Trabecular Bone Score in Women with Premature Ovarian Insufficiency and Correlation with Bone Mineral Density

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BACKGROUND AND AIMS

Oestrogen deficiency associated with premature ovarian insufficiency (POI) results in increased osteoclastic activity leading to decreased bone density, earlier onset osteoporosis, and increased fracture risk. Hence, evaluation of baseline bone health is recommended for all women diagnosed with POI, including adolescents. Conventionally, bone health is assessed by a dual-energy X-ray absorptiometry (DEXA) scan, which quantitatively analyses bone mineral density (BMD). However, bone strength depends not only on bone density, but also on bone microarchitecture. Trabecular Bone Score (TBS) evaluates bone microarchitecture by textural analysis of lumbar spine DEXA images, with only a few studies in POI.[1-3] Already existing fractures can be detected by Vertebral Fracture Assessment (VFA). The objective of this study was to assess bone health by TBS in women with POI and how it correlates with BMD.

MATERIALS AND METHODS

This was a prospective, cross-sectional study undertaken from April 2024–October 2025 after obtaining ethical approval. The trial was registered under Clinical Trials Registry India (CTRI). Women with POI, meeting all following criteria, were enrolled: age <40 years; primary amenorrhoea or secondary amenorrhoea for at least 4 months; and elevated follicle-stimulating hormone (FSH) >25.0 IU/L on two occasions at least 4 weeks apart. Exclusion criteria included history of surgery on tubes/ovaries, post radiation, post chemotherapy, history of chronic renal disease, untreated thyroid disorders, and corticosteroids/anticonvulsant treatment.

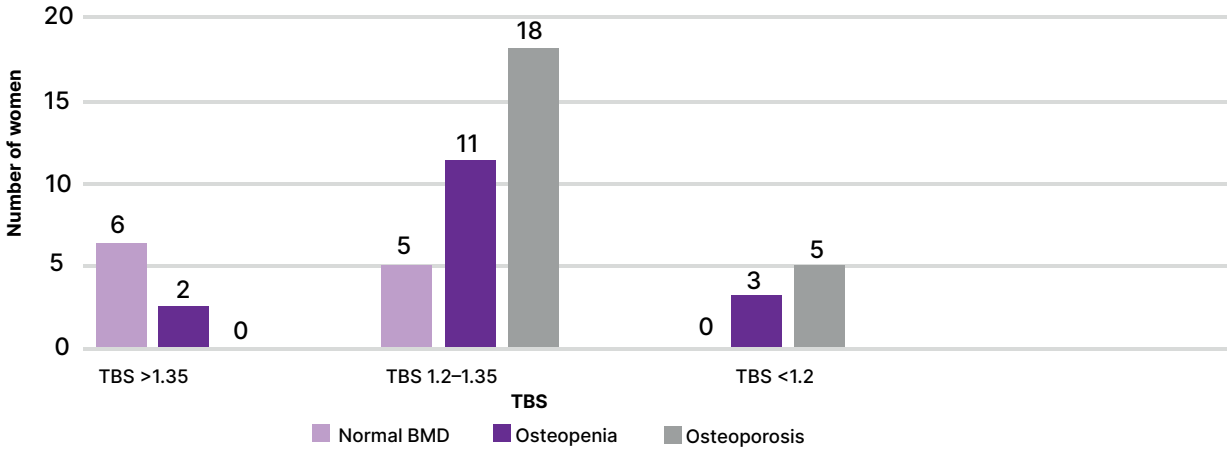
All eligible subjects underwent a DEXA scan to measure BMD, TBS, and VFA. BMD was measured at lumbar spine (L1–L4) and left hip. TBS was measured at lumbar spine (L1–L4) using TBS iNsight™ (Medimaps Group, Geneva, Switzerland) software installed in the DEXA machine. Images at T6–L4 levels were used for VFA.

DEXA scan T-scores of >–1.0, –1.0–-2.5, and <-2.5 indicated normal bone density, osteopenia, and osteoporosis, respectively. TBS scores of >1.35, 1.2–1.35, and <1.2 reflected dense trabeculae with good bone microarchitecture, partially degraded microarchitecture, and degraded microarchitecture with high susceptibility to vertebral fracture, respectively. VFA could detect any wedge, biconcave, or crush fractures.

