

Navigating The Silent Connection: Exploring The Relationship Between Menopause And Bladder Problems

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Abstract:

Introduction: Primarily, the bladder and its surrounding structures are quite rich in receptors of estrogen and there are significant anatomical and physiological changes that take place immediately after or around menopause. Even though the prevalence of several bladder symptoms such as incontinence, urgency, and frequency does appear to increase around menopause, there is still continuing debate on whether these symptoms are due to menopause, ageing, or their combination. Therefore, the relationship between menopause and bladder problems is unclear.

Methods: A qualitative-descriptive design is used for performing the research. Corresponding to this design, a comprehensive literature review has been carried out, which covers multiple journal articles related to the topic.

Results: The influence of menopause tends to vary with individual symptoms such as stress urinary incontinence is associated more with the deficiency of estrogen than urge incontinence, which appears to be related more to age. The data in the literature, however, is far from clear and it also appears that topical estrogens do possess several positive effects, particularly on the symptoms of urge incontinence, frequency, urgency, and even urogenital atrophy's prevention.

Conclusions: Menopause and bladder problems are not directly related to each other. Instead, the deficiency of estrogen is related to stress urinary incontinence. On the basis of current evidence, it would be more reasonable to consider and use vaginal estrogens instead of systemic as a part of the treatment or management of different bladder problems related to menopause.

Keywords: menopause; stress urinary incontinence; deficiency of estrogen; urge continence; estrogen replacement; bladder problems

Introduction:

Generally, menopause refers to a cessation of menstruation for a year or more among women, especially middle-aged women. It is quite a unique phase of the female reproductive cycle and while it is a rather normal physiological change, there are times when its symptoms can be severe to such an extent that they can adversely influence the daily activities of women. Menopause has a large impact on the body, which leads to changes and alterations in many systems and organs with the lower urinary tract and bladder being no exception. In addition, most women are unfortunately unaware of some menopausal changes they experience. Even though clinical issues related to the lower urinary tract and bladder are not exclusively linked to menopause, most women experience bladder symptoms after or around menopause. Urinary incontinence is often believed to be an inevitable part that comes with aging, which is a rather common misconception among women. There

are times when it can be related to menopause as well. This manuscript seeks to evaluate and shed light on the relationship between bladder problems and menopause and the possible ways how the symptoms can be managed and addressed

1.1 Background:

The prevalence of UI or urinary incontinence is twice as common in women as compared to men and it increases with age. 55% of elder women reported symptoms of UI as reported by Timothy Hillard in his research study, 1. In postmenopausal women, the prevalence of UI varies rather widely based on the description of incontinence in the literature, the diagnostic tools used, and the population studied. Data acquired from the MRC or Medical Research Council Survey highlighted that a little under half of the women between the ages of 48-54 years reported stress incontinence. Meanwhile, a quarter reported their experience with urge incontinence, 2. From a clinical perspective, even though it has been long assumed that menopausal transition is associated with urinary symptoms, the actual relation is far from apparent, 3 and 4. Many studies have highlighted a peak prevalence of urge and stress incontinence in mid-life, 5, 6, and 7. Although this would suggest that menopause is a clear cause of bladder issues, other studies have identified a rise in urinary symptoms with increasing age, 8 and 9. When focusing on individual symptoms, the presence of stress UI tends to peak during 45-49 years while the presence of urge UI rises primarily with age, 10 and 11. Meanwhile, epidemiological studies comparing diverse post- and premenopausal women have identified quite mixed connections based on the type of UI and symptoms, 12 and 13. Therefore, the effect of menopause on different urinary symptoms is quite interesting and controversial. Actually, ovarian activity tends to fluctuate for several years prior to menopause but in epidemiological terms, menopause is usually noted as a certain time point. It might be confounded further by delayed reporting and communication of urinary symptoms. A large number of women continue to bear with their specific symptoms for a long period of time before actually consulting a health professional. Furthermore, the relationship of symptoms with critical life events such as menopause is rather variable. In a study by Losif, 2, 2200 women aged 61 were included and around 70% of these women related the onset of incontinence to menopause, 14. On the other hand, Barlow, et al. identified that even though around 50% of women with their ages in between 55-85 had already had urinary symptoms, most of them did not relate these symptoms to menopause, 15. Therefore, longitudinal studies should offer the most accurate and adequate information. However, even in this category, the results are quite mixed. In Australia, the SWAN study did not find any specific relationship between the menopausal transition and urinary symptoms, 3. But more data acquired from the 1946 Birth cohort of MRC points out that females who had already been perimenopausal for over a year or became perimenopausal were more likely to experience symptoms of stress UI instead of women who remained premenopausal, 16. In the cohort, women were segregated into eight categories with ages between 54 and 49 on the basis of menopausal status. Actually, for stress incontinence, the highest prevalence was in women who had been perimenopausal for over a year at the age of 54. In contrast, the lowest prevalence of 43% was in women who were postmenopausal, 16. But experiencing the menopausal

transition was not related to any symptom change in severe or urge UI. Therefore, it can be deduced that menopause is not the primary cause of urge or stress incontinence. However, it does affect the presence of stress incontinence, which may be evident through the decreasing estrogen levels due to decreased collagen synthesis and urogenital atrophy. Thus, it is a contributory factor in incontinence and urinary symptoms among women in the least. In addition, the prevalence of other menopausal symptoms might affect the incontinence symptoms' reporting around menopause. After menopause, the prevalence appears to decrease, which means women can learn how to better manage their symptoms while urge incontinence appears to be more associated with age instead of menopausal status.

1.0 Materials and Methods:

In order to perform this research, a qualitative-descriptive design is selected. While there are various designs that may be used, a design that suits the subjective nature of the problem is the qualitative descriptive design. It helps recognize the different experiences of participants and present findings in a way that closely resembles or reflects the perspectives of different authors and participants. Another reason why this design has been selected is its appropriateness for health-related research studies, which are commonly associated with how patients experience certain issues and which interventions might be adequate for those problems. A qualitative-descriptive design is also to be used when a researcher hopes to survey and navigate the literature before presenting findings in the study. In this manner, such a design can be quite helpful in highlighting why certain problems occur and which interventions might be the most adequate for them. In addition, it helps generate findings that describe the why and how of events from a subjective perspective of participants. Meanwhile, from a more philosophical perspective, this design aligned the best with constructionism and naturalistic methods. Fundamentally, these philosophical perspectives indicate that reality is subjective and multiple. In qualitative-descriptive research, methods for data collection are quite diverse and aim to identify the why and how of a certain problem. While it primarily relies on interviews, it can also use a comprehensive literature review as a method for acquiring and interpreting data. A review of the literature can help find the different perspectives of researchers and help look at a problem or issue from multiple directions. It can also help better understand the problem and why it exists in the first place. In this research, a review of the literature is used as a research method. Furthermore, online libraries and databases such as Google Scholar and PubMed are used for acquiring relevant and credible data sources, 17.

