**Menopause and Musculoskeletal Health**

**Dr Sonia Davison:** Hello, this is Dr Sonia Davison. I'm presenting a webinar today on secondary causes of osteoporosis, looking at causes and then working out how to investigate. This is me, I'm the past president of the Australasian Menopause Society and a clinical fellow at Jean Hailes for Women's Health. I have delivered a number of educational presentations. I always get my say in what I say in presentations, and I've done these for various organisations.

So when we look at bones, there's a little bit of debate about this, but there's 213 bones in total. Some say there's a few more, some say there's a few less. So we've got a lot of bones. We need to look after them, and as practitioners and clinicians, we need to be advising others. Bones are not just mechanical struts that keep us up. They're alive, they're metabolically active, and they're constantly being remodelled, which is very useful because we are very active, we take a lot of different forces and impacts as humans, and we need to adapt to a changing environment as well.

We also need to remove old and damaged bone, for example, like a fracture, and that's an amazing process that bones can undergo to actually repair a fracture. And we need to replace that with stronger, more mechanically robust bone. When we're looking at bones, 70% to 80% is that harder outer layer, and that's called 'cortical' bone. And we have 'cancellous' or 'trabecular' bone, which makes up 20% of bone, and is lighter and gives us the flexibility that we need in terms of bones, because if they were very rigid they would just snap. This is a picture of a worm. We have bones because as humans, and as mammals, we're not worms. Worms do not need to weight bear. They're just gliding or propelling themselves through the earth. They don't need bones. But we do, for all of the different things we do in life. To remain functional and active, we need those mechanical struts, but we need them to also be active. So bones support us, they enable movement. They protect vital organs such as our skull protects our brain, our rib cage protects our heart and our lungs, which we need to survive. They also produce blood cells, so red cells, white cells, platelets. And they store fat and minerals such as calcium, phosphate and vitamin D.

Bones also have very important metabolic functions. They produce the precursor substances to hormones. They also balance the calcium and pH, and they also detoxify, so absorption of heavy metals, for example, is a process that bones looks into. When we're looking at the content of bones, up to 70% is mineral, so mostly calcium and phosphate, that's our body's depository of calcium. 20 to 40% is organic matrix, which is collagens. Up to 10% water, and less than 3% fats. You'll know this as practitioners, but on the left of both of these pictures here you can see that normal bone is reticulated, there are holes within bone, they are not hollowed, they're filled with fat and blood cells, red cells, platelets, developing white cells, et cetera. And then you will see on the right of both of these images here, what happens with osteoporosis. So the bones become thinner, those connections become thinner, the holes get bigger, they're still filled with things but they are bigger, and you can see very easily that with minimal impact a fracture could occur, because the bone has lost essential structure and substance that it needs.

When we're looking at secondary osteoporosis, the important thing to know is that most osteoporosis in postmenopausal women is just due to a loss of oestrogen, but you don't want to depend on that. So less than 30% of women who present with postmenopausal osteoporosis will have a secondary cause, so we need to think about it for those women. And more than 50% who would present premenopausally, so it's not normal to have osteoporosis when a woman comes before menopause. But men don't have osteoporosis that often. So 50 to 80% of men will have a secondary cause of osteoporosis and definitely need to be investigated.

As I said, most osteoporosis is postmenopausal osteoporosis, but consider secondary causes when there's a fragility fracture without sufficient traditional risk factors. And when there's a Z score, which is the age-matched score on a DXA scan, that's less than, some say -2 and some say less than -2.5, and that's a standard deviation, if you remember back to your studies of a DXA scan and what it measures with bone density. So when we're assessing for osteoporosis and fracture, we need to really take a very good history and look at the person in front of us, and really know about family history. So general health, risk factors for bone health decline, smoking is very important, alcohol use too. Medication use, critical importance, because there can be interactions with bone and interactions with other medications for bone. Family history, especially a fracture. And when we're examining that person, it's very important to see what they physically look like. Are they strong? Are they fit? What their BMI is, that's particularly important. Is there a kyphosis or scoliosis that might be impacting on the way that they can exercise and carry themselves? And then finally we look at investigations to see if there is a secondary cause of osteoporosis present. And really we're doing that because if there is a secondary cause, many times that we can actually treat that secondary cause, or modify that risk factor and hopefully therefore improve bone density by moderating that.