RESULTS

A total of 50 women with POI were enrolled: seven had primary amenorrhoea and 43 had secondary amenorrhea. Mean age was 25.47 years. Only 11 (22%) had normal bone density, 16 (32%) had osteopenia, and 23 (46%) women were osteoporotic.

Figure 1: Distribution of women with POI according to TBS and BMD, N=50.



BMD: bone mineral density; POI: primary ovarian insufficiency; TBS: Trabecular Bone Score.

Among the 11 women with normal BMD, illustrated by pink in Figure 1, who would be labelled as having good bone health, only 6/11 (54.5%) had good microarchitecture, and the other 5/11 (45.5%) had a TBS of 1.2–1.35. None had a TBS <1.2. In 16 women with osteopenia,, illustrated by purple in Figure 1, three, 11, and two women, respectively, had a TBS <1.2, 1.2–1.35, and >1.35. Thus, 68.7% of women had a TBS of 1.2–1.35, indicating that degradation has started, only 12.5% maintained good architecture and 18% had a TBS <1.2. Among the 23 women who were osteoporotic, illustrated by gray in Figure 1, none had a TBS score of >1.35. Respectively, 18 and five women had a TBS of 1.2–1.35 and <1.2.

Overall, only 6/50 (12%) women with POI had good bone health, in terms of both BMD and TBS. Figure 1 shows correlation between TBS and BMD. VFA-detected fractures were present in 3/50 (6%) women with POI. Of these three women, one had osteoporosis and two had osteopenia; none had a TBS of >1.35 and two had a TBS of <1.2.

CONCLUSION

TBS is a complimentary tool in the evaluation of bone health, as it assesses bone architecture and compliments fracture risk evaluation by BMD on DEXA scans. The combination of BMD, TBS, and VFA has the potential for early detection of poor bone health in women with POI. Early diagnosis of poor bone health may alleviate long-term consequences through timely counselling, lifestyle modifications, and intervention.

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Congress Interviews

This year, we had the pleasure of speaking with several leading voices in gynaecological endocrinology at the International Society of Gynecological Endocrinology (ISGE) 2026 Congress. Tommaso Simoncini, President of ISGE, reflects on his career journey and the evolving understanding of hormone therapy, particularly its role in cardiovascular health and menopause care. Andrea R. Genazzani, Founder and Executive Director of ISGE, shares his vision of endocrinology across the female lifespan and the central role of hormones in health and disease.

We also hear from Roberta Diaz Brinton, Director of the Center for Innovation in Brain Science, Tucson, Arizona, USA, who explores the intersection between menopause and Alzheimer's disease, and the future of precision approaches to brain health. Basil C. Tarlatzis, Past President of the European Society of Human Reproduction and Embryology (ESHRE), discusses reproductive ageing and fertility preservation, while Peter A. Chedraui, Universidad Espíritu Santo, Samborondón, Ecuador, offers a global perspective on menopause, cardiometabolic risk, and culturally responsive care. Together, they reflect on the latest advances presented at ISGE 2026 and the future of women's health worldwide.

Featuring: Tommaso Simoncini, Andrea R. Genazzani, Roberta Diaz Brinton, Basil C. Tarlatzis, and Peter A. Chedraui

Tommaso Simoncini

Professor of Obstetrics and Gynaecology, University of Pisa; Head of the Obstetrics and Gynaecology Unit, University Hospital of Pisa, Italy; President, International Society of Gynaecological Endocrinology (ISGE)

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Q1 Could you begin by outlining your professional journey and how your early scientific training shaped your focus on hormonal biology within obstetrics and gynaecology?

I started as a medical student and, as often happens, the early steps of your career are shaped by the people you meet, sometimes purely by chance. I happened to meet my mentor, Andrea Riccardo Genazzani, University of Pisa, Italy, who had just come to my university. He was an incredibly bright and inspiring person, and that encounter drew me into obstetrics and gynaecology, particularly gynaecological endocrinology.

From the beginning, I was very interested in research. I had the opportunity to spend a long period abroad studying the molecular actions of steroid receptors in vascular cells. At the time, researchers were beginning to investigate why hormonal therapies and the hormonal changes associated with menopause influence cardiovascular health and disease.

