

Grand rounds: osteodensosis

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Gerry recovered from his fit of drowsiness just as rounds were coming to a close. It always happened after a night on call: as soon as the lights dimmed and the projection was launched, he would be fighting sleep — a tussle he happily lost when he sat far enough from the podium to avoid detection and insult.

Today seemed typical of other weekly grand rounds of his first residency year. A couple of residents had deliberately set off their beepers and left. The B Team gang, led by the obnoxious PGY-3, T.J. Schmidt, strode in late, wearing greens pilfered from obstetrics to make it look like they (and not he) had spent the night on call. They had promptly gone to sleep in the back row. Other housestaff and attendings sat scattered throughout the half-empty auditorium, where wafted the usual whiff of limp, souring lettuce from cellophane-wrapped sandwiches. The front row was occupied, as always, by a collection of retired doctors, still enthusiastic but now deaf. Clinical clerks in their stigmatizing short white jackets sat on one side, taking notes.

A few things were different today, however. The better-than-average turnout included a few professors from physiology who normally shunned hospital sessions. Gerry also noticed scarf-bedecked technologists from the laboratory, as well as the head of radiology. No doubt they intended to please by showing up for the VIP from away — a former classmate, a personal friend, a leading light in research, or so the chief's introduction claimed. But the most startling difference was that Gerry was actually paying attention.

Dr. Massey Hyde-Jones was the epitome of a distinguished visitor: tall, silver-haired, well-tailored and articulate, with an Oxbridge accent that Gerry knew the chief would kill to emulate. Close to retirement, like the chief, Hyde-Jones was proving that age need not inhibit deep thoughts and great discoveries. The heady topic was no less than a new disease.

"Osteodensosis," the speaker concluded, "is the most prevalent and least-recognized condition in the aging male population. It may account for the long-acknowledged gender difference in death over age 60. We must face up to this serious issue and embark on clinical trials to investigate its management."

The item that had roused Gerry to consciousness was a graph displaying the frequency of osteodensosis. It rose steadily with age, reaching nearly 100% of the male population at age 84. "How can you have a disease that affects 100% of the population?" he muttered. "At least those guys are alive! I hope I'm still alive at 84."

What was the definition of this new disease, anyway?

What were its symptoms, and how was it treated? "Hormones, I'll bet," thought Gerry smugly, suspecting that a pharmaceutical company must be paying the visitor's expenses. But he wasn't about to ask, especially since the answers might have been given while he was asleep. He wished he hadn't dozed off. Perhaps the discussion would compensate.

The lights came up, and polite applause ensued. The B-Team housestaffers stirred, leaning forward and knitting their brows in feigned interest. The chief stood, all smiles. "Thank you, Massey. Most excellent! Dr. Hyde-Jones is willing and, indeed, eager for your questions — and I'm sure you'll have lots after those impressive revelations."

Hands rose throughout the room, but the first questioner didn't wait to be recognized. It was old Ferenczi, in the front row, the last general internist in town. Formal, with a charming accent, Ferenczi always had to have the first question, sometimes droning on for minutes. It was embarrassing. Gerry wondered why the chief tolerated it. Perhaps having no questions would be worse. Besides, Gerry had to admit, Ferenczi was nobody's fool.

"My congratulations, Dr. Hyde-Jones. It's not every day that we learn of a new disease, especially one that is right under our noses without our knowing it. I predict that we will soon be calling it Hyde-Jones syndrome."

Hyde-Jones made a gracious gesture that simultaneously acknowledged the praise and indicated that Ferenczi should get on with the question. "I was wondering if you would go over the definition. As I understood it, you propose not only a new disease — of dense bones — but a new way of thinking of *any* disease. It is to be diagnosed in relative terms by comparison with the rest of the population. Could you explain that again?"

"With pleasure, doctor." Hyde-Jones flashed a slide used earlier. "Osteodensosis went unrecognized because no one was looking for it. We assume that strong bones are healthy because they break less readily when exposed to trauma. But osteodensotic bones carry untold risks that become apparent only when we draw novel comparisons.

"Women live longer than men, and, among the physiological characteristics of elderly women, one of the most striking is thinning bone. It could be said that all women over 80 have thin bones, as compared to the male population. But let's face it, at age 80, half the women who could be alive still are; most of the men are already dead."

A rumble of laughter greeted this statement. Hyde-Jones glanced archly at the audience, eyebrows raised as a sign that the joke was shared, and continued.