2.1 Statement on Ethics:

Considering the fact that it is a review article, informed written consent was not obtained. However, all the sources from which information has been obtained are referenced properly.

2.0 Results and Discussion:

Most menopausal symptoms are resulted directly from the depletion of estrogen levels as females approach their menopausal stages. Some of these women even begin to experience these symptoms in the early perimenopausal phase. Primarily, the

common symptoms can be segregated into sexual, psychological, physical, and vasomotor complaints. In some postmenopausal women with a significant deficiency of estrogen, changes occurred in bone and cardiovascular health. In the literature, it is documented well that menopausal symptoms tend to influence the quality of life of women, 18.

3.1 Epidemiology:

Generally, over the years, life expectancy has increased significantly, which has led to an increase in the number of women experiencing postmenopausal periods. Currently, women spend around a third of their lives in a postmenopausal state when they experience estrogen deficiency on average, 19. After menopause, the prevalence of conditions that occur and take place more frequently is likely to increase and result in a similar increase in the expenditure of healthcare. With time, epidemiological studies have increasingly focused on documenting and recording the prevalence of UI or urinary incontinence in postmenopausal women, 20. However, a large number of women are still reluctant to admit that they are suffering from incontinence. Therefore, the actual magnitude of this severe issue is underestimated to a significant extent. With age, there is an increase in the prevalence of UI, though there are several reasons other than menopause why it is experienced. Urethral and bladder function both tend to become less efficient with age, 21. In addition, Malone Lee has indicated that elderly women tend to have a reduced flow rate of urine, higher end-filling pressures, increased urinary residual, decreased maximum voiding pressures, and reduced bladder capacity, 22. Furthermore, while younger women tend to excrete most of their daily fluid intake before going to bed, this pattern is almost reversed in the elderly and nocturia becomes common with increasing age. Urinary incontinence is undoubtedly the end result of various pathological processes. Not to mention, urinary symptoms alone are not really adequate for the proper diagnosis of the dysfunction of the lower urinary tract. Mixed urinary symptoms, unfortunately, are rather common and the correlation between urodynamic and symptomatic diagnosis is still known to be inadequate, 23 and 24. In the literature, Jarvis and his fellow researchers identified that urodynamic studies changed the management of females with UI in more than 30% of cases after the execution of a clinical diagnosis, 25. In fact, in the literature, it has been stressed multiple times that urodynamic studies are essential for the effective assessment of patients experiencing different symptoms of the dysfunction of the lower urinary tract. Even today, this statement continues to remain true. Urodynamic studies might be complex or simple, the former is usually only available and accessible at specialist centres. Some of the prime causes of urinary incontinence include genuine stress incontinence, overflow incontinence, and detrusor instability. Meanwhile, some other temporary causes include drugs, fecal impaction, and urinary tract infections. Some additional causes in the elderly include endocrine abnormalities, metabolic abnormalities, heart failure, deficiency of estrogen, decreased mobility, and dementia. In some elderly women, impaired physical status results in some additional causes of incontinence, which are not frequently experienced or faced by younger women. Urinary incontinence is quite common in the post-menopausal period but the data on its prevalence does not accurately explain the role of deficiency of estrogen. For

instance, in a survey that included over 10,000 women, it was highlighted by Thomas, Plymat, and Blannin that incontinence's prevalence increases with age but not particularly at the time of menopause, 26. On the other hand, it was indicated by Iosif and Bekassey that 70% of elderly Swedish women related the presence and onset of their symptoms to their menstrual period, 27. It was identified by Jolleys that the presence of stress incontinence tends to reach a peak at the age of 50 and decreases after it, 28. In research by Kondo and his fellow researchers, it was identified that stress incontinence's incidence tends to decrease after the age of 55 among 1105 Japanese women. Meanwhile, the incidence of urge incontinence tends to increase with age, 29. Actually, in a combined urodynamics and symptoms study, which was carried out at Dulwich menopause clinic, around 228 women were included and they were referred for climacteric complaints. They completed a comprehensive urinary symptom questionnaire and even underwent urodynamic studies that comprised urethral pressure profilometry, cystometry, uroflowmetry, and pad testing. In addition, stress incontinence symptoms were identified to take place in more than 50% of women and urge incontinence symptoms in 26%. Not to mention, only 60% of women had normal investigations. In spite of the common finding of urodynamic abnormalities and urinary symptoms, no correlation with menopause timing was identified, 30. Therefore, it would appear that SI or stress incontinence is not caused by menopause whereas UI or urge incontinence and other bladder symptoms, which are irritative might be related. Even though urinary symptoms are rather common in postmenopausal and climacteric women, and the lower urinary tract is recognized to be sensitive to estrogen, it is still difficult to demonstrate a causal relationship or association with menopause. Epidemiological data, unfortunately, is quite complex to acquire and, in the elderly, incontinence might be attributable to many other identified factors. Therefore, the significance of estrogen deficiency can only be measured by improvements in urodynamic assessments, cytology, and symptoms following ERT or estrogen replacement therapy.

3.2 Hormonal Influences and the Lower Urinary Tract:

Throughout the lower urinary tract, progesterone and estrogen receptors are found. Basically, it represents its shared origin or connection with the lower genital tract. The urogenital sinus, during 4-7 weeks of development, develops into the vestibule of the vagina, distal urethra, proximal urethra, and bladder. ERs or estrogen receptors, in the lower urinary tract, are widespread and can be traced in the epithelial tissues of the urethra, trigone, bladder, and even the supporting structure like uterosacral ligaments, levator muscles, and pubocervical fascia, 31. In the lower urinary tract, functional changes that occur after menopause can be attributed to the loss of estrogen and age-related changes. The gradual atrophy of mucosal muscles and skin, nerve degeneration, and decrease in smooth muscle tone, and skeletal muscle volume are caused by aging, which influences the lower urinary tract. In fact, histologically, there is primarily an age-related decrease in muscle fibres in the pelvic floor, a number of muscle fibres, and a rise in fibrosis at the bladder neck. Urodynamic studies have functionally shown that with age, the efficiency of the bladder decreases with higher residuals, reduced flow rate, and increased bladder capacity. After menopause,

estrogen deficiency leads to estrogen-sensitive tissues' progressive atrophy, which causes a thinning of the urethral and vaginal mucosa, weakening of different supporting ligaments and tissues, and thinning of the bladder's trigone, 32.

