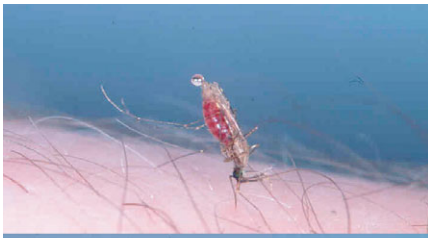
Inside JEB is a twice monthly feature, which highlights the key developments in the *Journal of Experimental Biology*. Written by science journalists, the short reports give the inside view of the science in JEB.

Inside JEB

MOSQUITOES' DRINKING PROBLEM



Pictures by Jon Wilson, Birkbeck photographic unit

During steamy summers, itchy bites remind us that female mosquitoes are remarkably adept at tracking us down. To add insult to injury, mosquitoes urinate on us while they greedily gorge on our blood. As Geoff Coast explains, feeding mosquitoes swell up to twice their size, and to make sure that they can still take off after their feast, the insects urgently need to pump out all the unwanted water and salts from their blood meal. In the 1980s, Klaus Beyenbach and his colleagues reported that mosquitoes solve this problem by flushing out copious amounts of sodium-rich urine. They found that the insects release a peptide that triggers sodium-rich urine production, and they dubbed this hormone mosquito natriuretic peptide, or MNP. For years, MNP's chemical identity remained elusive. Now, Coast and his colleagues reveal that MNP is a calcitonin-like diuretic hormone (p. 3281).

Coast explains that MNP acts on mosquitoes' Malpighian tubules, the insect equivalent of a kidney. When MNP binds to its unique receptor on the membranes of the Malpighian tubules' principal cells, it triggers the production of cyclic AMP, an intracellular messenger that causes sodium channels in the cell membrane to open, flushing sodium out of the insect's body. 'There were two likely candidates for MNP's chemical identity', Coast says; MNP was either a corticotropin releasing factor (CRF)-related peptide or a calcitonin (CT)-like peptide, because both are recognised diuretic hormones in fruit flies, and both produce cyclic AMP as their messenger.

First, Coast and his colleagues confirmed that mosquitoes are able to produce these two peptides. David Schooley scoured the genome of the malaria mosquito (*Anopheles gambiae*) for sequences that match the known fruit fly sequences for the CRF-related and CT-like peptides. Sure enough, he found the two candidate peptides in the mosquito genome, synthesised them and sent them off to Coast.

The team was now ready to test the effect of the two peptides on mosquitoes' Malpighian tubules. They carefully dissected out insects' tubules and moved them to a microscopic droplet of bathing fluid held under liquid paraffin, where the tubules continued to exude urine. Would either of the two candidate peptides have a diuretic effect, just as MNP does? Disappointingly, when the team added the CRF-related peptide to the bathing fluid, the tubules' secretion rates only increased a little. But when they added the CT-like peptide, the secretion rates shot up 10-fold, exactly as you would expect from a diuretic hormone. So far, the CT-like peptide was the most likely suspect in the search for MNP's identity.

But the defining feature of MNP is that it helps mosquitoes pump out sodium ions, so the real test was still to come; the team needed to show that the CT-like peptide also triggers increased sodium ion transport. Sure enough, when the team bathed mosquito tubules in the CT-like peptide and examined ion concentrations in the tubules' secretions, they saw a dramatic increase in sodium ion transport. But they didn't see a change in sodium ion transport when they bathed tubules in the CRF-related peptide. Clearly, only the CT-like peptide acts as a sodium-expelling hormone. As a finishing touch, the team showed that the CT-like peptide, but not the CRF-related peptide, mimics the effects of MNP on tubule electrophysiology. The CT-like peptide had passed all the tests with flying colours; the team concluded that MNP is a CT-like peptide. Now they just need to show that mosquitoes actually release the CT-like peptide into their bloodstream when they feed, which is easier said than done when you're working on such diminutive creatures!

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Coast, G. M., Garside, C. S., Webster, S. G., Schegg, K. M. and Schooley, D. A. (2005). Mosquito natriuretic peptide identified as a calcitonin-like diuretic hormone in *Anopheles gambiae* (Giles). *J. Exp. Biol.* **208**, 3281-3291.