a sterile, closed drainage system. AU medium was supplied to</p>

							the bladder at a constant flow rate of 0.75 ml min ⁻¹ .
Andreas Reisner (33)	2013	Austria	E. coli K-12, CFT073	Foley all-silicone catheter	artificial urine, human urine (5 to 15 healthy volunteers, both men and women)	a dynamic catheterized bladder model in vitro	The dynamic catheterized bladder model originally developed in the David Stickler laboratory was performed as previously described (49) , with minor modifications. In brief, the outer glass compartment was 5 cm longer than the inner compartment of two-compartment glass chambers (200ml). A size 14 sterile Foley all-silicone catheter was inserted into the inner compartment of the glass chambers, followed by inflation of the catheter retention balloon with 10 ml sterile water. After connection of catheters to standard drainage bags, sterile urine was pumped (30ml/h) into the inner chambers to a level just below the eyeholes of the catheter tips.
Thomas E. Andersen (34)	2012	Denmark	E. coli UTI89, NU14, 34476, ATCC 25922	silicone rubber disks	artificial urine	laminar flow conditions	Cell infections were performed in custom built FCs based on a previously described principle (37) : A four-chamber setup was used in each experiment, with each chamber consisting of a polycarbonate (PC) top disc, a bottom glass plate with a confluent PD07i layer, and a 0.5-mm-thick silicone gasket with a central 20-by-3-mm slit sandwiched between the PC disc and the glass plate. In this arrangement, the silicone gasket slit defines the flow channel dimensions and medium is brought to and moved through this channel by internal connecting pipes drilled in the PC disc. Flow is maintained with an

							extremely low-pulsation roller pump (Ismatec IPC-N4; Glattbrugg, Switzerland) attached to the exit tubing of the chambers. During growth periods, a flow rate of 0.9 ml/h was used, which equals a wall shear rate of $2s^{-1}$ as calculated from the chamber dimensions specified above and the volumetric flow rate. The calculation is valid under laminar flow conditions.
Sladjana Malic (35)	2012	UK	P. mirabilis, P. vulgaris, K. pneumoniae, M. morgani, S. aureus, NSM, P. rettgeri, E. coli, E. cloacae, P. stuartii, E. faecalis, S. aureus P10, P. aeruginosa	all-silicone catheter	artificial urine	in vitro bladder model	The in vitro bladder model has previously been described and comprised a glass chamber (bladder) (49). The base of the bladder chamber had an outlet into which a size 14 Ch all-silicone catheter was introduced, and this served to drain the bladder of artificial urine. The catheter retention balloon was inflated with 10-mL sterile water and the catheter connected to a drainage bag. Artificial urine was continuously introduced into the bladder at a flow rate of 0.5 mL/min using a peristaltic pump.
Weiling Fu (36)	2010	Georgia	P. aeruginosa M4	Lubri-sil all-silicone 16 French Foley catheters	10% (vol/vol) TSB	phage or phage cocktail-treated catheters vs untreated	A modified drip flow reactor (mDFR): contained four chambers, each with a sealing lid. The original device was modified to allow the connection of catheter segments to the influent and effluent ports within the device. The catheters in the mDFR each were connected by means of silicone tubing to glass vessels containing (i) phage lysate, (ii) bacterial inoculum, (iii) sterile medium, and (iv) an empty waste

							container.
Thomas Emil Andersen (37)	2010	Denmark	E. coli34476, 14608, 14782 and 11036, ATCC25922	silicone rubber	artificial urine	35 °C vs 30 °C, silicone rubber vs coated with plasma polymerized vinylpyrrolidone	A flow chamber with controlled shear forces: the chamber channel dimensions 15 mm×3 mm×0.5 mm were formed by a silicone gasket sandwiched between a top optically clear polycarbonate corpus and the silicone disc as bottom plate serving as substratum. Liquid flow passes through inlet holes in the corpus into the channel and exits through the corpus. A steady flow through the chamber was maintained with an extremely low pulsation roller pump attached to the exit tubing of the chamber. In all experiments four chambers were used in a parallel setup and connected to the same medium source and driven by the same multichannel pump. The same flow rate of 15 ml h ⁻¹ was used in all steps of the experiment. This flow rate equals a wall shear rate of 33 s ⁻¹ as calculated.
Katarzyna A (38)	2010	UK	P. mirabilis	all-silicone catheters	artificial urine	the hydrogel coating (with and without triclosan, 0.5%, 1%, 4% and 4% shorter exposure time) vs. uncoated catheters, hydrogel coated and impregnated with PHMB or iodine	The bladder model was described previously by Stickler et al. (49): The tested catheter was placed into the glass bladder model through the section of silicone tubing mimicking the urethra. Flow of artificial urine set to 0.5 mL/min by peristaltic pump. Volume of liquid inside bladder was 13 mL.
Gareth J. Williams (39)	2008	UK	P. mirabilis, P. aeruginosa	latex Foley catheters	artificial urine	All-silicone catheters vs nitrofurazone-impregnated catheters vs impregnated all-silicone catheters with triclosan	A laboratory model based on that developed by Gaonkar et al. (43): The spaces below and above the agar columns represented the urethral meatus and bladder, respectively. The agar surrounding the catheter

