

The In-Flow™

Device for Women: Clinical and Scientific Background





inflow™

Advanced Technology for More Natural Voiding

- How do you get urine out of the bladder without causing infection?
 - 100,000,000 urinary catheters are used globally every year, but they cause infections that kill tens of thousands and cost \$billions in medical care
- The In-Flow has been shown to have by far the lowest infection rate of any indwelling device for bladder drainage
 - **Active** stent-like device replaces **passive** urinary catheters
- Widespread use of the In-Flow has the potential to save lives, lower healthcare costs and improve quality of life for many women

This Presentation

- In-Flow Overview
- Indication and Patient Selection
- Clinical Evidence and Issues
- Discussion of UTI Mechanisms
- Status, Summary and Contact Info

Urinary Catheters

- Bladder drainage is typically done with urinary catheters, which may be the simplest of medical devices, often consisting of nothing more than a tube
- Two types of urinary catheters are most often used for women
 - Intermittent catheters, wherein the patient must insert a tube into their urethra 4-8 times per day as required for voiding
 - Indwelling (Foley) catheters, wherein the patient is literally tied to a bag of their own urine
- Although urinary catheters are among the most commonly used medical devices, they cause serious problems, notably:
 - Low quality of life, and
 - High rates of urinary tract infection (UTI)

How Serious is the Infection Problem?

- UTIs due to urinary catheters result in as many as 32,000 deaths, cost \$1.85 Billion in direct medical expenses annually*
 - Deaths and expenses are expected to increase with emergence of resistant bacteria (“super-bugs”)
- The most commonly used type of catheter (Foley) has 5% risk of UTI per day
 - Virtually 100% in 30 days



*CDC estimates for U.S. hospitals alone (2002)

The In-Flow™ Solution

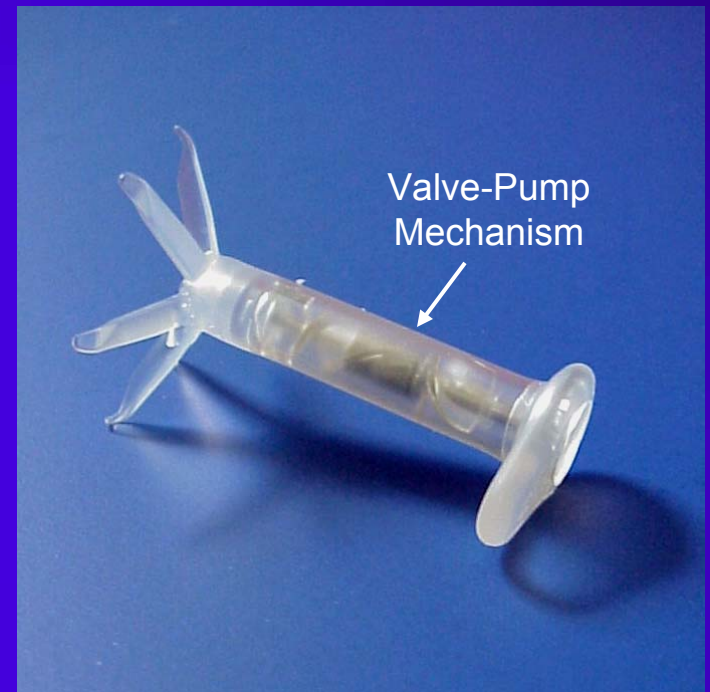


The In-Flow Device

Activator (Remote Control)

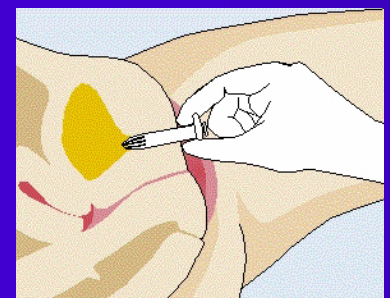
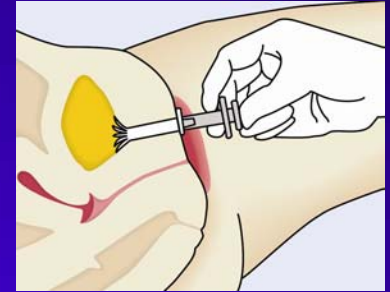
What is the In-Flow?