3.3 Influence of Sex Hormones:

When the impacts of estrogen treatment are considered, it becomes possible to find evidence about the role of sex steroids in lower urinary tract dysfunction during the postmenopausal period. Fundamentally, a complex interaction of different extrinsic and intrinsic factors helps maintain urinary continence. Urethral integrity typically relies on the strength of supporting structures, collagen content, the tone of its striated and smooth muscle, elasticity, vascularity, and epithelium. With age, there is a decrease in both functional urethral length and urethral closure pressure. Urethral closure pressure is improved by estrogens, which might be achieved by several mechanisms, 33.

- Estrogens improve smooth muscle contractility and alpha-adrenergic tone.
- Estrogens raise periurethral vascularity, contributing to around a third of overall urethral pressure.
- Estrogens improve squamous epithelium's proliferation and cellular maturation, which might lead to a healthier mucosal seal.
- Estrogens might have an effect on supporting structures' connective tissues. After menopause, there is a decline in skin collagen content and there is a correlation between closure pressure, urethral length, and skin collagen content. In periurethral tissues, collagen turnover and synthesis are increased by estrogens, which may weaken the urethral tone.
- It is suggested by animal studies that the volume of detrusor muscle fibers might be increased by estrogens, which can lead to an overall decrease in the smooth muscle/collagen ratio in the urethra and detrusor, 34.

Furthermore, there are other reported and often speculated impacts of estrogen, which might affect the function of the lower urinary tract:

- The bladder's sensory threshold might be increased by estrogens.
- In the rat pelvis, the neuromodulation function is increased by estrogens.
- There is a direct effect of estrogens on detrusor function, which results in reduced amplitude and frequency of spontaneous detrusor contractions. It might be due to a reduction of extracellular calcium's movement into the muscle cells or so, 35.

3.4 Progesterone:

In the urinary tract, although progesterone receptors are also identified, they are not prevalent as consistently as ERs and they appear to have an adverse influence on the function of the lower urinary tract, often related to the worsening of premenstrual urinary symptoms and irritative bladder symptoms during the HRT or

hormone replacement therapy's combined phase, 36. Actually, its mechanisms are understood poorly and the limited data on progesterone's physiological effects is often related to pregnancy. It is believed that progesterone modifies estrogens' blocking effect on the responsiveness and efficiency of muscarinic receptors, which increases the beta-adrenergic response effectively 37. In postmenopausal women, estrogen replacement therapy is used in conjunction with cyclical progestogens for the prevention of endometrial atypia and hyperplasia. Both of them are attributable to UET or unopposed estrogen therapy. The uterus's smooth muscle is relaxed by progesterone. In fact, progesterone induces beta-adrenergic receptor formation and since genital and urinary tracts tend to share the embryological origin and receptors of progesterone have been demonstrated in the urethra and bladder, a similar mechanism of action would be expected in the lower urinary tract. In female rats, it has been shown by Raz, Ziegler, and Laine that beta-adrenergic activity is facilitated by progesterone, producing significant ureteral relaxation on proper exposure to adrenaline, 38. The same group has also studied progesterone's effects on pregnant dogs' urethra and showed a similar beta-adrenergic receptors' facilitation to that seen and observed in the ureter. Zedric and his fellows have indicated that the bladder tissue strips from pregnant rabbits tend to generate at least 50% less tension than controls when exposed to bethanechol in response to calcium, 39. Meanwhile, Levin, Tong, and Wein have exhibited similar results, suggesting that progesterone might also possess an anticholinergic effect or influence on the bladder, 40. On the smooth muscle of the bladder or urethra, progestogenic effects might, therefore, be attributable to beta-adrenergic relaxation and anticholinergic effects. When it comes to the lower urinary tract, the effects of progesterone have been studied extensively during pregnancy when the urethra, bladder, and ureters are affected by progesterone.

Physiological hydroureter, during pregnancy, is attributed to both the gravid uterus's obstructive effects and progesterone's relaxant effects. It was noted by Langworth and Brack during a series of experiments that it was essential to exclude pregnant cats when evaluating the vesical activity of a healthy cat, 41. It is primarily because the bladder capacities of pregnant cats were increased significantly. Over the years, similar studies have been performed on animals and it has been identified that bladder capacities are usually increased during pregnancy. Supine cystometrograms were performed by Youssef on ten women during pregnancy and it was identified by him that bladder capacity had increased, 42. Actually, these changes have also been identified following exogenous progesterone administration and during the normal menstrual cycle's luteal phase. There are a few studies that evaluate and study the effects or influence of the administration of exogenous progestogen on the urethra. In fact, it is recognized that more than 35% of pregnant women tend to complain of SI at some time during their pregnancy. Keeping it in mind, it has been suggested that it is associated with progesterone levels. 43 pregnant women were evaluated by Van Geelen and his fellows using urethral pressure profilometry, 43. They also measured levels of serum 17 alpha-hydroxyprogesterone and found no change or alteration in the maximum pressure of urethral closure despite the rising levels of hydroxyprogesterone. They concluded that the tone of the urethra is not altered significantly by progesterone. Progesterone's effect

was studied by Rud on the urethra of incontinent and continent women and did not find any change in the maximal pressure of urethral closure, 44. However, he did manage to find a slight decrease in the transmission of urethral pressure during the cough profile. In addition, 14 postmenopausal women were evaluated by Benness and his fellows on cyclical progestogen and continuous estrogen, 45. In ten patients, they identified increased incontinence through pad testing during the cycle's progestational phase. Meanwhile, eight of their patients suffered from GSI or genuine stress incontinence and progesterone managed to adversely influence urethral incompetence in seven of these patients. However, Raz and Ziegler have indicated that in the urethral pressure profile, there is no change in continent women following the addition of a component of progestogen to HRT or hormone replacement therapy. Therefore, progesterone might inhibit and limit the urethral closure mechanism by reducing the peri-urethral blood flow and pressure transmission ratio, and this is most prominent in women who are incontinent with compromised urethral function. In patients with urinary complaints, exogenous progesterone's clinical value tends to await evaluation. Meanwhile, in HRT, it might play a positive role in women with DI or detrusor instability through its anticholinergic and beta-adrenergic properties. However, it might also offset estrogen's beneficial effects in women's GSI or genuine stress incontinence. In continent postmenopausal women though, this effect would be identified to be minimal.

