Since the first long-term silicone stent was created in 1967, the materials used and the design of the stents were continuously modified. The requirements to be met are the biocompatibility of the stent, retaining of the position and a certain draining of urine between the renal pelvis and the bladder. The stent designs currently used are the „double pigtail“, the „double J“ as well as variations in between.

**Indications and Complications**

The indications for the use of an ureteric stent are to relieve or prevent obstruction of the ureter
• by stone, tumour or stricture
• post ureteric surgery
• prior to ESWL
• ureteric perforation
• ureteric fistula

Complications of long-term stents include stent migration, reflux, encrustation and infections. Patients suffer from urination frequency, lower abdominal pain, dysuria, haematuria and loin pain. All these symptoms are resolved immediately on removal of the stent.

**Demands Upon the Stent Material**

The ideal stent material has to be totally biocompatible without provoking any biological response. Biomaterials currently used often consist of synthetic polymers. Alternatively they can be coated and subsequently show more advantageous properties. Hydrogel-coated stents, especially, allow easy insertion and reduce mechanical irritations, which are of great advantage for the patient’s comfort. In human urine, however, this material increases the amount of encrustation and infection (1). On the other hand a phosphorylcholine (PC) coating reduces patient comfort of encrustation surface friction.

**Table 1: Properties of different coating materials (according to S. J. Wood)**

<table>
<thead>
<tr>
<th>Material</th>
<th>Effect</th>
<th>Advantage</th>
<th>Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogels</td>
<td>Water drawn into the coating reduces surface friction</td>
<td>Easier of insertion patient comfort</td>
<td>May increase risk of encrustation</td>
</tr>
<tr>
<td>Silver</td>
<td>Prevents adherence and growth of pseudomonas on latex coated material</td>
<td>Reduces infection and encrustation</td>
<td>Leaching of coating</td>
</tr>
<tr>
<td>Heparin</td>
<td>Decreases bacterial adherence to surface of catheter</td>
<td>Reduces infection and encrustation</td>
<td>Leaching of coating</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Ciprofloxacin coating – reduces biofilm formation</td>
<td>Reduces infection and encrustation</td>
<td>Confirming results</td>
</tr>
<tr>
<td>Phosphorylcholine</td>
<td>Reduces protein and bacterial adhesion</td>
<td>Reduces infection and encrustation</td>
<td>Short-term potential only</td>
</tr>
</tbody>
</table>

| What is Phosphorylcholine (PC)? |

PC is found in the membrane of all living cells. The outer membrane lipid layer of human erythrocytes consists about 88% of PC containing lipids (picture 1). This high quantity is responsible for the hemocompatibility of the red blood cells and prevents blood clotting. To get a synthetic biomaterial with similar properties, lipophilic monomers and the PC monomers were combined together with other co-monomers to a polymer capable of coating the surface of a medical device. These polymers effectively mimic the surface chemistry of the body’s own natural membrane (picture 2), thereby minimizing adverse interactions with body fluids (blood, tear film and urine). PC containing materials have been used in cardiological (stents and vascular grafts) and ophthalmic (intraocular lenses, contact lenses, contact lens solutions) applications for many years. They have shown to improve the biocompatibilities in contact with blood and tear-films because they are highly effective in preventing thrombus formation in blood contacting applications and the deposition of proteins and lipids onto contact lenses.

**Properties of Phosphorylcholine (PC)**

The main property of PC is to keep the surface electrically neutral over a wide pH range and to preserve a hydrophilic nature. Accordingly devices with PC have a permanent water layer on the surface. That (among other things) makes it very difficult for biomolecules to displace the water and bind to the surface. Normally the bacteria adhere and fre-
quently will become established in a biofilm, which is a complex of micro- and macroorganisms embedded in an organic polymer matrix. Biofilms lead to the deposition of organic salts (struvite and hydroxyapatite). The resulting encrustation can block the ureteric catheters or stents, inducing leakage or retention of urine. Data from a clinical study show that much less biofilm was observed on the PC coated ureteric stents, implanted for three months (70% coverage on uncoated stents versus 30% on PC coated stents, picture 3) (3). Another laboratory test in an accepted urine model also shows a 90% reduction in E. coli adhesion on a range of PC coated surfaces after 18 hours of incubation. The data of some in vitro studies show that PC treated materials reduce the adsorption of proteins and the adhesion of bacteria in urological devices as well as the risk of encrustation (3, 4, 5) and urinary tract infection. This latter infection constitutes the most common infection acquired within the hospital setting.