							simulated the urethral tissue.
Jessica M.T. Barford (40)	2007	UK	E. coli (SGH031), S. epidermidis, P. putida, K. oxytoca, Ent. Faecalis, Ent. Faecalis	silicone catheters	artificial urine	different sections of latex Foley catheters coated lubricating jelly	The in vitro model of a catheterized lower urinary tract was set up to create realistic flow conditions for investigating factors. The model was set up according to schedule. The catheter was pushed through and when the balloon protruded from the other end, a rubber ring cut though one side was placed on the catheter below the balloon (to prevent the leakage that occurred during preliminary tests when the balloon was inflated, and mimicking the internal urethral sphincter). The attached screw-cap was then screwed onto the bladder chamber, adjusting the catheter so the balloon was just inside the chamber. The waste container was placed on the floor to obtain optimum drainage. The pump was operated at 40–50 mL/h.
Aniruddha Chakravarti (41)	2005	UK	P. mirabilis NSM6	Silicone catheters	artificial urine	electrified catheters with silver wires vs control	The 4 bladder models used were glass fermentation flasks, as previously described (58). The catheter balloons were then inflated, securing the catheter in position and sealing the outlet from the bladder. Sterile artificial urine was pumped into the bladder by a peristaltic pump at 0.5 ml per minute. In this way a residual volume of 30 ml collected in the bladder below the catheter eyelet and then flowed through the lumen into collecting bags with a closed drainage system.
David S. Jones (42)	2004	UK	?	Silitek and Percuflex polyolefin copolymer ureteral stent	artificial urine	the urease inhibitor, acetohydroxamic acid, or urease substrates	In vitro bladder encrustation model: The reaction vessels consisted of 700-mL volume plastic tanks with

						(methylurea or ethylurea)	firmly attached lids on the top. Sections (2.5 cm) of the ureteral stents were dissected, heat-sealed at both ends, and suspended into the artificial urine using Microlance 3 needles (60-mm length), which were themselves firmly attached within the vessel. An opening in the middle of the lid provided an easy way to replace artificial urine on a daily basis. The vessels were placed in an orbital shaker and their contents were exposed to a physiological temperature of $37.0 \pm 0.1^\circ\text{C}$ and a rotation speed of 100 rotations min ⁻¹ .
Trupti A. Gaonkar (43)	2003	USA	<i>S. aureus</i> , <i>S. epidermidis</i> , <i>E. coli</i> , <i>E. faecalis</i> , <i>P. aeruginosa</i> , <i>C. albicans</i>	latex and silicone catheters	fresh sterile urine, trypticase soy agar	Uncoated latex and silicone catheters vs impregnated with combinations of (1) chlorhexidine and silver sulfadiazine (CXS) and (2) chlorhexidine, silver sulfadiazine, and triclosan (CXST)	In vitro CAUTI model: The model consisted of two tubes, one of which was open and cylindrical with one end capped and the other end sealed with a rubber cork with a hole in the center (tube 1). The tube was crimped from both of the sides at the center. The second tube, which was open at one end, was used for collecting urine (tube 2). The sterile modified trypticase soy agar was cooled to 40°C and then poured along the sides of the tube around the catheter, leaving the upper 1 cm of the catheter protruding out in the space above the agar tract, which represents the bladder. This lower end of the agar column with the catheter protruding represents the meatus, and the agar surrounding the catheter simulates the urethra.
Sean P. Gorman (44)	2003	UK	<i>P. mirabilis</i>	polyurethane, Percuflex, silicone extruded tubing	artificial urine	the dynamic model vs a static model	The dynamic encrustation model consisted of a purpose designed glass

							reaction vessel linked to a pumping system to circulate artificial urine through the vessel containing biomaterial samples attached onto stainless steel mandrels. Artificial urine was pumped from a 5-L reservoir of artificial urine through silicone tubing using a Watson-Marlow pump. A pump speed of 10 mL min ⁻¹ was required to maintain the urine level in the reaction vessel. Several reaction vessels were clamped in parallel to a vertical steel pole. Each vessel had a separate inflow and outflow of urine and all outflowing urine was pumped back into the reservoir.
Jae Hyung Park (45)	2002	South Korea	E. coli ATCC 11775, P. mirabilis ATCC 25993, S. epidermidis, ATCC12228)	the copolymer/SPU blends coated silicone foley catheter	artificial urine	silicone catheter vs coating with SPU vs coated with copolymer/SPU blends (PEO-PTMO, 0, 5, 10, 20, 30 wt%)	Artificial bladder model was composed of a cylindrical glass flask (5 cm in diameter and 10 cm in height) similar to that designed by Stickler et al. (55) , a peristaltic pump, and a drainage bag. The catheters coated with SPU and blends were inserted into the autoclaved flask and inflated using a polystyrene syringe to fix the position like a catheterization in the human body. With a peristaltic pump, the sterile urine was supplied to the flask at a rate of 0.7 ml/min, which made 30 ml of residual volume below the level of the catheter eyelet.
S.K.S. Choong (46)	2000	UK	?	the polymer membranes, stents and catheters	fresh human urine	PTFE urethral catheter vs hydrogel coated urethral catheter, C-Flex ureteric stents vs Hydrogel-coated ureteric stents vs uncoated stents	The 'bladder' reservoir was 8 cm in diameter and 10 cm in height, and had a side-arm 8 cm high to which was attached a ureteric segment. This 'ureteric' segment had a straight section of 14.5 cm long, and

