Shared, Rented, Occupied: Expanding Our Concept Of Who We Are

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"I am large, I contain multitudes."
—Walt Whitman, *Leaves of Grass*, 1855[1]

Cotard's syndrome is a rare mental disorder in which people believe they are already dead or that their body does not exist. The condition is named after Jules Cotard, the French neurologist who first described it in 1880. The problem occurs in schizophrenia and has been reported rarely in migraine sufferers. Some Cotard patients have been demonstrated to have lesions in the parietal lobe or atrophy of the frontal area of the brain.

People who experience an absent body are considered delusional. The delusion, however, may lie in the other direction: those who think they have a complete human body may be the ones who are harboring a false belief.

Researchers at the NIH's National Human Genome Research Institute and the Human Microbiome Project have recently estimated that 90% of the cells in *Homo sapiens* are not human at all, but are microbial. Numerically, of the roughly 75 trillion cells in our body, around 68 trillion are bacterial.[2] Because they are so small, however, they account for only one to 3% of the body's mass. For example, a 200-lb individual is made up of only two to six lb of bacteria. Gene-wise, however, the balance is hugely in favor of the bacteria: our bodies contain 360 times more bacterial genes than human genes.[3]

In recent decades, researchers isolated a few hundred bacterial species from healthy humans, largely by standard culture techniques. Now, however, using genome sequencing methods, they have identified more than 10,000 microbial species that constitute the body's ecosystem, with perhaps 20% remaining to be identified.[3]

There is a tendency to think that these bacteria are something of a nuisance, contaminants or invaders looking for a free ride. It is not so; the microbes are essential for our survival. "Humans don't have all the enzymes we need to digest our own diet," says Lita Proctor, PhD, who manages the Human Genome Project. "Microbes in the gut break down many of the proteins, lipids and carbohydrates in our diet into nutrients that we can then absorb. Moreover, the microbes produce beneficial compounds, like vitamins and anti-inflammatories that our genome cannot produce."[4]

We speak of "the" human genome, but, strictly speaking, *Homo sapiens* has more than one genome. We are a superorganism in which a multitude of bacterial genomes live in concert with our human genome. And not just bacterial genomes, we are also partly virus. Our genome also contains about 100,000 fragments of DNA from retroviruses, making up 8% of our total genetic material.[5]

A torrent of DNA swapping goes on between these microbes through gene transfers, resulting in the creation of new organisms. Some experts believe that the number of microbes created through genetic recombination is so high that the concept of distinct bacterial species may become obsolete.[6]

Our microbial community produces a flood of metabolites that have been dubbed the Human Metabolome.[7] It is suspected that these metabolites stimulate human cells to produce autoantibodies that play key roles in autoimmune and other diseases.[8,9]

CLINICAL APPLICATIONS

Attention to the human microbiome and metabolome may already be paying off. An example concerns type 2 diabetes mellitus, which affects one in eight Americans.[10] With the sequencing of the human genome, many researchers believed it would be possible to identify the genes that render an individual susceptible to developing this disease. Unfortunately, although several of the approximately 22,000 human genes have indeed been linked to diabetes, they are not powerful predictors of who will develop the disease. Traditional risk factors, such as obesity, diet, and sedentary lifestyle, remain better predictors than known genes. Scandinavian researchers have demonstrated, however, that the bacteria that live in our gastrointestinal tract are more powerful predictors of type 2 diabetes than either human genes or traditional risk factors. In the study, which involved European women, the "signature" of the gut microbiome discriminated between women who did and did not have type 2 diabetes and also predicted which women with impaired glucose tolerance would go on to develop diabetes.[11] The possibility has been raised that this common disease, afflicting around 80 million Americans, may one day be prevented or treated by manipulating gut flora.[12]