So I'll go through some case studies for you today. And this is the first one, who is Susie. She's 61 years of age. She's post-menopausal. She's coming to you for a general health check. There is a family history of osteoporosis and fracture in her mother, and she's had a bone density before performed, and we'll see that in a minute. She's asking if there is a need for a DXA scan. So it's really tricky, because under Medicare guidelines, she doesn't receive a rebate for the DXA scan, and for some people paying out of pocket for a DXA scan, which can be between $100 and $200 currently, I believe, depending on where you have the scan performed, that's a lot of money for some people. But I also think that in this context it's a good investment in her health to have a check of bone density, given that the family history is there of osteoporosis and fracture.

And I just thought I'd walk you through what a DXA scan looks like. I know you are very busy in your practices, especially if you're a general practitioner. But it is very nice when you are able to look at the scans, and the patients really like to see them as well. So on the left there you can see a picture of the spine. That's not really important and not diagnostic, but it is if you can see a scoliosis or if there's particular degenerative disease, and there's sort of some white spots highlighted there in the picture which might indicate that. It's also important for the patients to see a general picture of their spine, too, to see if it looks a little bit out of whack. The middle coloured picture that looks like a rainbow with the green, yellow and red, you can see some three black bands coursing through that, and they're showing the decline in bone density to the right as people age.

The bottom line on that graph is the age, and the density is to the left axis of that graph. You can see where Susie lies, that little black dot in the middle is where she's lying. Green is normal, yellow is osteopenia and red is osteoporosis. You can also see on the graph to the right of the slide, this was her baseline, the first dot. She had an increase in bone density, which was exciting, which is the second dot in the middle. And you can see the black dot on the right of that final graph on the right, which means she hasn't actually lost much bone, she's actually had a net improvement in bone. But when you do look at the T scores, she does have osteoporosis at the spine, and of course we don't want that, especially in a 61-year-old.

This is her neck of hip, and again, you can see the picture on the left. They do a few different regions at the hip. We do look at neck of hip, usually, rather than total hip or Ward's triangle, although they're often always measured. And you can see there where her black dot is situated within the rainbow graph in the middle, she is down at the osteoporotic level there. And you can see on the right graph she was a little bit low, increased, but unfortunately has had a substantial decline after that, and I think it's about a 9% decline since the last scan. So it's a nice way to be able to physically look at the pictures, and when someone is very reluctant to have treatment, this can actually be very motivating to see, well this is where you are, this is your, and the other thing is their age-matched scores. So the Z score is their age-matched score. This is appearing on the information down the bottom there, you can see.

We want to have an age-matched score of zero, so you don't want to be any way deviating from the normal age expectations for bone density. So a Z score of zero is what we're really asking for. And if it's less than zero, that can also be a motivator for people, because they don't like to have bones that are less than what would be expected. And you can also see, which is very useful, height and weight on DXA scan, if you look carefully enough. So you'll see there for this lady, her weight is 37.6 kilograms, and for a height of 157 centimetres, this means her BMI is in the underweight range at 15.3, and Susie just doesn't have enough mass for her bones to be well supported. So you do need to have a healthy BMI of at least 20 to 21 to support, to give enough mass for your bones to perform their normal functions, and to have normal bone density.

So we'll start with nutritional causes of bone loss, which Susie obviously has being so thin. Poor dietary habits can contribute. Anorexia nervosa, so 30% of them will have osteoporosis, and there's a threefold lifetime increase and fracture risk. Bulimics can also have osteoporosis too, depending on what their net weight has been, if it's been low. Alcohol excess. So hence that's a very important part of history taking.

