

## Fish in space

OK, we are now going to spend a whole podcast dealing with one rather extraordinary issue. If you fly a fish up into orbit, letting it swim around while it's in free-fall, it will start losing bone density.

This takes time of course, at least ten days, although for many fish that is a lifetime. And of course, we are talking about bony fish – rather than sharks and rays, which have a cartilaginous skeleton. For the record, Science on the ISS is right behind any initiative to get a shark into space – and return it safely to the Earth – particularly if it's a great white. But, that is another story.

The fish we do send up are generally medaka and zebra fish, which are small and harmless – and are ideal pisco-nauts. Firstly, they are popular aquarium fish. This means they survive well in artificial environments and their nutritional and environmental needs are well understood. They are also short-lived and fecund, so you might be able to make observations on several generations of them over the course of one space mission. They grow in transparent eggs, so you can watch their embryos develop, and even the hatchlings are semi-transparent and can stay that way until adulthood. So you can watch, for example, their bones developing.

Of course, we not only want to watch their bones developing, but also see what happens to their bones when we change their food, put additives in their water and even manipulate their genomes. Since fish really do lose bone density in microgravity, if we can find something that will substantially reduce that bone density loss, then it could be Nobel prize time. Not just because you found a cure that might stop astronauts getting osteoporosis in microgravity, but because you found a cure that could also help billions of people back down on Earth.

But just why the heck do fish get osteoporosis in microgravity? Fish don't walk, they float. And they float whether they are down here on Earth or up there in free fall within the ISS Aquatic Habitat, which is installed aboard the Japanese Kibo module.

It's not hard to understand why human astronauts lose bone density in microgravity. On Earth, their skeletons have to constantly hold back more than 60 kg of body mass from accelerating towards the centre of the Earth at 9.8 metres per second per second. On top of that, their skeletons also have to deal with the additional stresses of getting out of bed, walking down stairs and even picking up the shopping.

In orbit, astronauts and the ISS itself, are still trying to accelerate towards the centre of the Earth. But by falling along a curving, orbital trajectory that keeps them at a constant altitude above the Earth's surface – the astronauts and everything around them just keep on falling at the same velocity around and around the Earth. Under such free-fall conditions, human bones are no longer subjected to the regular compression forces they experience on the Earth – and so, they begin to change.

You see, a completely rigid bone is not a good thing. Expose it to too much force and it won't bend, it will break. Out in the wild, away from an organised health care system, once you break a major limb bone, you're pretty-much dead. So, natural selection has ensured that your bones can flex under stress. But a completely flexible bone is not a good thing either.

You can't chase down an antelope or pick up the shopping if your arms and legs are all floppy.

So we are all genetically-programmed to ensure that our skeletons always have just the right balance of rigidity versus flexibility – to support our body mass, but also to absorb the routine physical shocks that we are all exposed to on a daily basis. And our skeletons manage to do this, all the way from toddling-child up to running and shopping adult.

The right balance of rigidity and flexibility is achieved through an ongoing competition between two types of bone cells, the osteoclasts – whose mission in life is to make your bones flexible – and the osteoblasts, who are determined to make your bones are rigid.

Which cell population gets the upper hand seems to depend on just how much stress your bones are exposed to, day by day. In microgravity, the osteoblasts quieten down, while the osteoclasts continue deconstructing bone and returning calcium salts to your circulation. This turns out to be a significant issue for the ISS water-recycling system. Each time a new crew comes aboard they start unloading lots of calcium salts, which risk clogging up the filters. Indeed, it is also an issue for the astronauts' *internal* plumbing, since the increased calcium outflow increases the risk of them forming kidney stones.

We don't really understand the link between physical stress and bone density. We know a lot about the hormones that control bone density changes, but we don't really know what actually triggers those changes. It might be the compression of fluids in bone tissue, or it might be the formation of microfractures in physically-stressed bone. If we can identify the trigger and if we can then *mimic* that trigger with some kind of drug – well, there's that Nobel Prize again.

But anyway, we are still skirting around the main issue of this podcast – just why the heck do *fish* lose bone density in microgravity? On Earth they don't spend their lives pressed down upon a surface, they *float*. And on the International Space Station, in the Aquatic Habitat, they also *float*.

So, here at Science on the ISS we started googling *bone density loss, fish, ISS...* nope. Then *piscine osteoporosis*, nope. Then *fish in space, WTF...* nope, nothing. Sure there were lots of webpages reporting that fish lose bone density in orbit, but no explanations of *why* were being offered.

So, it was time to bring out the big guns. We posted to the Cosmoquest forum, outlining the problem, seeking suggestions and after two weeks... nope, not one person replied. So, then we tried... *Dr Karl*. You always get an answer from Dr Karl. Although... the answer we got was *because there's no forces acting on their bones in microgravity*. No, really?

So, here's what *we think* the answer is. Imagine you have fish A floating on Earth and fish B floating in microgravity. Is there a difference in forces? Well, yes. There are pressure differences within the water that the different fish are floating in. On Earth, you might have experienced that you can swim around on the surface, no problem. But dive down a few metres and your ears begin to hurt, as external water pressure starts to press in on them. That pressure you find in deep water is because of gravity. Layers of water, that are trying to accelerate towards the centre of the Earth, press down on layers below them and the

pressure builds and builds, depending on just how many layers of water there are above you.

So this is at least half of the story. If a fish swim downwards on Earth it will be exposed to more pressure. Its body-form and its skeleton will be compressed and stressed, and so its own little osteoblasts will be working hard to keep its bones rigid. But up in orbit, in microgravity... there is no up or down. There are no layers of water pressing down, one on top of the other. Instead, *water itself* floats in microgravity – and with no pressure differentials.

The other half of the story is that most bony fish have swim bladders, which help them to maintain buoyancy, much like the vests that scuba divers wear. This is a useful thing for fish on Earth, under gravity, since the low density gas in their bladder will keep them at a certain level in the water, without having to constantly expend energy on swimming up or down. But it also means that the fish must *occasionally* work against this buoyancy to swim down – perhaps to pursue food or to avoid becoming food. These short bursts of effort are what help to keep their muscles, as well as their bones, in good shape.

But of course in microgravity, the swim bladder becomes irrelevant, since the pressure and density of the surrounding water never change. So just like astronauts, fish in orbit just float around, without needing to expend the slightest amount of effort.

So, that is the answer to why fish lose bone density in microgravity. Without gravity, the fish do a lot more floating than they ever do on Earth – and so, their bones lose density. This of course means that Dr Karl was right. Fish lose bone density in microgravity because there's less gravity.