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The fifth parasite: Malaysia studies new malarial strain

Shelf of curiosities: Dr Sharma with part of UPM's national parasite reference collection. Jars of parasites dating back to the 1970s are stored at the building's parasitology lab. Current research focuses on P. knowlesi, a type of simian malaria shown to be an emerging zoonotic disease.

A deadly malarial strain has made the leap from monkeys to humans, and Malaysia is at the forefront of the research.

A SHELVING unit running across the length of a wall draws curious stares to its collection of bottled curiosities: a pickled cow hoof, floating specimens of parasitic helminths, tangles of worm-like ascaris, muscle tissue dotted with sarcocystis, and at the far right corner, a collection of Anopheles mosquitoes suspended in a clear viscous substance.

"We're trying to set up a national parasite reference collection," explains Dr Reuben Sharma. Not many people visit this parasitology lab, headed by Dr Sharma and tucked away in a remote corner of Universiti Putra Malaysia's (UPM) Faculty of Veterinary Medicine in Serdang, Selangor. But the work being done here is of national importance.

In some ways, UPM is the new kid on the block, having recently joined other research institutions in the country working on a deadly, emerging malaria parasite – Plasmodium knowlesi.

Caused by microscopic single-celled organisms known as plasmodia, it's not as bad as it sounds. A malarial infection of this kind is only deadly if not treated, and malaria drugs are widely available.

The trick is knowing you have it. And that's what makes P. knowlesi so interesting. Up until about 10 years ago, no one had any idea that humans could get infected.

There were four human malaria parasites, and P. knowlesi was not one of them, hitherto known only to infect monkeys.

Primary contributor

That is, until eminent Sarawak-based parasitologist Dr Balbir Singh got curious about some statistics.

Having spent many years studying malaria at the Liverpool School of Tropical Medicine, Britain, Dr Balbir believed in academia with a focus – and his focus was malaria, although mostly involving human malarias.

His research, however, is one of the main reasons we now know that the biggest contributor of Malaysia's hospitalised malaria cases is not human malaria, but P. knowlesi.

In 1999, he and his wife Dr Janet Cox-Singh started work at the Faculty of Medicine & Health Sciences, Universiti Malaysia Sarawak (Unimas). While trawling data to get acquainted with malaria transmission dynamics in Sarawak, they noticed an anomaly, and decided to investigate.

This was the problem: in Kapit, a relatively inaccessible town on the banks of the Rajang river in Sarawak's vast Kapit division, people were being hospitalised for P. malariae.

This was strange for two reasons. One, P. malariae symptoms are mild, hospitalisations are very unusual. And two, very few of the patients were children – usually the most vulnerable to severe infections through a lack of acquired immunity. Dr Balbir was baffled why 95% of the cases reported involved adults.

So Dr Balbir packed his bags and went to Kapit, drawing blood samples from sick patients at the hospital.

Under the microscope, the plasmodia did indeed look like P. malariae. But when Dr Balbir turned to DNA-based detection, the plot thickened. The samples tested negative for any of the four parasites known to infect humans – P. malariae, P. falciparum, P. vivax and P. ovale – but tested positive for .

In other words, it was malaria all right – just not a form of human malaria.

Eventually, when he ran the DNA sequence information gathered from his team's research through the DNA database, P. knowlesi showed up as a complete match.

Pandora's Box

That moment determined the course of Dr Balbir and Dr Cox-Singh's research for the next decade, and beyond. It has also put Malaysia at the forefront of investigations into P. knowlesi. Their team at the Malaria Research Centre at Unimas developed a molecular detection test for the parasite, and launched a study. They travelled to hospitals scattered throughout Sarawak, as well as longhouses in the interior, in order to find out how widespread the disease was.

Four years, two hundred patients and one publication in leading medical journal The Lancet later, the world was in for a surprise: a fifth human malaria had emerged on the scene.

Of all the malaria cases observed in the Kapit division, 58% were caused by the simian or monkey malaria P. knowlesi.

Once the news emerged, cases began popping up all over South-East Asia, in areas that are home to both its macaque hosts and Anopheles mosquito vectors. The team published a second study in 2008, which showed that P. knowlesi was not restricted to Sarawak either; cases have been confirmed in Sabah and Pahang too. More importantly, the medical community took notice when they reported that P. knowlesi could lead to fatal infections.

So far, Malaysia has the highest number of cases, but that's probably because it is the only country where there has been a focused scientific drive to study it with molecular detection tools.

But why is P. knowlesi even important?

Most cases happen to people who live or work in the jungle, or adventurers coming out of it.

Right?

Killers in the blood

Here's why it matters: some malaria parasites are more dangerous than others.

P. falciparum for example, is a killer.

P. vivax is not as bad, but it is a potential killer, and can be severely debilitating.

P. malariae – which Dr Balbir discovered looks a lot like P. knowlesi under a microscope – and P. ovale don't do too much damage.

What makes some forms of Plasmodium infections deadlier than others is the ability and speed with which the parasite replicates within the blood.

When Plasmodium first infects a human, it migrates to the liver and transforms into a new form capable of tunnelling into red blood cells, eventually exploding out of your liver cells into the bloodstream.

Tens of thousands of individual parasites then penetrate your body's red blood cells, stealing their nutrients and replicating like crazy, before surging forth in great numbers to invade yet more red blood cells. Without prompt treatment, a bad case of malaria will lead to severe fever, muscle pain and chills.

For P. malariae, a fresh invasion occurs every 72 hours.

In P. knowlesi however, the red blood cells burst open with new parasites every 24 hours.

Each assault is synchronised, which is why malaria is associated with periodic fevers.

Your body's temperature rises as your immune system reacts to the shock.

With every replication cycle, the patient grows weaker, left with fewer red blood cells to pass oxygen around the body. This puts stress on organs such as the heart and lungs, leaving victims struggling for breath.

High parasite counts within the blood are part of what makes P. falciparum deadly.

And from the limited experience with human case studies, P. knowlesi infections can involve a comparable, if not higher, parasite count than P. falciparum.

That's one reason why knowing more about P. knowlesi is important.

For one thing, we need to make sure our healthcare systems – especially in rural jungle regions – are fully aware of this new threat.

The severity of an infection will vary from patient to patient. Unfortunately, a microscopy-based misdiagnosis of P. malariae can prove deadly, and probably has in the past.

In 2011, the World Health Organisation (WHO) facilitated an informal consultation on the public health importance of P. knowlesi.

One of its recommendations was to treat any case diagnosed by microscopy as P. malariae with the possibility that it may also be P. knowlesi as a guide to case management. This has since been adopted by Malaysia's health care system. WHO also acknowledged that surveillance is needed to detect whether or not any human-to-human transmission is occurring.

If it is, that would be a big blow to global ambitions for malaria eradication.

Source: The Star Online