Those were really pioneering years. I was fortunate to work in a fantastic laboratory at Brigham and Women's Hospital (BWH), as part of Harvard Medical School, Boston, Massachusetts, USA. I spent 2–3 years there doing basic research, essentially training as both a molecular biologist and a gynaecologist, while working closely with cardiologists in a multidisciplinary environment.

That experience shaped my professional trajectory. Later, I returned to Italy, joined the University of Pisa, and gradually developed my career there, first as a trainee and then as a practising physician and academic.

Q2 Did you enjoy combining scientific research with clinical practice?

Yes, very much. I think that combination was the real added value of my career.

> **It is very clear that oestrogens have profound protective effects on the cardiovascular system**

Of course, as you move forward professionally and take on more responsibilities, administrative duties and leadership roles tend to take up more of your time, but, for nearly 20 years, I had the privilege of doing both basic research and clinical work simultaneously.

I established a research laboratory in my department that remains very active today, with technicians, students, and young investigators. I was constantly moving between the laboratory and the clinic, which created a very stimulating professional environment.

Q3 Over the years, how has your perspective on hormone therapy evolved, particularly regarding cardiovascular risk and endothelial function?

Interestingly, my perspective has not changed very much; what has changed is the general perception within the medical community.

The scientific evidence has been remarkably consistent. It is very clear that oestrogens have profound protective effects on the cardiovascular system. This applies to both men and women, although women experience a dramatic shift in oestrogen levels at a specific point in life: menopause.

From an evolutionary perspective, oestrogens developed to support the enormous cardiovascular adjustments required during pregnancy. Pregnancy demands substantial changes in blood

flow and vascular function, and oestrogens play a central role in facilitating those changes.

When women lose oestrogen at menopause, the cardiovascular system is affected. Endothelial function changes significantly, and this contributes to the increase in cardiovascular disease risk observed after menopause, eventually reaching levels similar to those seen in men.

We now know that steroid receptors, including oestrogen, progesterone, and androgen receptors play key roles in cardiovascular biology. Endothelial cells are one of their most important targets, and the presence or absence of these hormones can substantially alter endothelial function.

Q4 Would you say that hormone replacement therapy reduces cardiovascular risk after menopause?

Yes, there is clear evidence that it does. This evidence comes not only from basic science and animal studies, but also from clinical research.

We have many biomarkers that allow us to assess vascular function, such as measures of vessel dilation, blood pressure regulation, and endothelial activity. These biomarkers consistently show that oestrogen replacement improves vascular function.

Even the clinical trials that generated controversy around hormone therapy show that, when used appropriately, oestrogen therapy reduces cardiovascular risk rather than increasing it.

However, that does not mean hormone therapy should automatically be used in every menopausal woman. Medicine requires clear therapeutic goals.

Cardiovascular risk is multifactorial. It depends on genetics, lifestyle, and comorbidities. Lifestyle interventions, such as maintaining a healthy weight, exercising regularly, and controlling blood pressure, remain the cornerstone of cardiovascular prevention.

Hormone therapy can play an important role, particularly for women who have symptoms or who may benefit from it, but it should not replace healthy lifestyle measures.

Q5 Translating laboratory findings into clinical practice is often challenging. What have been the key barriers in bringing mechanistic insights into routine patient care?

This is a complex issue. Interestingly, the main difficulty is not translating laboratory findings to patients, but rather translating them to other physicians.

Clinicians in fields such as cardiology or oncology are often well placed to understand molecular and biomarker data, but modern medicine tends to simplify information excessively. Many physicians simply do not have the time or energy to explore the underlying evidence in detail.

A good example is the reaction to the Women's Health Initiative (WHI). When those results were published, many people focused on the headlines rather than the full data.

For more than 20 years, we have been discussing and clarifying the findings, pointing out that hormone therapy is not harmful for the heart when used appropriately. The evidence supporting this is extensive and entirely consistent with basic science research.

Another challenge is that women's health has historically received less research investment compared with areas such as oncology, cardiology, or diabetes. These fields attract significant pharmaceutical investment, whereas preventive approaches in women's health have often been neglected.

