To life, love and loss

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Turning and turning in the widening gyre
The falcon cannot hear the falconer;
Things fall apart; the centre cannot hold;
Mere anarchy is loosed upon the world

W.B. Yeats

INTRODUCTION

'Cancer starts when a cell picks up genetic mutations and multiplies out of control.'

I don't know how many times I've written some variation of that sentence during my career as a science writer, including the twelve years I spent in the communications team at the world's leading cancer research charity. Never once did I stop to consider what it really means. Or that it might be wrong.

Cancer is a disease that affects us all. Even if you've been lucky enough not to see its effects up close, either in yourself or in someone you love, cancer is a global health problem that kills millions of people around the world every year. Scientists and doctors have been trying to discover its causes, consequences and cures for thousands of years, arguably only making any significant progress in the latter half of the twentieth century. Today, around half of the people diagnosed with cancer in the UK can expect to survive for ten years or more – a figure that's only likely to rise in the future. To an optimist, this is a glass half full.

We already know how to cure cancer. Or rather, we already know how to cure *some* cancers. The best way is to spot them as soon as possible and remove them with careful surgery before they've started spreading round the body (known as metastasis). Radiotherapy can be curative and hormone therapy can be very effective for keeping breast and prostate cancers at bay, if used at the right time. Many blood cancers respond strikingly well to chemotherapy – particularly in children – and drugs can completely cure testicular cancer even at an advanced stage. There have been startling results with the new generation of immunotherapies, yet they currently only work for fewer than one in five patients who take them. But for most of the unlucky ones

whose disease has started its unrelenting march through the body, the question changes from 'Will I get better?' to 'How long have I got left?' Not *if*, but *when*.

This is pretty much the same situation we've been in since American President Richard Nixon infamously declared 'War on Cancer' in 1971. Seeking a distraction from the conflict in Vietnam and hoping to capitalise on the pioneering spirit engendered by the recent Apollo moon landings, Nixon pledged millions of dollars towards the quest for a cure within a decade. Alas, in an unfortunate parallel with the situation in the Far East, he had wildly underestimated his enemy. In 1986, statistician John Bailar ran the numbers: despite a few successes here and there, the vast majority of late-stage cancers still remained stubbornly incurable. In Bailar's own words, the War on Cancer was to be judged a 'qualified failure'.

Although there's been a fair bit of successful tinkering around the edges for certain types of cancer – most notably malignant melanoma – a close look at today's statistics reveals the same patterns. More and more people are being diagnosed at an early stage when treatment is much more likely to be effective, boosting the overall figures. But survival from advanced metastatic cancer is still likely to be measured in months or single-digit years rather than decades.

The big problem is that precision tools of surgery and radiotherapy are virtually useless against rampant disease, and chemotherapy is a blunt weapon based on the principle of killing cancer cells faster than it kills the healthy ones. Even when it works, the tumours almost inevitably come back – weeks, months or even years later – and every subsequent round of treatment is a more brutal assault on health, with diminishing returns. The empty half of the glass is proving difficult to fill.

At the turn of the twentieth century, scientists working for the newly-founded Imperial Cancer Research Fund in London were busying themselves growing cancerous mouse cells in the laboratory in the hope of figuring out the secret of their prodigious multiplication. The researchers marvelled at the seemingly inexhaustible regenerative capacity of the cells in their care, with General Superintendent of Research Ernest Bashford

noting in the charity's 1905 annual scientific report that, 'Under artificial propagation a mouse tumour has produced an amount of tissue sufficient to yield a giant mouse as large as a St Bernard.'

Today, we have a more complete picture of what happens when cells throw off their molecular shackles. Cheats emerge from the civilised multicellular society of cells, growing and dividing out of control in a shambolic mockery of normal life. One cell becomes two, two cells become four, four become eight, piling up to make a multimillion-strong mob. But they don't stop there. These rebels invade and corrupt the well-behaved tissues around them, persuading the immune system – the body's police force – to look the other way. They slip unnoticed into the bloodstream, travelling through arteries and veins to set up splinter groups and sleeper cells. Every single one of them is driven by rogue versions of our own genes – the genetic instruction manual that tells cells when to divide, what to become and even when to die.

There's a long-standing belief that the 'cure for cancer' lies in understanding the faulty genes and molecules within tumour cells – a task that has occupied a small army of scientists for the best part of a century, at a cost of countless billions of dollars. Researchers have extracted, read and analysed DNA from tumours and healthy tissue samples from thousands of cancer patients around the world: endless letters spelling out the recipe book of life and the typos within it that are thought to be responsible for driving cancers to grow and spread. But rather than providing clarity, this information reveals more than ever before about the genetic chaos within tumours.

We can see the scars left in the genome by tobacco smoke or ultraviolet light from the sun. There's evidence showing how the biological defence mechanisms that are meant to protect our cells can fail, or even turn against us. There are strange marks with unknown causes, which may one day be pinned down to damaging chemicals in the environment or new molecular processes. DNA analysis has revealed remnants of large- and small-scale damage, from a handful of typos to scenes of epic genetic disaster as whole chromosomes are shattered and stitched back together again. To make things even more confusing, it now turns out that even perfectly healthy tissues are a mess of mutated cells by the time

we get to middle age, many of them carrying what would normally be classified as cancerous mutations.

More disturbingly, these studies have shown that the genetic changes that turn a single cell into a tumour aren't consistent or fixed. There is no one 'cancer gene' just as there is no one 'cancer cure'. There are major differences in the genetic makeup of tumours from person to person, and even variations in gene faults across the miniature landscape of an individual tumour. Every cancer is a genetic patchwork made up of distinct groups of cells, any one of which could be carrying gene changes that make it immune to the effects of treatment. Once a cancer has grown to a certain size and diversity, relapse is inevitable.

Scientists have begun to see the progress of cancer as a microcosm of evolution, with cells picking up new mutations and undergoing natural selection as they grow and spread, akin to Darwin's great tree of life. And it's here we discover another uncomfortable biological truth about cancer: the very processes that have driven the evolution of life on this planet are inescapably at work within our own bodies as cancer develops.

To make things worse, some of these selective pressures come in the form of supposedly life-saving therapies, which strip away drug-sensitive cancer cells and allow resistant ones to flourish. Unfortunately, what doesn't kill cancer only makes it stronger and when it comes back, it's unstoppable. It's no wonder that our current approaches to treatment are powerless against such a malignant monster.