I'll take you to the next case study now, who is Rose. Rose is also 61. She's postmenopausal. She has Crohn's disease. She's had partial removal of some of her small intestine and long-term steroid use. So you can see alarm bells ringing in terms of, we need to be able to absorb things from our gut, including calcium, vitamin D, those sort of things, and steroids can also have a negative impact on bones. She was referred for advice, she had multiple fractures and osteoporosis on a DXA scan. Her BMI is reasonable, 20.9, and her vitamin D was very low at 15. So at that level she has vitamin D deficiency. No doubt that's from poor absorption, but she also might live in a cold area and be very sun smart, and that's something that we can really address very easily. I know the government don't want us to look at vitamin D levels, but for this lady it was critical, and I would want her vitamin D to be at least 75 nanomoles per litre. Looking at her DXA scans here, slightly different presentation and different DXA scans will give you a different image.

You are definitely allowed to request the images. Most facilities that do these scans can easily print them or email them. I know a lot aren't printing them anymore, but you can definitely request them, and the patient can as well. You'll see on the left, the bone density is in the red there, she has osteoporosis. And you'll see at the hip on the right, she did have osteoporosis and a further decline of about 11%, which is disappointing. And we don't want anyone to be osteoporotic when they don't need to. We don't want to, we want to prevent a fracture if we can, and that's the main aim of all of this. So when we're looking at gastrointestinal causes of bone loss, inflammatory bowel disease is one cause, and that was what Rose had. Pernicious anaemia, liver disease, and also coeliac disease. You can also see on the right, the most common site of fracture, and mostly the vertebrae, but with coeliac it can be the distal radius as well.

Medications are important cause of bone loss. Some of them, it's very minimal, and some of them it depends on how much they're using and how long, for example. Corticosteroids, so a prednisolone equivalent dose of 5mg or more daily. At 5mg, that's sort of replacement dose and their bones should be fine. And it's for more than three months. So just be aware of what they're using. Topical steroids not so much, but again, it's all a combination effect for some people. Some anti-epileptic agents. The SSRIs have a very modest effect. Thyroxine excess, not thyroxine to achieve normal thyroid function tests, it's just excess. Aromatase inhibitors. Tamoxifen in premenopausal women can have a deleterious effect on bone. However, when it's taken in a normal situation in postmenopausal situation, it's actually beneficial for bones. And chemotherapy is also another cause of bone loss. So we just need to be aware of what people are on.

Also, immunosuppressants such as methotrexate, lithium, heparin, not used so much anymore. Proton pump inhibitors have a limited effect on bones, but again, you need to consider it. Depo-Provera, depot medroxy progesterone acetate, over some time with repeated doses, yes, can cause bone density loss, it is reversible. Aluminium containing antacids, and some antipsychotics.

I'll go now to case study 3. I'm so sorry. So this is Sandy. Sandy's 52. She's perimenopausal. she's had tremor, weight loss, intestinal hurry. She's felt on edge generally, and she has dry and gritty eyes. So given that you look at her and she looks to be hyperthyroid, you look at her thyroid function test, her TSH is suppressed, and her free-T4 is elevated at 36, should be up to 19. Her TSH receptor antibody was also markedly elevated at 35, and her DXA scan revealed osteopenia of the lumbar spine and osteoporosis, unfortunately, at the femoral neck.

So Sandy's perimenopausal, not postmenopausal, and she has thyrotoxicosis due to Graves disease. So when we look at endocrine causes of bone loss, premature menopause is a very important cause, so menopause before age 40 years. Hypopituitarism, primary hyperparathyroidism, hyperprolactinemia, Cushing's syndrome, acromegaly, diabetes mellitus, and hyperthyroidism, and you can see the different sites that are generally affected there, in terms of those things. Primary hyperparathyroidism is a sort of a very useful thing to find, because if there's a parathyroid adenoma present, removing that can often mean that there's an improvement in bone density, following the removal of that and appropriate treatment. There are also immunological causes of bone loss, rheumatoid arthritis, lupus, multiple sclerosis, they tend to affect, the fracture site tends to be at the hip.