- Intraurethral device for female bladder drainage (29 day use)
 - **Active** stent-like device replaces **passive** urinary catheters
- The only device with a pump
 - Internal pump provides periodic, forceful evacuation of urine, full bladder emptying
- The result of extensive development
 - \$100M previously invested by Medtronic, J&J and Influence



How Does the In-Flow Work?

- Following device sizing, In-Flow is inserted using disposable introducer
- To void, the patient or her caregiver holds remote control over lower pelvic area and presses a button
 - This activates the internal turbine pump, which spins at 10,000 rpm and quickly drains the bladder
- When the button is released, a valve is engaged, blocking further urine flow
- Device can be easily and safely removed at any time by simply grasping and pulling forward



Patient Benefits

- **Lowest** UTI rate by far for any indwelling device
 - Same or better than for intermittent catheters
- **Highest** quality-of-life of any means of bladder drainage
 - Eliminates need to self-cath 4-8 times daily
 - Eliminates tubes, drainage bags
 - Improves self-image, hygiene
 - Allows use of a toilet
- **In-Flow** increases self-reliance, personal dignity



Transformational Technology

“It can simply, yet absolutely transform the quality of individuals’ lives.”

- Brother of IDE patient

“...the device has been an unqualified success. It is difficult to put into words the effect that (In-Flow) has had on (my daughter’s) life.”

- Father of IDE patient



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Indication

- The In-Flow device is a **replaceable urinary prosthesis** intended to normalize toileting in women with chronic voiding dysfunction
 - A prosthetic device compensates for a specific physiologic deficiency
 - The In-Flow compensates for two physiologic deficiencies
 - Its **valve** simulates normal **sphincter** function by closing at the control of the patient to block the flow of urine
 - Its **pump** simulates normal **bladder** function by fully evacuating urine even in patients who cannot generate bladder pressure, i.e. with hypotonic/acontractile (atonic) bladder



Atonic Bladder

- Inability to spontaneously urinate due to neurologic disease or injury
 - Typically secondary to a life-altering condition such as spina bifida, multiple sclerosis, stroke, spinal cord injury, or diabetic neuropathies
 - Complications include urinary retention, bacterial colonization, recurrent UTIs, bladder stones, impaired renal function
- Incurable condition with few clinical alternatives



Huge Need, but Limited Alternatives

The inability to void is one of life's most discouraging circumstances

- Medtronic InterStim has recently shown positive results for certain patients with non-obstructive retention, but involves surgery
 - Not appropriate for many patients, particularly given the compromised medical condition of many with atonic bladder
- Currently, the vast majority of atonic bladder patients use urinary catheters, despite high UTI rate and/or low quality of life
- The In-Flow device represents a conservative middle course
 - Well suited to majority of atonic bladder patients

Current Standard of Care

- CIC is the standard of care for long term bladder drainage
 - Known to have vastly superior UTI rate than Foleys
- However, many patients lack the necessary manual, visual or cognitive ability to perform the procedure reliably
- Others simply do not want to self-catheterize
 - Can be a time-consuming, malodorous procedure
 - Some find repeated touching of genital area to be distressing
 - Elderly patients in particular often opt for Foleys despite their well known problems



Clean Intermittent Catheterization

Who Should Use the In-Flow?

- As intended, its ability to work effectively even for patients who cannot generate bladder pressure makes the In-Flow particularly beneficial to women with atonic bladder
- Its unique characteristics as a urinary prosthesis also provide important advantages compared to urinary catheters
 - When used as an alternative to CIC, the IDE showed that In-Flow provides equivalent safety and effectiveness, but with improved quality of life (QoL), including the ability to void in a toilet
 - When used as an alternative to indwelling (Foley) catheters, the In-Flow provides vastly superior safety and effectiveness, as well as improved QoL

Patient Care

- As an indwelling device, the In-Flow can be used by a number of patients who would otherwise use indwelling (Foley) catheters
- When used by non-ambulatory patients (confined to bed or wheelchairs), additional assistive devices may be required:



Feminal
Female Urinal



Whiz Freedom
Female Voiding Aid

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IDE G970029 ($n=273$)

- Compared the In-Flow to clean intermittent catheterization (CIC) in population limited to women with atonic bladder
 - CIC is the current standard of care for long-term bladder drainage and is known to have lowest UTI rate of any urinary catheter