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"Obviously a young man has denser bones than an older man. This difference is not disease. We identify osteodensosis by calculation: comparing bone density of the patient to the average for age- and race-matched groups of both women and men who lived beyond 80 years. The mathematical formula shown on this slide indicates when excess density becomes pathological. Yes, it may be a new way of diagnosis.

"Of course, men do not die of dense bones. They die of stroke, heart attack, diabetes, emphysema and cancer. But — bone density in cadavers of men who died of these conditions is greater than the average for males and females. I suggest that osteodensosis constitutes as reliable a risk factor for early death in males as the established indices of cholesterol, blood pressure, weight and family history. How it engenders the risk still needs to be elucidated."

"Just one more thing," Ferenczi said, noticing the chief's impatience and speaking quickly, "if you'll indulge me a second longer. I really must protest the name you give to the disease with its jarring *mélange* of Latin and Greek."

Gerry now imagined that Ferenczi had seized the first question simply to flaunt that Old World erudition once again.

"Yes, you're quite right. It bothers us too. We wanted to avoid confusion with the rare hereditary condition of osteopetrosis. But, quite frankly, we thought that the etymologically purer constructs, such as osteopyknosis, osteobarosis, osteolithiasis or osteo-ostosis, offered no more elegance and far less clarity for lay people needing education. We live in a multicultural age, after all." Hyde-Jones shrugged, calmly but surely trumping in erudition.

Seeing that Ferenczi was nodding, the chief invited the head of radiology to take the floor. "Did I hear correctly that osteodensosis has no symptoms? Isn't that problematic for a new disease?"

Irritation flickered across Hyde-Jones' smooth features. "That's right. No symptoms at all, other than acute death from other causes! That's why it is so sinister. As you know, many serious diseases are asymptomatic until they are well advanced: hypertension, cervical cancer, lung cancer."

The questioner sat down, deflated.

Looking a little desperate, the chief turned to Professor Aidan Hill, the bright, young physiologist who had been waiting patiently, arm raised, since the floor had opened.

"Okay. I like your suggestion, and I can even imagine a metabolic connection between dense bones and cardiovascular effects. But can you really claim this is cause and effect? I mean, perhaps bone density is a "fellow-traveller," a trait that goes along with something else, as yet unknown, that is the real cause. For example, the patient could have a dietary preference for food that strengthens bone and also happens to damage the heart."

"I do not deny that," Hyde-Jones replied. "Correlation is not causation. But is it not more sensible to proceed as if correlation might be causation, at least until some better explanation comes along? Early male mortality has reached epidemic proportions, and we accept it. For years we've

been dithering with lipids, blood pressure, weight reduction and even exercise, yet where has all that taken us? It's time we tried something new."

"But how would you treat it?" T.J. Schmidt blurted from the back row, setting B Team tittering. The chief glared, but Hyde-Jones responded blithely.

"Good question back there. I'll get to it shortly. But let me finish with the physiological question. Healthy bones, sick hearts: a link is counterintuitive, but how do we know that it does not exist, if we don't look for one?"

This challenge brought the sound of (just) two hands clapping off to the left, where sat Sandy Chang, the born-again, local guru of evidence-based medicine. Hyde-Jones beamed with interest at Chang and pointed at the clock in an interrogative manner that shocked Gerry for its obvious implication: "Will I see you at lunch?"

"As for treatment, we could consider parathyroid hormone and vitamin D in acute settings, although I'd prefer synthetics with less risk of mental and gastric disturbance. But the honest answer is that I don't know, and I'd like someone to help me find out." The speaker aimed a bemused, sidelong glance at Chang, who grinned.

"To lighten male bones, we could remove or modify those factors that build bone: exercise, vitamin D, calcium and anabolic steroids, including testosterone. But we'd have to be careful: vitamins and minerals affect a host of other things, including heart function. My inclination would be to avoid disturbing that axis. Same could be said for exercise." Hyde-Jones paused, evidently for effect. Something big was coming.

"Prevention may be simpler than treatment, and here, hormones strike me as very interesting. Males are subjected to unopposed, unrelieved testosterone. Women have a natural break at regular intervals. I've often wondered if the lack of a hormonal cycle in males explains their extraordinarily dense bones. Sometime in adult life, then, preferably after reproduction but before climacteric, we could administer estrogen, then withdraw it, and thereby create a cycle."

Gerry could not believe his ears. Hyde-Jones plowed on. "We could consider antitestosterone with drugs, like Testoxifen." A ripple of protest ran through the audience. "Yes. I know. We reserve Testoxifen for malignancies and other life-threatening situations, and it has unpleasant side effects — loss of libido, sore nipples and hot flashes. But osteodensosis could well be a life-threatening situation that we refuse to recognize despite a wealth of epidemiologic evidence!"