3.5 Use of Estrogens for the Management of Disorders of Lower Urinary Tract:

Estrogens undoubtedly have a critical physiological action and impact on the lower urogenital tract. Meanwhile, the pathophysiology of the effect of deficiency of estrogen determined above would indicate that estrogen treatment must be capable of benefitting many conditions that influence and affect the postmenopausal bladder. The evidence, however, is quite contradictory and far from clear about it. Many studies are observational and have utilized different progestogens and doses, and have also used inconsistent follow-ups and varying outcome measures. More recent studies have attempted to resolve these problems but the role of estrogen in the management of the postmenopausal bladder is rather vague. As a part of HRT, it is possible for estrogen to be either administered systemically or topically, 46. Actually, for continence to exist, the pressure of urethral closure needs to exceed or go beyond intravesical pressure at all times with the exception of micturition. Continence might be improved by estrogens by increasing the urethral resistance, increasing the sensitivity of alpha-adrenoreceptor in the smooth muscle. Furthermore, estrogen therapy has been indicated to increase the number of superficial and immediate cells in postmenopausal women's vagina, and similar changes have actually been demonstrated in the bladder and urethra. While the utilization of estrogen therapy for the relief and treatment of different urinary disorders in postmenopausal women remains quite controversial, it has been used rather extensively for this indication with different degrees of success. The studies that have been performed unfortunately tend to vary in many critical respects such as the mode of administration, dose, route, and type of estrogen. Therefore, this heterogeneity has undoubtedly further

complicated the picture. A meta-analysis that focused on around 166 articles on female urinary incontinence treatment published during 1969-1992 revealed that only 17 uncontrolled and six controlled trials of estrogen therapy existed, 47. The meta-analysis identified a prominent subjective improvement in symptoms of incontinence for all participants following ET or estrogen therapy. However, there was a lack of evidence that pointed toward objective improvement.

3.6 Topical Estrogen:

In the evidence, it has been indicated that vaginally administered estrogens are capable of improving not only vaginal atrophy but also its related symptoms, 48. In addition, these estrogens are being used increasingly due to concerns raised about system HRT's long-term concerns. Actually, most of the RCTs or randomized controlled trials that compare placebo with vaginal estrogen for the treatment of different urinary symptoms have shown some improvement in postmenopausal women. However, the overall number in such trials has often been small with ineffective and short follow-ups. The HUT or hormones and urogenital therapy committee performed a meta-analysis, which indicated that topical estrogen was superior and better than systemic estrogens that lowered urinary tract symptoms' subjective improvement, 49. In a randomized double-blind placebo trial, the use of a placebo was compared with a 25ug estradiol tablet among 110 women with symptoms related to urgency and frequency and found only a slight improvement in urgency with no benefit in other areas, 50. On the other hand, a recent RCT that focused on 57 hysterectomized women found improvement in nocturia and urinal frequency upon receiving vaginal estrogens, 51. In addition, there does not appear to be a synergistic effect when an antimuscarinic is combined with topical estrogens. Many systematic reviews have all identified that vaginal estrogens are indeed capable of improving the symptoms of urge incontinence, urgency, and frequency to a varying extent. Still, there is insufficient evidence for any specific and continuing benefit after the discontinuation of the treatment.

3.7 Estrogens in Undiagnosed Incontinence:

Actually, early studies into estrogens' effect on the dysfunction of the lower urinary tract predates many urodynamic studies and were majorly uncontrolled and subjective. The first report was produced in 1941 by Salmon, Walter, and Gast who treated sixteen women with incontinence, urgency, frequency, and dysturia using intramuscular ET for 4 weeks. In 12 women, symptomatic improvement was observed and treatment was discontinued, 52. After discontinuation, symptoms recurred and were relieved again by intramuscular ET. Three decades later, 110 stress-incontinent women were given Quinestradiol by Musiani, and a 33% cure rate was reported with a 39% improvement rate, 53. Estradiol implants were used by Schleyer-Saunders in 1976 for the treatment of 100 women with post-menopause with undiagnosed UI. It was identified that 70% of participants were improved significantly, which reduced the need for surgery, 54.

3.8 Systemic HRT:

In general, most systematic reviews have focused both on topical

estrogens and systemic estrogens. For instance, Fantl, et al, identified an overall benefit for the treatment of estrogen with a subjective improvement in the symptoms of incontinence. It serves to highly data's relative paucity, 49. In addition, of the 166 papers that have been published between 1992 and 1969, only six were identified to be controlled trials while seventeen were uncontrolled. In 2003, it was followed by a systematic Cochrane review which helped identify 28 adequate randomized trials on the effects of preparations on UI and HRT doses on UI, 55. In estrogen-treated groups, a general impression was of higher cure rates as compared to placebo for almost all categories of incontinence, particularly for urge incontinence. Still, most evidence was not objective and it was unclear if it was maintained after the discontinuation of the treatment or not. In combined HRT, the addition of progestogen appeared to decrease the positive effect of estrogen, perhaps due to progesterone's negative effects on the bladder. Another meta-analysis in the same year determined that there was insufficient evidence about how stress UI was improved by estrogens. When it comes to more recent studies of systemic HRT, they appear to challenge the idea that estrogens are beneficially largely for the bladder. A large prospective cohort study in the form of the Nurses Health Study followed around 39,436 continent and postmenopausal women over a period of four years. A new UI's incidence was significantly higher between 1.64 and 1.34 based on the kind of hormone replacement in the users of HRT, 56. Regardless, this risk diminished after discontinuing HRT and it returned to baseline after a decade of no HRT. The Progestin Replacement Study also indicated an increased risk of UI in females who underwent HRT. A large RCT, the Women's Health Initiative, also reported a significant incidence of UI in the users of HRT at one and three years in both those with no reported symptoms at baseline and those who were actually symptomatic at baseline, 57. It is important to note that the risk remained highest for mixed and stress incontinence with no specific uniform impact on UI. The estrogen group appeared to have adversely influenced the incontinence instead of the combined medroxyprogesterone acetate and CEE. A recent systematic review that focused on 22 RCTs in postmenopausal women for hormone administration identified an inconsistent improvement in UI. In addition, oral administration caused a worsening of stress and mixed UI, 57. The risk, for both parameters, was lower with combined progestogen and estrogen therapy than for individual estrogen. It can be thus deduced that oral estrogen alone is capable of increasing stress UI. In contrast, estrogen gel and transdermal therapy were related to high rates of continence, but this study was specifically self-reporting. Actually, an RCT that focused on ultra-low-dose TT or transdermal therapy over a period of two years for bone protection did not show any worsening or improvement in postmenopausal women. Therefore, it can be said that the larger RCTs tend to contradict and challenge the previous assumptions based on pathological changes observed with the deficiency of estrogen and earlier data. Regardless, a conclusion is reached that either these studies are misleading due to an ineffective design or systemic estrogens indeed have an adverse influence over incontinence mechanisms. Primarily, estrogens are recognized to improve collagen remodeling and while this is mostly believed to be a positive effect, it tends to reduce cross-linking and total collagen initially, which may destabilize the detrusor muscle by weakening the pelvic floor, 59. Now, if this was really the case, it might be

