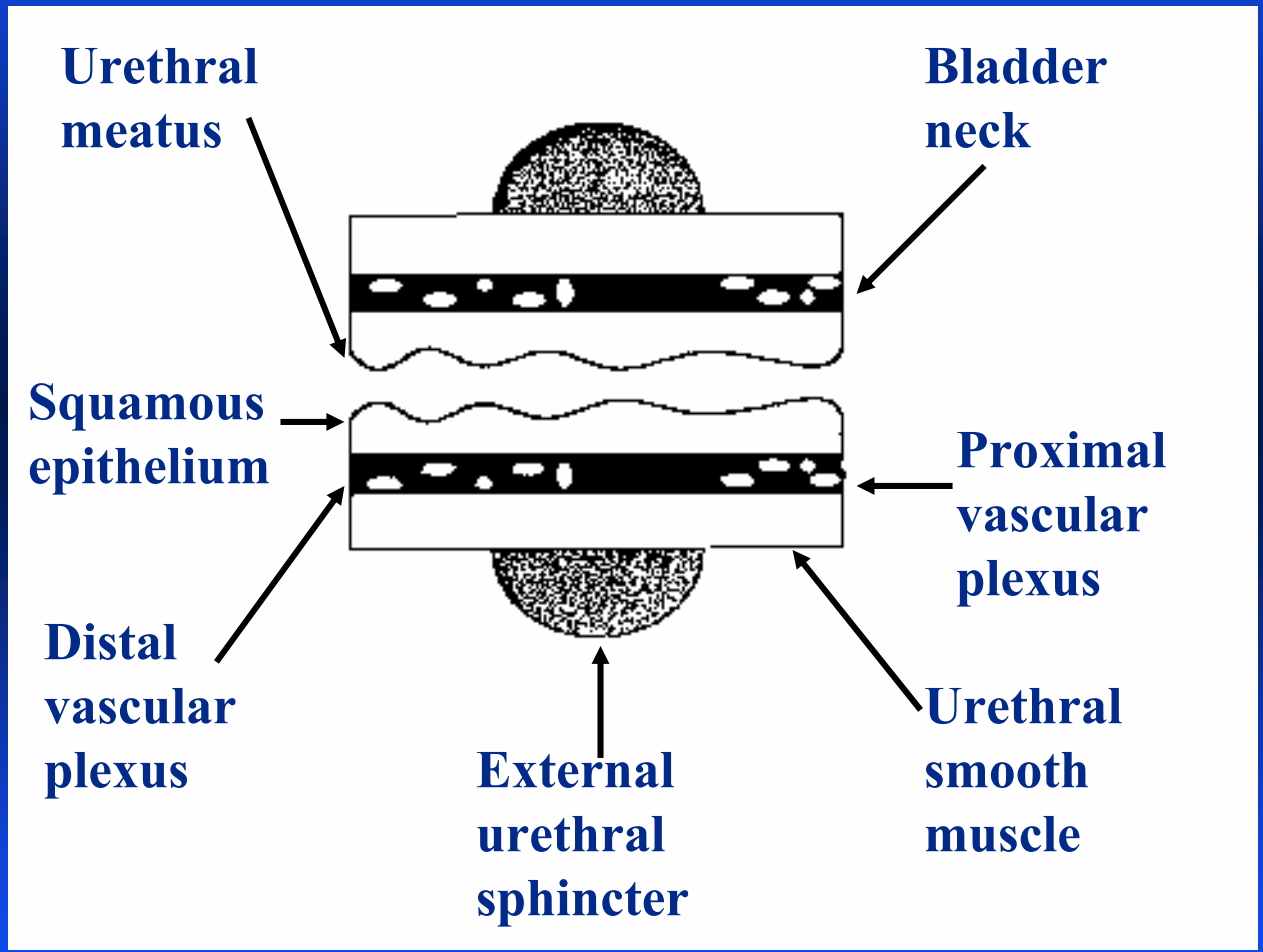
Place de l'oestrogénothérapie chez la femme âgée

Dr. F. Luzuy

FL

Tissue layers of the urethra



Periurethral collagen, stress urinary incontinence (SUI) and estrogen replacement therapy (ERT) among postmenopausal women

Collagen Parameter	*Postmenopausal SUI, on ERT compared to no ERT*	*Postmenopausal continent , on ERT compared to no ERT*
Cross-linking	↓↓	↓
Concentration	↓	↓
Fibril diameter	**unchanged**	**unchanged**
mRNA for collagen I, III	**I(I), T(III)**	**unchanged**
Proteoglycan (PG) concentration	↓	**unchanged**
PG: collagen ratio	**unchanged**	↑

