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ORIGINAL PAPER

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Why are Foley catheters so vulnerable to encrustation and blockage by crystalline bacterial biofilm?

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Abstract Many patients undergoing long-term bladder catheterisation experience blockage and encrustation of their catheters. The problem stems from infection by urease producing bacteria, particularly *Proteus mirabilis*. Bacterial biofilms colonise the catheters, the activity of urease raises the pH and induces the deposition of calcium and magnesium phosphate crystals. In this study, a laboratory model of the catheterised bladder has been used to examine the early stages in the formation of the crystalline biofilms. The results show that initial cell adhesion is to the irregular surfaces surrounding the catheter eye-holes. Microcolonies form in depressions in these surfaces and spread to cover the entire surface of the rims around the eye-holes. Crystals then form around the bacterial populations and the biofilm starts to move down the lumenal surfaces of the catheters. The encrustation develops most extensively and generally blocks the catheter at or just below the eye-hole. There is a need to improve catheter design and manufacturing procedures for the eye-holes if the problems associated with the current devices are to be reduced.

Keywords Catheter encrustation · Bacterial biofilms · *Proteus mirabilis*

Introduction

Foley indwelling bladder catheters continue to be a major cause of infection, morbidity and mortality [18]. Patients undergoing long-term catheterisation will inevitably develop urinary tract infections. While these are for the most part asymptomatic, they induce a vulnerablity to a range of complications including urolithiasis, pyelonephritis and septicaemia [8, 15]. Many acute symptomatic episodes are triggered by encrustation and blockage of the catheter lumen. A study in Bristol (UK) of 457 catheterized patients being cared for in the community, for example, recorded 506 emergency referrals over a 6 month period, predominantly related to blocked catheters [7]. Several surveys have reported that this complication is experienced by up to 50% of patients undergoing long-term catheterisation [3, 11, 12].

As with the formation of infection-associated stones, catheter encrustation stems from the infection of the catheterised urinary tract by urease producing bacteria, particularly *Proteus mirabilis* [10, 16]. These bacterial cells colonise the catheter surfaces, forming biofilm communities embedded in a polysaccharide matrix. Their urease activity generates ammonia and elevates the pH of the urine and the biofilm. Under these conditions struvite (magnesium ammonium phosphate) and apatite (calcium phosphate) crystals are formed and become trapped in the exo-polymer matrix which surrounds the cells [5, 14]. The crystalline deposits can be hard, abrasive and can traumatise the bladder mucosa and urethra. As the biofilm develops, the lumen of the catheter becomes increasingly obstructed causing either incontinence from urine leaking around the catheter or painful retention of urine and distention of the bladder. Other manifestations include vesico-ureteral reflux, ascending infection of the urinary tract culminating in episodes of pyelonephritis, septicaemia and shock [8]. Clinical experience and in vitro studies have shown that all of the currently available types of catheters are susceptible to blockage by crystalline biofilms [2, 13].

In this study, we have used a laboratory model of the catheterised bladder to examine the development of crystalline biofilms on catheters. The aim was to understand why catheters are so vulnerable to this complication and establish if there are sites on the catheter surface that are particularly susceptible to encrustation.

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Materials and methods

The bladder model

The model of the catheterised bladder has been described previously [13]. In essence, it consists of a glass chamber maintained at 37°C by a water jacket. After sterilisation of the model by autoclaving, a size 14 or 16 catheter (Bard, Crawley, UK) was inserted aseptically into the chamber through a section of silicone tubing (a ''urethra'') attached to a glass outlet at its base. The catheter balloon was then inflated, securing the catheter in position and sealing the outlet from the ''bladder''. 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 chamber below the level of the catheter eyelet and then, as this volume is exceeded, urine flows via the eye-hole through the catheter and drainage tube to a collecting bag.

The artificial urine used in the experimental work was based on that devised by Griffith et al. [6]. It contained calcium chloride 0.49 g/l, magnesium chloride hexahydrate 0.65 g/l, sodium chloride 4.6 g/l, di-sodium sulphate 2.3 g/l, tri-sodium citrate dihydrate 0.65 g/l, di-sodium oxalate 0.02 g/l, potassium dihydrogen phosphate 2.8 g/l, potassium chloride 1.6 g/l, ammonium chloride 1.0 g/l, urea 25g/l, gelatine 5.0 g/l. The pH of the medium was adjusted to 6.1 and it was then sterilised by membrane filtration. Tryptone soya broth (Oxoid, Basingstoke, UK) was prepared separately, autoclaved and added to the sterile basal medium to a final concentration of 1.0 g/l.