expected that the symptoms would improve over time as the collagen content would increase. However, this is yet to be proven and remains speculative. At the same time, why vaginal estrogens tend to have a better influence over urinary symptoms as compared to HRT is unclear. Actually, it may be possible that topical estrogen's effects on the genital mucosa and any improvements in atrophy are responsible for the improvements that occur in the symptoms of the lower urinary tract to some extent. It indicates that comprehensive randomized trials are required but they are not likely to occur with large samples. Even though estrogens' effect on UI is contentious, there is no doubt that estrogens are identified to have some proven and evident positive impacts on other symptoms of the bladder.

3.9 Recurrent Urinary Tract Infections:

Actually, the incidence of both asymptomatic bacteriuria and UTI or urinary tract infections increases significantly with age just like the severity of any other infection, 60. Fundamentally, bacteriuria is prevalent in one-fifth of people over 65 years of age and increases steadily with age. However, the extent of this infection related to menopause and ageing is rather unclear. It is important to note that in the vagina, loss of lactobacilli after menopause tends to result in acidic vaginal environment loss, which enables exposure to pathogenic bacteria. It also contributes to the excessive growth of different gram-negative organisms, which includes *Escherichia coli*. In addition to it, urethral and vaginal atrophy leads to the vagina's foreshortening and affects the reaction of the urethra as well, which reduces the natural defence of the body against different pathogens. Still, Hextall, et al. did not find any particular changes in infection rate related to menopause, 60. In the vaginal flora, estrogens tend to reverse these microbiological changes and are therefore used potentially for the prevention and treatment of recurrent UTIs. Even though there were progressive results from early studies, RTs have been less conclusive, though the success may again depend on the kind of estrogen used. Recurrent UTI was prevented by intravaginal estriol whereas there was little to no statistical difference between placebo and oral estriol cream. In the largest study, however, the vaginal ring was better to a significant extent at preventing recurrent UTI compared to a placebo. In their third report, the HUT committee concluded that in such a situation, estrogens proved to be beneficial, especially when used locally. A decrease in the incidence of different infections also appears to be related to a decrease in the severity of different urinary symptoms and problems, 61. Brandberg and his fellow researchers treated 41 elderly women with recurrent infections in the urinary tract using oral estriol and they indicated that their vaginal flora was treated and restored effectively, 62. At the same time, they indicated that the women required fewer antibiotics after it. Meanwhile, Privette and his fellow researchers, in a controlled study, evaluated 12 women who experienced and went through frequent infections of the urinary tract, 63. All of them were identified to have atrophic vaginitis and had also experienced a mean of four infections in each patient annually. The treatment itself consisted of a combination of antibiotics and short-term douche for 1 week together with estrogen therapy in the long term. The follow-up indicated only four infections in the whole group. Kjaergard and his fellow researchers studied around 23 women with postmenopausal

symptoms with recurrent infections of the urinary tract, 64. The participants were treated with a placebo or vaginal estradiol for five months following which improvement was observed in the estradiol group's vaginal cytology. However, there was no difference in patient satisfaction or urinary tract infections between the two groups. 40 elderly women with similar infections were randomized by Kirkengen and his fellows to receive either a matching placebo or oral estriol for four weeks, 65. No difference was identified between placebo and estriol after the first period of treatment but when a second treatment of eight weeks was followed and evaluated, estriol proved to be more effective than placebo in the reduction of urinary tract infections' incidence. One of the largest studies in the literature has been carried out by Raz and Stamm in which 93 postmenopausal women with recurrent infections of the urinary tract were randomized to receive either placebo or intravaginal estriol cream, 66. The study itself showed a prominent reduction in urinary tract infections' incidence with active treatment. In fact, even estriol is quite effective in preventing recurrent infections in the urinary tract in women, which suggests that it is a critical therapeutic role for ERT in postmenopausal women.

3.10 Urogenital Atrophy:

In postmenopausal women, urogenital atrophy is a rather common observation, affecting around 25% of women, even when they are undergoing SER or systemic estrogen replacement, 61. In a research study that spanned over 70 years with Australian women, a complaint of vaginal dryness appeared in 3% of all premenopausal women and up to 47% of women with three or more years into their menopause, 68. At a specialist menopause clinic, over a third of women were noted to suffer from urogenital atrophy. Urogenital atrophy is capable of causing dyspareunia and discomfort and may lead to a cessation of any sexual activity, which contributes to a lower quality of life. It is possible for atrophic trigonitis and urethritis to present with several presentations including vulval pruritis, increased awareness of prolapse, urinary urgency and frequency, recurrent UTIs, and bladder pain. Generally, it is possible to treat these symptoms effectively with either systemic or topical estrogen replacement. Furthermore, the vaginal route offers better relief of symptoms as compared to the systemic treatment. In vaginal preparations, the use of low doses also helps in avoiding the issue of endometrial stimulation. Even though the different vaginal preparations are quite effective, females have appeared to favor the vaginal ring or estradiol-releasing tablet for overall satisfaction, the comfort of the product, and ease of use. It might take several months for an improvement in symptoms and the treatment itself must be continued in long-term. Otherwise, it is possible for symptoms to return after cessation, 68.

