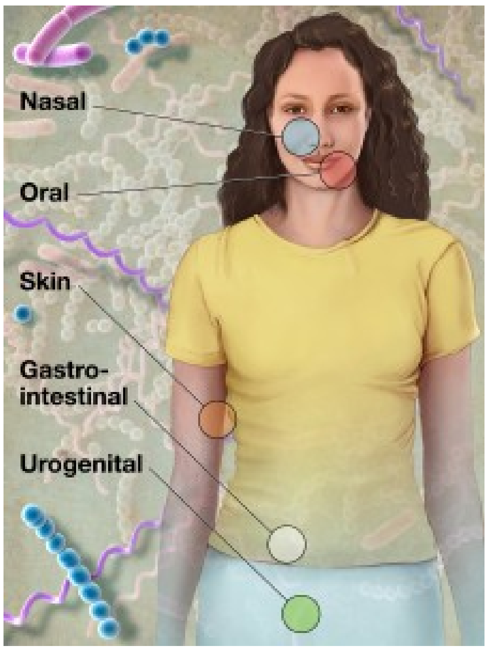
Medical Xpress

Why count stools in the human microbiome?

January 18 2016, by Ricki Lewis, Phd



Credit: NHGRI

Last week, a not-yet-accepted-for-publication paper challenged the long-held view that bacterial cells outnumber human cells in a body 10 to 1. As "rewriting the textbooks" fueled media attention, I took a look, because I actually write – and rewrite – human anatomy and physiology and human genetics textbooks.

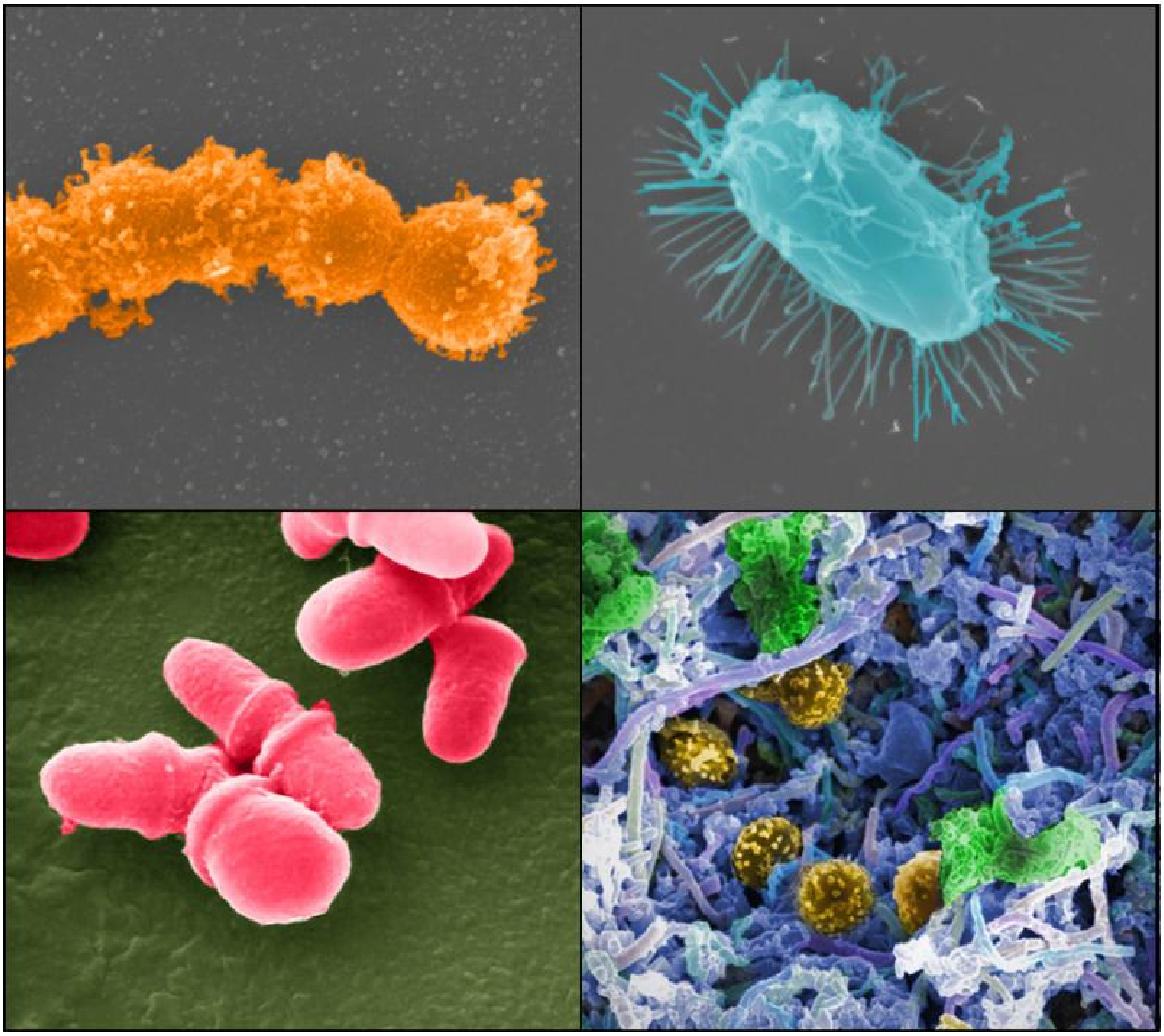
I had low expectations for the report, "Revised estimates for the number of human and bacteria (sic) cells in the body." But I was pleasantly surprised with the mental exercise the paper provoked, because I'd doubted the 10:1 ratio too, even though I cite it in my books.