Dr. Stanley Hazen of the Cleveland Clinic and his colleagues have apparently identified in an animal study why red meat may contribute to arteriosclerotic heart disease, America's biggest killer. In brief, specific bacteria in our GI tract metabolize carnitine, a substance found in red meat. This results in a compound called TMAO (trimethylamine-N-oxide), which promotes the growth of artery-clogging plaques. Diets high in red meat promote the growth of these bacteria, which leads to more TMAO and more atherosclerosis. "The bacteria living in our digestive tracts are

dictated by our long-term dietary patterns," says Hazen. "A diet high in carnitine actually shifts our gut microbe composition to those that like carnitine, making meat eaters even more susceptible to forming TMAO and its artery-clogging effects. Meanwhile, vegans and vegetarians have a significantly reduced capacity to synthesize TMAO from carnitine, which may explain the cardiovascular health benefits of these diets." Hazen notes that besides being found in red meats, carnitine is also added to dietary supplements to boost weight loss and is commonly found in another item linked to heart risks—energy drinks. "We need to examine the safety of chronically consuming carnitine supplements as we've shown that, under some conditions, it can foster the growth of bacteria that produce TMAO and potentially clog arteries," he noted.[13–16]

This shift in understanding toward a bacterial mediator of a common disease is similar to the transition in thinking about the pathogenesis of peptic ulcer disease. In 1982, Dr. Barry Marshall and Dr. Robin Warren of Perth, Western Australia, discovered the microbe *Helicobacter pylori* in the stomachs of patients with gastritis and stomach ulcers, and they demonstrated conclusively that these bacteria caused these diseases. They were ridiculed at the time, because the conventional thinking was that no bacterium could live in the human stomach, which produces acid similar in strength to that in a car battery. The textbooks were rewritten however, and Marshall and Warren were awarded the Nobel Prize in Physiology or Medicine in 2005.

Today, gastritis and peptic ulcer disease are treated with antibiotics in order to eradicate *H. pylori*, and researchers are attempting to produce vaccines against the bacterium. Such a vaccine would be a windfall for a pharmaceutical company, because at least half the world's population is infected with this bacterium, making it the most common infection in the world.[17]

Will we see an antibiotic approach in eaters of red meat? Will the new findings cause a shift toward vegetarianism? An indication of what may follow can perhaps be found in Dr. Hazen's decisions. Before his team's discoveries, he used to eat red meat several times a week, around 12 ounces at a time. Now he has cut back to eating it twice a month, in 4- to 6-ounce portions. "I am not a vegan," he says. "I like a good steak."[18]

SHARED, RENTED, OCCUPIED

Human and bacterial genomes started shaking hands eons ago. Among the scientists who saw the big picture was physician Lewis Thomas (1913–1993). Thomas was director of research at Memorial Sloan–Kettering Cancer Center for many years. In a collection of dazzling essays published in the early 1970s in the *New England Journal of Medicine*, he wrote, "The new, hard problem [of biological science] will be to cope with the dawning, intensifying realization of just how interlocked we are. The old, clung-to notions most of us have held about our special lordship are being deeply undermined…. We are shared, rented, occupied."[19]

Thomas believed we owe much of our intracellular machinery to "primitive bacteria that swam into ancestral precursors of our eukaryotic cells and stayed there." Thomas singled out intracellular structures, such as mitochondria, centrioles, and basal bodies, and "probably a good many other more obscure tiny beings…, each with its own special genome," as contributions from bacteria that have become necessary for human life. "Without them, we would not move a muscle, drum a finger, think a thought." There has been so much cross-linking of microbial DNA with our own, says Thomas, that by now "our genomes are catalogues of instructions from all kinds of sources in nature, filed for all kinds of contingencies."

There is an existential side to all this mixing. "As for me," Thomas said, "I am grateful for differentiation and speciation, but I cannot feel as separate an entity as I did a few years ago, before I was told these things; nor, I should think, can anyone else."