3.11 Estrogen Therapy and Stress Incontinence:

In the management of females with SI, the main parameter that has been used for assessments is urethral pressure profilometry. It was shown by Caine and Raz that 26 women with SI out of 40 had increased symptomatic improvement and maximum urethral pressures while taking conjugated oral estrogen, 69. Similarly, 24 women with SI were treated by Rud with high doses of oral estriol

and estradiol in combination. He identified a rather prominent increase in intra-abdominal pressure's increase to the urethra with an increase in the maximum urethral pressure as well, 70. In the study, around 70% of women were improved symptomatically but estrogen in high doses was administered over a short period of time and similar studies have not reported the same changes. Walter and his fellow researchers randomly allocated around 29 postmenopausal women with incontinence to cyclical treatment with either placebo or estriol and estradiol for four months. They identified a rather significant improvement in urge incontinence and urgency in 47% of the women but no improvement was observed in stress incontinence, 71. They were not really able to demonstrate a significant change in profile parameters of urethral pressure. In a similar manner, Wilson and his fellows allotted around 36 women with SI to a placebo-controlled double-blind study focusing on cyclical oral estrone for three months, 72. They identified no specific difference in the subjective response, quantity of urine loss, and parameters of urethral pressure. One of the few studies that have actually indicated a prominent objective improvement in SI with the use of estrogen therapy was performed by Walter and his fellow researchers. For instance, in a placebo-controlled randomized study that used estriol (4mg regularly) showed that nine out of twelve women preferred the use of estriol to placebo and that there was a prominent objective decrease in the loss of urine using estriol as compared to placebo, 73. In this study, however, the numbers were very small and it is one of the only few studies in the literature to actually highlight this effect.

3.12 Combination Therapy:

Based on the findings of studies found in the literature, estrogens alone appear to be useful for the symptoms of UI and urgency but not for SI, though there have been promising findings and reports of combination therapy using an alpha-adrenergic agonist and an estrogen. For instance, Beisland and his fellow researchers treated around 24 menopausal women with SI using vaginal estriol and oral phenylpropanolamine in combination and separately, 74. It was identified by them that the combination was effective in curing eight women and improved nine more, and proved to be more effective than either drug individually. Hilton and his fellow researchers reported the outcomes of a placebo-controlled double-blinded study using estrogen with phenylpropanolamine or estrogen alone in approximately 60 postmenopausal women with SI, 75. They identified that the symptoms of nocturia and frequency improved significantly using the combination of estrogen alone. They also identified that SI improved subjectively in all groups but it improved objectively only in the combined group. Actually, it is likely that in the urethra, phenylpropanolamine's effect on alpha-adrenergic receptors is potentiated significantly by estrogen replacement therapy's concomitant use in postmenopausal women.

3.13 Risk Factors and Causes:

Based on the literature and evidence acquired from it, it can be said that menopause is not the only cause of major bladder issues and problems. There are several other factors that are found to contribute to the development of different bladder problems and issues. One of the primary causes is infections of the bladder or urinary tract as it can result in urinary incontinence. Meanwhile,

when the infection is addressed and treated, urinary incontinence is found to improve to a significant extent. Among the several causes, the consumption of caffeine or alcohol in excessive amounts is also identified to cause different bladder problems and issues. For instance, the consumption of such beverages is identified to fill the bladder quickly, which often results in more urination, 76. Nerve damage is capable of interrupting different signals from the bladder to the brain. As a result, the urge to urinate is not really experienced by the person. It can adversely influence the ability of the person to control and manage urination. Some medications are also identified and found to be a side effects of some medicines such as steroids and diuretics. These medications have been identified in the literature to cause several bladder problems and issues. In addition to it, another factor that may contribute to different bladder problems and infections is concerned with constipation. In fact, long-term or chronic constipation has been identified to affect bladder control. For instance, it has been determined to adversely influence and weaken the pelvic floor muscles, which makes it harder for people to hold in their urine, 77. Other than these symptoms, an important yet often ignored cause or risk factor of bladder problems are concerned with being overweight. During menopause, carrying excess weight tends to increase the risk of urinary incontinence. The extra weight tends to put excessive pressure on the bladder, which can either cause incontinence or worsen it for a person. As it has been identified above, it is common for postmenopausal women to experience a deficiency of estrogen levels in their bodies, which can lead to significant changes in the issues of the urinary tract including the lining of the bladder as well, 78. As a result, thinning of tissues and decreased elasticity can be caused, which makes the bladder quite vulnerable and susceptible to inflammation and irritation. In addition to it, with a decrease in estrogen levels, the health of the urinary tract degrades to a significant extent, which promotes the growth of different bacteria within it. With a decline in the levels of estrogen, different infections are caused, which can cause different bladder symptoms such as discomfort, urgency, and frequent urination. Vaginal atrophy can also be caused by low levels of estrogen that may be associated with menopause. It is also recognized as GSM or genitourinary syndrome of menopause, which often takes place when the estrogen levels are decreased, 79. It involves the inflammation, drying, and thinning of vaginal issues and vaginal atrophy can also cause different urinary symptoms such as discomfort during urination, frequency, and urinary urgency. During menopause, decreased estrogen levels and hormonal changes might contribute to the development of an overactive bladder. It is important to note that an overactive bladder is characterised by a strong and sudden urge to urinate, which is often accompanied by waking up at night or nocturia. Bladder prolapse is yet another cause or risk factor for the development of different bladder issues. It is fundamentally a condition in which the bladder tends to descend into the vaginal canal. Due to hormonal changes, the weakening of tissues and pelvic floor muscles might contribute to the development of bladder prolapse, which can lead to different symptoms like difficulty emptying the bladder, urinary frequency, and urgency, 80.