Yet hormone therapy is one of the few treatments shown to prevent cardiovascular events and Type 2 diabetes in healthy women. That is an incredibly powerful effect, but it remains underutilised.

Q6 As President of the International Society of Gynaecological Endocrinology (ISGE), what has stepping into this role meant to you personally, and what vision do you hope to advance during your tenure?

It has been a great honour. I have worked with this society for many years, and it has grown into a truly global organisation.

We now have around 40 national or regional societies affiliated with ISGE, which gives us a very broad international presence.

My vision is that education should be the central mission of the society. Around the world, there is still a tremendous need for education in gynaecological endocrinology, reproductive medicine, and menopause.

> **Topics such as menopause or hormonal physiology are often covered only superficially**

In many countries, physicians receive little or no formal training in these areas. Some regions lack even the most basic hormonal therapies. The educational needs vary widely across the world, and our responsibility is to help meet those needs by providing appropriate training and resources.

Q7 Do you think current training programmes adequately cover gynaecological endocrinology?

Training varies greatly between countries, but in many places it is insufficient.

In the USA, for example, it has been estimated that many obstetrics and gynaecology residents receive little or no formal teaching on menopause.

In general, training programmes focus heavily on obstetrics, while functional gynaecology receives less attention. Topics such as menopause or hormonal physiology are often covered only superficially.

There is an enormous need for better education in this field, and addressing that gap is one of our priorities.

Q8 Which emerging themes or research presented at the ISGE 2026 Congress do you believe will have the greatest impact on clinical practice in the coming years?

This is a very exciting time for the field.

For about two decades, there were relatively few major pharmacological innovations in reproductive endocrinology. Treatments for ovulation induction, contraception, and menopause were well established, but there were limited new developments.

Now, we are seeing renewed interest. New therapeutic approaches are being developed for conditions such as endometriosis and other functional disorders that significantly affect women's quality of life.

We are also revisiting fundamental concepts, including the neuroendocrine control of reproduction and metabolism. Understanding how the brain regulates ovarian function is opening new possibilities for treatment.

Technological advances, including big data and AI, are also likely to transform the field. Although these approaches have already made major impacts in areas such as oncology, they are only beginning to influence reproductive medicine.

I am hopeful that, in the coming years, we will see significant innovations that improve women's health globally, ideally with treatments that are accessible and affordable, rather than limited to high-income settings.

Andrea R. Genazzani

Professor of Obstetrics and Gynaecology, Department of Clinical and Experimental Medicine, University of Pisa, Italy; Past President, International Society of Gynecological Endocrinology (ISGE)

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Q1 You are playing a key role at this year's International Society of Gynecological Endocrinology (ISGE) Congress. What was your vision in shaping the scientific programme?

My vision was that gynaecological endocrinology touches every moment of life, from the fertilisation of the oocyte to the death of the individual. In women, hormones are a fundamental part of not only the reproductive system, but also the function and development of the entire body. Every organ expresses oestrogen, progesterone, and androgen receptors. Every cell in the body is influenced by hormones.

We must also think about adolescence and the dramatic changes that occur throughout this period of life. These changes do not only affect gonadal function, but also personality development, body development, and the way an individual grows into adulthood. Hormones influence the capacity to reproduce and the way a woman thinks, lives, feels, and develops her identity.

That is why our society must bring together not only gynaecologists and endocrinologists, but also paediatricians, neurologists, psychiatrists, psychologists, and experts in metabolism, bone health, gut function, and cardiovascular medicine. Every system in the body is influenced by hormones.

Without hormonal support, a woman could not face pregnancy, delivery, or the physiological stresses that come with these events. Nature has protected the female body in remarkable ways, and hormones are central to that protection. They also help the body adapt to stress, both acute and chronic, which can dramatically affect health and reproductive capacity.

When you think of all this together, you can understand why it is essential to have a meeting like this: to exchange knowledge across disciplines and to understand the full impact of endocrinology on the female body.

> **Nature has protected the female body in remarkable ways, and hormones are central to that protection**

Q2 From your leadership perspective, where is gynaecological endocrinology heading over the next 5–10 years?

Over the next 5–10 years, we have several priorities.

First, we must better address adolescence and early female development, making these transitions easier, safer, and more protected. Second, we must continue improving contraception, making sexuality and conception safer. Through contraception and hormonal therapies, we can also help protect women from the later development of disease.