							connected to its upper end was a 'kidney' reservoir 3.5 cm in diameter and 5 cm high. The siphon was 7 cm high externally, with an external diameter of 1 cm and an internal tube 6.5 cm high and with a diameter of 0.5 cm. The adapter for a urethral catheter had a diameter of 14 F. Twice daily, the urine was emptied into the central reservoir containing a PTFE magnetic stirrer which gently mixed the urine. From the central reservoir urine was peristaltically pumped at 0.5 mL/min through silicone tubing into an inlet of the model.
Satoshi Takahashi (47)	2000	Japan	<i>P. aeruginosa</i> , <i>E. faecalis</i>	indwelling catheter	Mueller-Hinton medium	antibiotic medium of Gatifloxacin (AM-1155)	Briefly, the system consisted mainly of two flasks corresponding to a bladder and a kidney model, a peristaltic pump at a constant flow rate of 0.5 ml/ min medium was transferred to a bladder model. The medium (70 ml) in the bladder model was withdrawn except for 10 ml in the side arm in order to simulate the status of a patient having residual urine in the bladder diverticulum without an indwelling catheter.
K.A. Getliffe (48)	2000	UK	<i>P. mirabilis</i>	hydrogel-coated Foley catheter	pooled human urine (<7 L/day) was donated by four healthy individuals	different volumes of an acidic bladder washout solution (Suby G) and different washout delivery devices (Optifow, UroTainer, a bladder syringe) was compared to the "standardized" conditions	A model of the catheterized bladder adapted from (59) was used to produce catheter encrustation under controlled conditions. The model consisted of four glass bladders (inner capacity 250 mL). A 14 F hydrogel-coated Foley catheter was introduced into the base of each bladder through a size 19 silicone bung with an appropriately sized bore-hole. During experiments urine

							was pumped into each bladder from a 10-L Nalgene@ reservoir vessel at a flow rate of 1 ± 0.1 mL/min, using a multichannel peristaltic pump.
D J Stickler (49)	1999	UK	E. coli, P. aeruginosa, K. pneumoniae, P. stuartii, M. morgani, P. vulgaris, P. mirabilis	silicone tubing	Human urine, collected from healthy volunteers and an artificial urine	Formation of the biofilm on the luminal surfaces of the catheters	The model consists of a glass vessel (200 ml) maintained at 37 ° by a water jacket. Catheters (#14) are inserted aseptically into the vessel through a section of silicone tubing attached to a glass outlet at the base. The catheter is then attached to a drainage tube and reservoir bag. Sterile urine is supplied to the bladder via a peristaltic pump 0.5-1.0 ml/min (). A residual volume of urine (30 ml) collects in the bladder below the level of the catheter eyehole.
N. S. Morris (50)	1998	UK	P. mirabilis	latex catheters	artificial urine	all-silicone vs hydrogel-coated latex, hydrogel/silver-coated latex and silicone elastomer-coated latex catheters	The model of the catheterized bladder has been described previously (58). In essence it consists of a glass fermentation flask. A size 14 catheter was inserted into the flask through a section of silicone tubing (a 'urethra') attached to a glass outlet at the base of the flask. Sterile urine was then supplied to the bladder at 0.5 mL/min. In this way a residual volume of 30 mL collects in the bladder below the level of the catheter eyelet and then flows through the catheter and drainage tube to a collecting bag.
Nicola Sian Morris (51)	1998	UK	P. mirabilis NSM6	all-silicone catheter	artificial urine	various concentrations of the urease inhibitors acetohydroxamic acid or fluorofamide	The model of the catheterized bladder has been described previously (53). In essence it consists of a glass fermentation flask. A size 14 all-silicone catheter was inserted aseptically into the flask through a section of silicone tubing

							(a "urethra") attached to a glass outlet at the base of the flask. Sterile urine was then supplied to the bladder at 0.5 ml min ⁻¹ . In this way a residual volume of 30 ml collects in the bladder below the level of the catheter eyelet and then flows through the catheter and drainage tube to a collecting bag.
David J. Stickler (52)	1998	USA	A. tumefaciens, P. aeruginosa, P. stuartii, P. mirabilis, M. morgani, E. coli, K. pneumoniae	Silicone catheter	artificial urine	All silicone vs Silicone-coated latex, Hydrogel-coated latex catheter	The bacterial biofilms were produced in a simple physical model of the catheterized bladder (58). In essence, this model consists of a glass fermentation flask. A size 14 all-silicone catheter was inserted into the flask through a section of silicone tubing (a "urethra") attached to a glass outlet at the base of the flask. Sterile artificial urine was then supplied to the bladder at 0.5 ml min ⁻¹ . In this way, a residual volume of 30 ml collects in the bladder below the level of the catheter eyelet and then flows through the catheter and drainage tube to a collecting bag.
N. S. Morris (53)	1997	UK	P. mirabilis	Urethral catheter	artificial urine	hydrogel/silver coated latex, silicone treated latex, teflon coated latex, all silicone catheter	The model of the catheterized bladder has been described previously (58). In essence, this model consists of a glass fermentation flask. A size 14 all-silicone catheter was inserted into the flask through a section of silicone tubing (a "urethra") attached to a glass outlet at the base of the flask. Sterile artificial urine was then supplied to the bladder at 0.5 ml min ⁻¹ . In this way, a residual volume of 30 ml collects in the bladder below the level of the catheter eyelet

