## Royal Jelly Isn't What Makes a Queen Bee a Queen Bee



For decades, scientists thought an excess of something special, a substance called royal jelly, elevated a regular honey bee larva to a queen. New research suggests we had it backward: It's what future queens *aren't* fed that matters.

Royal jelly, which also is called "bee milk," looks like white snot. More than half of it is water, the rest is a combination of proteins and sugars. Special glands in the heads of worker bees secrete the stuff, which gets fed to babies.

A developing queen bee is fed royal jelly exclusively—not pollen and honey like her proletarian sisters. Some describe withholding royal jelly from worker bees as nutritional castration. These bees don't get the special Food of the Gods. Or, perhaps, food of genetic monarchies. And so, we thought, their ovaries shrivel, and they don't become a queen.

It turns out, it's the other way around. *Not* feeding an immature queen pollen and honey is what makes her royal, not her exclusive access to royal jelly.

## **Queens and Genes**

Radically different looking animals can be created from identical genetic material; a worker bee and a queen bee differ only in which genes are activated. Genes make proteins, which build the rest of our bodies. By manipulating the environment of their offspring, honey bees genetically alter their bodies via nutrition.

We've known for a while that bees' diet is involved in building different kinds of bee bodies. Science is still figuring out just how that happens. Queen larvae are surrounded by royal jelly; they float on a sea of sugary bee gland snot in enlarged cells. Worker bees eat beebread (a type of fermented pollen) and honey. Nurse bees mash this into a "worker jelly" and add glandular secretions as a garnish. Workers don't get the special stuff in queen jelly, and their ovaries shrivel.

That's the conventional explanation. But Dr. May Berenbaum, a professor at University of Illinois and an author of the new research, says there isn't a simple answer to the question *What do bee babies eat?* 

"We had the hardest time figuring out what larvae eat," she says. "Among other things, worker jelly and royal jelly appear to have, and there is no consensus, a slightly different ratio of mandibular to hypopharyngeal gland secretion ... It all happens in the dark surrounded by 50,000 stingers. So it isn't the easiest insect in the world to work on."

Beebread and honey are derived from plant materials, and like many plant materials, they contain a variety of phenolic chemicals. We eat them all the time; flavonoids are the plant chemicals that give plants their unique flavors (and help plants discourage plant-eating insects, among other functions).

Royal jelly, however, has no detectable phenolic acids. None. From previous research, the researchers knew that flavonoids increase immune responses of adult worker bees. That's a good thing; it has the side effect of helping bees detoxify pesticides faster. The scientists wondered how developing bees would react to phenolic compounds.

To find out, they fed two groups of bee larvae diets with and without p-coumaric acid, a common type of flavonoid. Then they looked closely at differences in gene activation between the groups. The results were startling, unexpected, and nifty.

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Bees reared on the p-coumaric acid diet had ovaries significantly smaller than those reared without that compound. That's the kicker, because what makes a

queen bee a queen? She's the only bee in the hive laying eggs. Fourteen genes known to be involved in worker-queen differentiation were upregulated, or increased in expression.



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Apis mellifera, Queen Honey Bee. Frank Greenaway/Getty Images

Queen bees also are bigger and live longer than worker bees. In one set of genes known to regulate organ size in animals, p-coumaric acid significantly changed the expression of over half of genes involved in that signaling pathway.

"We never set out to change perceptions on queens and caste determination," says Berenbaum. "I'm interested in detoxification; how insects cope with phytochemicals they consume. Much to our surprise and delight, a whole suite of other genes that were implicated in caste determination changed."

"It was one of those impossible to miss sorts of phenomena. I think ... the idea of royal jelly is so appealing, people haven't really questioned it."

## The Silencing of the Genes

With over four centuries of living with bees, why are humans still learning so much about them? To answer that question, I reached out to Dr. Ryszard Maleszka at Australian National University. Maleszka,

who is not an author of the new research, works specifically on honey bee epigenetics.

Epigenetics is the study of how environments affect gene expression. "With our current knowledge we only scratch the surface of biological systems, and honey bee biology is no exception," Maleszka says. "We are dealing with 500 million years of animal evolution so there is much to discover."

"[This research] is a wonderful example of an evolutionary invention whereby common plant chemicals have been recruited to be crucial elements of gene regulation ... By using environmental ingredients honey bees found a clever solution to a challenging problem: How to generate two contrasting organisms, long-lived reproductive queens and short-lived functionally sterile workers, using the same genetic hardware."

Lots of factors go into making a queen beyond the plant chemicals examined in the new research: A compound with the wonderful name of royalactin, for example, has been proposed as critical to queen development. Maleszka has delivered a stinging rebuke to the idea that a single compound in royal jelly is the "switch" that makes a queen, though. In 2008, his lab was able to create queen bees without any royal jelly consumption, by turning off (silencing) a set of genes. Other bee researchers have questioned the "one molecule to rule them all" idea of queen development. The reality is likely that, like everything else in biology, it's complex and many factors are involved.

The real power of this new research may be in explaining why worker bees don't become queens. Instead of chemical castration by denying workers royal jelly, this elaborate feeding process provides chemical protection for the queen's ovaries. She is sheltered from the potential toxic or metabolic effects of plant chemicals. As we continue to improve our techniques, hopefully we will come closer to a firm answer about just what honey bees eat in their hives, and why.

## Postscript: Um, Why Are Humans Eating Royal Jelly?

When we thought royal jelly was magic queen stuff, stealing and eating phlegm produced in insect heads made a kind of warped sense. Royal jelly proponents claim the stuff cures all sorts of human problems, infertility in particular. By deduction, the stuff that makes queen bees baby machines, laying up to 2,000 eggs a day, should increase human fertility. I am compelled to say this is not how scientists deduce cause and effect.

Royal jelly also is sold as an aphrodisiac, and like most erotic insect products, it's applied with "vigorous rubbing." That makes it hard to say just how firm evidence for this erectile remedy really is. Also, actual honey bee reproduction involves penis detachment and death, which doesn't sound like a good time to *me*, if we are sticking with that whole "what works for a bee will work for humans" analogy.

Royal jelly does have antibacterial and antifungal properties, since it's the gunk developing bees float in

until they metamorphose. It's marketed in many cosmetics as an anti-aging ingredient; queen bees live 40 times longer than worker bees. So far, there isn't much evidence of royal jelly having medical significance in humans. It's probably a good moisturizer, though. Especially if you don't think about where it comes from.

My best guess is that about 600 tons of royal jelly is produced and sold yearly; East Asia is the main producer. Prices vary widely, but based on a trip to my local health food store, seems to run about \$1 per gram. The market value of royal jelly is based on what we thought we knew about its magical properties; that doesn't seem likely to change in the foreseeable future.

But now you can have a lot of fun telling people where their royal bee goobers came from.

Wenfu Mao, Mary A. Schuler, and May R. Berenbaum. 2015. A dietary phytochemical alters caste-associated gene expression in honey bees. Science Advances 1(7).

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