3.14 Treatments for Bladder Problems During and After Menopause:

The treatment of bladder problems and urinary incontinence generally depends on a number of factors from the cause of incontinence to the type of incontinence. Based on these factors, it is likely that a doctor might suggest different lifestyle changes. In a study, it was identified lifestyle changes can help improve different bladder problems and symptoms. Decreasing the consumption of alcohol and caffeine, gradually retraining the bladder to hold more urine, losing weight to reduce the pressure on muscles and bladder, and using Kegel exercises or even pelvic floor exercises might be considered for strengthening the pelvic muscles and addressing the urinal problems, 81. Typically, Kegel exercises involve relaxing and squeezing the muscles in the genital and pelvic areas to strengthen them in an effective manner. It might play an important role in helping the person develop better bladder control. It is also possible that a doctor might consider recommending more than one treatment option, particularly if they do not believe that lifestyle changes are helping the individual treat and recover from different bladder problems. Therefore, it is likely that a combination of two or more treatments might be recommended or used to ensure that bladder issues and problems are treated and addressed in an effective manner. When it comes to the treatment of bladder problems through the use of medications, there are certain medications that might be considered or used. For instance, among the medications used for the treatment of bladder problems, anticholinergics might be prescribed by a doctor for calming the bladder in case it is identified and determined to be overactive. It is possible that mirabegron might be prescribed as a beta-3 adrenergic receptor agonist for increasing the amount of urine that can be held and maintained by the bladder. In addition to it, topical estrogen products might also be used for toning the vaginal areas and urethra, 82. Estrogen therapy is one of the most common treatments used in the form of medication for women with bladder issues. It is worth noting that low-dose local estrogen therapy is considered and applied to the vaginal in the form of tablets, rings, or even creams, 83. Estrogen plays an important role in improving the strength and elasticity of vaginal tissues and urethra, reducing different urinary symptoms such as incontinence, frequency, and urgency. It is identified to be particularly beneficial for menopausal women who are suffering from vaginal atrophy. As it has been determined above, anticholinergic drugs may also be considered and used for the treatment of different vaginal issues. These medications like tolterodine or oxybutynin tend to work by relaxing the bladder's muscles. Through the reduction of bladder muscle contractions, these medications are capable of alleviating incontinence, frequency, and urgency. They may have, however, some side effects like constipation and dry mouth. Topical estrogen creams might also be used, which are applied directly to the urethra. When it comes to the application of these creams, it is capable of helping improve the health of different urethral tissues while reducing various urinary symptoms. Electrical stimulation is yet another technique that might be considered or used for helping a person regain control of their bladder in case urinary incontinence is associated with nerve impairment. In fact, it is identified to be an effective technique or method for helping people regain control over urinary issues and problems. In addition to these treatments, there are also a number of devices that are found to be used for the treatment of different urinary diseases. There are several devices available that may be considered or used for helping women with urinary diseases during or after menopause. For instance, a pessary

is recognized as one of the most commonly used devices for the treatment of SI or stress incontinence, 84. In the case of a pessary, a stiff ring is inserted in the vagina for helping reposition the urethra for preventing the leakage of urine. In addition to it, it is possible that a doctor might even prescribe a urethral insert, which is a small disposable device that is often inserted into the urethra for plugging the leakage. Urethral inserts are also common devices that are considered and used for the treatment of different urinary problems and issues. these tampon-like devices are actually inserted into the urethra for blocking urine leakage during any form of physical activity. They tend to work through the application of gentle pressure to the urethra, which prevents urine from leaking. In addition, urethral inserts can be quite effective for women suffering from stress incontinence. Biofeedback has recently acquired extensive attention from many researchers as a potential treatment to address different urinal problems. For instance, it is possible for a candidate to actually work with a therapist to better comprehend how the body works. A wire is connected in biofeedback to an electrical patch over the urethral muscles and bladder, which sends a signal to a monitor. This helps alert the person when the muscles are contracting. By understanding just when the muscles tend to contract, it may be possible for a person to gain better control over their own body. Among the different treatments available that may be considered and used for the treatment of different urinary problems, surgery is also considered a solution. However, it is important to note that surgery to address and repair different problems is often recognized as the last resort for the treatment of incontinence. When it comes to surgical interventions, sling procedures might be considered or used. In sling procedures, a synthetic or mesh sling is placed surgically under the bladder neck, or urethra for offering support. The sling generally serves as a hammock, which helps in the elevation and support of the urethra. It helps in the reduction of stress incontinence and is used normally as a minimally invasive procedure, 85. Bladder neck suspension is also one of the surgical interventions that may be considered or used. This surgical procedure involves supporting the urethra and bladder neck for reducing stress incontinence. It can be performed through the use of different techniques as pubovaginal sling procedures of Burch colposuspension. Collagen injections may also be considered or used as a surgical method for the treatment of different bladder problems and issues. In such a procedure, bulking agents like collagen may be injected into different tissues around the urethra. Since the tissues are bulked up, it plays an important role in reducing urine leakage and increasing support. This surgical method or intervention is used primarily for the treatment of women suffering from stress incontinence. In some cases, however, it is possible that even surgery may be unable to treat or help with urinary incontinence. In such situations, it is essential for the person to take steps to better improve their symptoms and ensure that their condition does not worsen. For the improvement of symptoms, it is undoubtedly possible for the person to take several steps. For instance, the person can check their local drugstore for protective undergarments or absorbent pads for adults with incontinence. Since most of these products are quite thin, they can be worn easily under clothes. In this manner, it can be possible for the person to lead a normal life as they would without the condition. Among the treatments of different bladder issues and problems in postmenopausal women, behavioural therapies have

also acquired significant attention. In these therapies, bladder training is considered quite important. It involves scheduled urination. A person may start initially by going to the bathroom almost every hour and then gradually increase the time intervals in between each bathroom visit. Timed voiding is also one of the behavioural therapies that have been explored by researchers in the literature. It involves setting a specific schedule for regular bathroom visits even if the person does not really feel the urge to urinate. It can play an important role in helping control urgency and frequent urination. This behavioural therapy has been recognized to effectively benefit people with an overactive bladder. Even though there is a wide range of interventions and treatments available that may be considered for addressing and treating bladder issues and problems among postmenopausal women, the suitability of any intervention is identified and determined on the basis of the severity of symptoms and individual circumstances, 86. Typically, more complex treatments like surgical options may be considered and used when conservative treatments have stopped working or are unsuccessful for patients. In addition to it, surgical options are considered when traditional and more simpler methods do not work due to the severe symptoms of bladder problems. Therefore, in the literature, even researchers have determined that a person should be more open about their problems, especially the ones related to menopause. It can help the doctor better determine the problem and then select and recommend the treatment that will be more suitable and effective for the patient.

