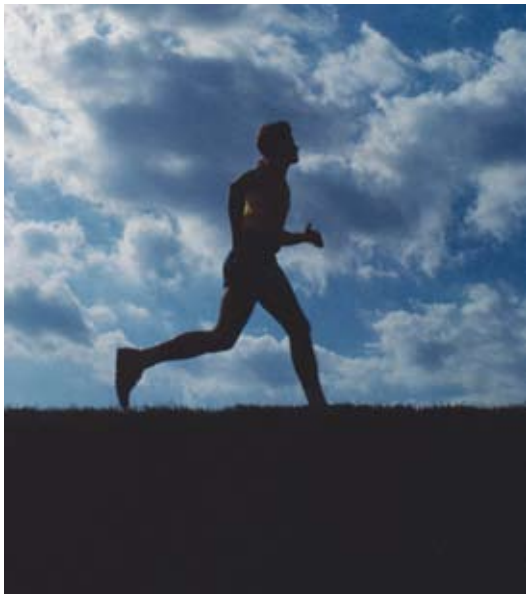
You might not see them but they see you



It is always important to be aware of, and take heed of, consensus expert opinion in medicine, but I feel it is equally important to not routinely accept it as gospel. Therefore I tend to love medical anecdotes where a doctor with a radical but intelligent idea which dissented from consensus opinion has later been proven to be correct. The most famous of these in recent Australian medical history was the story of *Helicobacter pylori*, which was proven by two Australian doctors to be a common cause of stomach ulcers.[1] Their story starts with a hypothesis that Robin Warren came up with and Barry Marshall tested. When they initially tried to publish the idea, it was considered so radical that they couldn't even get it accepted as a paper at the Gastroenterological Society of Australia annual conference.[1] Twenty years later they won the Nobel Prize for medicine.

The popular TV medical show *House* is based around a physician called Gregory House who routinely shows up his more conservative medical colleagues by thinking outside the square and coming up with radical but generally correct diagnosis. On the theme I am writing it is a refreshing show in that it paints the medical establishment as often being too conservative. Where *House* is a frustrating show is that it sets an unrealistic ideal that there is such a fantasy expert who is so clever that with enough tests and clever history taking that he can diagnose absolutely everyone. In the show of course, virtually everyone turns out to have a curable disease. If only the real world were so obliging.

I also like to ponder real world counter-arguments that sometimes it is better to just treat a problem functionally rather than insisting on making an anatomical diagnosis in every case. Low back pain is probably a classic example where a large number of patients can be most effectively managed by simply treating their condition (with, for example, mobilisation, core strengthening, NSAIDs, moderate exercise) rather than worrying about whether the pain is coming from their facet joints or discs.[2] I certainly wouldn't say that this is the case for every low back pain patient, but if you had to decide whether to spend someone's last $300 on a lumbar MRI scan or four sessions of functional treatment, in many cases you should probably opt for the latter.

However, in this article I want to write about a diagnosis that as a profession we haven't yet asked enough questions about, which is a sub-type of osteoarthritis. We should all be thinking more about its underlying cause and what we can do to perhaps treat it far more effectively than we do. This diagnosis I will call "Rapidly progressive osteoarthritis". This reminds me of a great line from the movie "A Few Good Men" where Lt Kaffee (Tom Cruise) asks Col Jessep (Jack Nicholson) if the danger in a certain situation was "grave danger"? The answer which Colonel Jessep gave was "Is there another kind?" Joints with osteoarthritis are obviously in danger of further degeneration, but are they are they all in "grave" danger? Is there another kind of osteoarthritis than rapidly progressive osteoarthritis?

These questions have a double answer in that all joints with osteoarthritis are in danger of deteriorating but you'd only call it "grave" danger once you have the benefit of hindsight and have seen the deterioration occur. It seems to be the current status quo in medicine that we tend to treat all cases of osteoarthritis as being the same animal. We genuinely can't give a straight answer to someone who asks "how many years does my knee (or hip or other joint) have left in it?". I can't understand why our profession isn't trying harder to work out what causes some joints to pack it in over a matter of months whereas others can go for years without any change for the worse.

With our regular private patients, who pay to see us each time, we tend to get disproportionate follow-up from the patients who are doing OK but aren't perfect. The complete cures generally don't return to tell us face to face that they are asymptomatic, whereas the complete failures probably seek alternate advice. This discrepancy is doubtless greatest of all for orthopaedic surgeons, who regularly hear vicious attacks on their colleagues by the patients in their offices. They make lots of money but are prone to becoming grumpy as sub-consciously they probably realise what some of their patients say about them in the offices of other surgeons.