The experimental protocol

Sets of models were assembled and the bladders primed with urine. The models were then inoculated with 10 ml of 4 h urine cultures of *P. mirabilis* B2 or NSM42, isolates from patients' encrusted catheters. After 1 h to allow the organisms to establish themselves in the model, the supply of urine was switched on. The models were run for 2–20 h before the urine supply was switched off, the catheters removed from the models, and examined by electron microscopy.

Electron microscopy

In some experiments, visual assessment of the encrustation was made on sets of catheters using low vacuum scanning electron microscopy. At the end of the incubation period, 1 cm cross-sections were cut at approximately 10 cm intervals along the lengths of the catheters, from just below the eye-holes to close to the drainage tube junction. They were viewed directly using the low vacuum setting of a JEOL 5200 SEM at 20kV. The low vacuum facility allows the direct examination of specimens that have not been fixed, stained or treated in any way.

In experiments to observe the early stages in the formation of bacterial biofilm on the catheters, after various incubation periods the flow of urine to the models was terminated and liquid contained in the bladder chamber replaced with approximately 100 ml 2.5% glutaraldehyde in 0.1 M Sörensen's sodium phosphate buffer, pH 8.0. The level of this fixative solution was adjusted such that the eyehole and tip of the catheter were completely submerged. Fixation was carried out for 30 min in situ to reduce the loss of biofilm during subsequent handling of the catheter. The fixative was then drained and the catheter removed from the bladder. Sections cut from the catheter were then transferred to 2.5% glutaraldehyde in 0.05 M sodium caodylate buffer, pH 8.0, containing 0.7% ruthenium hexaamine trichloride (RHT) for 18 h. RHT was employed to stabilise polyanionic components of the bacterial extracellular matrix. Surplus RHT was removed by two gentle rinses in buffer after which the samples were postfixed by immersion for 1 h in 1% osmium tetroxide. They were then dehydrated in an ascending series of ethanol solutions prior to immersion in two 15 min changes of hexamethyldisilazane (HMDS). The HMDS was allowed to evaporate away at room temperature in a fume hood. The air-dried samples were then mounted on aluminium specimen stubs with carbon cement (Leit C) and sputter-coated with gold in an Edwards S150A vacuum coater. They were examined in a Philips XL20 scanning electron microscope.

Results

In an initial set of experiments, all-silicone and hydrogel-coated latex catheters were run in the models for various times or until they blocked. The images obtained by low-vacuum SEM on the sequence of cross-sections from the all-silicone catheters after 16 h and 20 h incubation in the model are presented in Fig. 1. At 16 h, crystalline biofilm had formed around the eye-hole and balloon area but there was little sign of encrustation on the lumenal surfaces beyond the central portion of the catheter. After 20 h incubation and at the time of