We must remember that the female body evolved for a very different life pattern: early menarche, early pregnancy, repeated pregnancies, breastfeeding, and then the natural end of fertility. Today, society has changed completely, but the biology has not changed at the same pace.

One very important point is that fertility declines years before menopause. Women often think, 'Menopause happens around 50 years of age, so I still have plenty of time', but that is not correct. Fertility may be lost

7–8 years before menopause, and if menopause comes early, fertility may end much sooner than expected. For example, if menopause happens at age 50, fertility may already be markedly reduced in the early 40s. If menopause occurs at the age of 40 years, fertility may decline significantly in the early thirties. The problem is that no woman knows exactly when her menopause will occur, and prediction is difficult.

We must encourage women to achieve their reproductive goals within the optimal reproductive window. However, for that to happen, society must also support them. Women must have the possibility to work, to live fully, and to become pregnant without being penalised.

Another major issue is that menopause itself has changed in meaning, because women now live so much longer. Around 200 years ago, most women did not live long beyond menopause. Life expectancy was below 50 years.

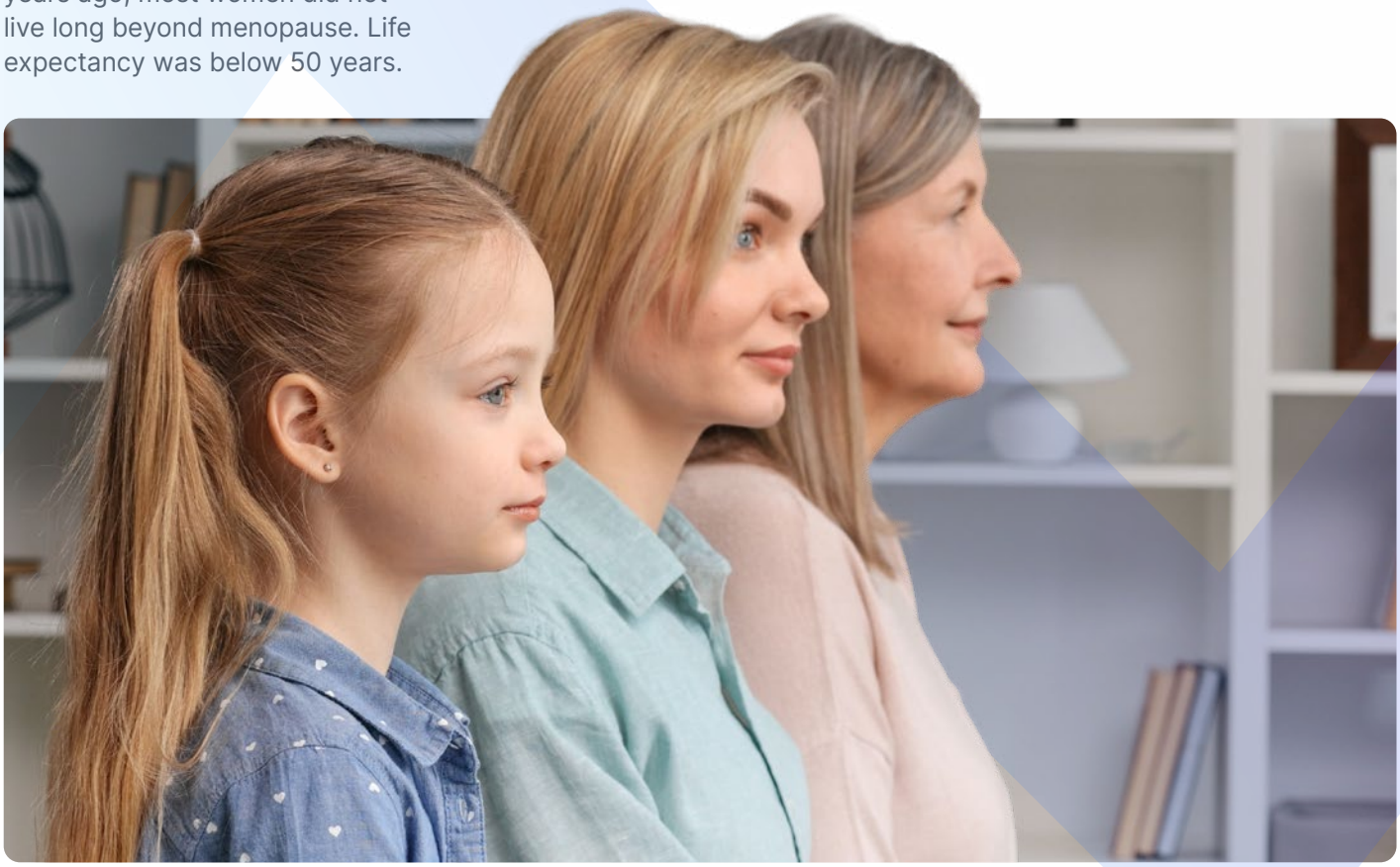
It is only in the last century that women began living well into their 60s, 70s, 80s, and beyond. In Italy, for example, the average life expectancy for women is now close to 88 years. This means that in just one century, we have effectively discovered postmenopausal life.