							and then flows through the catheter and drainage tube to a collecting bag.
Rabih O. Darouiche (54)	1997	USA	E. coli, P. aeruginosa, K. pneumoniae, E. faecalis, C. albicans	all-silicone Foley catheters	artificial urine	all-silicone Foley catheters coated with minocycline and rifampin vs uncoated catheters	A novel in vitro bladder model, consisted of the following sterile major components. The kidney was simulated by a 3-L plastic infusion bag that contained sterile artificial urine dripping via a volumetric pump at a fixed rate of 36 mL/h into the "bladder." The bladder was represented by a half-filled, seminverted glass flask with two outlets; the upper outlet provided a sampling port for access by a long needle that allowed collection of urine samples for culture and the lower outlet contained the plugged tip and the 5-mL inflated balloon of the catheter that was passed through an adaptor into the "urethra." The urethra was simulated by a 12.5-cm-long glass tube that contained the catheter, surrounded by a film of urine dripping down from the "bladder" through a hole in the adaptor, also at a rate of 36 mL/h. The urethral meatus was represented by a funnel that contained a segment of the catheter that was exposed to bacterial contamination originating from the source of infection dripping into the side outlet of the funnel over the external surface of the catheter at a fixed rate of 0.2 mL/min. The urine flowing around the catheter into the funnel was collected in the collection bag, represented by a glass flask with two side outlets; the overflowing urine drained through one side outlet,

							and the capped end of the catheter was externalized through the other side outlet.
D. J. Stickler (55)	1996	UK	<i>P. aeruginosa</i> , <i>E. coli</i> , <i>P. mirabilis</i>	all-silicone catheter	artificial urine	Comparison of drainage bags were fitted to the catheters: Mono-flo A6208 S4, P4 control, P4+AB device, PP2000N control, and PP2000N+AB device	The model of the catheterized bladder consisted of a glass fermentation flask (190mL). The catheter (14# Rusch all-silicone) was inserted into the flask through a section of silicone tubing (a 'urethra') attached to a glass outlet at the base of the flask. Sterile artificial urine was then supplied to the bladder at 1.0 mL/min via a peristaltic pump. In this way, a residual volume of 30 mL collected in the bladder below the level of the catheter eyelet. The catheter was connected to a drainage tube and bag, the bag being positioned on a stand below the bladder. A loop of tubing was introduced into the drainage system. Sets of six bladder models were used in each experiment.
A. Rasmussen (56)	1996	Denmark	<i>P. aeruginosa</i>	the urine-meter and the tubing	Mueller-Hinton broth diluted with saline	comparison of three urine-meters (the Braun Ureofix 511, the Kendall Curity 4000 and the Unoplast Unometer 500)	an experimental bladder-drainage model: a bladder catheter was connected to a plastic infusion-bag, mimicking the bladder. The kidneys were represented by an infusion-bottle, from which Mueller-Hinton broth diluted with sterile saline (1:9) flowed continuously at 1 L/day through an infusion-line and through the 'bladder'. The catheter was connected to the urine-meter and a connecting bag or, in the control, with a bag only. During the experiment the urine bag was emptied twice a day. With the urine-meter included, the system was

							operated for 12 days and samples taken once a day from the 'bladder' and tested for bacterial growth.
Hoo Yin Wong (57)	1995	USA	E. coli, K. pneumoniae, P. mirabilis, P. aeruginosa	a MacConkey blood agar biplate	human urine	Iontophoresis of therapeutic electrical current +gentamicin vs gentamicin, the dump valve set for intermittent filling and emptying vs continuous drainage	a dynamic in vitro artificial bladder model: Erlenmeyer flasks were used as the urine reservoir. Standard intravenous tubing was used to transport the urine from the Erlenmeyer flasks into the special "bladder" beakers. The Flo-Guard 6300 intravenous volumetric pump regulated the urine flow at 50cc per hour. The "bladder" beakers contained a side port at the bottom to act as an outlet. In this phase of the experiments, the urine outflow from the "bladder" beaker was regulated by a gravity dump valve and timer that opened the dump valve every 4 to 6 hours. Due to the configuration of the beakers, 10 to 40 cc of residual urine always persisted in the "bladder" beakers.
Stickler, D.J. (58)	1994	UK	P. aeruginosa, E. coli, P. stuartii, P. mirabilis	silicone or silicone coated latex urethral catheters	pooled human urine, artificial urine	ciprofloxacin treated silicone catheters vs uncoated	a physical model of the catheterized bladder (detailed data unavailable)
K.A. Getliffe (59)	1994	UK	P. mirabilis	catheter (18 Charribré)	synthetic urine	Suby G, mandelic acid 1% or saline 0.9% vs no bladder wash-outs	A model of the catheterized bladder: consisted of a glass 'bladder' composed of a specially converted five port, jacketed reaction vessel with 'quickfit' ground glass connections. A catheter (18 Charribré) was inserted into the base of the bladder through a glass 'urethra'. The bladder was supplied with synthetic urine, at a flow rate of 1.0 ± 0.1 ml/min, using a 502AA 4-channel peristaltic cassette pumphead connected to a 502s