We urgently need a new way of thinking about how cancer arises, and how we might prevent and treat it based on this evolutionary reality. We need a clearer understanding of the species of rogue cells evolving within a tumour and the landscape in which they live, seeing them as populations changing over time, not fixed entities that can be described with a simple list of mutations. German biologist Richard Goldschmidt coined the term 'hopeful monsters' to describe organisms that had evolved dramatic new properties in a relatively short timeframe in the prehistoric Cambrian seas. Cancer cells are 'selfish monsters', evolving wildly and rapidly in the space of a patient's lifetime. And just as famine or predators act as important selective pressures

that shape species, cancer cells respond to selection too, acting out an evolutionary drama within the ecosystem of the body.

In this brave new world, where every cancer is genetically unique and evolves its way out of trouble, the old models of drug development and clinical trials no longer stand up. It's become a hopelessly bureaucratic business, using ever more sophisticated tools to achieve a shrinking return. We need to be a lot smarter to beat such a wily foe. But we're finally starting to decipher cancer's secret evolutionary playbook, as well as revealing the ecology of the landscape in which these rogue cells live. And there is growing hope that we can use this knowledge to predict and confound its next moves, skilfully manipulating the processes of evolution itself to steer and shape exuberant tumour growth.

In January 2019, as I was working on the first draft of this book, my Twitter feed lit up with news that an Israeli biotech firm had apparently developed a cure for all cancers that would be available within a year. Despite the credulous retweets and media reporting, the therapy had only been tested in mice and had no clinical data to support these claims, suggesting that the announcement was likely to do more for the health of the company's finances rather than any cancer patient in the foreseeable future. Somewhat predictably, a year later this 'miracle cure' was still in development and not a single patient had been treated.

Infuriatingly, articles debunking such overhyped miracle cures and outright nonsense usually receive many times fewer clicks than the original coverage. This is hardly a modern problem. In 1904, Sir D'Arcy Power, a surgeon at St Bartholomew's Hospital in London, wrote a furious paper in the *British Medical Journal* railing against a quack cancer cure produced by one Dr Otto Schmidt, a German doctor. He noted that Schmidt's ineffectual treatment 'gained a somewhat wider circulation than was intended, as a long abstract appeared in the *Daily Mail*'.

We want to believe that there is a Cure for Cancer – a term that has embedded itself deep in our cultural consciousness to mean total eradication of the disease. We want to know that all the time, money, effort, pain and lost lives are getting us closer to finding such a cure. We are easily seduced by talk of smart drugs, magic

bullets and miracles. Shifting towards a new way of evolutionary and ecological thinking about cancer is going to require a change in mindset – not just from the scientific and medical community, but from patients and the public – if the long-awaited solution doesn't look quite like what we expected.

This isn't a story about cancer. It's a story about life. I want to show you that cancer isn't a modern human disease, but is hardwired into the fundamental processes of biology. We'll discover how the roots of this rebellion go all the way back to the origins of multicellular life, setting up the organised structures from which cheating cells emerge. Looking back over more than a century of research, we'll see how scientists have learned the genetic secrets of cancer – knowledge that has been both revolutionary and misleading at the same time. We'll find out how the same evolutionary forces that shape the spectacular diversity of life on Earth also act down at the level of rogue cells and how we must learn to work with them rather than against them in order to beat cancer. And while we can't deny our own biology – and nobody lives for ever – we'll look forward to a future when every person who is told, 'You have cancer' then hears the words, 'It's OK – we know what to do about it.'

1

LET'S BEGIN AT THE VERY BEGINNING

It all starts with one.

Though there may have been many other similar objects floating around in the primordial soup roughly 3.8 billion years ago, LUCA was the cell that got lucky.* Spawned in the hot, dark and suffocating environment around ancient deep-sea hydrothermal vents, LUCA was a simple bacteria-like cell that had somehow managed to accumulate all the components necessary for independent life: a set of molecular machinery and genetic instructions enabling it to generate energy, maintain itself and – most importantly – replicate.

One cell became two. Two became four. Four became eight, and on and on and on and on. And now, billions of years later, here we are. Every single cell in your body, every cell in the tree outside your window, every cell in the goldfinch that chirps in its branches or in the colonies of bacteria lurking in your toilet bowl can trace its origins all the way back to LUCA through an unbroken chain of cell divisions. This process of cell replication is the fundamental engine that drives the profusion of life on Earth. It's what turns an acorn into an oak, a lump of yeasty dough into a loaf of fluffy bread, a fertilised egg into a baby and a cancer cell into a deadly tumour.

ANCIENT AND MODERN

When someone hears the news that they have cancer, one of the first questions they often ask is, 'Why me?' But the first question I

want to ask is, 'Why us?'

If you follow the headlines declaring ever rising cancer rates, it's easy to fall into the trap of thinking that cancer is a recent disease caused by our unhealthy modern lifestyles. But given that cancer will inevitably emerge in almost any multicellular species, this simply isn't true.

In October 2010, while I was working in the science communications team at the charity Cancer Research UK, the University of Manchester put out a press release about a review written by two researchers, Rosalie David and Michael Zimmerman, published in the journal *Nature Reviews Cancer*. They concluded that because cancer is rare in Egyptian mummies and other ancient remains, it must be an almost entirely modern confection for which we only have ourselves to blame. Unsurprisingly, the story was media catnip. It quickly appeared in newspapers and online, stirring me into action to write a post for the charity's blog arguing that these claims were not only misleading, but also wrong.

For a start, rare doesn't mean non-existent. We have no way of knowing whether or not the proportion of cancers that turn up in the archaeological records is an accurate reflection of the health of the populace in which they arose. Calculating accurate cancer incidence statistics for long-dead human populations is almost impossible, given the relatively small proportion of remains that have been unearthed from ancient times in comparison to the number of humans who have ever lived. What's more, cancer is a disease that mostly affects older people, with the incidence rising sharply over the age of sixty. Many modern populations are lucky enough to avoid the hazards that sent our ancestors to early graves, such as infectious diseases, poor diets, death in childbirth and generally unpleasant living conditions. But as average life expectancy has significantly increased around the world, so too have the chances of living to an age where the risk of cancer becomes an issue.

You might make it to fifty or more in ancient Egypt if you were wealthy and well fed, but the poor folk would be lucky to scrape past thirty. In fifteenth-century England, men could expect to live to fifty on average, with women only reaching around thirty,

presumably thanks to high rates of death in childbirth. While archaeologists can have a good stab at guessing the age of an individual they've unearthed, perhaps by looking at the condition of their teeth and bones or any accompanying artefacts, it's very difficult to work out an age-standardised cancer incidence curve for people who shuffled off this mortal coil many thousands of years ago.