After menopause, women lose hormonal protection. You cannot change the genes or regenerate ovarian function once menopause has occurred, so we have had to learn how to help women live longer and better in this phase of life.

Women must have the possibility to work, to live fully, and to become pregnant without being penalised

That is why we discovered that hormone therapy can protect women, not only the genital tract and sexuality, but also the heart, the bones, and the brain. Hormone therapy can help a woman maintain her femininity, her mobility, her cognitive function, and her quality of life for decades after menopause.

Unfortunately, the Women's Health Initiative (WHI) damaged the field for more than 25 years. People became convinced that hormone therapy increased the risk of myocardial infarction, stroke, and cancer. While that was not the case, universities stopped teaching hormone therapy properly for years. Doctors were trained to view menopause as something 'natural' that women should simply accept, but menopause is natural in the same way that infection is natural; it does not mean we should not treat it when treatment can improve lives.



Q3 At this Congress, which emerging topic do you think deserves the most attention?

It is difficult to choose one single topic, because the programme is extremely broad. If you look through it, you will find major topics, including contraception, endometriosis, adenomyosis, abnormal uterine bleeding, adolescence and development, ageing, pelvic organ changes, gynaecological cancers, hormone-sensitive cancers such as breast cancer, menopause, fertility, and pregnancy protection.

Each person will be drawn to the area closest to their own expertise. I am particularly interested in the effects of hormones on the brain and other tissues, so I naturally follow those sessions.

Q4 What areas do you think the Congress should prioritise in the future?

Contraception, menopause, pregnancy protection, reduction of pre-eclampsia, reduction of recurrent pregnancy loss, and the prevention of unnecessary abortion through better reproductive care.

Q5 Having witnessed decades of evolution in the field, what gives you the greatest optimism, and what concerns you the most?

My concerns have changed over time. In the earlier years, many diseases, such as endometriosis, were poorly recognised. We had to define and characterise them properly as part of female reproductive and endocrine health.

Then, we focused greatly on the development of contraception, both to prevent unwanted pregnancies and to reduce abortion. We are not 'pro-abortion'; we want to protect women so they can have a healthy and satisfying sexual life without unnecessary risk or complication.

Now, we are moving beyond efficacy alone and focusing more on safety. For example, in contraception we have learned that only a few women, such as those with polycystic ovary syndrome or hyperandrogenism, truly need strong anti-androgenic approaches. For most women, we should be moving towards more natural oestrogens and well-selected progestogens that provide contraception without harmful androgenic effects.

In menopause, we have also learned that the old idea of oral treatment is not necessarily the best approach. If possible, we should use more physiological routes, especially transdermal oestrogen, which more closely matches the body's normal circulation and avoids some liver-related effects.

Another important development is the use of natural progesterone, not only to protect the endometrium, but because progesterone has major effects on the brain and nervous system. It plays a role in myelination and neural protection in ways that synthetic alternatives may not replicate as well.

This, to me, is a major direction for the future: more physiological, more natural, and more targeted hormonal treatment across the lifespan. In some cases, systemic treatment also needs to be combined with local therapy; for example, local oestrogen or androgen treatment at the vaginal level, to preserve vaginal function and quality of life.