Effect of menopause and estrogen replacement on periurethral collagen biochemistry stress urinary incontinence versus continent women (after Falconer et al)

FL

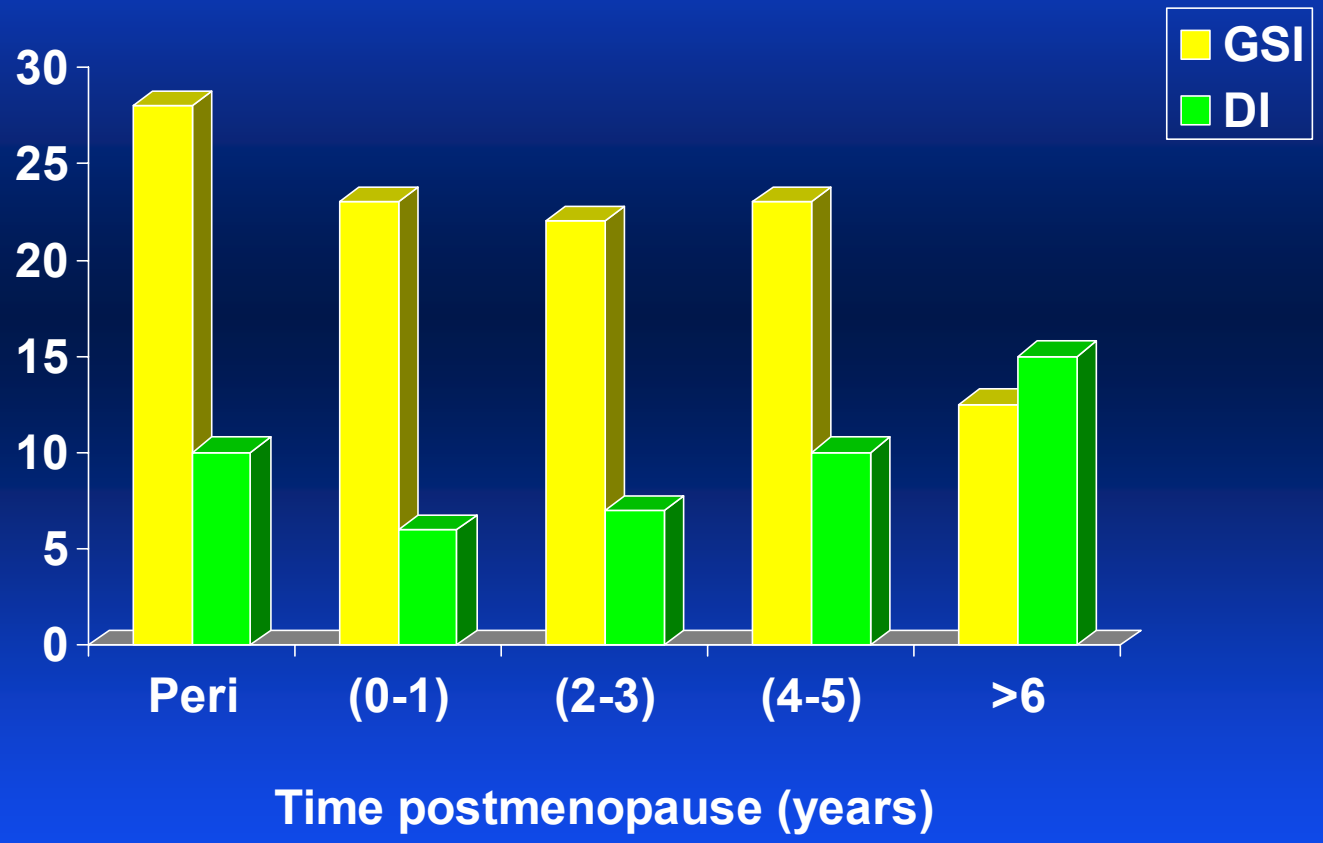
Estrogen effects on stress incontinence

Parameter	*Effect of estrogen*	*Effect on continence*
Pressure transmission ratio	possibly increases proximally	probably minimal
Contraction of external urethral sphincter/levator ani	no evidence of direct effect	none
Urethral tone	possibly increases baseline tone	unclear