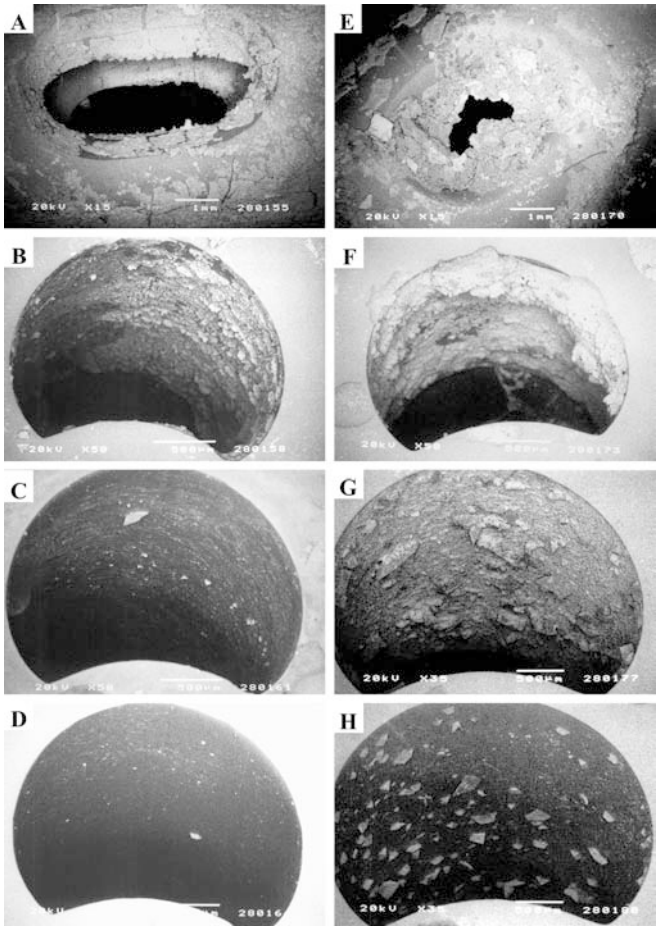

Fig. 1 The development of encrustation along all-silicone catheters. Scanning electron micrographs of size 16 all-silicone catheters removed from *Proteus mirabilis* infected models after 16 h (**A**–**D**) and 20 h (**E**–**H**) incubation. **A** and **E** are images of the eye-holes; **B** and **F** show cross-sections of catheters taken from just below the eye-hole region; **C** and **G** are from the mid-sections below the inflation balloon; **D** and **H** are from the drainage tube end of the catheters

blockage, while encrustation was visible along the full length of both types of catheter, it formed most extensively in the eye-hole region. These catheters eventually blocked at the eye-hole or the central channel just below the eye-hole after a mean time of 35 h. This profile of encrustation is similar to that generally observed in blocked catheters removed from patients (Fig. 2).

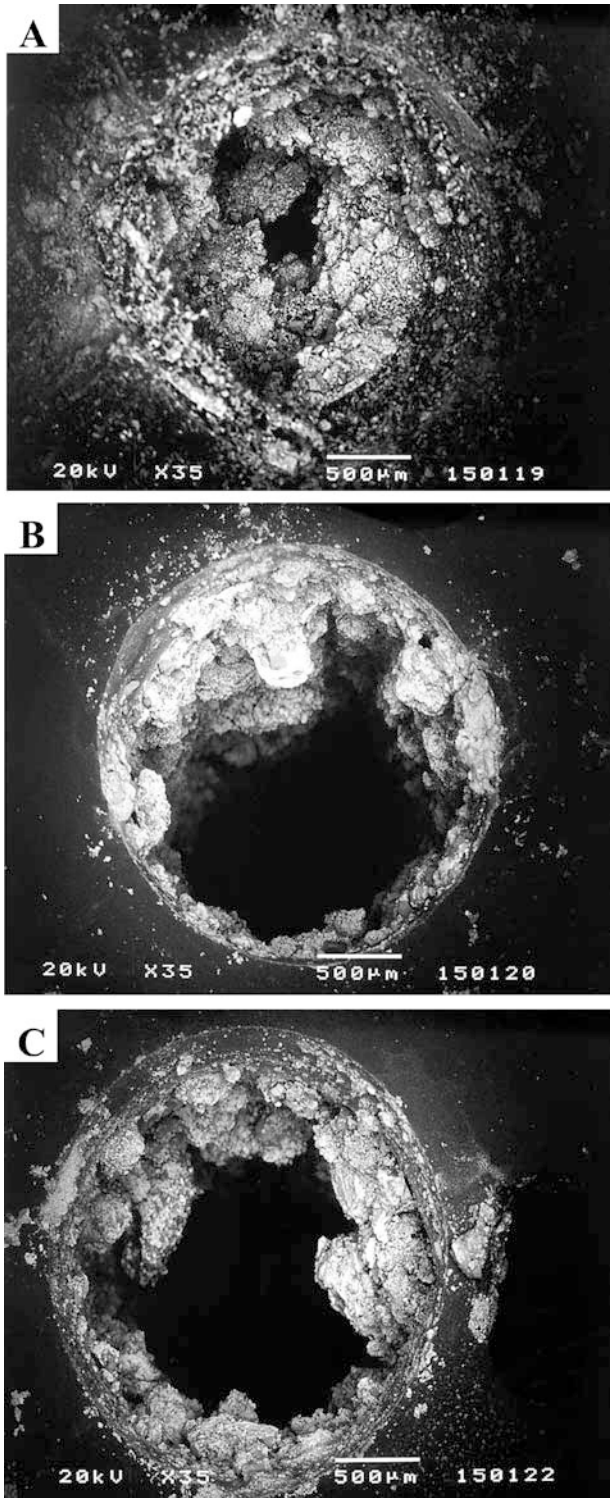

Fig. 2 Profile of encrustation on a catheter recovered from a patient. The catheter had been in situ for 14 days before it blocked. **A** is from just under the eye-hole; **B** is from the middle section of the catheter and **C** is from the drainage tube end