							Drive. Residual urine collected below the catheter eyes and excess urine drained through the catheter into a collecting vessel. Urine flowed from the reservoir to this vessel within a sealed system.
W. Schmitz (60)	1993	Germany	<i>P. mirabilis</i>	Silicone coated (inner and outer surface) latex catheters	artificial urine supplemented with 15 g/l trypticase soy broth	the tested citric acid containing solutions (Suby-G and Solution-R)	A model has been established with six glass bladders (double walled glass vessels, capacity 250 ml) connected in parallel. The system (the urine vessel and the bladder) was kept at 37 °C by a thermostatic water circulation. Sterilized synthetic urine were supplemented with 15 g/l trypticase soy broth was pumped into each bladder at a rate of 81 ml/h and was collected separately after single bladder passage. Each bladder had a separate urine supply. Silicone coated latex catheters were installed into a silicone rubber plug closing the bottom of the bladders. The residual urine volume was 22.1 ml per bladder.
Anne Mulhall (61)	1992	UK	?	?	10 per cent Nutrient Broth	investigate the spread of micro-organisms from artificially contaminated drainage bags of different design	Following pilot experiments using Quickfit apparatus, a more sophisticated model incorporating a peristaltic pump, a top filling bladder, and a glass 'urethra' was assembled. Flow of sterile 'urine' from a 10 litre reservoir was maintained by a peristaltic pump at 1 ml per minute, which is the normal rate of secretion of ureteric urine. The residual volume of urine in the bladder was 20 ml, the excess draining via the catheter into the collecting bag in a direct simulation of the situation in vivo.

J. B. King (62)	1992	UK	P. aeruginosa, P. mirabilis, P. stuartii, E. coli	CLED Agar	sterile pooled urine	three antiseptic bladder washout solutions (chlorhexidine (0.02% w/v), supplementing chlorhexidine with EDTA and TRIS) vs saline	The details of the model of the catheterized bladder have been described previously (64). In essence, sterile pooled urine is delivered by a peristaltic pump at a rate of 1 ml/min to a fermentation flask (100 ml) which acts as the bladder. The flask is kept at 37~ and the residual volume of urine is maintained at 10 ml by the positioning of the catheter and drainage tube system. Excess urine is drawn off by a vacuum pump to a Buchner flask, which represents the urine drainage bag.
Koji Mnrnaka (63)	1988	UK	S. faecalis	?	the 'complete' broth agar	ciprofloxacin, norfloxadn or enoxadn	The design of the model has been described in detail elsewhere [Greenwood & O'Grady, 1978 (77); Greenwood, 1985 (67)]. In the present experiments, an overnight culture of S. faecalis in complete broth was diluted with fresh broth at a rate of 1 ml/min; to simulate frequent micturition a pump automatically removed accumulated broth at hourly intervals, leaving a residual volume of 20 ml. By use of a gradient-forming device, the concentration of drug in the broth entering the system was allowed to reach a peak concentration over 4h.
D J Stickler (64)	1987	UK	E. coll, Klebsiella-Enterobacter, P. mirabilis, P. stuartii, S. faecalis, P. aeruginosa	Infected urines	pooled urine	antibacterial solution (100 ml of chlorhexidine 200 mg l-1) vs saline	A simple physical model of the catheterized bladder: Urine flows into the bladder from the ureters and reservoir of urine is maintained in the bladder by the catheter. A glass model was set up at half-scale with a 10mL residual volume of urine, a 1 mL min-1 urine dilution rate and a

							capacity of 90mL. The bladder was represented by a small fermentation flask. The residual volume of urine was kept at 10mL by catheter drainage system connected to a vacuum pump via a Buchner flask which represented the urine drainage bag. The urine in the bladder was mixed gently by a magnetic bar. An aspirator bottle represented the kidney and this provided sterile pooled urine which was pumped into the bladder flask at 1mL min ⁻¹ by a peristaltic pump.
C. Pinosi (65)	1987	Italy	E. coll, Klebsiella-Enterobacter, P. mirabilis, P. stuartii, S. faecalis, P. aeruginosa	MHB agar	human urine	Fosfomycin trometamol with or without G6P	The experimental model described by Greenwood and O'Grady (77) was used with some modifications. 120 ml of sterile urine containing the suitable concentration of antibiotic were introduced into the flask simulating renal excretion and were transferred by a peristaltic pump at a flow rate of 1 ml/min into a second flask simulating the bladder which contained 5 ml of urine and 10 ⁸ bacteria/ml of the tested organism. After 2 h, 120 ml of urine were withdrawn in order to simulate micturition. The test was performed in two steps. The first simulated a daily treatment of about 12 h, with micturition every 2 h and a flow rate of 1 ml/min. The second was a 'night phase' of 12 h, during which there was no micturition and a reduced flow rate of 0.25 ml/min.
D. Greenwood (66)	1986	England	E. coli ECSA 1, PAT, 89/317, 25/1	continuous opacity monitoring device, disc diffusion tests	broth	trometamol fosfomycin	Bladder model: The design and use of the model have been described elsewhere (77,67). In the present