Literature
(2) S. J. Wood: Ureteric stents - materials and design, Urology News Online, 3/3
(5) S. J. Wood et al.: Phosphorylcholine: a coating that is hydrophilic but does not increase encrustation, J. Endourology, (1998), 12, 6-20

PC coating of ureteric stents reduces the rate of UTI

A Contribution to the Management of Nosocomial Infections

During the „First International Workshop on Phosphorylcholine Stents in Urology“ in Starnberg, Dr. Ulf Salzmann from the University of Munich presented a complete summary of former studies regarding the role and function of phosphorylcholine in ureteric stenting. Common complications of ureteric stents were urinary tract infections. Up to 31% of the patients with ureteric stents suffered from these infections, 16-19% of the patients experienced flank pain and often needed painkillers. As much as 34% of the patients suffered an obstruction, in up to 8% a dislocation and haematuria was experienced by up to 64%. Almost 68% of the stents were infected with micro-organisms. Pseudomonas aeruginosa was the most common pathogen isolated.

Reasons for the complications of ureteric stents

There are two main problems that account for most of the common complications of ureteric stents:
- Bacterial adhesion and formation of a biofilm
  Bacteria adhere to biomaterials within hours. They do this by aggregating and encasing in a protective mucoid glycokalix. This biofilm is resistant to host defences and protects the micro-organisms from antimicrobial agents. It therefore makes a perfect reservoir for bacteria to live in.
• Encrustation

By producing urease, some bacteria induce crystallization processes in ureteric stents: urease splits urea in ammonia and carbon dioxide, increasing the pH level. That leads to a precipitation of organic salts, especially ammonium magnesium phosphate (struvite) and calcium phosphate (hydroxyapatite). All these processes increase the incidence of urinary tract infections and lower the patients quality of life.

PC coating helps to prevent complications

To prevent these above mentioned complications, the phosphorylcholine (PC) coating was developed. The advantage of PC is the nearly perfect mimicry of the surface chemistry of natural cell membranes. This makes it possible for medical devices to become biocompatible. Cardiologic studies can also demonstrate the effect of PC coating: the platelet activity decreased in PC coated stents and endothelial cells were not activated. In uncoated stents, cardiac endothelia was activated, along with an unchanged platelet activity (picture 4). In addition the risk of infection was reduced.

Some in vitro studies have shown the effects PC coating has in urology: In an incubation test with E. coli, researchers have shown, that there is less bacterial adhesion in PC coated surface, than in uncoated (picture 5). In addition, it has been shown, that Proteus mirabilis, Pseudomonas aeruginosa and Staphylococcus epidermidis do not adhere as strongly to coated samples, as they do to uncoated controls. Furthermore, the encrustation could also be significantly reduced in PC coated catheters (picture 6).

A clinical investigation of 45 patients with PC coated ureteric stents (implantation 3.9-12.8 weeks) only led to very few complications:
- obstruction in 3 patients (6,6% versus 34% in uncoated stents)
- dislocation of stents in 2 cases (4,4% versus 8%)
- pain in 6 cases (13,3% versus 19%)
- large portions of encrustation in 13%
- UTI (infection) in 6 patients (13,1% versus 31%)

Conclusion

In vitro studies in urine have shown, that PC coating of materials used for urological devices leads to a reduction of bacterial adhesion, fewer encrustation and less protein adhesion. In addition, PC coating of ureteric stents improves the patients quality of life and is therefore of great clinical importance.

Use of ureteric stents: PC coating improves the quality of life

Initial Findings in the Use of Phosphorylcholine Coated Double-J-Catheters

A small clinical investigations performed retrospectively at the university hospital of Jena could also show advantages of PC coated stents for patients with longterm ureteric stent therapy:

Dr. Volker Janitzky Ph.D., currently urology Heidenau, examined 10 patients with a malignant obstruction of the ureter and chronic UTI, which were referred to his hospital clinic. His results were presented by Dr. Tor-
sten Weinrich during the workshop in Starnberg. All patients had previously been treated with ureteral stents for at least 3 months.