Writing four decades before the Human Genome and Human Microbiome projects existed, Thomas did not realize the extent to which we humans are colonized by bacteria. How he would have marveled had he known that 90% of the cells in his body were microbial.

ENDOSYMBIOSIS

A major figure in advancing this area of science was Lynn Margulis (1938–2011), a biologist at the University of Amherst, where she developed her "endosymbiotic theory." Margulis showed how certain organelles, such as those specified by Thomas, came to occupy human cells. She demonstrated with actual photographic evidence how a primitive, prokaryotic organism could engulf another, with both entities surviving, a sequence that presumably was common millions of years ago.

I attended a lecture in the 1980s at the Isthmus Institute in Dallas, TX, in which Margulis showed actual film footage of one microorganism eating another, with the eaten organism suddenly popping up inside the eater, apparently unchanged and flourishing, merrily going about its quivering business. I was astonished, along with everyone else in the audience. I suspect Thomas had seen these famous film sequences at some point, and that they influenced the opinions he expressed in his essays.

At the age of 19 years, Margulis married astronomer Carl Sagan, who would become well known for his 1980 *Cosmos* public television series and his advocacy for SETI, the search for extraterrestrial intelligence. Their marriage lasted for eight years. Their careers were a striking symmetry—Margulis probing the microscopic, invisible world of microorganisms for the origins of life, while Sagan looked to stars and galaxies for signs of life and intelligence.

THEY CAME FROM OUTER SPACE

We are "rented" in another way. The most basic occupants of our bodies—the atoms—are continually breaking their rental agreements and moving on.[20] Radio-isotopic techniques allow us to trace the chemicals that enter and leave our body. Roughly 98% of the 10^{28} atoms of the human body are replaced annually. Some tissue, such as bone, is especially dynamic. Each body structure has its own rate of dissolution and reformation: the lining of the stomach renews itself in a week; the skin is entirely replaced in a month; and the liver is regenerated in six weeks. Some tissue is relatively resistant to the

constant turnover, such as collagen, and the iron in the blood's hemoglobin molecules. But after five years the entire body is renewed, down to the very last atom.

This means that five years ago our current body literally did not exist. And if we survive for five years from today, we will have a completely new body.

Many of our replacement parts do not originate on Earth. For example, the phosphorous in our bones and the iron in our blood were formed at an early stage in the evolution of our galaxy. Like many heavy elements in Earth's crust, they were cycled through the lifetime of several exploding stars, eventually finding their way to Earth and our body.

If we live to be 80, we will have had 16 different bodies. Maybe those individuals with Cotard's syndrome are onto something. Could they be extraordinarily sensitive to their vanishing body, while the rest of us are fixated on a stable, unchanging physical form that does not reflect reality?

WHITHER?

We now know we are a biological crazy quilt, a tangled web of building blocks that spans a mind-boggling spectrum, from humble bacteria to star stuff. Our self-image is in serious need of an overhaul that broadens what we mean by "the web of life." The new image would be a kind of ontological spandex, stretching and enlarging our sense of connectedness with other life forms, some of which constitute our physical bodies and help make life possible. Connecting with these creatures and processes would not debase us, as some fear, but could contribute to a more intense sense of belongingness and unity with the natural world. As Thomas said with ambiguous excitement on learning of these things, "I cannot feel as separate as I did a few years ago."

In his inspiring book *Wayfinders*, anthropologist and ethnobotanist Wade Davis describes how we have been whipsawed between the extremes of individuality and unity. He writes, "During the Renaissance and well into the Enlightenment, in our quest for personal freedom, we in the European tradition liberated the human mind from the tyranny of absolute faith, even as we freed the individual from the collective, which was the sociological equivalent of splitting the atom…." [21] The result, Davis shows, has been a forgetting of our interdependence and interlocked unity with the natural world in favor of glorification of the solitary individual who can secede from the natural world without penalty—the supremacy of "special lordship" to which Thomas refers.