3.0 Conclusion:

A critical role is played by estrogens in the maintenance, function, and development of the urogenital tract. After menopause, the deficiency of estrogen is related to the pathogenesis of several conditions that affect or influence the postmenopausal bladder. But even though it is true that urogenital atrophy is improved by estrogens, its role in addressing different bladder symptoms is still unclear. For instance, topical estrogens are not only capable of reversing the impacts of urogenital atrophy but also for positively affecting urinary urgency, frequency, and incontinence to some extent. It can be achieved without any sort of concerns about ES or endometrial stimulation and wider concerns and issues about the safety of systemic HRT. In clinical practice when faced with the treatment of urogenital symptoms among postmenopausal women, the optimal solution is concerned with using vaginal estrogens for correcting underlying atrophy initially. It can be carried out in conjunction with other suggested interventions like anticholinergics and pelvic floor re-education. In case systemic HRT is utilized for other indications, there may be a need to use vaginal estrogens as well for acquiring optimal effects.

4.1 Personal Measures:

In the literature, many studies have been performed that actually highlight and determine the need for personal measures that postmenopausal women can take to better manage the symptoms they experience. It is essential for postmenopausal women to actually develop and maintain an adequate and healthy lifestyle. In the maintenance of a healthy lifestyle, it is necessary to maintain a healthy and proper weight. Actually, additional pressure can be put by excess weight on the bladder, which is capable of worsening and

exacerbating different bladder issues and problems. Therefore, it is necessary for postmenopausal women to engage in regular physical activity and then follow or use a balanced diet to make sure that a healthy weight is achieved and maintained. Even though the maintenance of a healthy weight can be challenging and difficult, it is essential for combatting different problems including bladder issues. In fact, it can be said that being overweight is associated with many other health problems such as diabetes. Therefore, the maintenance of a healthy weight is not only capable of helping with bladder problems but also other major issues and problems that postmenopausal women tend to face and experience. It is possible for postmenopausal women to maintain an adequate and healthy weight by actually using a proper and healthy diet and exercising regularly. In addition to it, it is essential for postmenopausal women to stay hydrated. They need to drink an adequate and suitable amount of water throughout the day to stay hydrated properly. Even though the reduction of fluid intake before bedtime can help significantly with night-time urination, it is still necessary for a person to ensure that they consume enough fluids to ensure they are not dehydrated. Otherwise, it is highly likely they may experience different issues and problems related to dehydration. In order to avoid dehydration and related problems, it is necessary for postmenopausal women to drink and consume enough fluids. Another important measure that postmenopausal women need to consider and take is concerned with avoiding different bladder irritants. Actually, there are certain beverages and foods that are capable of irritating the bladder such as artificial sweeteners, spicy foods, alcohol, and even caffeine. It is essential for postmenopausal women to ensure that they either limit or completely avoid these types of foods to ensure that urinary symptoms are minimized in an effective manner. In dietary studies and research, it has been confirmed multiple times that these foods are indeed capable of worsening the bladder problems and issues that people tend to experience. Furthermore, in postmenopausal women, these issues can be more challenging to address and these foods are capable of further exacerbating bladder problems. Therefore, it is essential for postmenopausal women to make sure that such foods and items are avoided or limited to positively influence and affect bladder issues and problems. An important measure that can be considered and used by postmenopausal women for the treatment of different bladder issues and problems is concerned with practicing different pelvic floor exercises. It is essential to perform and carry out different Kegel exercises. Improving and strengthening the pelvic floor muscles through different Kegel exercises and activities is capable of improving bladder control and reducing urinary incontinence. It is essential for postmenopausal women to first locate the pelvic floor muscles by relaxing and contracting the muscles that are used for stopping the flow of urine midstream. These exercises can be performed and carried out regularly by postmenopausal women for strengthening and improving the muscles over time. It can be quite beneficial for postmenopausal women in helping them address their bladder issues and problems. In addition to it, it is necessary for postmenopausal women to consider and adopt different healthy bathroom habits. For instance, it is important to maintain regular bathroom routines. They can consider establishing a regular schedule for using and considering the bathroom to avoid holding urine for a long period of time or rushing to urinate when it is not necessary. Timed voiding can be quite helpful in regulating urination and reducing urgency. At the

same time, it is essential for postmenopausal women to actually take their time. For instance, when the restroom is being used, they should take their time to fully empty the bladder and lean forward slightly on the toilet to make sure of complete voiding. They can even consider and use double voiding. For instance, after urinating, they can consider waiting for a few seconds and trying to empty the bladder again. It can play an important role in making sure that the bladder is completely empty. One of the most important personal measures that can be considered and used by postmenopausal women is concerned with the use of protective devices or measures. An important protective measure is concerned with wearing protective undergarments or absorbent pads. In case the women experience occasional leakage of urine, they can use different absorbent pads or even protective undergarments to make sure that the leakage is prevented in an effective manner. These undergarments or pads can undoubtedly offer a sense of security and even prevent a sense of embarrassment in case of accidents. Therefore, it is essential for postmenopausal women to make sure that they consider this protective measure as it is meant to not only help them but even provide them with a sense of security. At the same time, it is possible for them to even carry a change of clothes. For instance, for different situations and circumstances where accidents might be more likely to occur or take place such as long outings or tips, it can be rather helpful to have a spare set of undergarments or clothes on hand. In case any accident does happen, the person can just use this spare set of clothes to make sure that they avoid any type of embarrassment. Other than these measures, it is essential for postmenopausal women to actually seek out professional assistance once they identify and determine the symptoms that indicate and point toward urinary problems. Many postmenopausal women are quite hesitant in reaching out to get professional assistance. However, it is undoubtedly one of the most effective personal measures that postmenopausal women can consider and take. They need to discuss their bladder issues or problems with an experienced healthcare professional who is capable of offering comprehensive evaluation and personalised treatment and advice. In addition to it, it is also possible for postmenopausal women to consider and undergo pelvic floor physical therapy. In case the healthcare professional has recommended different pelvic floor exercises, postmenopausal women can consult a professional therapist to participate in and undergo pelvic floor physical therapy. A trained and experienced professional is capable of offering exercises and techniques that are specific to the needs of postmenopausal women. Overall, these are some personal measures that can be considered and used by postmenopausal women to make sure they manage and positively affect their bladder problems and issues. They can consider these steps to better respond to the symptoms they experience and face, and even manage them in a timely manner. Regardless, it is essential for postmenopausal women to consult an experienced healthcare professional and seek out personalized treatment plans that are designed to help them effectively. It can help them manage and quickly address their bladder problems and issues.

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Conflicts of Interest

None

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