Impact of estrogen on resting continence

Tissue	*Effect of estrogen*	*Effect on continence*
Urethral mucosa	softens, increases pliability	aids hermetic seal, aids continence
Submucosal vascular plexuses	increases fullness and tortuosity of proximal plexus no effect on distal plexus	increased closing pressure, aids resting continence
Periurethral collagen	increases elasticity, collagen synthesis	effect on continence unclear
Striated muscle	no effect	no direct effect
Urethral smooth muscle	may increase tone synergistically with α-agonist	effect unclear when used alone
Detrusor smooth muscle	probably decreased irritability	possible decrease in urge incontinence

Age distribution of genuine stress incontinence and detrusor instability; after Versi and co-workers



FL

Estrogen therapy in stress incontinence : uncontrolled trials

Ref.	*Subjects*	*Type*	*Outcome variable*	*Intervention*	*Result*	*Notes*
Hilton (83)	11 PM, GSI	cohort	MUCP PTR	2 g vaginal conjugated E_2 daily x 4 weeks	significant improvement in MUCP and PTR, non significant improvement in symptoms	
Bhatia (89)	11 PM, GSI	cohort	UPP	2 g vaginal conjugated E_2 daily x 6 weeks	6/11 cured or improved. Improved UPP in cured patients	no UPP changes in patients who were not cured
Bergman (90)	11 PM, GSI	cohort	UPP	vaginal conjugated E_2 x 6 weeks	5/10 improved urethral cytology only among improved GSI	Proposes urethral mucosal factor to explain results
Sartori (95)	30 PM, GSI	cohort	Leakage at maximum capacity	Premarin 0.625/ Provera 2.5 oral qd x 3 months	70 % had no leaking at maximum bladder capacity	No discussion of their GSI criteria. Significant subjective improvement

PM, postmenopausal; GSI, genuine stress incontinence; UPP, urethral pressure profile., MUCP, maximum urethral closure pressure; PTR, pressure transmission ratio

Estrogen and stress incontinence; randomized placebo-controlled trials

Ref.	*Subjects*	*Study Type*	*Outcome variable*	*Intervention*	*Result*
Judge (69)	20 PM hospital-based geriatric patients	R	Incontinence	Quinestrol po qd x 5 weeks	significant reduction in frequency of incontinence at 5th week placebo had no effect
Walter (81)	29 PM with UI	R	SI, UPP	Cyclic po E_2/E_3 x 20 days	no improvement in SI or UPP
Samside (85)	34 PM with UI	R	SI	po estriol x 3 months	no significant change in SI

PM, postmenopausal; S1, stress incontinence; Ul, urinary incontinence; F, frequency; GSI, genuine stress **in**continence; UPP, urethal pressure profile; R, randomized, double-blind, placebo-controlled

Estrogen and stress incontinence; randomized placebo-controlled trials

Ref.	*Subjects*	*Study Type*	*Outcome variable*	*Intervention*	*Result*
Wilson (87)	36 PM with UI	R	SI, F, pad change frequency	po estrone x 3 months	no significant change in no of pad changes, UPP, or frequency
Walter (90)	12 PM with UI	R	Urine leakage	po estriol 4 mg qd plus α-agonist	significant objective decrease in amount of urine loss
Fantl (96)	83 PM, GSI hypoestro-genism	R	GSI, hypoestro-genism, subjective	po estrogen x 3 months	no improvement in GSI vs, placebo significant improvement in vaginal and urethral estrogenization significant improvement in subjective symptoms

PM, postmenopausal; S1, stress incontinence; Ul, urinary incontinence; F, frequency; GSI, genuine stress **in**continence; UPP, urethal pressure profile; R, randomized, double-blind, placebo-controlled

FL

Estrogen plus α-agonist therapy in treating urinary incontinence

Ref.	*Subjects*	*Type*	*Outcome variable*	*Intervention*	*Result*
Beisland (81)	13 PM UI, USI	R	Symptoms, UPP	Oral E_2 versus oral E_2 & PPA	8/13 became continent with combination therapy ve E_2 alone. Significantly improved UPP with combination therapy
Beisland (84)	20 PM UI, USI	R, X	UPP	PPA 50 mg po bid vaginal estriol 1 mg qd	8 cured, 9 improved with combination therapy
Kinn (88)	36 PM GSI	R	UPP, leakage	Oral E_2 versus oral E_2 & PPA	Significant objective improvement with comibnation therapy vs E_2 alone

postmenopausal; Ul, urinary incontinence; GSI, genuine stress incontinence; R, randomized, double-blind, placebo-controlled; X, cross-over; UPP, urethral pressure profile; USI, urethral sphincter insufficiency (low urethral closure pressure); PPA, phenylpropanolamine (α-adrenergic agonist; E2, estradiol; E3, estriol