							experiments, overnight cultures of E. coli in 20 ml Eugon Broth were continuously diluted with fresh broth at a rate of 1 ml per minute to simulate the flow of ureteric urine into the bladder; at 1 h intervals a pump removed accumulated broth, leaving a residual volume of 20 ml. The changing concentration of antibiotic in the broth inflow was achieved by use of a gradient-forming device. The response of the bacterial culture to the antibiotic was continuously monitored photometrically.
D. Greenwood (67)	1985	England	E. coli, K. aerogenes	Turbidimetric measurement	broth	Antibiotic	The bladder model system that we have developed has been described in detail elsewhere [Greenwood & O'Grady, 1978 (77)]. Basically, a dense bacterial culture, held at 37°C, is diluted at a rate which simulates the flow of ureteric urine and at intervals a 'micturition' episode removes accumulated culture. The inflow can be altered to simulate normal, reduced or increased ureteric flow rates, and the frequency of 'micturition' can also be readily varied. Broth has been used in the system in preference to urine, since it is more convenient to work with and provides more reproducible growth conditions.
D. Greenwood (68)	1984	England	Escherichia coli MAS, Escherichia coli 23T and Klebsiella aerogenes RN4	DST agar, disc diffusion tests	"complete" broth	ciprofloxacin, norfloxacin, nalidixic acid and cinoxacin	Bladder Model. The model has been described in detail elsewhere (77). An overnight culture of bacteria in "complete" broth was diluted with fresh broth at a rate of 1 ml/min to simulate the dilution of infected

							bladder urine with ureteric urine. To simulate frequent micturition, a pump automatic. ally removed accumulated broth at hourly intervals, leaving behind a residue of 20 ml. After 4 h of such dilution and periodic "micturition", exposure to the antibacterial agent commenced.
David Greenwood (69)	1984	England	nalidixic acid sensitive strains of E. coli, E. coli strain 23T and Klebsiella aerogenes strain RN4	?	broth	quinolone compounds of the nalidixic acid series	The model that we have developed for this purpose has been described in detail elsewhere [Greenwood & O'Grady, 1978 (77)]. Briefly, the model consists of a glass flask designed so that the turbidity of the culture contained within it can be continuously monitored photometrically. The flask is primed with 20 ml of an overnight broth culture of the organism under study and the culture is diluted with fresh broth at a rate equivalent to the rate of flow of ureteric urine into the bladder (which, in the absence of diuresis, is normally about 1 ml/min during the day). At predetermined intervals (usually 1 h) a pump is automatically activated in order to empty the flask of accumulated culture fluid ('micturition') leaving behind a residual volume of 20 ml. This residual volume is rather higher than the normal human value of about 1 ml so that the model represents a 'difficult' patient with impaired ability to clear infection by the normal hydrokinetic washout mechanism. The required renal excretion profile of the agent under study is achieved by use of a

							gradient former which arranges for the concentration of drug in the inflow to the flask to rise to a peak and then decline in a pre-selected fashion.
D. Greenwood (70)	1984	England	E. coli ECSA 1, K. aerogenes RN4, E. coli 23 T	male urine agar plates, DST agar plates	broth	norfloxacin (and nalidixic acid)	Bladder model: The design and use of the model have been described elsewhere (Greenwood & O'Grady, 1978(77)). In the present experiments, 20 ml of an overnight broth culture were diluted (1 ml/min) with fresh broth to simulate the dilution of bacteria in the bladder with ureteric urine. At 1 h intervals, a pump removed accumulated broth ('micturition') leaving a residuum of 20 ml. The response of the bacterial culture was continuously monitored photometrically.
John D. Anderson (71)	1983	Canada	Enterobacteriaceae	Mueller-Hinton agar plates.	healthy adult volunteers urine	ampicillin, amdinocillin and the combination	The apparatus was constructed of glass and fitted together with ground glass and polytetrafluorethylene joints to facilitate steam sterilization. A cylindrical glass vessel served as culture chamber. The "bladder" was emptied every four hours via an electromagnetic valve activated by an electronic timing device. The base of the apparatus was constructed in such a way that a residual volume of 4 ml remained when the apparatus emptied. Sterile urine was pumped into the bladder at a rate of 60 ml/hour.
D. Greenwood (72)	1981	England	E. coli ECSA 1, K. aerogenes	continuous turbidimetric monitoring	phosphate-buffered "complete" broth, fresh, filtered, pooled urine	Ampicillin, hexamine, hexamine hippurate and hexamine mandelate	Bladder model: The design and use of the bladder model have been described elsewhere (77). In the present experiments 20 ml of an overnight broth culture of bacteria

							were diluted with flesh broth at a rate of 1 ml per minute (the normal diurnal ureteric urine flow rate). At one or four hour intervals the system was automatically emptied, leaving behind a residual volume of 100 20 ml. After four hours of dilution and emptying, exposure to antibacterial agent was commenced. In order to simulate the renal excretion profile of drug, a gradient-former was used. The "micturition" occurred every four hours.
J. D. Anderson (73)	1980	Canada	E. coli, Enterobacteriaceae	Plates of Mueller-Hinton medium	Pooled midstream urine specimens from healthy males and females	Amoxicillin trihydrate, ampicillin sodium	Human urinary bladder model: a full description and details of the operation of this apparatus have been described previously (76). For these experiments facilities were provided to pump urine or urinary solutions of antibiotic from a reservoir maintained at 4°C. Principal features of the apparatus (outline only) are as follows. A cylindrical glass vessel (volume 500 ml) served as a culture chamber. Cultures were aerated and mixed by passing air through the urine. The apparatus was maintained at 37 °C by heating lamps controlled by a thermistor in the base of the apparatus. Sterile urine with or without antibiotic was pumped into the bladder with a peristaltic metering pump (60 ml/h). The culture vessel was automatically emptied every 4 h to leave a residual volume of 4 ml. Culture samples for viable count determinations were withdrawn with a hypodermic

