

A coronavirus patient is evacuated from Mulhouse civil hospital in eastern France last month



Solving a puzzle with world looking over their shoulders

Scientists are some way off unravelling the deadly mysteries of COVID-19

JAMIE WALKER
ASSOCIATE EDITOR



As doctors see more and more of COVID-19, they are getting a handle on what the coronavirus does to people. It hits seniors much harder than young adults; kills many more men than women; and is inexplicably gentle on children.

But the why of this is another matter. Four months and more than two million cases worldwide into the pandemic, with deaths nearing 150,000, questions outweigh the few, hard-won answers gleaned from the hit-and-miss of patient care and preliminary lab studies.

A vaccine, the only sure way to stop the disease, is at least a year away and for all the optimism of the researchers nobody can be sure one will emerge. Several re-purposed drugs show promise as treatments but they, too, have a long way to go before being proven. For now, Australians can take comfort that the stopgap of border closures, shutdowns and social restrictions are working better than just about anywhere else.

But as the clamps come off in the coming months — assuming the spread of infection continues to be controlled — understanding the ins and outs of the virus, its strengths and weaknesses, will become even more vital in the absence of a vaccine.

Take the best-known feature of COVID-19: lethality to the elderly. From the time the first cases were identified in the Chinese city of Wuhan in December last year, deaths skewed overwhelmingly to the over-70s. No surprise there. Sorry, boomer, but the healthiest septuagenarian still has the im-

mune system of, well, a septuagenarian. What puzzled doctors and scientists were the ancillary outcomes. Babies, small children and pregnant women usually rank with the elderly as the most vulnerable in an epidemic. Yet from day one, COVID-19 largely spared them, as well as teenagers and to a lesser degree young adults. A study of 72,314 patient files in central China's Hubei province, enfolding Wuhan, found that fewer than 10 per cent of those infected were under 30.

The gender disparity has proved to be even more mystifying. In Italy, men account for 60 per cent of cases and 70 per cent of all deaths, again weighted heavily to the grey and white-haired cohort. New York City counts 43 COVID-19 fatalities for every 100,000 men against 23 per 100,000 women, according to its health department.

Here, the story is much the same. Of Australia's 65 fatalities to date, 39 have been men, just two of them aged under 60. Interestingly, the number of young women infected is considerably higher in the 20 to 30 age bracket — more than 750 to about 600 men — something that has epidemiologists thinking about smoking. Could it be the missing link?

At first glance, this makes sense. COVID-19 starts as an upper respiratory infection, the virus lodging in the throat and nasal passages, but in its severest form it settles in the lungs to choke oxygen supply, eventually damaging other organs. Men also have higher rates of hypertension, a related risk factor. If an individual has pre-existing pulmonary and/or cardiovascular problems arising from smoking, it stands to reason they would have a tougher time of it.

The theory gained early traction in China because the difference in smoking rates between the

sexes there is striking: 61 per cent of men to barely 4.2 per cent of women, according to the World Health Organisation.

However, in wealthy Western societies the discrepancy is much less pronounced: 16.5 per cent of men and 11.1 per cent of women smoke daily in Australia. And here's the problem when it comes to extrapolating the data to COVID-19: contrary to popular belief, the gender gap widens when it comes to young adults smoking. In 2018, men aged 18 to 24 led their female peers 17.5 per cent to 10.4 per cent in regularly using tobacco products, the Australian Bureau of Statistics reports. So smoking may be part of the jigsaw but it doesn't solve the puzzle, not here anyway.

Katherine Gibney of the Peter Doherty Institute for Infection and Immunology in Melbourne, where epidemiologists are modelling the epidemic for the federal government, cautions against

With deaths in the hundreds of thousands, questions outweigh the few, hard-won answers

drawing conclusions off a thankfully low base of cases in this country. "Certainly in China it was bit easier to put it down to things like smoking because there was a big gender disparity in smoking there," she says. "That is not the case in other countries. If you look at some studies of disease burden in Australia they do say there is more disease caused in men than women ... but I don't think there is one clear single reason."

The answer may lie in the immune system itself, how it works differently in men and women, coupled with other compounding factors. Gibney, an infectious diseases physician and medical epidemiologist, says this is apparent with several diseases. It may be that behaviour increases the exposure of men to a particular virus — as is the case with HIV.

Then there is tuberculosis.