Secondly, most archaeological specimens are little more than skeletons. Although some cancers leave their mark in the bone, others are more likely to stay confined to swiftly decomposing internal organs. The fact that tumours have been spotted in a number of mummified bodies, whose soft tissues are preserved, doesn't particularly scream 'extremely rare' to me. Certainly, the disease was common enough to be worth mentioning by ancient Egyptian, Roman and Greek doctors, with the second-century Greek physician Galen noting, 'We have often seen in the breasts a tumour ... This disease we have cured often in its beginning, but when it has progressed to a substantial size no one can cure it without surgery.' As we'll see, more than 275 examples of cancer have been documented in people who lived before the turn of the twentieth century, including extremely rare childhood tumours as well as more common cancers. And those are just the ones we know about. How many of Galen's breast cancer patients are lost to history because we have no physical or written trace of their existence?

In fact, the original review is far more circumspect than the press stories. Michael Zimmerman is a respected scientist who has produced detailed studies of tumours in mummies, and the paper goes into great detail about the archaeological and cultural evidence for cancer in antiquity. We could argue endlessly about whether or not this meets a definition of 'rare', but by far my biggest issue with the story lay in the university's original press release, which contains the following quote from Rosalie David: 'There is nothing in the natural environment that can cause cancer. So it has to be a man-made disease, down to pollution and changes to our diet and lifestyle.'

Sorry, but no. It simply isn't true that the ancient past was some kind of wellness utopia. As we'll see in the next few chapters,

although modern lifestyles and habits can undoubtedly increase the risk of cancer, the natural environment is awash with things that cause cancer, from viruses and other infectious diseases to food moulds and naturally occurring chemicals in plants (even the 'organic' ones). Radioactive radon gas seeps out of the ground in many parts of the world as a result of natural processes, especially areas rich in volcanic rocks. It's thought to be responsible for the unusually high rates of cancer discovered in the remains of a group of villagers living in the American Southwest about a thousand years ago. Our very own sun showers us with cancer-causing ultraviolet radiation every day. Carcinogenic compounds abound in the soot and smoke produced by open fires, used by humans for food and warmth for more than a hundred thousand years and particularly noxious in confined spaces like caves or kitchens. And most childhood cancers have very little to do with any environmental factors, instead arising as a consequence of normal developmental processes running amok (see here).

To get a better idea of the way that cancer has haunted the human race throughout our history, I met up with Casey Kirkpatrick, one of the co-founders of the Paleo-oncology Research Organization (PRO) – a small but determined group of women scientists dedicated to investigating cancer throughout antiquity. They're following in the footsteps of a handful of pioneers of ancient disease research (paleopathology), notably doctor-turned-Egyptologist Eugen Strouhal and American anthropologist Jane Buikstra, and taking a very systematic approach to the problem. One of the PRO's first projects was to set up the Cancer Research in Ancient Bodies Database (known as CRAB, as a nod to the ancient etymology of the disease, here), where they gathered all the information they could find about cancer in humans who lived before the twentieth century.

It's still a work in progress, but at the time of writing there were around 275 entries – significantly more than had been described by 2010 when Zimmerman and David's review came out. That still might not seem like a lot, but there will be many more ancient cancers out there that have simply gone unnoticed. It is, after all, remarkably difficult to diagnose someone who's been dead for

more than a thousand years, especially if all you have to go on are a few bits of bone.

The main tools for diagnosing cancer in ancient remains are X-rays and CT scans. In fact, the first X-ray image of a mummy was published by pioneering English Egyptologist Flinders Petrie in early 1896, just four months after the discovery of X-rays (although he was searching for jewels or amulets hidden under funereal wrappings rather than tumours). The first cancers in mummies were spotted in the 1950s, but the development of three-dimensional CT scanning in the 1970s was a game changer. Archaeologists could now virtually unwrap mummies and see what lay within, leading to the identification of many more cases.

Spotting a strange lump or abnormal structure in an ancient skeleton or mummy doesn't automatically signify cancer: it could be a benign tumour, a cyst, or any one of a number of other diseases. It might be a sign of fluorosis – a condition in which soft tissue turns into bone owing to high levels of fluorine in the environment, commonly found near volcanoes. Or it could be something known as pseudopathology, where the normal decomposition of bone creates an illusion of disease. However, there are some giveaway clues.

Certain cancers look very distinctive – what Casey Kirkpatrick and her colleagues would describe as having a specific *pathognomic*. Others aren't so obvious. While CT scanning and X-rays might reveal there's some kind of cancer present, it can be hard to say exactly which type, so the best a paleopathologist can offer is a selection of options rather than a definitive answer. Myeloma – a cancer affecting white blood cells in the bone marrow – leaves the same kind of traces in bones as tumours that have spread through the body from elsewhere, while the blood cancers leukaemia and lymphoma are virtually indistinguishable in ancient remains. And while a modern-day patient with suspected cancer will be put through a systematic battery of tests and scans to pin down their disease, there isn't a similar standardised pathway for assessing cancer in ancient remains – something the PRO team is working to address.

Another problem is figuring out how diseases manifested within in the body in the distant past. There are big differences around

the world in the causes, numbers and types of cancer that turn up in modern populations, and it's rare that someone living in a wealthy country today would die of cancer without receiving any treatment at all. So trying to compare 4000-year-old Egyptians, third-century Inuit or precolonial Peruvian villagers with modern Westerners is a tricky task. Some researchers are trying to make more realistic comparisons with less developed cultures and populations without good access to medical care, although gathering accurate data and statistics in these parts of the world can be challenging.

The difficulty of diagnosis has led to long-running arguments about whether or not strange lumps and bumps found in ancient remains are true examples of cancer or if they could have been caused by other means. One of the most famous (and controversial) examples is the mass bulging from the jawbone of Kanam Man, a fossilised remnant of an ancient human dug up by fossil-hunter Louis Leakey and his team near the Kenyan shore of Lake Victoria in 1932. The exact age of the fossil and its position in our ancestral family tree is disputed – although it's thought to be at least 700,000 years old – as is the true nature of the mass protruding from its surface. If it is, as some people argue, the remnants of a bone tumour or Burkitt's lymphoma, then this lump is one of the oldest hominin cancers that we know of. Or, as others believe, it could just be overgrown bone resulting from a poorly healed fractured jaw.