These observations suggest that the initiation sites for encrustation by crystalline *P. mirabilis* biofilm lie close to the catheter eyelets. Fresh unused catheters were therefore examined by SEM to determine the nature of the surfaces in this region. The images presented in Fig. 3 illustrate that the surfaces of the rims around the eye-holes, particularly of latex-based catheters, are rough and irregular.

To examine the hypothesis that the biofilm is laid down initially on these irregular surfaces around the eye-holes, hydrogel-coated latex catheters were examined after periods of incubation ranging from 2–20 h in the bladder model. After 2 h incubation there was little evidence of biofilm or crystalline material colonising the surfaces (Fig. 4). The irregular surface of the eye-hole region was visible and a number of isolated cells appear to have adhered in some of the crevices. Few cells seem to have colonised the main body of the catheter at this stage. After 4 h incubation, microcolonies of cells are clearly visible on the rim of the eyehole. These clumps of cells seem to have developed in depressions in the uneven surface (Fig. 5). At this stage there was no sign of biofilm developing in the central channel. At 6 h, encrustation becomes visible in the biofilm. The microcolonies on the eye-holes have developed further and amorphous crystalline material typical of calcium

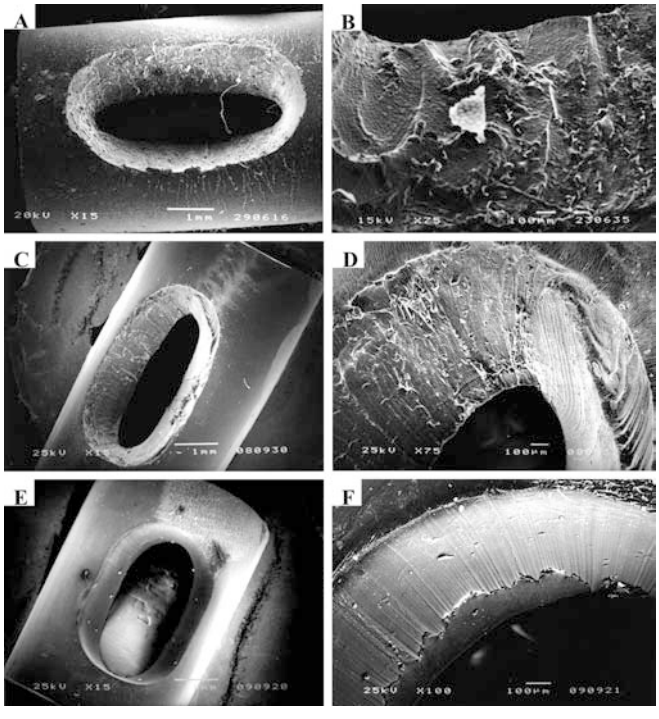

Fig. 3 The nature of the surfaces around the catheter eye-holes. Scanning electron micrographs of the surfaces around the eye-holes of un-used catheters are shown. **A** and **B** are of silicone-coated latex catheters; **C** and **D** are of hydrogel-coated latex catheters; **E** and **F** are of all-silicone catheters