Men are twice as likely to catch that deadly lung disease because the genes on their lone X chromosome interact differently with the predatory mycobacterium than the double-X combination in women. This can also be a double-edged sword for women, making them more prone to auto-immune diseases such as rheumatoid arthritis and lupus when a hyper-immune response is triggered. Talk about swings and roundabouts. The thinking with COVID-19 is that a more robust immune reaction works for women, empowering their body's defences to go after the pathogen.

"In very general terms, women's immune systems may get on top of the disease more effectively than men," Gibney says. Another theory scientists are pursuing is that the receptor the coronavirus uses to bind to human cells — known as ACE2, for angiotensin converting enzyme 2 — is more prevalent in older people or shaped in a way that assists it, increasing the patient's susceptibility. In severe illness, the virus seems to trigger an explosive immune over-response in which proteins called cytokines are rapidly released into the bloodstream, clogging the lungs and compromising other organs in a grim struggle for survival where the person's odds are at best 50-50.

As for children, there is no explanation for why they generally experience milder symptoms or none at all, a feature of other diseases caused by coronaviruses, such as severe acute respiratory syndrome and Middle East respiratory syndrome. One theory holds that their immune systems, being less developed, don't have the capacity to overreact and unleash a cytokine storm. Gibney says there is always the possibility that childhood vaccinations confer some cross-immunity to COVID-19. Even though children appear less likely to become dangerously sick, they aren't insulated from the virus.

"They get the infection, but they don't seem to be important to spreading it on to others and in most cases they don't get severe disease," Gibney says. She points to another redeem-

ing quality of the virus: its genetic stability. To date, there is no sign that it is as prone as influenza is to mutate, which would compound the already formidable challenge of developing a vaccine and therapeutics.

Perversely, Australia's achievement in "flattening the curve" of the pandemic serves to underline how dangerous COVID-19 is. With a mortality rate of less than 1 per cent here, it pales against the lethality of MERS, which kills more than a third of those struck by it.

But that's not the number that counts in pandemic modelling. The R0 — pronounced R-nought — is the basic reproductive number used by epidemiologists to predict how many people will be infected when an epidemic takes hold. COVID-19's R0 is 2.5. That means 10 carriers will infect 25 others, who will infect 62 more people and so on, increasing exponentially at nearly twice the rate of seasonal flu unless checked.

The good news is the shutdown of borders, workplaces and social activity in Australia has pushed the effective reproductive rate of the virus below 1, a manageable level. Let us get carried away, Gibney says the danger is far from over. In one sense, COVID-19 would pose less of a collective threat if it killed more people sooner. Yes, it's a bit to get the head around. But there's no place for the human heart in these calculations, as Australians will learn in the coming months. "It almost seems like a perfect storm as a disease," Gibney tells Inquirer.

"It's reasonably infectious and it causes mild disease in most people, so most people are well enough to be out and about ... doing their own thing and spreading it to more people. If it was more like SARS, it would actually be easier to contain ... because the majority of people would be much sicker and they would not be going out and spreading it.

"So what we have to learn to live with until a vaccine turns up ... is that this virus is a very effective reproducer and very effective at infecting and spreading through communities. We can't afford to underestimate it at any point."

Brits emerge with caution — and smell hope in the air

Symptomatic weeks of dread passed; so many aren't as lucky

PAOLA TOTARO
LONDON



It is a moment that will be seared into my memory forever: we were six days into lockdown in London and I'd gone to the bathroom to wash my hands when I realised my hand cream, scented with a powerful mix of mandarin rind and rosemary leaf, had no smell.

I quickly sprayed a puddle of my favourite perfume on to my wrist and sniffed deeply. Again, zero. Nil. Zilch.

Panicked but still incredulous, I fumbled with the childproof cap of the toilet disinfectant and put my nose to the bottle: usually this yields an unbearable bleach-laden, floral reek. Nothing.

As the realisation dawned, my veins turned to ice.

It was March 26 and I was in the middle of researching the events that led Italy into its terrible coronavirus death spiral. In my reading, I'd come across a report by British ear, nose and throat specialists warning that their colleagues in Italy, South Korea and China were seeing significant numbers of patients with the sudden onset of anosmia/hyposmia and dysgeusia/ageusia — the loss of smell and taste. In Germany, more than two in three confirmed cases have anosmia. In South Korea, where testing has been more widespread, 30 per cent of patients testing positive stated loss of smell as their major presenting symptom in otherwise mild cases.