Ron Sender and Ron Milo from the Weizmann Institute of Science and Shai Fuchs from Weizmann and the Hospital for Sick Children in Toronto methodically and mathematically revised downwards the mantra of 10 bacterial cells for every human cell, to something closer to equality. The last sentence of the abstract is the most tantalizing teaser ending to a scientific paper since Watson and Crick hinted at the mechanism of DNA replication in their famous 1953 paper. Wrote Sender, Fuchs, and Milo: "Indeed, the numbers are similar enough that each defecation event may flip the ratio to favor human cells over bacteria."

But that's the end of the story, no pun intended.

Anatomy of a bowel movement

Biology instructors teach that the contents of the alimentary canal are not actually part of the body. So why do fecal bacteria dominate descriptions of the human microbiome?



Clockwise from top left: Streptococcus [Tom Schmidt], microbial biofilm of mixed species [A. Earl, Broad Institute/MIT], Bacillus [Tom Schmidt], Malassezia lopophilis [J.H. Carr, CDC]; NHGRI

A BM forms as the organs of the digestive tract chop and mix food into chyme, then absorb the nutrients. What's left accumulates in the large intestine (colon) and consists of about 75% water, plus undigested matter, mucus, electrolytes, intestinal lining cells, bile pigments, and a huge community of thriving bacteria.

In 1920 John Harvey Kellogg, MD, of Battle Creek, Michigan, captured the gastrointestinal journey in his "Itinerary of a Breakfast" graphic, part of which opens this post. An expert in enemas, Dr. Kellogg, with his brother Will, invented cornflakes.

The species that dwell in our colons, including Bifidobacteria, Faecalibacteria, and Bacteroides, were once and are still known as "intestinal flora," but over the past few decades they've been subsumed under the buzzword "microbiome." The time of origin of the term is under some debate; this article refers to 1988. And the advent of metagenomics has certainly broadened the scope. But the first peek into the human microbiome was actually in 1676, when Antonie van Leeuwenhoek described the curious "animalcules" in his mouth.

Rebranding our intestinal flora as the colon microbiome opened up economic niches. Grants could be granted, companies formed ("Explore your microbiome; get sequenced"), articles assigned to journalists trumpeting science news that perhaps wasn't, and the makers of probiotics well, probably doing something in their pants with joy, equalizing that ratio.