They compared PC coated to hydrogel-coated indwelling ureteric stents. The stents were replaced every 4-8 weeks. The team examined the internal stent encrustation (endoscopic), the irritation of the bladder mucosa (according to a patient questionnaire) as well as any occurring urinary tract infections (pathological results in the urine diagnostic).

**The study came up with striking results:**

In spite of the progressing malignant disease which all ten patients had, stone formation and encrustation could be reduced, bladder discomfort relieved and the frequency and severity of UTI could be cut down in nearly all patients (picture 7, 8, 9).

Normally the long term use of common ureteric stents, especially in patients with malignant diseases, is limited due to bladder and kidney discomfort. Most chronic UTI become resistant to antibiotics and are very annoying to the patients concerned. The reason for these UTI to become chronic may be a biofilm formation in the ureteric stent. This biofilm - consisting of organic and anorganic material - "protects" the bacteria. Bacteria become less accessible to antibiotics and the UTIs develop antibiotic resistance.

**Conclusion**

The clinical improvement achieved by PC coated stents was impressive. The quality of life was increased and the co-medication could be reduced. Since UTI in patients with commonly used indwelling stents is often resistant to antibiotic therapy, PC coated stents should be considered for use for the palliative urinary drainage.

**Comparison between PC coated and conventional stents**

**A Study on Safety and Performance**

The first experiences with PC coated stents were made 1999 in an open multi-centre study in the UK. The main goal of the study was to examine the safety and performance of PC coated stents. 28 uncoated and 44 PC coated stents were examined, as well as 19 patients who had both, reports Dr. Graham Watson from the Esperance Hospital, Eastbourne, UK. Whether encrustation occurred was determined macroscopically, on different sections of the stent as well as the biofilm was analysed via electron microscopy.

**Better performance of PC coated stents**

In comparison to the uncoated stents the grade of encrustation was far lower in the PC coated stents. In addition a biofilm occurred twice as frequently in uncoated stents as in PC coated stents (76% versus 36%). The results of the patients who received both stents simultaneously were especially impressive. Here the biofilm rate was only 26% in the PC coated stents compared to 74% in the uncoated stents.

The authors conclude, that PC coated stents achieved better results in all measured parameters in comparison to the uncoated stents.

**Picture 8: Bladder mucosa irritation comparing hydrogel coated versus PC coated ureteric stents (n=10)**

- never = no irritation
- seldom = bladder sensation (foreign body) up to twice a week
- frequently = occasional sensation of foreign body (especially after voiding)
- mostly = permanent sensation of foreign body, required spasmoanalgetic drugs

**Picture 9: UTI-rate comparing hydrogel coated versus PC coated ureteric stents (n=10)**

- never = no bacteria, no symptoms
- rarely = less than once per month
- recurrent = up to two pathological results per month
- permanent = urine microscopy: >10⁵ bacteria/ml, resistant to antibiotic therapy
Development of a New Outcome Measure

Side effects of a ureteric stent therapy affect the quality of life of the patients. To evaluate the effects of stents with a reliable and valid instrument the „Ureteric Stent Symptoms Questionnaire“ (USSQ) was developed in UK. This study compared the QoL of patients with or post stents, stone patients without stents, patients with LUTS (Lower Urinary Tract Symptoms) and healthy controls.

Dr. Anthony Timoney from the Southmead Hospital in Bristol, UK, presented the USSQ (picture 10) in Starnberg.

Final draft of the questionnaire was developed by pilot testing to clear ambiguities and to delete redundant items. The response categories based on interval scale: not at all / occasionally / sometimes / most of times / all times.

The final draft of the USSQ includes 38 items in 6 sections:
- Urinary symptoms: storage, voiding, incontinence, haematuria (11 items)
- Stent related pain affecting general health (8 items)
- General health: difficulty in usual activities and mobility (6 items)
- Reduced work performance (5 items)
- Sexual matters (3 items)
- Additional problems (5 items)

The USSQ demonstrated a good construct validity and a high sensitivity. Significant changes (p<0.005) across all domains with and without stent in situ. The reliability shows a high degree of internal consistency and test-retest reliability for all sections. The sum of each item score is very simple, high scores indicate worse outcome. Some results are shown in picture 12 and 13.