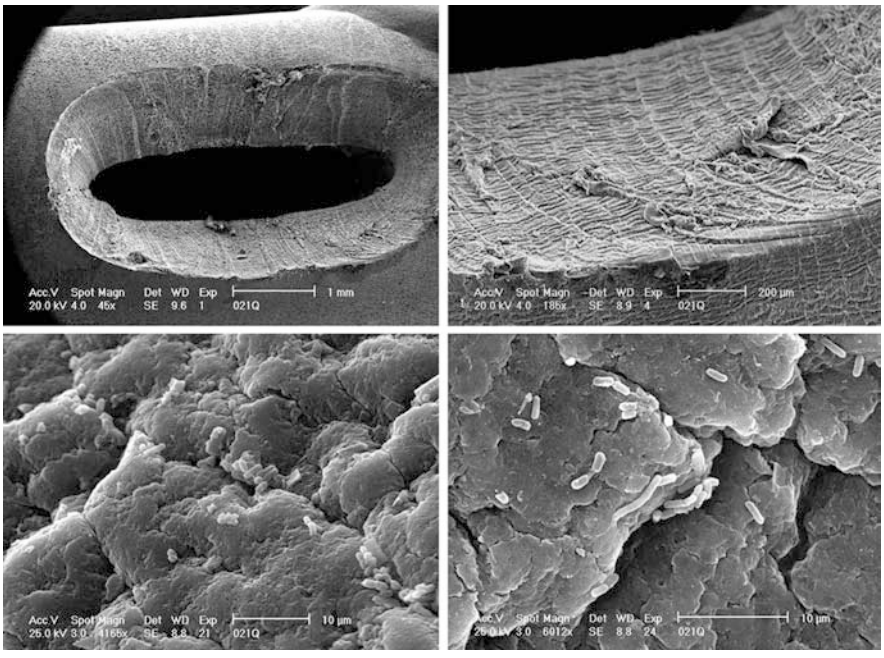

Fig. 4 The colonisation of a hydrogel-coated latex catheter by *P. mirabilis* cells after 2 h incubation in the model. The micrographs all show the surfaces of the rims of the eye-holes. *P. mirabilis* cells can be seen adhering in the crevices of the rough, un-even surface

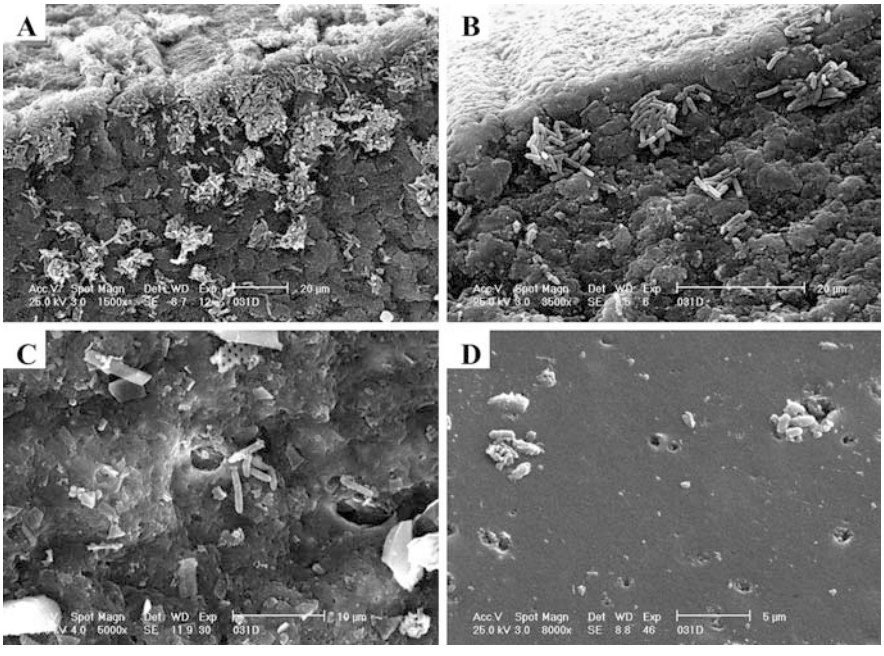

Fig. 5 Microcolony formation on a hydrogel-coated latex catheter by *P. mirabilis* biofilm after 4 h incubation in the model. **A** and **B** show the presence of microcolonies of cells developing in depressions in the un-even surface of the eye-hole rim; **C** was taken from the lumenal surface immediately below the balloon region of the catheter and **D** shows small numbers of cells adhering to imperfections in the lumenal surface at the drainage tube end of the catheter

apatite has appeared in association with these populations. There are signs that the biofilm is starting to move down the catheter lumen (Fig. 6). At 20 h the eye-hole is extensively encrusted and biofilm has formed below the balloon region (Fig. 7).