Although elite athletes are different to regular patients in many ways, one of the biggest differences is that we actually get better follow-up than we do with most of our normal patients, even if it is just watching them on TV. To illustrate the lack of predictability about joint degeneration I'd like to draw on an example that is already in the public sphere.[3] Joel Selwood, now one of the gun midfielders with the Geelong Cats in the AFL, was a particularly outstanding junior, but had two knee operations for significant chondral damage in the year before he was drafted. A number of clubs apparently were put off drafting him because of his medical history. His story is now a happy one for the player and for Geelong, who took the risk with him. However, I don't believe that this warning, presuming it was given, should be seen as a black mark against any of the medical teams who made it to their recruiting staff. Just as it is thorough to know whether a prospective recruit is a bad kick, it is thorough to know whether he has a good or a bad injury history. There is even a recent paper from the NFL showing how much greater the risk is (of not playing games) for a significant orthopaedic injuries such as knee chondral damage.[4] Sometimes it might be worth recruiting someone in spite of a major injury query – Chris Judd and his shoulders pre-drafting by West Coast and then his groin injury pre-Carlton would be a good example of a risk that has twice paid off, with the benefit of hindsight. It is probably not in as good taste to discuss the many examples of poor recruits who have had ongoing problems with pre-existing injuries and have therefore turned out to be risks which didn't pay off.

As hard as it is for recruiting staff to pick which of the top eighteen year old players will be the best players three years later, it seems to be equally hard for us as doctors to tell which grade III chondral lesions will be asymptomatic in three years and which ones will have progressed on to frank osteoarthritis. I have had two patients this year who were extremes in lack of progression. One was told he needed a knee replacement in 1970 and still hadn't needed it yet and another was told in the same decade he should stop running because of knee osteoarthritis yet has run a dozen marathons since. Both of these patients were seeing me because of Achilles tendon pain. Yet all of us have seen patients who have had a knee which had rapidly progressed from being OK for running to being in knee replacement territory within a few years or even months.

A similar dilemma relates to the value of knee chondroplasty as a procedure itself.[5–7] There are multiple major published papers showing that knee chondroplasty, *on average*, is no better – or may even be worse than – conservative management. Our medical system, which won't fund hyaluranon injections, shoe wedging or physiotherapy interventions that have been shown to be helpful in osteoarthritis, continues to fund a procedure that a Cochrane review claims has "gold" evidence of not being helpful.[8] The problem for the government is that there would be widespread outrage (particularly from surgeons, but also from some patients) if arthroscopic chondroplasty was no longer funded by Medicare. I feel this is because there *are* a significant number of patients who get substantial improvement from a chondroplasty and these patients would be furious to have to pay for the procedure fully themselves. The problem is that – if you believe the RCTs which we know should be more reliable than our clinical observations – there must be an equal body of patients who are made substantially worse by arthroscopic chondroplasty which balance out the ones who get better. Clinical optimism leads us to hope that every arthroscopic chondroplasty will turn out like Joel Selwood, but if we are honest we admit that we see some dismal failures.

So having led in with all of these questions, I want to re-toss up a hypothesis[9] which, if correct, could explain all of these paradoxical findings. The hypothesis is that "Rapidly progressive osteoarthritis" is caused by subtle intra-articular (or subchondral bone) infection and that the progress of osteoarthritis, in the absence of infection, is relatively slow and

benign. When I use the terms infection, I mean possibly any infection (bacterial, viral, fungal or other microorganis) – but what I don't mean is "in-your-face" *Staph. aureus* septic arthritis. Classic septic arthritis certainly causes extremely rapid joint degeneration but it also generally gets rapidly diagnosed and (usually successfully) treated with joint lavage plus intravenous antibiotics.

Current dogma is that bacteria which cause septic arthritis can be routinely grown in pathology laboratories and that the main defence that bacteria has against modern medicine is to develop antibiotic resistance. The medical profession hasn't taken seriously a very plausible defence mechanism that microbes may develop against modern medicine – the inability to grow on an agar plate in a pathology laboratory.[9] The average doctor has the view that if a biopsy or fluid tap is taken from a knee and doesn't grow microbes then there are no microbes present. In other words: the same intellectual error that stopped doctors before Marshall and Warren from thinking of a microbial cause of stomach ulcers.