But today, we are in a position to put back together what we tore apart. We can now observe and measure what was once considered mythological—that we are literally made up of those tiny beasties and animalcules that our ancestors fantasized, and that we have stardust in our blood and bones. What the shamans and poets intuited is no longer metaphor, but demonstrable fact.

JETTISONING THE SILVER

Our expanding view of our body and its place in the web of life is not simply an esoteric advance in cell biology, but an issue whose appreciation may influence our survival. Our beliefs can either help preserve or destroy us by shaping our belongingness and fittingness in the world. This is not idle philosophy. History provides endless examples of people who misconstrued how they fit into natural patterns, with tragic consequences, as geographer Jared Diamond shows in his chilling book *Collapse: How Societies Choose to Fail or Succeed*.[22]

A telling example at the group level is that of Sir John Franklin (1786–1847), described by anthropologists Owen Beattie and John Geiger in their riveting book *Frozen in Time: The Fate of the Franklin Expedition*.[23] Franklin was one of the most famous British admirals of his day. In 1845, he was sent by the British government to complete the charting of the Northwest Passage through the Arctic latitudes. Franklin's two sailing ships contained 25 officers and 110 crewmen. But in September 1846, both ships became trapped in the winter ice off King William Island. Franklin died a few months later. Both ships were eventually crushed, and they sank.

When the expedition did not return to England, several rescue missions were launched. In 1854, Inuit hunters told a Scottish explorer on the scene what they had witnessed. Franklin's men had abandoned the icebound ships and tried to reach safety on foot. The Inuit found them frozen to death at Starvation Cove on the Adelaide peninsula, stiff in their leather traces. The natives reported that some of the starving men had resorted to cannibalism. As evidence, the Inuit gave the explorer items they had scavenged from the site, which made their way back to England.

Unlike the Inuit, who used light sleds that could be easily pulled by men or dogs, Franklin's men had tried to man-haul a 650-lb sled made of iron and oak. On top of it, they tied an 800-lb lifeboat loaded with all the personal effects that British military officers of the day considered indispensible in the field. When this lifeboat was subsequently discovered by explorers in 1858, it was loaded with an astonishing variety of articles, "a mere accumulation of dead weight, of little use, and very likely to break down the strength of the sledge-crews."[24] The articles included silver dinner plates, monogrammed silver forks and spoons, silk handkerchiefs, curtain rods, scented soap, sponges, slippers, toothbrushes, and combs. There were also six books, including the novel *The Vicar of Wakefield*, which the officers had taken from the 1000-book library of the icebound ships. These weakened men planned to drag this mountain of gear across the immense polar wastes and the boreal forests of northern Canada, hoping to encounter another coastal ship or an outpost of the Hudson's Bay Company. None of them survived. They perished, it was later determined, from hypothermia, starvation, tuberculosis, scurvy, and lead poisoning from eating badly tinned canned foods.[25,24]

Franklin's men sadly misunderstood how to fit into their environment. They may not have survived no matter what they did, but their chances for survival would have been greater if they had discarded the worthless tonnage and befriended the native Inuit, who might have fed them. Because of who they were and what they believed, they found both options impossible. They considered the Inuit as beneath them. Charles Dickens, who followed reports of these events closely in London, defended the

men by insulting the Inuit. In 1854, he described the natives as "covetous, treacherous and cruel…a gross handful of uncivilized people, with a domesticity of blood and blubber." The flower of the trained English Navy, Dickens crowed, needed no help from primitive Eskimos.[26] This was effervescent Victorian snobbery at its zenith.

Perhaps the crew's minds were muddled because of malnutrition and grave circumstances, but they believed they could bludgeon their way past the obstacles they confronted. Their failure to befriend the Inuit was a dreadful miscalculation, and their decision to haul unnecessary, weighty items, such as silver plate and monogrammed cutlery, can only be considered suicidal. This was not a singular incident, but the British way at the time. Robert Falcon Scott, another heroic British naval officer and polar explorer, reached the South Pole in 1912, only to find that the Norwegian Roald Amundsen had preceded him. Scott's fatal journey was marked by similar manly exertions that exhausted Franklin's crew, resulting in the death of himself and his four comrades.