Recalculating

Sender, Fuchs, and Milo convincingly argue that the bacterial/human (B/H) cell number ratio is more like 39 trillion/30 trillion, based on a "Reference Man" who is between 20 and 30 years old, weighs about 154 and is 5 feet 6 inches tall. Caveats lump females with males and the old with the young because the variability among them is less than that of microbiomes among individuals.

The absolute numbers of both bacterial and human cells is lower than previously thought. The authors trace the 10:1 mantra back through the literature to an ancestral lone "back-of-the-envelope" estimate published in 1972 from one Sir Samurai T. D. Luckey, PhD. Dr. Luckey was apparently a very interesting and influential man, according to this autobiographical piece in Dose Response: An International Journal that opens with the fact that his mother nearly died giving birth to him.

The new paper begins with past estimates, touching briefly on the methodology for conducting a bacterial census in the colon—"direct microscopic clump counts from diluted samples"—which I imagine might resemble weak iced coffee. "The bacterial content of the colon exceeds all other organs by at least two orders of magnitude," point out the authors, with 100 trillion cells, compared to a mere trillion bacteria in dental plaque and 100 billion each in saliva, skin, and the small intestine.

Colon bacteria are not us

Clearly most of the human microbiome is in the colon, the jettisoning with each "defecation event" notwithstanding. But why are we counting these temporary residents of the colon at all? Isn't that skewing the census based on excrement? Since when is a turd an organ?

The contents of the alimentary canal – mouth, esophagus, stomach, intestines – are IN our bodies, but not technically PART of our bodies. As one of my co-authors eloquently told his students in describing the digestive tract, "Contents of the tunnel are not part of the mountain." The colon microbiota are transients, compared to say bacteria under the foreskin (which I wrote about here) or tucked around a hair follicle.

Red cells rule

More interesting than the widely-reported B/H ratio to me were the human cell type counts. Sender, Fuchs, and Milo discovered that red blood cells and platelets comprise 90% of our cells – some earlier studies omitted these cells because they lack nuclei.

A wonderful graphic shows a field of colored sectors. Red encompasses 84% of the image, the red blood cells. Platelets are 4.9%. Muscle cells take up 0.001% and the dreaded fat cells 0.2%. Put another way, fat cells and muscle cells make up 75% of total cell mass, but together account for about 0.1% of total cell number. Red cells predominate because they are tiny, about a hundredth of the volume of a fat or muscle cell, and short-lived, shipped to the spleen for dismantling after a mere 3 months. Muscle and fat cells, as we know all too well, persist although they may shrink, with disuse or exercise, respectively.

Sender, Fuchs, and Milo re-examined and updated data used to estimate human cell counts, lowering the numbers. And this is where the brilliance of their paper lies.

Consider:

- The ratio of glia to neurons isn't 10:1, but 1:1.
- Evaluating all blood vessels, not just capillaries, drops the number of lining (endothelial) cells from 2.5 trillion to 600 billion.
- Analysis of the skin considers dermal thickness, not just surface area. This reduces the number of dermal fibroblasts 100-fold, accounting for only 0.05% of human cells.

Omitting the red blood cell and platelet contributions gives a human cell count of a mere 900 billion. What would it mean if we recalculate the B/H ratio to exclude these cells coursing briefly through our vasculature as well as the bacteria exiting in our feces? I have no idea. Perhaps a mathematically inclined reader will elaborate. But I don't think the 10:1 or even 1:1 are very meaningful, or useful.

Why are we even counting and cataloging the bacteria in and on us anyway? I realize microbiomes are being tracked and associated with diseases and responses to treatment. But the number of variables, the difficulty of separating cause and effect, and the populations of bacterial species that can wax or wane with a giant meal or ensuing dump, seem overwhelmingly complex.

The bigger picture of the downgrading of the bacteria within us from 10:1 to 1:1? Maybe we need to challenge and re-evaluate accepted figures more often than every 40 years—or even the 3 years between textbook revisions.

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