Discussion

The images presented in Figs. 1 and 2 show that encrustation develops most extensively at or just below the eye-hole region in both the experimental and patient's catheters. Several studies have shown that the lumenal surfaces of catheters, particularly latex-based catheters, are uneven [1, 4, 17]. The micrographs of the unused catheters presented in Fig. 3 demonstrate that the engineering techniques used in catheter manufacture produce particularly rough irregular surfaces on the rims of the eye-holes. It is also clear that the eye-holes, especially of latex-based catheters, are often just narrow slits (some 1 mm wide) in the tubing. In the case of all-silicone catheters, the eye-holes are larger and the surfaces smoother than those of the latex-based catheters. Striations and irregularities were

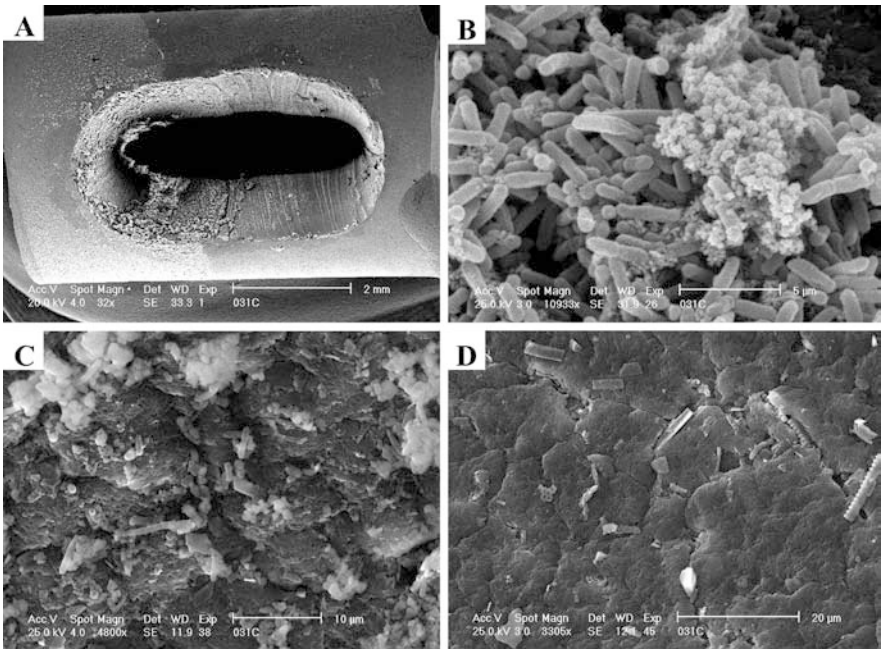

Fig. 6 The formation of a crystalline biofilm on a hydrogel-coated latex catheter by *P. mirabilis* biofilm after 6 h incubation in the model. **A** and **B** are images of the eye-hole where encrustation has formed and amorphous crystalline material can be seen associated with the developing bacterial biofilm; **C** shows some cells and crystalline material on the lumenal surface below the balloon; **D** shows that biofilm formation has not reached the drainage tube end of the catheter