There are also haematological and neoplastic causes of bone loss, multiple myeloma, myeloproliferative disease, systemic mastocytosis, and primary or secondary malignancy. Most commonly affected fracture site is vertebrae, but of course with a malignancy it's the affected bones. Renal causes of bone loss is very important as well. Adynamic bone disease, secondary hyperparathyroidism and osteomalacia. So just be very aware of their family history there, the medications, and check their UEC. Other causes of bone loss. Smoking definitely can have a negative impact on bone density, especially when it's more smoking history over time. Disuse. So that's again, we're not designed to be worms, we're designed to be active, weightbearing, using our bodies. There are some genetic causes of bone loss. And infections, which can be general, which means they're just generally not well, versus bone-specific causes such as osteomyelitis.

This is a nice slide, which is a nice image, I thought, taken from this journal, Journal of Clinical Medicine last year, 2022. And it just nicely shows that, really, anything that can go wrong with the body, if it in fact impacts on nutritional aspects, or the structure of the body, can definitely, or lead to another medication, can definitely lead to a negative impact on bone density and secondary osteoporosis. So I thought that was a neat way of looking at it, that this author has looked at.

So all very well and good, but how do we investigate for secondary causes of bone density loss resulting in osteoporosis? So for anyone who comes along to you with osteoporosis, just remember, I wouldn't look at someone and think that they're postmenopausal, oh, this is postmenopausal osteoporosis. I would do these tests in everyone. Blood count, ESR, UEC. Liver function, ALP is a bony marker that's within the LFTs, but also to see if they're unwell with other disease that might be affecting their liver. TSH. Calcium, phosphate and magnesium sort of go as a parcel. Parathyroid hormone. And a vitamin D level is also very important, and needs to be correlated with the LFTs and the PTH as well, and the calcium.

But when might we do additional investigations? Well, if the Z score is less than 2, -2, or -2.5, some others say. If they're premenopausal women or men less than 50, and if there's a lack of specific clinical findings or risk factors for osteoporosis. So these additional investigations would be useful. So if they're premenopausal an estrogen level, oestradiol and FSH. If they're male, an LH or a morning testosterone. Serum protein electrophoresis, and free light chain assays, which is essentially urinary protein electrophoresis. Coeliac serology, you might just be, even if they don't have symptoms, you might be surprised, they might have coeliac disease. A total IGA needs to be measured with that too. HbA1c. 24-hour urinary cortisol, if they look like, what we used to say, a lemon on sticks, so a big truncal mass and very skinny legs and arms, Cushing's disease might be something. So I wouldn't do 24-hour urinary cortisol without a good reason to do it, it is a hard test for patients to do. And you might want to do a 24-hour urinary calcium if they have an abnormal calcium or PTH. And we talked about medications before, and the HbA1c you'll see there, it's very interesting that metformin can actually have a positive impact on bone density. So some medications can certainly do the reverse of other medications that have a negative impact.

There's a lovely review article, it is lengthy, but if you need further information, Professor Peter Ebeling, who's one of the Jean Hailes endocrinologist, and has a vast experience and research experience in bone health, does a lovely article with others on secondary osteoporosis, for further reading. There are lots of resources out there. So if you are new to Jean Hailes, or new to this area, there are lots of women's health resources here. These are not particularly noted for bone health down the bottom here. But just to show you, when it comes to anything such as menopause, endometriosis, et cetera, there are health professional tools, and then there are educational components to our website as well, such as webinars. Ask an Expert is very useful if you have difficult cases, you can submit those. Hormone therapy cases, postmenopausal health, there's lots out there. And if there's something that you think is not out there, we'd be delighted to try and include that on our website if we thought it would benefit you and your patients. But there are some consumer resources on bone health, which are very useful for patients to look at. I'll go back to those again. And they're very useful for general advice for women, and they will touch on general advice about how to maintain good bone density and how to improve bone health in general.

It's been delightful today to speak with you. I hope you've learned something. I hope you feel comfortable now about looking at secondary causes of osteoporosis. It's been a pleasure to be here today. Take care.

**End of transcript**

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