Other contentious examples are an apparent spinal tumour in the fossilised skeleton of a young australopithecine – one of our ancient primate ancestors in east Africa, who lived nearly 2 million years ago – and a strange growth in a rib belonging to a 120,000-year-old Neanderthal from what is now Krapina in Croatia. That last one is most likely the result of a non-cancerous condition called fibrous dysplasia, where normal bone is gradually replaced with weak fibrous tissue.

A more definite diagnosis comes from a toe bone from the South African Swartkrans cave – the 'Cradle of Humankind' where our species is first thought to have emerged. Although it's impossible to pin a precise species on the bone, which dates back more than 1.6 million years, it very likely belonged to an individual who was

related to humans. Unfortunately, they were probably afflicted with a type of aggressive bone cancer known as osteosarcoma, which tends to affect teenagers and isn't known to be related to anything in the environment or lifestyle. This is the oldest known identifiable cancer in a human ancestor to date, but that may change in the future as more bones are discovered and diagnostic techniques improve.

There are many other examples of possible ancient cancers dotted around the world. A benign tumour was spotted in the 250,000-year-old jawbone of an adult *Homo naledi* – a member of the most recently identified group of extinct human ancestors, whose numerous bones were discovered in the Rising Star cave system in South Africa in 2015. There's a skull bone belonging to an ancestor of the Neanderthals, *Homo heidelbergensis,* who possibly died of a brain tumour up to 350,000 years ago in the region of Europe we now call Germany. Then there's Lemdubu woman – a sturdy, rugged-jawed, twenty-something female who was buried 18,000 years ago in an Indonesian cave. Her bones are peppered with holes that look just like the cavities caused by metastatic cancer. Frustratingly, ancient fossilised skeletons don't come with neatly preserved medical notes, so we may never know the truth about these long-gone souls.

New molecular biology techniques offer a potential way forwards. As DNA detection techniques have become more sensitive and much cheaper, researchers can now analyse tiny fragments of DNA gathered from historic remains. This tactic has most famously been used in the case of the mummified body of Italian Renaissance ruler King Ferrante I of Aragon, which was found to harbour an exceptionally well-preserved tumour in the pelvis. Under the microscope, the cancer cells looked like they could have either started life in the king's bowel or in his prostate. Genetic testing revealed that the tumour carried a fault in a gene called KRAS, which is common in bowel tumours but virtually unknown in prostate cancer. This provided Ferrante with a definitive diagnosis a mere 500 years after his death.

However, genetic techniques have limited usefulness, because they rely on capturing a sample of DNA from a tumour, either in a preserved organ or where it's spread into the bone. And it may be

of limited benefit now that we know even normal cells can contain apparently 'cancerous' mutations (see here). An alternative idea is to look for faulty protein molecules that might be a more reliable indicator of cancer – an approach known as proteomics. It's more technically challenging and expensive to identify proteins than it is to do more straightforward DNA sequencing, so proteomic analysis tends to be reserved for the most special samples in a paleopathologist's collection. Costs are coming down all the time, though, so it's likely to be more widely applied in the future.

Despite the increasing availability of tools, the limiting factor will always be the supply of human remains on which to use them. Perfectly statistically balanced populations of skeletons can't be magicked out of the ground – you get what you get and you get on with it. There's also something called the 'osteological paradox', first proposed in 1992 by anthropologist James Wood and his colleagues, which says that any archaeological record will never be truly representative of the state of pathology in that population. This is partly because some people will succumb quickly to diseases that leave no trace in their mortal remains and also because you can only ever know about someone's health at the point of their death. For example, finding the skeleton of a fifteen-year-old girl who died 2000 years ago tells you nothing about the health of her friends who survived to an older age. But we do know that many different types of cancer have been found all over the world in many cultures spanning many thousands of years, including what would be considered as very rare tumour types by today's standards.

There are other, more nebulous, things that affect whether researchers are more or less likely to find certain types of people and diseases in the archaeological record or information about them. If someone had a very fast-growing cancer, they might just suddenly die without it ever being diagnosed or leaving a mark on their bones. Even if an autopsy was performed, many cultures have a stigma around cancer, believing it's sinful or infectious, so families might not want the cause of death recorded. There are also cultural traditions around death and burial that can affect the kinds of remains that archaeologists might stumble upon many years later. For example, some societies buried babies in the walls

or floors of houses. Others separated male and female graves, or buried people with certain diseases like plague or leprosy in a specific place.

Ultimately, this is a number problem. Finding three skeletons with signs of cancer in a particular area might represent 3 per cent of people in a village of a hundred, 0.3 per cent in a town of a thousand, or 10 per cent of a group of thirty. Maybe cancer is genuinely rare in historical and prehistorical populations. Or it may have been much more common than we think, because scientists haven't systematically been looking for it. It's exciting to think about the new clues that might be revealed by DNA or protein analysis, as well as a more methodical approach towards X-ray or CT-scanning remains for signs of cancer. But what's becoming clear is that the more people look for evidence of cancer in ancient remains, the more they find.

Even though some of the most striking examples of ancient cancer have come from mummies, who have more flesh on their bones than typical skeletal remains, there's still a lot we don't know about how well tumours are preserved during the mummification process. You can't just grab a scalpel and do a post-mortem on a mummy, so researchers rely on CT scans to see what might be going on inside. But according to Casey Kirkpatrick, we don't actually know how well mummified tumours show up on a scan, so we don't know what we might be missing. To find out, she and her colleague Jennifer Willoughby decided to do an unusual experiment.

First, they teamed up with a group of researchers at a nearby hospital who had a steady supply of mice with various types of cancer. Next, they set about mummifying these animals in every way they could imagine. Some were dropped in a local swamp to replicate the mummies found in peat bogs. Others were encased in ice or ended up buried in hot sand. And for a final flourish, Kirkpatrick and Willoughby even gave a few mice a full ancient Egyptian ritual burial, carefully removing their tiny internal organs and packing the corpses with natron and natural resins before bandaging them up.* Once mummification was complete, the final stage was to put the mice into a CT scanner to see how well their tumours had been preserved through the process.

Reassuringly, the signs of cancer showed up clearly in all the mummified mice, suggesting that CT scanning probably isn't missing much in the way of solid tumours when it comes to studying ancient human mummies. 'Cancer is not a modern disease,' Kirkpatrick emphasises. 'It has happened throughout our entire history. There are carcinogens in the environment, there are also genetic factors and infections – it's near impossible to avoid. I think we really need to reach out to the public and inform them about this, especially when people are suffering and thinking that cancer is all their fault.'