- The In-Flow device clearly met its clinical endpoints:
 1. Primary Endpoint: Post-void residuals (PVRs) - CIC and the In-Flow were equivalent in their ability to fully empty the bladder
 2. Secondary Endpoint: Quality of life per Wagner I-QOL - Scores were 50% higher for In-Flow than for CIC (clinically & statistically significant)
 3. Comparative safety: UTI rates were equivalent, although In-Flow is *indwelling* and CIC is *intermittent* (breakthrough technology)
 - Discomfort was higher with the In-Flow

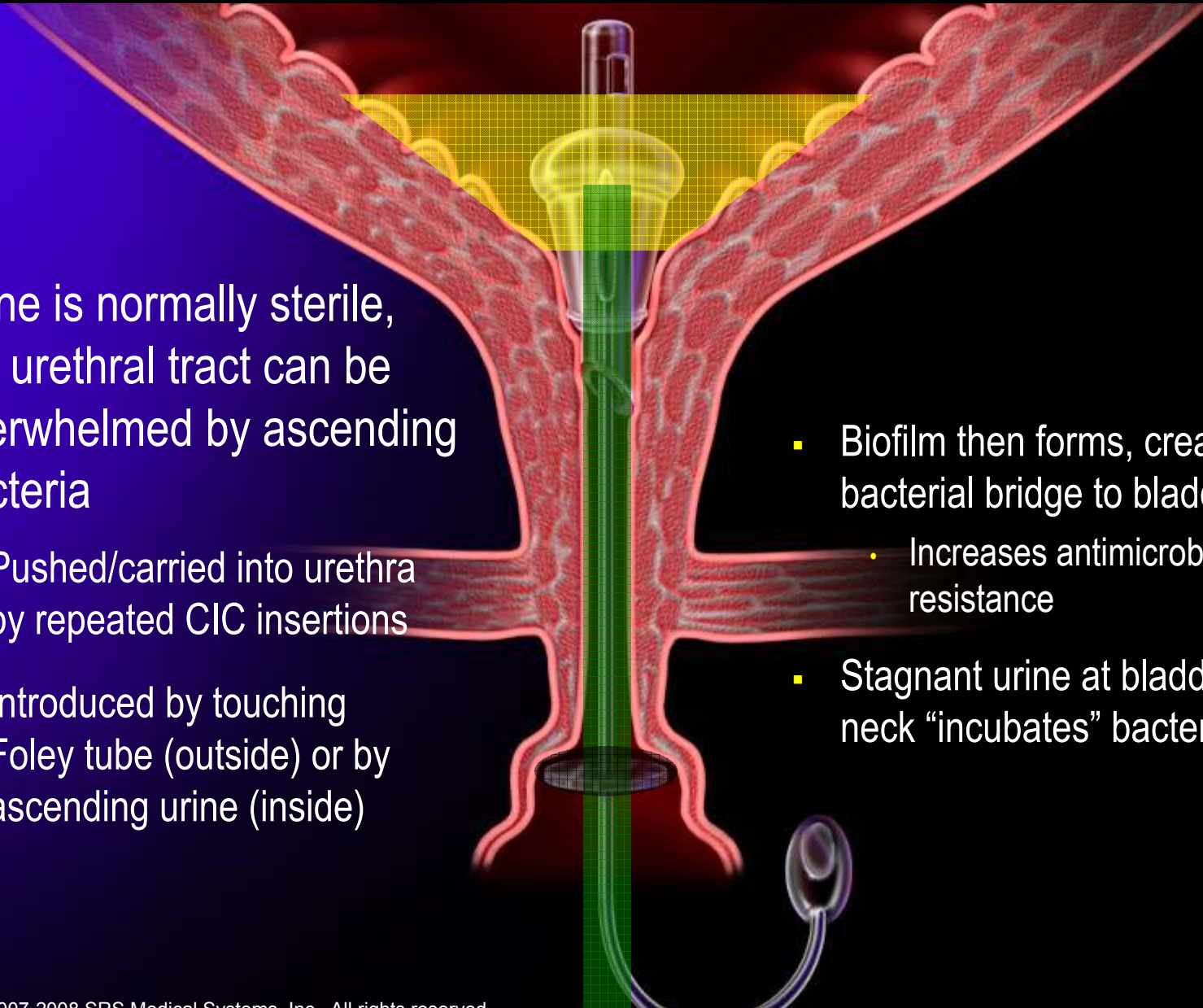
Long-term Clinical Studies

- Four peer-reviewed clinical studies (total $n=222$), report similar findings to IDE
 - No serious or lasting adverse events were reported in any study
- Specific findings from the two long-term studies include:
 - In a one-year study of 20 acontractile (atonic) bladder patients, Lynch et al reported 80% improvement in quality of life (QoL) and no negative tissue changes: “This study shows that the Inflow device provides an effective method of bladder drainage, with few side-effects and significant improvement in QoL.”
 - In an earlier study of 40 patients with voiding dysfunction in which 21 patients were followed for more than a year with a mean follow-up time of 24.6 months, Madjar et al concluded that, although dropout was a problem (due largely to discomfort): “Women who continue treatment for a prolonged time are satisfied with the device use.” In fact, “All patients were satisfied with the device and preferred it to previous treatment modalities used.”
- In a four-year follow-on to the IDE study ($n=15$), Tu reported unprecedentedly low UTI rates after 4-6 months and for years thereafter

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Catheter-related UTI Mechanisms

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- Urine is normally sterile, but urethral tract can be overwhelmed by ascending bacteria
 - Pushed/carried into urethra by repeated CIC insertions
 - Introduced by touching Foley tube (outside) or by ascending urine (inside)
 - Biofilm then forms, creating a bacterial bridge to bladder
 - Increases antimicrobial resistance
 - Stagnant urine at bladder neck “incubates” bacteria

Anti-Infection Efforts to Date

- Catheter manufacturers have applied bactericidal coatings to outer catheter body
 - Intended to retard biofilms, prevent bacterial bridge to bladder neck
- Effects are measurable, but not powerful
 - Studies re silver alloy and antibiotic impregnated catheters show reduced rate of asymptomatic bacteriuria for about 1 week
 - Since studies did not track clinical symptoms of UTI, actual effectiveness is uncertain



How Does the Body Protect Itself?

➤ Voiding normally flushes ascending bacteria