							syringe and needle via a rubber cap in the base of the apparatus.
D. Greenwood (74)	1980	UK	E. coli	a simple photometer is built into the system to provide a continuous record of the opacity of the culture.	broth	three 13-tactam antibiotics	a simple semi-continuous cultivation apparatus in which a bacterial culture is diluted at a rate equivalent to the normal ureteric urine flow rate (about 1 ml per minute during the day, falling to about a quarter of that value during the night) and is periodically discharged, in simulation of the act of micturition, at regular preset intervals. A commercially available gradient forming device, which represents, in this model, the kidney in that it arranges for the broth diluent to contain a continuously changing concentration of antibiotic according to any predetermined profile. rate was 1 ml per minute and the interval between "micturition" episodes was one hour. The residual bladder volume was held at 20 ml.
Y. Kawada (75)	1980	UK	E. coli, S. epidermidis	?	"Complete" broth	ampicillin	Bladder model: The design and use of the bladder model have been described elsewhere (77,78).
J. D. Anderson (76)	1979	Canada	E. coli, P. mirabilis, S. epidermidis, S. faecalis, C. perfringens, B. melaninogenicus, B. fragilis	Viable counts were determined and oxygen tensions were monitored by withdrawing samples with a hypodermic syringe and needle via a rubber cap in the base of the apparatus.	Pooled midstream urine samples from males and females	Role of Bacterial Growth Rates in the Pathogenesis of Urinary Infections	The bladder model was an apparatus fitted together with ground glass and polytetrafluoroethylene joints which facilitated steam sterilization. A cylindrical glass vessel (volume, 500 ml) served as the culture chamber. The lower part tapered, and interchangeable glass bases could be fitted to vary the residual volume. A residual volume of 1±0.2 ml was chosen for all experiments described here. The "bladder" emptied via a sterilizable electromagnetic valve

							activated every 4 h by a timing device. Urine was pumped into the bladder through a peristaltic metering pump. An urine flow rate of 50 ml/h was used.
David Greenwood (77)	1978	England	E. coli, P. mirabilis.	Bacterial suspension	A synthetic urine, broths were added	antimicrobial drugs	The model, in its original form [O'Grady & Pennington, 1966 (86)]. The lay-out of the bladder model: the flask which constitutes the 'bladder' containing the bacterial culture, clamped in its supporting framework which is housed in an incubator. A motor-driven stainless steel paddle (Q, held just above the light path of the photometer, gently mixes the culture. Fresh broth enters through a port at the top of the flask and the system is emptied periodically through a sidearm, the height of which controls the level of the residual volume of 20 ml. Broth is delivered to the 'bladder' at a rate simulating that of the secretion of urine by the peristaltic pump; this pump receives broth from two reservoirs, one of which contains antibiotic at the required peak concentration. The relative proportions of antibiotic-containing and antibiotic-free broth are controlled by a slider-valve arrangement operated by the continuous gradient former according to a predetermined profile cut from graph paper, which is 'read' as it travels past a sensing device on the gradient former.
David Greenwood (78)	1977	UK	Ampicillin sensitive and resistant strain E. coli,	the opacity of the culture was continuously	"complete" broth	Penicillins and cephalosporins	Every hour the accumulated broth was pumped from the bladder model

			Ampicillin sensitive strain <i>P. mirabilis</i>	monitored photometrically			(simulating micturition), leaving a 20-ml residuum. The "bladder" temperature was kept at 37 C and the opacity of the culture was continuously monitored photometrically. A changing concentration of antibiotic was introduced into the system with the broth inflow by use of a suitably programmed gradient forming device.
D. Greenwo (79)	1976	UK	<i>E. coli</i> ECSA1	Changes in the turbidity of the culture are continuously monitored photometrically.	the "complete" broth	polymyxin B, colistin (polymyxin E) and their sulphomethyl derivatives, sulphomycin and colistin sulphomethate	The design of the in-vitro bladder model and its application to the study of antibiotic effects have been described elsewhere (80,85). In this device, a fully grown broth culture of bacteria is diluted with fresh broth at a rate of 1 ml per min. (the normal diurnal rate of secretion of urine into the bladder) and at hourly intervals a "micturition" episode empties the "bladder", leaving a residual volume of 20 ml. To simulate conditions encountered in vivo, arrangements were made for the antibiotic to be instilled in gradually increasing concentrations into the "bladder" over a period of 8 h, by use of an automatic gradient former linked to twin reservoirs of broth. Once the maximum concentration of antibiotic had been achieved, it was maintained for the remainder of the experiment, including an 8-h "sleep" period during which the inflow rate was reduced to 0.25 ml per min. (the normal nocturnal rate of secretion of urine) and "micturition" was