ALL CREATURES GREAT AND SMALL

Cancer isn't a uniquely human affliction – something I've been all too aware of since our first dog, a much-loved Welsh springer spaniel named Sheba, died of leukaemia. But while it's sometimes argued that the artificial pressures of domestication cause tumours to turn up in pets as well as people (therefore putting it in the category of a 'modern disease'), framing cancer as the inevitable consequence of multicellularity tells us that we should expect to see cancer occurring in any and every species. And, with some notable exceptions, that's exactly the case.

In 2014, Croatian geneticist Tomislav Domazet-Lošo and his colleagues at the University of Kiel in Germany published a mind-boggling paper describing tumours in two different species of a tiny freshwater creature called *Hydra* – the simplest organism currently known to develop cancer. Little more than a tube with tentacles, each *Hydra* is made of two layers of cells, maintained by three distinct groups of stem cells. Two of them make the layers of the tube, while the third – known as interstitial stem cells – is multitalented, capable of producing various bits of the *Hydra*'s simple body as well as germ cells, which eventually become eggs and sperm. And it's from these stem cells, interrupted somewhere along their journey to making eggs, that a tumour grows. While it's hard to tell whether a *Hydra* is feeling unwell, the presence of this cancer certainly has an effect, severely reducing their growth rate and fertility. It's also important to point out that Domazet-Lošo and his team didn't interfere with these creatures in any way, such

as making genetic tweaks or putting nasty chemicals in the water – the tumours popped up entirely spontaneously. Their discovery raises an interesting question: if something as basic as *Hydra* can develop cancer, what about other animals?

One person who's trying to answer that question is Amy Boddy, Assistant Professor in the Department of Anthropology at the University of California, Santa Barbara. She and her team have been pulling together an impressive amount of data about tumour incidence across a huge range of species – a concept known as comparative oncology.

'One of the hardest things is figuring out exactly how we define cancer in the first place, especially when looking across wildly different organisms. We can be fairly sure that a cancer in a dog or mouse will be recognisably similar to a human tumour. But what about strange cells in a mussel, or a peculiar bulge on a mushroom? When you start talking about concepts of cancer in other organisms, you realise we don't know a lot about the disease,' Boddy says. 'There were huge arguments when we wrote our first review of cancer across the tree of life about what we should class as cancer, because the medical definition is very human-centric.'

Invasive cancer in humans is defined by whether or not tumour cells have broken through the basement membrane – a thin protective sheet of molecular 'cling film' wrapped around our tissues and organs. Plenty of organisms don't have this barrier layer yet can still be affected by rogue cells multiplying out of control. Plants develop large growths known as galls, usually the result of bacterial, viral or fungal infection, or the work of wasps. And there are other strange phenomena like the fasciated cacti that we'll encounter in the next chapter.

Tumour-like masses can be found in red algae and even fungi aren't in the clear: non-invasive growths have been spotted in mushrooms, while simple moulds can start growing in abnormally excessive ways. Although these lumps are a symptom of over-enthusiastic cell proliferation, it's not quite right to call them cancers as the rigid cell walls and sturdy internal structures of fungi and plants prevent rogue cells from spreading throughout the organism.

Moving on to animals, cancer turns up almost everywhere you look. One recently published list of animals known to be affected by cancer stretches over more than twenty pages, while the line-up of marine creatures that have been found with tumours reads like the menu from the world's weirdest sushi restaurant: cockles, clams, crabs, catfish, cavefish, cod, corals and quahogs. Damselfish, angelfish, jewelfish and goldfish. Smelt, salmon, sea bream and weedy seadragons ... the list goes on and on.

Tumours turn up in frogs, toads and other amphibians, and have been spotted in a range of reptiles such as snakes, turtles, tortoises and lizards. Cancers appear in many species of bird, from parakeets to penguins, cockatoos to cassowaries and black-bellied whistling ducks to common or garden budgerigars. Not to mention the curious case of a three-legged robin with a cancerous mass in its belly, which arrived in the possession of a Mr H.K. Coale of Chicago one day in 1919. From aardwolves to zebras, our fellow mammals are also affected by all manner of cancers: whales, wallabies, baboons, badgers, bongos and almost everything in between.

Just as tumours turn up in long-dead human remains, there's evidence of cancer stretching way back through the fossil record. In 2003, a team led by Bruce Rothschild from Northeastern Ohio Universities College of Medicine trawled the museums of North America with a portable X-ray machine, taking images of more than 10,000 dinosaur bones. Although they found tumours in only one family of dinos – herbivorous duck-billed hadrosaurs from around 70 million years ago – they detected a staggering twenty-nine tumours in ninety-seven individuals. There's even a tumour in the leg bone of a fossilised proto turtle that roamed the Triassic seas washing over what's now modern Germany about 240 million years ago. Evidence of cancer has come to light in other dinosaur species, including a giant titanosaur, although some of these observations are controversial.*

These surveys of cancer across life have also challenged the persistently popular but incorrect belief that sharks don't get cancer. This strange idea sprang up in the 1970s when Judah Folkman and Henry Brem at The Johns Hopkins University School of Medicine in Baltimore, Maryland noticed that cartilage – the

protective layer on the ends of bones – prevented new blood vessels from growing into tumours. Shark skeletons are made entirely of cartilage rather than bones, so people started to wonder if they might be more resistant to cancer than other animals.

Lab experiments suggested that shark cartilage was very effective at stopping tumour blood vessel growth, while attempts to induce tumours chemically in these fish failed. Given that nobody had spotted cancer in any sharks in the wild, the theory seemed to check out. From there, it was a relatively simple mental leap to suggest that shark cartilage might prevent or even cure cancer. Boosted by the publication of the 1992 bestseller *Sharks Don't Get Cancer* by William Lane, a multimillion-dollar industry was born. Sharks were caught, farmed and slaughtered in their millions to make cartilage pills for desperate cancer patients, despite at least three clinical trials showing that they were ineffective.

More importantly, the fundamental premise isn't true: tumours have been spotted in multiple species of sharks, including in the mighty jaws of a great white found off the coast of Australia in 2013. As marine biologist David Shiffman pointed out in an article about the discovery of the great white tumour, 'Sharks get cancer. And even if they didn't get cancer, eating shark products won't cure cancer any more than me eating Michael Jordan would make me better at basketball.'