A few days before, I had developed a disconcerting burning feeling up high in my lungs, my nose felt dry as if I'd come off a long-haul flight and I was inordinately tired. But my husband and I had spent the week before completing a marathon 125km walk following Hadrian's Wall across Britain. We'd trudged through mud, battling sleet and high winds over five exhilarating but physically challenging days and I figured I was paying the price with a cough.

A day or so later, however, my husband also began to cough; a harsh, hacking, painful bark. With growing dread, we had to accept that as we'd returned to London from Newcastle in a crowded train carriage, we could well have contracted "it".

In Britain, coronavirus testing is offered only to health workers or if you require hospitalisation: we had little choice but to wait it out at home. In self-isolation lockdown — and, at night, from each other — the next fortnight unfolded in a mix of anxiety, hyper-vigilance and occasionally sheer terror. Every ache, every wheezy breath, every slight perception of temperature change unleashed the fear that symptoms might cascade and worsen.

Thankfully, our 18-year-old daughter remained asymptomatic, and as no temperature appeared and the cough didn't worsen, we began to relax a little when, boom — British Prime Minister Boris Johnson was admitted to intensive care.

Strangely, and in retrospect, that was probably the worst moment psychologically: Johnson



A cyclist crosses empty Westminster Bridge in London

had been isolating for close to a week before his lungs seized and the reality that a dramatic turn for the worst could unfold for anyone in just hours pervaded both our dreams that night.

Three weeks later, I am inordinately grateful that we are among the fortunate ones who have had the virus and, hopefully, have developed immunity. But the nation and its capital are in mourning. To date, nearly 14,000 people have lost their lives to COVID-19 and Britain has mirrored the dizzying number of daily deaths reported in Italy last month.

Statistically, it is likely that England and Wales have reached the peak of the so-called curve, although nobody has made that call in public yet. But experts warn there may be another hidden epidemic inside the nation's care homes that has yet to be properly quantified.

Three weeks later, I am inordinately grateful that we are among the fortunate ones ... But the nation and its capital are in mourning

The Office for National Statistics reported 217 deaths in care homes in the fortnight to April 3, but the lack of widespread testing and British GPs' understandable reluctance to register COVID-19 as a reason for death without confirmation suggests a further 4000 elderly or vulnerable people will probably have lost their lives.

Johnson, meanwhile, continues to convalesce at Chequer's, his country residence, and has yet to return to the helm, leaving his increasingly beleaguered stand-in, Secretary of State Dominic Raab, to face growing questions about the continuing shortfall in personal protection equipment for National Health Service workers and his government's failure to deliver an adequate testing regimen.

This week, Britain was still carrying out fewer than 15,000 virus tests each day despite pledges to swab 100,000 people daily by the end of the month. More detail also has since emerged of an inexcusable post-Brexit government bung that resulted in Britain being excluded from an EU-wide mass purchase of medical kit including ventilators and PPE.

Nearly all EU countries — reportedly 25 of 27 — are taking part in the project for shared purchase of ventilators as well as joining

forces to buy protective kits for medical staff. Joint procurement makes sense because it ensures purchase at wholesale price, reduces red tape and offers a helping hand for medical purchases to smaller nations that have less bargaining power.

Addressing initial questions about the mess, Cabinet Office Minister Michael Gove insisted Britain had not received an email inviting it to join the EU procurement scheme, a stand British officials, inexplicably, continued to repeat this week.

For its part, the British opposition has stood by the word of newly installed Labour leader Sir Keir Starmer, who announced immediately that his new team would work closely with the government to ensure bipartisan support in the campaign to defeat the virus. Starmer, who took the reins from Jeremy Corbyn on April 4 as the virus began to really ravage the nation, has balanced a difficult tightrope, questioning government policy failings without scoring political points.

Yet beneath these horrors, the herculean efforts of the NHS, its 14 million staff — including 10,000 retiree doctors and nurses who have returned to the frontline — are paying dividends. Early last month there were fears that London's intensive care units, which had around 770 beds combined, would be overwhelmed by coronavirus, sparking the transformation, in just nine days, of the Excel Stadium, an integral part of the 2012 Olympic Games, into a 3650-bed field "Nightingale" hospital — complete with grim, ground-floor makeshift morgue.

But interior figures reported by the British Health Services Journal on Wednesday showed the Nightingale treated only 19 patients across the Easter weekend and that despite rising levels of infection, hospitals have been able to double their ICU capacity to 1555 beds.

Chances are Britain will continue in lockdown for several weeks but already there have been cogent opposition calls for the government to release details of its strategy to ease restrictions — whenever the scientists deemed it possible.