Like Franklin's crew, we are burdened with flawed ideas of how to fit in. We have attempted to secede from the natural order in ways too numerous to name. We are largely oblivious to the problems we have created in our planet's life-support systems, which we perpetuate through denial that is every bit as outrageous as anything Franklin's crew believed. Our misbehavior is far more serious. Fewer than two hundred lives were at stake in their situation; we are flirting with seven billion lives.

There must have come a point when those unfortunate Englishmen realized that their pride would not save them and that they would never see England again. Will we too reach a point when we realize we should have viewed things differently? That we should have jettisoned the silver plate? Made friends with the natives? Lightened our load? Reevaluated our "special lordship," as Thomas characterized our misperceived place in the world?

BEYOND THE YUCK FACTOR

I recently discussed in broad strokes the concept of the human microbiome with a friend of mine. He was repulsed at the thought that he was "infested" with bacteria and viruses. He bridled when I said that numerically the genetic contribution of microbes to his body dwarfed the strictly human genome. I suggested that, since none of us would be alive without them, we might be grateful to the bugs. No sale. Gathering himself for a final retort, he sniffed, "I am not a bacterium!" I felt that if he would have had a prescription for a potent antibiotic, he would have taken a double dose to cleanse himself. It was Franklin's men all over again.

Some humans got it right in the past. Among them was the Greek philosopher Democritus (460–370 BC). Democritus liked small things; he was among the first westerners to champion the idea of atoms. He considered it disrespectful to look down on diminutive members of the animal world. Instead, he said, we should honor them for their teachings —"the spider for weaving and mending; the swallow for architecture; the swan and the nightingale for singing."[27] Today, this practice of looking to nature for principles of design and innovation is becoming increasingly valued and is known as "biomimicry."[28] Had Democritus known about microbes, he would probably have stood up for them too.

THE OTHER? WHAT OTHER?

Mistrust of nature is not an attitude we can afford. Unless we learn to embrace the natural world that sustains us, we are guaranteed a dismal future. The insights that are flowing from the Human Microbiome Project and our understanding of human origins—that we are a fusion of the microbial and the galactic—is a template on which we can claw our way back to a sense of connectedness with all of life, on which our future increasingly depends.

Historian Robert Nadeau and physicist Menas Kafatos, of George Mason University, in their book *The Non-Local Universe: The New Physics and Matters of the Mind*, maintain that "a profound sense of identification with the other that operates at the deepest levels of our emotional lives" is necessary if we are to deal with the ecological challenges we face.[29] "Other" comes from an Indo-European root meaning "different." An important step in identifying with the other is to make peace with that part of ourselves that many reflexively consider to be different, repulsive, and non-human—our indispensable human microbiome.

There are many paths to this understanding. Lewis Thomas, as we have seen, saw through the error of separateness through a confrontation with the facts of cellular biology. But most people do not need scientific laboratories to reach the same place. For them, sunsets, music, and a child's laughter work quite well.

I am fascinated by people who champion both intellectual and non-rational approaches to unity. An outstanding example is Wolfgang Pauli, who won the Nobel Prize in Physics in 1945. Pauli came to this place through the lessons of quantum physics marinated in what he called "the mystical." He said, "Contrary to the strict division of the activity of the human spirit into separate departments—a division prevailing since the nineteenth century—I consider the ambition of overcoming opposites, including also a synthesis embracing both rational understanding and the mystical experience of unity, to be the mythos, spoken and unspoken, of our present day and age."[30]

"Microbial" comes from Greek words meaning "small life." Our microbiome may be small life, but it makes possible large life, human life.

Life, not size, is what matters most.

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