Although shark cartilage may not be able to prevent or cure any disease, comparing cancer across species can provide useful insights into what might be going on in our own bodies. This becomes particularly interesting when we ask not *whether* a singular example of a tumour has been found in any given type of animal – something that should be entirely expected, if cancer is a process that inevitably arises in any multicellular organism – but *how often* it turns up.

Perhaps surprisingly, not only can we definitively say that cancer isn't a human-specific disease, but we also aren't even the species that gets it the most. It's a commonly held assumption that humans get cancer more than other species, yet it's based on woefully incomplete information. Just as we have no idea about

the frequency of cancer in ancient human populations without systematic data collection, nobody has really looked at the incidence of cancer across species in a methodical way.

It's one thing to generate a huge list of all the species where any kind of cancer has been spotted, but it's quite another to work out whether any of them are particularly rare or commonplace. Amy Boddy and her colleagues in Santa Barbara have become animal epidemiologists, sifting through data from zoos – plus as much information as is possible to glean about wild populations – to see how common the disease really is across different species.

'Zoo animals do have unusually long lifespans compared with animals in the wild, and we have quite small sample sizes for some of these,' she warns. 'But our preliminary data suggests that there are quite high rates of cancer in small mammals compared with humans – we see quite a lot of tumours in ferrets, and also it looks like little mouse lemurs seem to be getting a lot of cancers too.'

Boddy explains that cancer seems to be more common in animals that have been through a bottleneck – an event that drastically reduced the population at some point – meaning that today's individuals are more genetically similar than they would be if they hadn't been through the crash. Golden Syrian hamsters have squeezed through a particularly drastic bottleneck, with the majority of domesticated hamsters in the world being descended from a single litter found in the Syrian Desert in 1930. As a result, they have unusually high rates of spontaneously occurring tumours.

Other pure-bred and domesticated species are also more susceptible to cancer. Dogs have a roughly similar risk of cancer to humans, with different types of tumour being more or less common in particular breeds. And up to a third of farmed hens will develop ovarian cancer owing to the pressure of constantly having to churn out eggs.

Interestingly, humans have been through several such precarious situations in our history. For example, there's good evidence that our ancestral population collapsed to fewer than 20,000 breeding individuals around a million years ago, taking our species to the brink of extinction – something that may play a part in our susceptibility to cancer today.

bigger than a 20-gram mouse, meaning that a mouse-sized piece of blue whale flesh must be at least 10 million times more cancer-proof than an actual mouse.

Humans are a clear outlier, with higher than expected rates of cancer for our size. But when you take our bad habits out of the equation (particularly smoking), then we seem to be remarkably resistant to cancer compared with smaller creatures but much more susceptible than the giants of the mammalian world. The observation that cancer risk doesn't track with body size is known as Peto's Paradox, named after Richard Peto, the British statistician who first noticed it back in 1976. While it may seem contradictory, this eponymous Paradox is a fascinating lens through which to think about why humans – or any other organism – might or might not get cancer at a given point in their lifetime. And all that's required to solve it is a little strategic thinking.

As well as differing in size, animals also differ in lifespan. In the wild, under constant risk of predation, a mouse might be lucky to make it to a year. Even in the cosy confines of a laboratory, the oldest are lucky to make it past two. By contrast, the Greenland shark – the oldest known vertebrate – reaches sexual maturity at the ripe old age of 150. Using a dating technique that looks for the impact of 1950s radioactive bomb tests in the lens of the eye, the oldest of the Greenland sharks tested so far was thought to have been alive for up to 500 years, first slipping through the chilly Arctic seas when Queen Elizabeth I was on the throne. African elephants average about sixty to seventy years, but guinea pigs are unlikely to reach eight. Global human average lifespan is now around seventy, while our chimpanzee relatives can expect to hit fifty. On the other end of the primate spectrum, mouse lemurs have an average reproductive lifespan of around five, although they can live to fifteen in a zoo.

Solving Peto's Paradox requires an evolutionary trade-off between growth, longevity and sex. To put it simply, either you evolve to live fast and die young – existing for just a few short, dangerous years filled with as much reproduction as possible – or you're a slow burner that grows large, tends to eat rather than be

eaten, has offspring later in life and looks after them for a long time.

Obviously, if humans all got cancer before any of us could reproduce, we wouldn't have got very far as a species – that's how natural selection works. But maintaining a large body in a healthy, cancer-free state for decades takes a lot of energy and resources, so species have evolved to stay healthy for the duration of their reproductive phase, however long that may be, succumbing to cancer when the effort to maintain the body is no longer worth it. It therefore makes perfect sense that 90 per cent of all human cancers occur in people over the age of fifty: we've evolved to get through the prime of life in good health, but once the kids are born and raised then all bets are off.*

The ultimate expression of the 'live fast, die young' strategy comes from a marsupial mouse known as *Antechinus*. For around two weeks in August, in the depths of the Australian winter, males will mate with as many females as possible in frantic bouts lasting up to fourteen hours. But as the mating period draws to a close, bad things start to happen to the little guys. Their fur falls out, their internal organs start to break down and infections quickly take hold. Within a few short weeks all the males are dead, having invested all of their energy in reproduction and literally gone out with a bang.

Their mates fare little better and the mothers usually die after their pups are weaned, leaving the orphans to fend for themselves until the following year, when the whole cycle starts again. The reproductive strategy of these creatures may seem strange in comparison to our human lifestyles, but to them it makes perfect evolutionary sense. *Antechinus* live on insects, which tend to appear in cyclical gluts. The frenzy of mating happens just around the time of the biggest food bonanza, so the mothers are well fed as they suckle their young, while the males are little more than disposable sperm-delivery vehicles.

On the other end of the spectrum, researchers studying nature's slow burners are making some intriguing findings about how these species manage to stave off cancer for so long. Advances in DNA sequencing mean that we can now rummage around in these animals' genomes and find out what keeps them ticking.

One of the most famous examples of a long-lived, cancer-resistant mammal is the naked mole rat. These sand puppies live in large colonies beneath the African desert, constantly tunnelling in an effort to find tasty plant roots and keep their continually growing teeth in check. Shielded from the sub-Saharan sun, their burrows stay at a constant 30°C, so they've dispensed with the effort of maintaining the high body temperature common to all other mammals. They don't seem to feel pain, can survive in perilously low oxygen levels, aren't pestered by predators and rarely venture out into the scorching sunlight. Even more strangely for rodents, they're eusocial; only a few animals in the colony are sexually active – a sole dominant queen who rules the roost and a handful of lucky stud males – while the rest are non-breeding workers responsible for digging, maintaining and guarding the twisting network of tunnels.