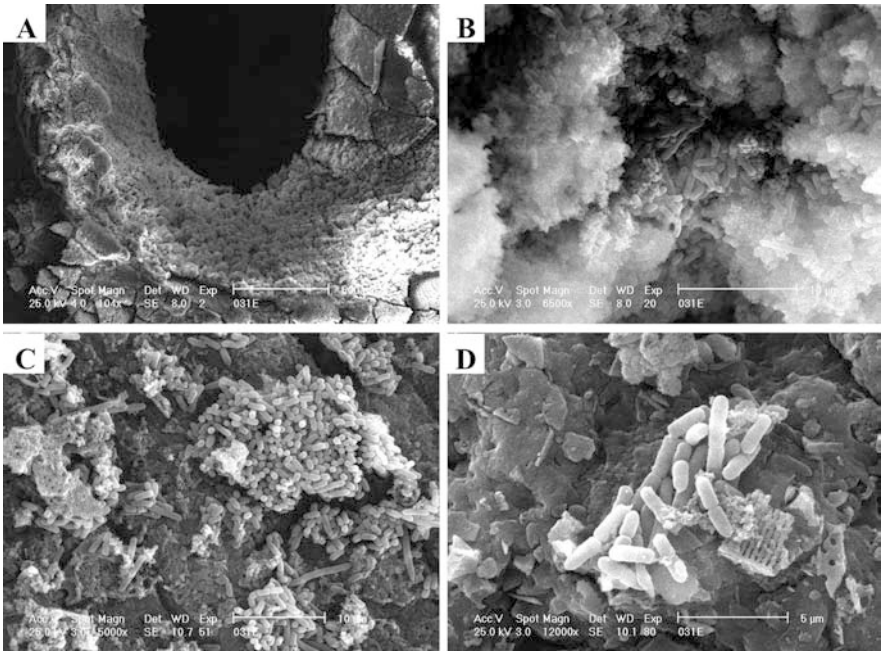

Fig. 7 The development of encrustation along the lumenal surface of a hydrogel-coated latex catheter by *P. mirabilis* after 20 h incubation in the model. **A** and **B** show extensive encrustation on the sculpted surfaces of the eye-holes; **C** shows biofilm formation on the lumenal surface 10 cm below the balloon; **D** shows a microcolony and some crystalline material forming on the lumenal surface of the catheter just above the drainage tube connector

commonly found however, on the surfaces around the eye-holes.

The images presented in Figs. 4, 5, 6 and 7 illustrate the development of biofilm over the first 20 h of exposure to *P. mirabilis* in urine. It is clear that initial cell adhesion is to the rough surfaces that surround the catheter eye-holes. Microcolonies form in depressions in these surfaces and then spread to cover the entire surface of the eye-hole rims. Crystalline material becomes associated with the bacterial populations at about 6 h and the biofilm starts to spread along the lumenal surfaces of the catheters. While the encrustation eventually forms along the full length of the catheter, it develops most extensively and generally blocks the lumen just below the eye-hole.

Most catheters in use today are manufactured from latex. The physical properties of this natural rubber material mean that the walls of the tubing have to be thick. Size 14 catheters have an external diameter of 4.7 mm. Cross-sections cut from these catheters reveal that the central channels, however, can be as narrow as 1.5 mm in diameter and are easily blocked (Fig. 8). Catheters manufactured from silicone have thinner walls than their latex counterparts. For example size 14

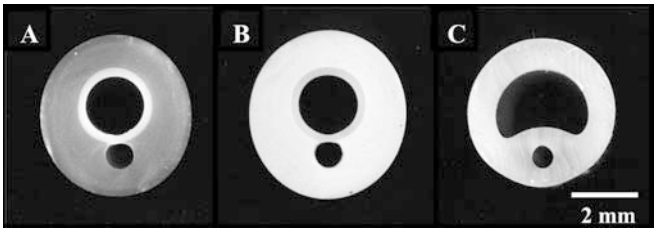

Fig. 8 Cross-sections of unused catheters. **A** is a silicone-coated latex catheter; **B** is a hydrogel-coated latex catheter; **C** is an all-silicone catheter

all-silicone catheters have internal diameters of around 2.5 mm. The central channels of the silicone catheters however are crescent shaped (Fig. 8) and the corners of the crescents are sites which often trap crystalline debris and initiate encrustation and blockage. Silicone surfaces are smoother than latex and the catheter eye-holes are larger and not so crudely formed. Surface striations and irregularities are found, however, particularly around the eye-holes (Fig. 3). Examination of the development of crystalline biofilm on all-silicone catheters showed a similar pattern to that observed on the hydrogel-coated latex catheters.

In 1988, Calvin Kunin posed the question "Can we build a better urinary catheter?" [9]. He made the point that in an era when significant technological advances were being made on all fronts, we should be able to solve the simple problem of draining urine from the bladder without producing infections and all the associated complications. Kunin commented that catheter manufacturers have been reluctant to invest in research and development. Little has changed since this call for action. The design of the urinary catheters in current use is driven not by the requirements for effective patient care but by the manufacturer's requirements for low-cost and convenient production processes.

As a result, the catheters available today with their roughly engineered, irregular surfaces around the eye-holes and narrow central channels are readily colonised and blocked by crystalline bacterial biofilm. The development of catheters with larger internal diameters and smoother surfaces especially around the eye-holes, would substantially reduce the problems associated with the current devices. Building a better catheter is surely possible. The morbidity associated with the currently available devices undermines the quality of life for many individuals and is no longer acceptable. The medical device industry must be persuaded to take up the challenge.

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