"Would you castrate them, doctor?" came an anonymous voice from the rear. Gasps filled the air. The chief, looking weak, sat down. Hyde-Jones was cool as a cucumber. Clearly the question was not new; perhaps the visitor welcomed it.

"I might. In this era of sperm-bank technology and tolerance for gender identity, I see no reason why any human being should be subjected to the raging effects of a hormone that could well mean an untimely death. If family history for

early male mortality were strong, and if the patient had already reproduced or banked his sperm, then why not?"

Silence. Gerry's mind was racing with reasons why not.

Hyde-Jones was completely in charge. "Just think, the benefits could go well beyond prevention of this disease. The vast majority of crimes are committed by men, and most crimes committed by women are provoked by men. What is the relationship of unopposed, lifelong testosterone to those statistics? Has anyone thought to look?"

"There'd be other spinoffs too." Now Hyde-Jones adopted a frivolous tone. "No more shaving, for example. I've long suspected that Procter and Gamble and the rest of the soap industry have a vested interest in preventing us from making this important discovery." Another smile at Sandy Chang confirmed what everyone was suspecting — a budding December–June romance.

"But Massey!" the chief moaned from the front row. "That's like suggesting that the paper industries want to keep us menstruating!"

"Well, my dear, how do you know that they don't?"

Gerry liked that answer, and he was beginning to like Hyde-Jones. Shaking her head, the chief rose again to face the audience. "One more question, and then I think we should let our guest go to lunch."

"What the hell," Gerry thought. He raised his hand.

"Speaking as the only man in the room," he began, "in fact, speaking as the only male doctor ever to have served in this hospital, I can't help but ..."

"See how he has his legs crossed!" called out T.J. from the back. Peals of merriment rang out. Offended, Hyde-Jones glared at the chief, but she was laughing too. Seeing her old friend's annoyance, the chief recovered, wiped her eyes (smudging her makeup) and bellowed: "Silence!"

"Dr. Hyde-Jones, I enjoyed your presentation, especially how you've encouraged us to see things in a different way. But — and forgive me for saying this — I wonder if we've come to this new diagnosis simply because most medical practitioners are, and have always been, women. Perhaps this is like one of the 'hidden industrial forces' that you alluded to a moment ago. I mean, you could build a case for women being sick with something — oh, like the opposite of osteodensosis — what would you call it?"

"Osteoporosis, Gerry."

"Yeah, thanks chief. Osteoporosis. You could say that all women have it at age 80 and that we need to treat it because it correlates with death. Unlike your disease, we could even say it has symptoms, like fractures and pain."

"Fractures are caused by trauma, Gerry," the chief inter-

rupted with exaggerated forbearance. "By accidents, unshovelled sidewalks, social decay. I'm tired of your patient-blaming attitude."

"Let him continue," said Hyde-Jones.

"Sorry. Okay. Forget the symptoms with osteoporosis. My point is that maybe you don't see female thinning of bones as a disease because you are women and you think changes in women are normal. Do you see what I mean? Differences in women are physiological — those in men are abnormal, pathological."

B Team started to groan, but Hyde-Jones raised her hand for silence.

"Gerry's point is well taken. It's the best comment I've heard today, and the only one to focus on how discoveries are made. The pervasive female character of the profession may well explain why it took so long for osteodensosis to be identified."

Gerry felt pretty good about these remarks and began to relax — which made the final blow all the more painful.

"But I'm afraid the justification for this new disease is obvious. Lose sight of it and you've lost the whole match. *We* are alive, and *they* are dead."

The audience exploded, B Team included. Laughter, whistles, applause, even foot stamping, none of which had been heard at grand rounds within living memory. The chief was in her element. Despite the awkward moments, rounds had never been better: new science, well presented, a speaker with great poise. She shook hands with Hyde-Jones and, in a magnanimous mood, gathered up faculty for that hot lunch with libation: Aidan Hill, Sandy Chang and even Elisabeth Ferenczi, knowing she'd regret it later.

Humiliated, Gerry watched them swagger out the door, tottering on their heels, their skirts swishing. He had to agree with old Ferenczi that Hyde-Jones had an eponymic future; her syndrome might appear on fellowship exams. But he wasn't convinced of this new disease. And although it was still early in his residency, he already knew some things were worse than being dead. Living without his gonads ranked high on that list.

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