Although researchers initially became interested in naked mole rats for their unusual social structure, they soon realised something odd about the animals they'd brought into their captive lab colonies: they just weren't dying. In 2002, researchers in New York published a report of a naked mole rat in their laboratory colony that had made it to at least twenty-eight, beating the previous rodent longevity record holder (a 27-year-old porcupine). This was smashed in 2010 by a naked mole rat nicknamed Old Man, who was thirty-two when he finally passed on to the great colony in the sky. Most mole rats make it into their late twenties and cancers are virtually unheard of, with only a handful of cases documented in more than a thousand captive animals.

It's still not entirely clear how naked mole rats manage to live so long and stay cancer-free. Maybe it's their low-calorie, low-temperature lifestyle, which is thought to reduce the production of damaging chemicals called free radicals that are created as cells generate energy. Perhaps the explanation lies in altered levels of hormones and other molecules that drive cell growth, or in their polyphenol-rich vegetarian diet. In 2013, scientists discovered that the mole rats make an unusually large and sticky version of a kind of cellular glue called hyaluronan. They suspected that this helps to reinforce contacts and communication between their cells, stopping them from running out of control and turning cancerous.

Certain genes involved in energy production are much more active and present in many more copies in mole rats than in mice. Perhaps this extra dose of DNA acts to buffer the carcinogenic effects of genetic damage, keeping mole rats powering through well into old age. There are other key differences in genes involved in the response to DNA damage and other ageing-related pathways. Cells from naked mole rats are more resistant to stress and damage than those from other small rodents. And a study published in 2019 showed that naked mole rats also have a highly unusual repertoire of immune cells compared with mice, which may help to keep them healthy for so long.

As if that wasn't enough, they have yet another layer of protection against excessive cell growth: it's simply not tolerated. There's a phenomenon in biology known as contact inhibition, best described as a cell's 'personal space', which stops them proliferating if things start to get too crowded. Naked mole rat cells are exquisitely sensitive to contact inhibition and will freeze as soon as they detect another cell getting too close, preventing any pile-ups that could herald the start of a tumour.

Similarly long-lived blind mole rats (no relation to the naked ones) have solved Peto's Paradox in a different way. Although these rodents are about the same size as regular rats, they live five times as long and have very low cancer rates, often making it to their twentieth birthday. This longevity seems to result from the ability of blind mole rat cells to repair potentially cancer-causing DNA damage five times more efficiently than those of a normal rat – a property that might have evolved to protect the animals from the harmful cycles of high and low oxygen levels that they experience in their subterranean burrows.

Capybaras – those delightfully chilled South American giant guinea pigs with a reputation as being the friendliest creatures in the zoo – have a different answer. Their unusually large body size appears to be the result of overenthusiastic activity of the hormone insulin, which controls cell growth and metabolism. At the same time as becoming King of the Rodents, they must have also evolved a way to suppress cancer (remember, the bigger the body, the more cells and the greater the cancer risk). Researchers digging in the capybara genome have recently found that although

these animals seem to have higher than normal levels of harmful genetic mutations compared with other rodents, they also seem to have particularly vigilant immune cells that seek out and destroy rogue cells before they can grow into a tumour.

Elephants are a whole other story. Rather than attempting to fix any potentially cancerous damage to their DNA or ramp up their immune system, they've evolved multiple copies of a gene encoding a molecule called p53 – the so-called Guardian of the Genome – which triggers cells to die for the greater good at the first hint of trouble. This makes sense considering their huge size: you've got cells to burn if you're an elephant, so it's better to get rid of any dodgy ones straight away.

Scientists have also been diving deep into the genes of the 100-tonne bowhead whale, whose 200 years of relatively cancer-free living make it a good candidate for the longest-lived mammal on the planet. At the moment it's not clear how they achieve this, but it may be to do with having gained or lost certain genes associated with DNA damage repair or by controlling cell proliferation.

On the other end of the size scale, a teeny Brandt's bat clocks in at less than 10 grams – one ten millionth the weight of a mighty bowhead and about half the size of a typical laboratory mouse. Yet it holds the record for lifespan in a creature that small, with the oldest documented individual living for a staggering forty-one years. While Brandt's bats are the winners of the old age Olympics, all other species of bats also live for an unusually long time compared with ground-based rodents of similar sizes. There's certainly a built-in longevity advantage to being able to fly, as bats can zip off at the first sign of predators. But they seem to have some useful molecular adaptations, too.

In 1961, American microbiologist Leonard Hayflick realised that most cells could only divide fifty or so times before they ran out of steam and died. We now know that this Hayflick limit is imposed by telomeres – the caps of DNA and protein on the ends of chromosomes that protect the fragile ends in the same way the plastic aglet wrapped around the end of a shoelace stops it from fraying. In most normal animal cells, the telomeres get a tiny bit shorter every time a cell divides, owing to the vagaries of the DNA copying machinery. Once the telomeres shrink to a certain size,

takes me into his lab to look at a salty tankful of prickly white spheres, each about the size of a Mint Imperial (or Mentos candy if you're American). These are *Tethya wilhelma* – just one of the many species of sponge that appear to be untroubled by any form of cancer.

'We wanted to find a new model organism that would be good to study, where its genome has already been sequenced, and we can grow it in the lab,' Maley tells me, explaining how one of his colleagues, Angelo Fortunato, has spent months of his life setting up the perfect saltwater system to keep these sponges happy in their new home. And then, after all that, he's bombarding them with X-rays.

This is no gentle zapping – it's a full-on nuclear assault. By way of comparison, a short, sharp dose of just five grays of high-energy radiation is enough to kill a human within two weeks of exposure. Fortunato's giving his sponges a staggering *seven hundred*, and they just carry on like nothing happened. No obvious signs of harm and certainly no cancers.

Maley and his team are busy figuring out exactly how these super-sponges manage to shrug off such a colossal blast, in the hope that it might reveal new insights into how to protect our own cells from radiation damage. This might be useful when it comes to finding ways to enhance the fatal effects of radiotherapy on cancer cells or to protect healthy tissue around them. At the time of writing, they're still searching for clues, although other researchers have found a number of chemicals in sponges that block tumour growth. These little marine creatures definitely have something interesting going on inside their unassuming exteriors that needs to be wrung out.

