

Are you okay? You smell like cytokines.

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Nurses and hospice workers say they can smell the final approach of death. Not with sudden death, but with the slow march toward the grave, the body's systems begin to shut down and metabolism changes, so that breath and skin and fluids give off a distinctive odor that signals the end is near.

This is not surprising. In fact it's more perplexing that deadly diseases don't announce their presence earlier. From an evolutionary perspective, it would be more advantageous if we could all detect early warning signals, olfactory cues that the immune system is gearing up to ward off a new and threatening disease. Psychological scientists call this the behavioral immune response. The idea is that the healthy would have a better chance of surviving an epidemic if they could identify its first victims—while they are still looking well—and steer clear. Unfortunately, those early churnings of the immune system are far too subtle to detect.

Or maybe not. Scientists at Sweden's Karolinska Institutet, working with colleagues at the Monell Chemical Senses Center, are reporting the first evidence that disease not only smells but can be detected in chemical cues of the body's frontline immune response. The team, led by Mats Olsson, wanted to test the idea that humans can perceive a difference between the body odors of healthy and sick people—even when they don't appear any different. Assuming that such a sickness cue has evolved to lessen contamination risk, they wanted to see if they could detect such a cue in the early stages of the body's sickness response. Here's how they ran the test.

They recruited healthy volunteers for two experimental sessions in the hospital lab. On one occasion, they injected the volunteers with a toxin known as lipopolysaccharide, or LPS. LPS is a bacterial toxin known to elicit a strong immune response in humans. On another occasion, they injected the same volunteers with a saline solution. The volunteers wore tight t-shirts to absorb their sweat, which the scientists sampled four hours following the injections. The scientists confirmed an inflammatory response in those injected with LPS: Their temperatures rose and blood samples showed clear rise in cytokines, known to mediate the body's immune response.

Other volunteers then smelled the sweat samples, and rated them for intensity, pleasantness and health. Here's what they found, and report in a forthcoming article in the journal *Psychological Science*:

The body odors of those injected with LPS, who had mounted an early immune response, smelled much more intense and much more unpleasant. Their odors also smelled less healthy, though that effect was much less powerful. These findings suggest that humans can indeed tell the difference between the smells of sick and healthy people. Importantly, this test was just four hours after the immune activation—way too early to detect any overt signs of sickness.

It could be that the sick body is simply emitting more of the same volatile and odorous chemicals as the healthy body. Or it could be that the sick body is emitting unique and aversive odors—cues that announce

sickness and trigger a behavioral response. The scientists find this interpretation more intriguing, and found preliminary evidence to support it. They also found that the smell of disease was mediated by the volunteers' actual immune activation, as indicated by their cytokine levels. Taken together, these findings strongly suggest that humans send out an olfactory cue when they just start to get sick, a cue that can be used by others to stay healthy.

The scientists want to look at the role that disgust plays in the behavioral immune response. It's been suggested that this emotion evolved as a disease avoidance mechanism, which would be consistent with this evidence of aversive odors. Avoidance of the sick—especially soon after infection—would be a highly effective strategy in containing an epidemic.

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