Q6 If you had to summarise the core message of this Congress in one sentence, what would it be?

Hormones are essential to protect human life, maintain human health, and make the transmission of life possible.

Roberta Diaz Brinton

Director, Center for Innovation in Brain Science; Regents Professor of Pharmacology and Pharmaceutical Sciences, University of Arizona, Tucson, USA

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Q1 Could you begin by telling us about your professional journey and how you first became interested in women's brain health and Alzheimer's disease?

My journey began when I was a postdoctoral fellow at The Rockefeller University, New York, USA. I had the remarkable opportunity to be a basic science observer on a clinical trial led by Howard M. Fillit, who was then an Assistant Professor and Associate Physician at Rockefeller, investigating the effects of oestrogen in women diagnosed with Alzheimer's disease.

There was a clear rationale for the study. Oestrogen promotes the activity of choline acetyltransferase, which generates acetylcholine. At that time, the degeneration of cholinergic neurons in the basal forebrain was one of the earliest recognised hallmarks of Alzheimer's pathology. These neurons produce acetylcholine, which is a neurotransmitter involved in learning and memory.

Through that trial, I came to know one of the participating women. She was an Adlerian psychologist and a wonderful storyteller. I would walk with her on the Rockefeller campus, and she would regale me with stories about the intellectual rivalries between Jung, Adler, and Freud.

One evening I walked her back to her room at the hospital. I bid her good night, closed the door, waited about 30 seconds, and then knocked and entered again. I asked her "Do you remember me?" Her reply was "I am so sorry, should I?"

In that moment, that one woman with Alzheimer's transformed this neuroscientist's journey. She could not remember me for 30 seconds, and I have remembered her for over 30 years.

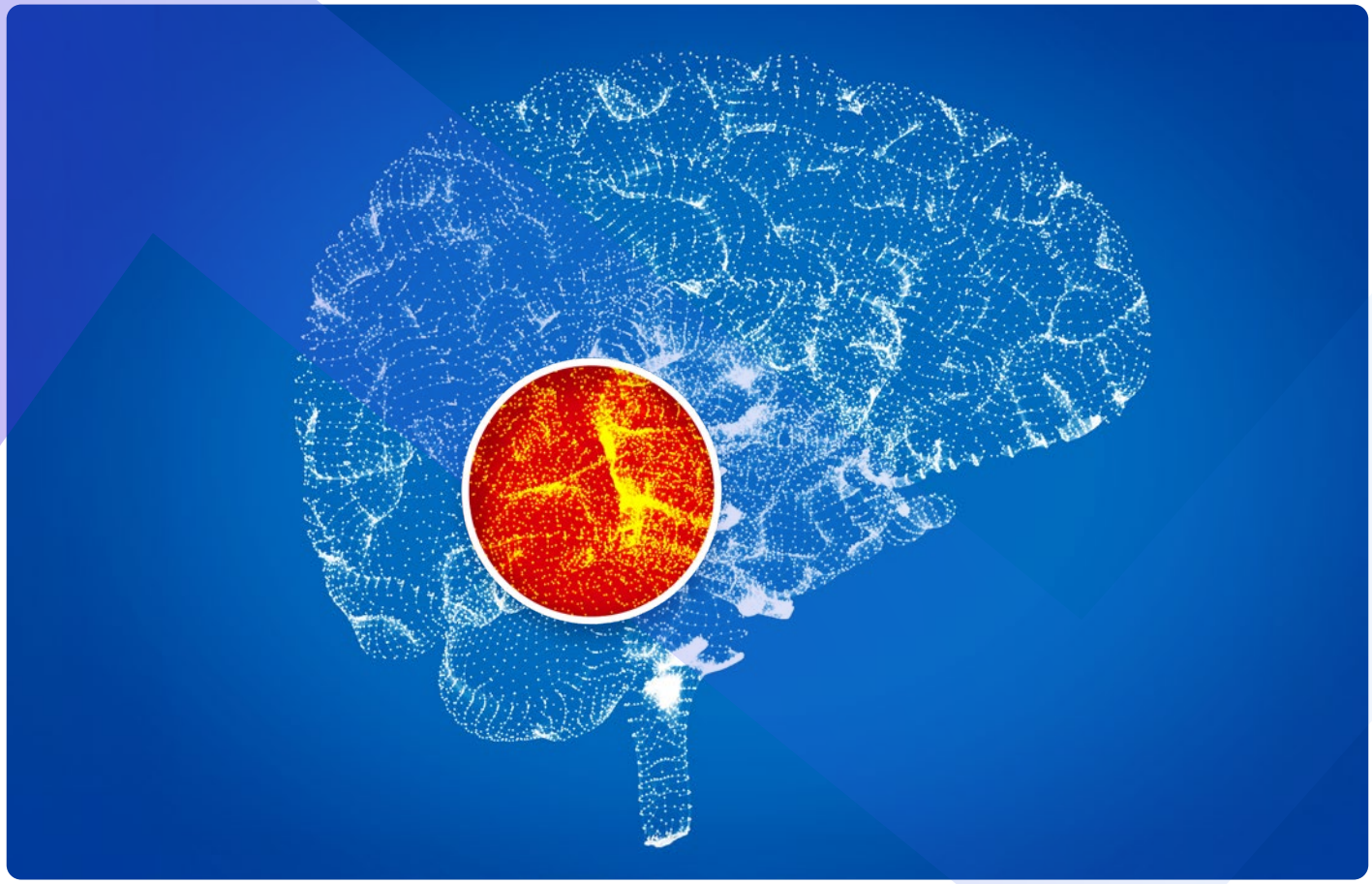
That moment changed the course of my scientific career and set me on a lifelong path to understand why women are at greater risk for Alzheimer's and to develop therapies that could prevent and even cure this disease.