							suspended.
D. Greenwood (80)	1976	UK	E. coli ECSA1	The turbidity of the culture was continuously monitored photometrically.	broth	ampicillin, cephalothin and cephalixin, polymyxin B sulphate, tetracycline hydrochloride, chloramphenicol, nalidixic acid	Details of the bladder model and its application to the investigation of antibiotic effects have been described elsewhere (85). 20 ml of an overnight broth culture of E. coli were diluted with fresh broth either at 1 ml/min, simulating the normal diurnal rate of urine flow into the bladder, or 2 ml/min, simulating a state of diuresis. At preset intervals of 1, 2 or 4 h, controlled by an automatically resetting clock, the accumulated broth was pumped out of the system (simulating the act of micturition) leaving a residual volume of 20 ml. Antibiotic was added as a single pulse, immediately after the fourth hourly "micturition".
D. Greenwood (81)	1976	UK	TMP and SMX sensitive strain E. coli ECSA 1	the turbidity is continuously monitored photometrically	Wellcotest broth	trimethoprim (TMP) and sulfamethoxazole (SMX)	Details of the design of the 'bladder' model and its application to the study of antibiotic effects have been described elsewhere (85). In the model, a fully grown broth culture of bacteria is diluted with fresh broth at a rate equivalent to the normal diurnal ureteric urine flow rate (1 ml per minute) and at preset intervals (1 hour in the present series of experiments) a 'micturition' episode empties the 'bladder' leaving a residual volume of 20 ml. The culture is mixed by a stainless steel paddle.
D. Greenwood (82)	1975	UK	E. coli	the opacity is continuously monitored photometrically	"complete" broth	Cephaloridine, cephalothin and cephalixin, ampicillin	In the in vitro bladder model (85) 20 ml of a fully grown overnight broth culture (representing an arbitrary residual bladder volume) is

							diluted with fresh broth at 1 ml/min to simulate the ureteric urine flow. At pre-set intervals a "micturition" episode empties the bladder of all but the residual volume. The culture is gently mixed by a stainless steel paddle. 4 cycles of dilution and micturition.
D. Greenwood (83)	1975	UK	E. coli, Klebsiella sp., P. mirabilis, P. vulgaris, P. morgani, E. sp., S. marcescens, Hafnia sp., Providencia, Citrobacter sp.	continuous turbidimetric monitoring	broth	cefazolin	Bladder model. A full description of the model and the experimental rationale have been provided in previous reports (85). Briefly. 20 ml of an overnight broth culture (representing an arbitrary residual bladder volume) are diluted with fresh broth at 1 ml per min to simulate the ureteric urine flow rate. At preset intervals (1 h in the present experiments), a "micturition" episode empties the bladder of all but the residual volume.
D. Greenwood (84)	1975	UK	E. coli, Klebsiella spp., Enterobacter spp., P. mirabilis, P. vulgaris, Hafnia spp., S. marcescens, Providence, Citrobacter sp.	the opacity level	the 'complete' broth	Ampicillin, nafcillin, cloxacillin, carbenicillin, 6-aminopenicillanic acid and BRL 1437	The model and rationale of the experimental design have been described in detail elsewhere (85). In brief, 20 ml of a fully grown broth culture (representing an arbitrary residual bladder volume) was diluted with fresh broth at a rate of 1 ml/min simulating the diurnal ureteric urine flow into the bladder. At pre-set intervals (1 h in the present experiments), a 'micturition' episode emptied the 'bladder' down to the residual 20 ml volume.
F. O'grady (85)	1973	UK	E. coli	the opacity of the growing culture, the Eh of the culture.	broth	ampicillin	Two new models based on those previously described (86) have been constructed: The "bladder" in this model consists of a 250 ml glass cylinder on to the base of which a 20

							ml glass syringe barrel is welded. A stainless steel plate is attached to the top of the flask and is used to clamp the flask into its frame. The plate also provides location for the inlet and outlet tubes as well as electrodes for the measurement of pH, Eh and temperature. The vessel is sterilized with the plate and electrodes in position. The piston system is so arranged that the syringe plunger is held flush with the floor of the bladder cylinder and is withdrawn only for sufficient time to allow the opacity reading to be taken. A specially designed electronic clock selects in turn the signals from each electrode and, having caused the plunger to be withdrawn, from the photometer. The same clock arranges for micturition to occur at preset intervals, ensuring that at the same time the syringe plunger is in the correct position and that digital readings are not taken during the turbulent conditions which exist while the bladder is being emptied. The voltages generated by each of the electrodes are fed to a voltmeter and paper tape pump which are programmed to generate a digital multiplexed record of the opacity, pH, Redox and temperature signals on paper tape. The characteristic effect of diluting at 1 ml/min a fully grown broth culture with a residual volume of approximately 20 ml and hourly micturition is seen.
F O'Grady (86)	1966	UK	E. coli or P. mirabilis	the opacity of the culture	fresh broth	Continuously mixed and	An in vitro system simulating

						diluted cultures	various possible conditions in the urinary bladder: a glass vessel holding about 400 ml. with a tubular prolongation at the base, was maintained at 37° and provision made for stirring the contents. The basal tube was fixed in the light path of a Spekker photometer and the wedge set close to maximum occlusion with inoculated broth in the tube. A suitable filter was adapted to reset the instrument to the same values for each test. Fresh broth was added to the culture by a metering pump at rates simulating ureteric urine flow (0.5-1.0 ml./min.). "Micturition" leaving a residual volume of 30 ml.
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