The infective theory of osteoarthritis progression would explainwhy surgery is curative for some patients with chondral damage but actually worsens the condition in others. If a chondroplasty manages to drill away the focus of infection it might fix the problem, but surgery also runs the risk of introducing further organisms through the surgical portals. But we shouldn't expect a revolution any time soon in surgeons diagnosing a whole lot more post-operative infections in order to better treat those patients who are made worse by their surgical procedure. Since infection is seen as a black mark against the treating surgeon, the dogma that osteoarthritis "is sometimes rapidly progressive for unexplained reasons" is one that sits far more comfortably with surgeons that the thought that post-operative infections are quite common.

So how does one treat an infection in a joint when the causative organism is unknown? Perhaps it has unwittingly already been done – a RCT shows improvement in osteoarthritis with the antibiotic doxycycline,[10] although most experts regard that doxcycline in this trial was working as an MMP-inhibitor. My instinct would be to treat with one or a combination of broad-spectrum antibiotics actually injected intra-articularly. This would mean attacking another one of medicine's sacred cows – that you shouldn't inject antibiotics directly into joints! Of interest is that some vets are happy to inject antibiotics into horse joints[11–12] and it seems to be safe in rabbits.[13] I've tried to work out why and how it became medical dogma that antibiotics shouldn't be injected intra-articularly in humans. The logic is certainly at least thirty years old, but it seems that the argument against intra-articular injection of antibiotics is twofold: (1) that it can lead to "synovitis" and (2) that intravenous antibiotics enter the synovium efficiently and are therefore effective at treating septic arthritis, so that intra-articular antibiotics are not necessary.[14] These two arguments together seem somewhat illogical – if antibiotics can successfully enter the synovium and, antibiotics can cause synovitis, then we should see synovitis caused by intravenous antibiotics as well. Antibiotics in the joint may have benefits and risks and these should be equally pertinent whether or not the antibiotic got to the joint via the bloodstream or via an intraarticular injection. One confounder with observation of "synovitis" in a joint after an intra-articular injection is that it could have been caused by an infection itself. It probably comes down to a question of dose, in that the local dose from an intra-articular injection would probably be higher and be more likely to be closer to a toxic dose. There is only one antibiotic on the market –

flucloxacillin – approved for intra-articular injection (at a dose of 250–500mg/day) and so with the other major antibiotics there is very little data available about toxicity in local tissues like joint. It may simply be defensive medicine to avoid intra-articular injections given that these are not approved by the manufacturers of most antibiotics. Of course the big advantage of intra-articular antibiotics would be that it could be done as an outpatient procedure in minutes, as opposed to intravenous antibiotics which require an expensive hospital stay. There may be some patients, particularly those awaiting joint replacement who have already given up their joint as being beyond the point of no return. The practical advantage of a single rather than ongoing injection(s) is obviously of great benefit in animals[11] who might be less obliging if asked to sit still with an IV drip in situ for three days.

The problem with my hypothesis is that it is very difficult to prove, although you can manage osteoarthritis according to Table 1 and admit you don't fully understand the pathogenesis. Marshall and Warren took over a decade to convince the medical establishment of the common existence of one organism in the stomach. If there were regularly more than a dozen fastidious organisms that can cause hard-to-prove infections in joints, then exhibiting instances of these is only proof for that individual case rather than for the disease in general. The only answer to the solution I can see is a much better medical records database. If there was a country-wide database of all cases of osteoarthritis and, over a large number of patients, perhaps it could be shown that certain patients could have joint replacements successfully deferred with the use of intra-articular antibiotics.

The current status quo possibly suits some of the bacteria which don't get seen and possibly suits the surgeons who don't see them. Remember that there are over 50,000 joint replacements getting performed per year in Australia under a health system which handsomely rewards procedural treatment and pays next to nothing towards surveillance and prevention. So whether we have a problem depends on whether you are a doctor, bureaucrat or an unlucky patient.

	Septic arthritis	Rapidly progressive osteoarthritis	Relatively benign osteoarthritis
Joint swelling	Substantial, red, hot	Effusion mild-moderate	Effusion mild or not present
Lab results	High ESR, CRP, WCC, high joint aspirate white cell	?moderately high ESR, CRP, white cells present in aspirate	Normal
Joint fluid culture	Positive	Negative	Negative
Cause	Pathogenic bacteria (e.g. *Staphylococcus aureus*)	?fastidious bacteria (e.g. *Kingella Kingae*9),?rheumatological condition, ?localised osteoporosis	Trauma
Treatment	Rest & intravenous antibiotics, ?joint lavage	Hyaluranon injections, ?doxycycline, ?other antibiotics (including perhaps intra-articular), ?surgery	Physiotherapy, moderate loading, orthotics, glucosamine

Table 1 – Possible management protocol for osteoarthritis

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