The USSQ is expected to be a useful outcome measure when comparing different types of stents.
Assessment of Quality of Life in Clinical Study Protocols

In order to compare the impact different stents have on patients’ quality of life an efficient questionnaire has to be realized. Dr. Silke Schmidt from the University Hospital of Hamburg gave some recommendations.

The quality of life of patients has become an important and widely accepted measure of the efficacy of a medicine or a treatment in clinical trials. The scope of definition usually depends on the reason why subjective health parameters are being assessed, the particular concerns of patients, clinicians and researchers and the specific setting the concept is used in. The term health-related quality of life (HRQOL) is used, because many different valued aspects of life exist, including income, environmental aspects etc. These are not necessarily related to the health of an individual. The HRQOL is the most interesting parameter for clinicians, keeping in mind that when a patient experiences disease, almost all aspects of life become health-related. The HRQOL is usually considered to be a multidimensional construct which includes the physical, emotional, mental, social and behavioural components of both well-being and function, as perceived by the patients and/or by observers. There are different arguments why either generic or disease specific measures should be used. While generic health status measures can provide an effective overall assessment of functional status and general quality of life in a number of different domains, such measures may not provide sufficient detail to characterize the particular ways in which different treatments affect different aspects of the disease process and the subjective experience of the patient. In order to be sure to capture the relevant aspects of quality of life, it may be necessary to include both more generic and more disease-specific measures. This strategy enables us to include other populations when using the generic measures as well as to include other treatment modalities with the same population when using the disease-specific instrument.

However the term disease-specific QoL not only covers a large range of health conditions, its meaning also varies, depending on the research context. In clinical trials measures are needed which are sensitive to occurring changes and thus may characterize the effect of a new intervention. For such measures the term intervention-specific instrument might be more appropriate. When evaluating the QoL of patients with urologic stents both disease-specific and intervention-specific issues of QoL assessment are addressed.

Data Collection

An elementary conclusion of QoL evaluation studies is that it is impossible to fill in missing data by collecting data retrospectively. Therefore one of the most crucial elements of QoL research is that the logistics of data collection have to be well organised. There are a number of recommendations to improve the quality of data and to enhance compliance in multicenter clinical trials. The EORTC group has proposed the following steps in order to help the QoL study to succeed:

1. Identify one person in each centre who is responsible for the logistics of data collection.
2. Ensure that the protocol is available to those persons who collect data.
3. Provide regular feedback on the progress of the study with respect to the evaluation of QoL.
4. Provide detailed explanations of study objectives, the importance of QoL evaluation and instructions for data-collection to both the person responsible at each centre as well as the patient.
5. Collect questionnaires when completed, check for omissions, check for incorrectly answered questions, and check for inconsistent answers.

Translation issues

There are different ways to convey a translation process in the development of QoL measures. In general we recommend two translations of the original instrument in advance, done by two independent translators. The translators then have to agree on a common version of the items. This agreed-upon version is quality-rated according to the conceptual equivalence, colloquial language and clarity by a set of raters. Finally an English retranslation should be performed which is compared to the original version by one of the authors. A pilot study should be conducted in the target nation in order to evaluate the comprehensibility, feasibility and acceptability of the instrument and in order to test it psychometrically.

Conclusions

The process of choosing (or developing), translating and implementing an existing QoL instrument is a complex task involving a thoroughly planned study design. There are some obvious issues which have to be addressed in studies that plan to evaluate a treatment with a specific technology. Though the effect of the intervention modalities on the QoL of patients is supposed to be beneficial, specific hypotheses of the effectiveness of treatment have to be formulated. The most crucial aspects which have to be addressed in a study testing the effects of specific stents are (a) whether it is appropriate to investigate the large variety of conditions which call for stents, (b) whether it is appropriate to mix males and females in a study involving symptoms of continence and sexual dysfunction and (c) how to choose the right study design.

Timoney et al. have addressed these issues and showed some promising results on treatment specific aspects of QoL in this population. To summarize it has to be kept in mind that QoL reflects the views and perspectives of the patient who undergoes this specific treatment and that any conception should always consider these views.