- Urethral inserts impede this flush mechanism
- Urine no longer contacts urethral tissue

Why is the In-Flow Protective?

- **Intraurethral design minimizes introduction of bacteria**
 - Sterile device is inserted aseptically only once every 28 days
 - No extracorporeal tubes minimizes hand contact, eliminates ascending urine
- **Internal pump ensures full emptying of the bladder**
 - Eliminates stagnant pool of urine that can incubate bacteria
- **Internal valve/pump mimics normal voiding functions**
 - Valve allows fill-void cycling, maintaining bladder tone
 - Pump provides turbulent evacuation of urine, preventing encrustation
 - Combination of fill-void cycling and turbulent evacuation mimics “flush mechanism” the body normally uses to prevent bacterial buildup (and compensates for biofilm?)

Is Turbulent Evacuation the Key?

- An in vitro study by Stickler and the Microbiology Research Group at Cardiff UK reported:
 - “Under conditions that simulated a heavy infection of *P. mirabilis*, where a conventional Foley catheter blocked with crystalline biofilm after 25.7 hours, the *In-Flow* device drained the bladder for at least 9 days at which point the experiment was stopped. (Its) central lumen appeared to be essentially clear.”



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Status

- The In-Flow has demonstrated a unique and important effect: the ability of an indwelling device to have long-term UTI resistance
 - Achieved primarily by mechanical means and using stable patient-contacting material (silicone without any deposition)
 - Also shown to improve quality of life by 50-80% compared to CIC
- CE-marked, available in Europe
 - Not yet actively marketed, but granted reimbursement in Germany
- FDA submission planned Q4-09



Summary



- Urinary catheters cause infections
 - These infections kill tens of thousands and cost \$billions in medical care
- The In-Flow has been shown to have by far the lowest infection rate of any indwelling device for bladder drainage
 - **Active** stent-like device replaces **passive** urinary catheters
- Widespread use of the In-Flow has the potential to save lives, lower healthcare costs and improve quality of life for many women

CE 0459

The In-Flow device conforms to Council Directive 93/42/EEC and bears the CE mark.

Authorized European Representative:

mtm medical | technology | marketing

www.mtm-med.com

CAUTION: Not cleared by the FDA for sale in the USA. Investigational device. Limited by US law to investigational use.

U.S. Patent Nos. 5,762,599 and 6,417,750 and related patents worldwide. Additional patents pending. In-Flow is a trademark of SRS Medical Systems, Inc.

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