MODERN LIFE IS RUBBISH

Cancer is neither new nor a uniquely human disease, so we can't blame it entirely on the evils of modern living. But we should question why the rates are so high in affluent societies, with one in two people in the UK born after 1960 predicted to get cancer at some point in their lifetime. Some of this can be explained by the impressive increase in life expectancy – more and more of us are

simply living long enough for cancer to kill us in old age rather than succumbing to violence, predators, misadventure, infectious diseases, starvation or death in childbirth.

Nineteenth-century doctors were convinced that cancer was a disease of civilisation but, as we've seen, it's difficult to generate accurate figures for cancer in ancient populations. Gathering stats on more recent hunter-gatherer societies and current populations with less 'modern' lifestyles is also a major challenge. Countries like the UK have incredibly detailed cancer statistics, fed by the detailed medical records kept by the National Health Service. It's therefore unlikely that anybody would die from cancer in the UK without it being noted at some point. But there are still many parts of the world where cancer goes undiagnosed and unrecorded.

Humans are immensely adaptable to the changing world around us and our genes are changing, too. We can see evidence of genetic changes that have swept through populations at a relatively quick pace, such as the ability to digest milk after infancy owing to a specific genetic change that became widespread during the rise of dairy farming around 10,000 years ago. Genetic variations for blue eyes are also fairly new, popping up between 6,000 and 10,000 years ago. But the world we live in today is changing far faster than this.

Our modern bodies evolved in a world with an uncertain food supply and more physical activity, and probably a different suite of infectious diseases and exposures to carcinogens. Ancient humans may have been exposed to indoor fires and chemicals from tanning or smelting, but they didn't deliberately inhale cigarette smoke or roast themselves in the midday sun. Our lifestyles are very different, too. For example, women in more developed countries tend to have fewer children and breastfeed for a relatively short time, as well as starting their periods earlier and having the option of hormone replacement therapy during the menopause. Given the role of hormones in driving the growth of many breast cancers, it's not a huge logical leap to suggest that altering the balance of hormones over a lifetime might have an impact on risk.

All this talk of evolutionary strategies makes me wonder whether or not humans will gradually start to evolve our way out of cancer as our lifespans increase and the average age at which we

have children also rises. Disappointingly, every scientist I've asked tells me that this is wishful thinking. Evolution works on a timescale of millennia, not centuries, and there simply hasn't been enough time for our species to adapt to all the changes that have happened. There's nothing we can do about the slow tick of time working in our tissues, honed by hundreds of thousands of years of natural selection.

As I head into my forties, I'm increasingly aware that I'm approaching the age where evolution gives up on me. I can do my best by not smoking, watching my weight, being careful what I eat, taking care in the sun and cutting down on alcohol, but ultimately I'm trying to wage war against my biological destiny.* Even so, as I talk to Amy Boddy about her research menagerie, I'm excited to think that this broader view of cancer could reveal important truths about the disease; although it feels like the whole field of comparative oncology is only just getting started.

'I think we need a better understanding of cancer in other organisms and how important that could be in revealing the basic biology of the vulnerabilities in humans, and I'm also sad to see that there isn't more work looking at human variation across the world in different populations and small-scale societies compared with Western populations,' she says. 'This is nature's toolbox, giving us all the recipes and ingredients that it has developed over millions of years of evolutionary history to produce different cancer defence mechanisms and modify risk – evolution has given us a pretty good code for what works.'

There's one final reason why we should care about cancer in animals as well as humans and that's for the sake of the animals themselves – an argument that often gets lost in the anthropocentric world of cancer research. Boddy is passionate that we should care about why animals get cancer as much as we should care about why humans do. For a start, vets and conservationists are keen to discover more about cancer in domesticated, captive and wild animal populations, both to understand the causes and to figure out how best to treat it. And the unexpected appearance of cancer in animals living in a particular area might reveal the presence of carcinogens that their human neighbours would do well to avoid, too. We could even

learn something from our animal friends along the way, perhaps stealing their best anti-cancer innovations to apply to our own failing bodies.

Still, knowing that cancer has always been with us and affects almost every branch of the tree of life still doesn't tell us *why* it happens. What turns a normal, well-behaved cell into a nasty one that grows out of control and causes trouble? To understand that, we need to uncover the rules governing the cellular societies within all living things and see what happens when they get broken.

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* LUCA – the Last Universal Common Ancestor – is the name given to the most recent organism from which all life on Earth evolved [although nearly 4 billion years is arguably stretching the concept of 'recent' to breaking point].

* Kirkpatrick tells me they drew the line at building a miniature pyramid.

* As with the challenge of correctly diagnosing ancient humans, tumours in soft tissue don't get preserved. Unfortunately, fossils don't come with an accompanying veterinary report, so there's plenty of room for argument.

* There's an intriguing difference in cancer incidence between the sexes that seems to be independent of anything else, with men being slightly more likely to get cancer at a younger age. It's a controversial idea, but the so-called Grandmother Hypothesis suggests that while grannies are useful because they help out with the grandkids, grandpas who take less of a role in childrearing are more dispensable in evolutionary terms.

* You can't cheat this destiny, either. Although evolution has got humans to a point where we're unlikely to get cancer during our prime reproductive years, you can't dodge it by not having children.

2

THE PRICE OF LIFE

Back in the early days of life on Earth, every cell was its own entity – an island in a sea of other free-living cells. But after a billion or so years of the single life, it was time to settle down. Cells began to club together and communicate with each other, forming small multicellular organisms. At first these were little more than loose collectives, but over millennia they evolved into highly organised creatures. They learned to specialise and differentiate their many parts, forming distinct tissues and organs: a place for every cell and every cell in its place.

Cells have decided that it's better to buddy up and form multicellular organisms than go it alone at several points during the history of life, creating the progenitors of fungi, algae and plants. Multicellular animals are thought to have evolved only once, first appearing on the scene around 600 million years ago. Although becoming multicellular means that each individual cell loses its autonomy, only replicating exactly when and where is necessary – during development, growth or repair, for example – there are some big advantages to being part of a larger whole.

For a start, multicellular organisms can grow large, providing a significant survival advantage (because it's hard to get eaten when you're bigger than everything else around you). They can eat a wider range of foods and evolve adaptations to cope with a range of environments, moving further and faster than unicellular slowpokes. Having lots of cells also means that specific tasks can be allocated to particular parts of the body – known as differentiation – allowing much more sophisticated functions to

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