Q2 You continue to attend meetings such as the International Society of Gynaecological Endocrinology (ISGE) Congress. What draws you to clinically focused meetings as a neuroscientist?

I come to ISGE for two broad reasons. First, the ISGE Congress is an opportunity to interact with clinicians. These are the people on the front lines of medicine. They are the ones making clinical decisions every day that affect women's health. Their knowledge and their challenges bring perspective that can inform our scientific research and our clinical trials. Medicine, especially around transitions such as menopause, is not linear. The complexity of human biology means that progress requires collaboration. None of us have all the answers.

Because of the interaction between scientists and clinicians, ISGE creates an innovative environment that encourages strategic innovative thinking and advances innovative solutions to challenges in women's health.

> **ISGE creates an innovative environment that encourages strategic innovative thinking**



Q3 Your research focuses on why women are disproportionately affected by Alzheimer's disease. Why is the female brain such an important area of investigation?

Two-thirds of all people living with Alzheimer's disease are women. If we want to prevent or treat this disease effectively, we must understand women's brain health.

Studying the female brain has revealed important biological insights, particularly around hormonal transitions such as the menopause. These transitions profoundly affect brain metabolism and neurological function. Interestingly, research in women has also advanced our understanding of the male brain. In men, testosterone can be converted to oestrogen within the brain. When testosterone production is suppressed, for example through certain medical treatments, the risk of Alzheimer's disease increases. Studying the female brain therefore helps illuminate broader mechanisms of brain ageing.

Q4 You mentioned a therapeutic currently being investigated in clinical trials. Could you describe the approach behind its development?

One of the therapeutics we are developing for Alzheiner's is based on allopregnanolone, a neurosteroid designed to stimulate regenerative mechanisms in the brain. This programme is currently in a Phase II clinical trial supported by the National Institute on Aging (NIA) within the National Institutes of Health (NIH).

More than 20 years ago, when we first proposed the idea of regenerating the Alzheimer's brain, regenerative medicine was not yet a well-established concept in neurology. Yet, the NIA supported the idea and encouraged us to pursue it.

Our goal is to activate the brain's intrinsic regenerative capacity. The Alzheimer's brain retains survival mechanisms that persist even as the disease progresses. If we can activate those mechanisms, we may be able to restore function.

Q5 Another area of your research involves PhytoSERM (NEUTherapeutics, Tucson, Arizona, USA). What is the concept behind this approach?

PhytoSERMs are plant-derived selective oestrogen receptor modulators designed to support both brain health and breast health.

Evidence suggests that menopausal hormone therapy can reduce the risk of Alzheimer's disease and other neurological conditions. However, many women hesitate to use hormone therapy because