As the first bloom of spring envelops London in a riot of cherry blossoms and birdsong in the absence of traffic and crowds, I feel enormously thankful to be alive and that, unlike hundreds of thousands around the world, my family has suffered no loss. I still have no sense of smell or taste and can only imagine the special fragrances of spring — while thanking my lucky stars, of course.

Who can they be now? Life sucks for Men Not At Work

I feel for them, stuck at home, unable to roam, but at least they're learning how women feel

CAROLINE OVERINGTON
ASSOCIATE EDITOR



Do you know anyone who is sick with COVID-19? I don't yet, and that is such a good thing. But I do know people who are struggling.

Men, in particular. Men who are between the ages of 18 and, let's say, 44. The suicide ideationists in our productive cohort.

They are struggling. Even before COVID-19, men were at greater risk of doing harm to themselves. And now so much has been taken from them.

I don't mean financially, although it's true that many men are worrying about how they're going to pay the mortgage and the bills if they lose their job or can't find a new one.

More worrying is their loss of direction and purpose, as well as the foundations on which we so often ask men to build their lives. I'm going to generalise a little bit

here, but many women are, I think, more used to being out of the workforce, at least some of the time. They are used to spending time at home, with small children.

They have experience with isolation. They know what it means to be a bit bored and frustrated. They have learnt, over time, how to manage, inventing things such as mothers' groups to support and encourage each other during the lonely years.

Women were the first to see the internet as a place where they could gather together to share tips, tricks and recipes — and, of course, their fury.

They are also used to working reduced hours, for less money. They tend to feel less connected to the office than men do. And they know the juggle, having long ago



Two young surfers walk past a 'beach closed' sign

mastered managing childcare with a working life.

Men, by contrast, are conditioned to work. And it's really quite wonderful how willingly and cheerfully so many of them take on the task of shouldering financial burdens on behalf of those they love. Much has been written

through the years about how Australian women do the bulk of the housework and the child rearing, even now in 2020. Less has been written about the other side of that coin. Men still do most of the paid work, and they do so, in the main, because they want to shelter and protect women and children.

It's a source of pride to them. Their self-esteem comes, in part, from being able to reassure their family: hey, it's OK, I've got this.

Taking responsibility protects men against dolorous feelings. It's hard to stay well, mentally, when you don't have to get up and go to work in the morning. When you can't provide, or even protect.

These are very old-fashioned notions, I know. There is an argument that men will benefit from the sudden changes to their working life wrought by COVID-19.

It's probably not a bad thing for them to know what it's actually like to "work from home" when you've got small children under foot. To have no boundary between your work and play. To be unable to roam at will. To know how exasperating it can be when you're trying to supervise school-work and your adorable kid just doesn't get the lesson at hand. To think, surely, child of mine, you cannot be this stupid?

We do, however, need to weigh these feelings against the experience of not being able to go any-

where or do anything. Because so much of what men love has also been taken from them.

They can't go to the football. They can't even watch it. They can't go to the pub. Or the gym.

Where I live — the caged city of Bondi — it's the ocean that's closed, and that is traumatic for surfers, many of whom use their time in the waves to manage their mental health.

It's much more than self-medicating with, say, alcohol, or nicotine. There is a sense of healing around the ocean. Stand on a cliff and look out to sea, and you'll know in your bones: we came from there. The ocean calls to us.

Some young men have not been able to resist. I see them most days, barefoot in their wetsuits, slipping around the barriers, trotting down to the sea. They're young and full of energy and champing at the bit. They just need to go in, and I feel for them.

Yet, at the same time, I know it's not right. It has to be the same rules for everyone because otherwise this frustrated young man

thinks, well, I can just sneak into the water, it won't do any harm. Then the next one thinks, well, I can just do this or that, and before long there is no social distancing and then you have emergency beds overrun, and beleaguered doctors in scrubs begging for assistance because it has become a choice: do I ventilate the COVID-19 patient, or the woman dying in childbirth, or the child battling cancer?

And that is not who we are, as a people.

So yes, I see them, sneaking out beneath the crepuscular sky, and I try not to judge. Then again, I see Sam Newman, a grown man in silly pants, wailing outside the Victorian parliament, demanding to know why he can't golf. This just as the Premier was receiving news that another much-loved Victorian had succumbed to the coronavirus, and I thought, please be quiet, Sam. We are none of us imprisoned, we are sheltering. This is a storm, and it will pass. And imagine how it will feel when we are all able to hold each other again.