Estrogen plus α-agonist therapy in treating urinary incontinence

Ref.	*Subjects*	*Type*	*Outcome variable*	*Intervention*	*Result*
Hilton (90)	60 PM GSI	R	GSI , frequency, nocturia, subjective	Oral E_2 versus oral E_2 & PPA	Significant objective improvement with comibnation therapy vs E_2 alone Significant,nocturia iimproved more with combined vs single therapy
Walter (90)	12 PM with GSI	R	Urine leakage	po estriol 4 mg qd plus α-agonist	Significant objective decrease in amouont of urine loss
Ahlstrom (90)	29 PM, GSI	R	UPP, symptoms	Oral E_3 placebo vs oral E_3 & PPA	Significant subjective improvement in E_3 + PPA vs E_3 + placebo Significant objective improvement in UPP variables in E_3 + PPA group vs E_3 + placebo Significant decrease in leakage episodes, decrease in urine loss on standard stress test

postmenopausal; Ul, urinary incontinence; GSI, genuine stress incontinence; R, randomized, double-blind, placebo-controlled; X, cross-over; UPP, urethral pressure profile; USI, urethral sphincter insufficiency (low urethral closure pressure); PPA, phenylpropanolamine (α-adrenergic agonist; E2, estradiol; E3, estriol

Estrogen therapy for urinary frequency, and urge incontinence

Ref.	*Subjects*	*Type*	*Outcome variable*	*Intervention*	*Result*
Wlater (81)	21 PM, F, UI	R	UI, F	Estrogen vs placebo x 6 weeks	7/11 study subjects improved 1/10 controls improved ($p < 0.05$)
Sanside (85)	34 PM with UI	R	Urge, mixed	po estriol x 3 months	Significant improvement in urge symptoms and mixed incontinence symptoms
Carrozo (93)	64 PM	R	UI, F	Oral estriol	No significant difference between estriol and placebo Both groups showed significant improvement over pre-intervention
Eriksen (92)	154 PM	R	UI, F, SI, dysuria	Vaginal estradiol tablets	Significant improvement in study group over placebo

PM, postmenopausal., R, randomized, double-blind, placebo controlled; Ul, urge incontinence; SI, stress **in**-continence; F, frequency

Controlled trials of estrogen therapy, for recurrent urinary tract infections

Ref	*Subjects*	*Type*	*Outcome variable*	*Intervention*	*Result*
Kjaergaard (90)	23 PM, R-UTI	R	Frequency of UTI	Vaginal estriol x 5 months	No significant improvement in study vs placebo. Significant improvement in vaginal cytology
Kirkengen (92)	40 PM, R-UTI	R	Frequency of UTI	oral estriol x 12 weeks	Significant reduction in UTI vs placebo
Raz (93)	93 PM, R-UTI	R	Frequency of UTI	vaginal estriol vs placebo x 8 months	Reduction in UTI in study group vs placebo Improvement in vaginal cytology in study group
Cardoso (98)	72 PM, R-UTI	R	Frequency of UTI	vaginal estriol vs placebo x 3 months	Improvement in study and placebo groups; no significant

PM, postmenopausal., R-UFI; recurrent urinary tract infection; R; randomized, double-blind placebo controlled trial

FL

Trials of estrogen effects on urethral pressure variables

Year		
1977	41	Improved resting UPP
1983	10	Improved PTR
1984	20	Improved resting UPP
1988	64	No changes in UPP
1989	6	Enhanced PTR to proximal mid-urethra
1990	12	No change in UPP
1991	12	No change in UPP after GnRH-induced menopause
1992	80	Improved pressure to proxiimal urethra. No change in other UPP variables

UPP, urethral pressure profile; GnRH, gonadotropin releasing hormone

FL

Summary of estrogen effects in the postmenopausal lower urinary tract

Parameter	*Effect of estrogen*
Symptoms of urinary incontinence	Improved
Genuine stress incontinence (objective diagnosis)	Not improved with estrogen alone Objective improvement with combination estrogen and α-agonist therapy
Urge incontinence	Probably improved
Recurrent urinary tract infections	Improved
Urethral pressure profile	Inconclusive
Nocturia	Improved
Frequency	Probably improved
Voiding difficulty	Probably improved