## Sex ratios: Bad times wallop extra sons

Nearly 30 years of deer-watching on a Scottish island have revealed a quirk of male-female sex ratios. It may explain why a famous biological hypothesis has been maddeningly hard to prove.

The Trivers-Willard hypothesis, named for the scientists who devised it in 1973, predicts that to maximize their chances for heirs, the flossiest, fittest females in some species give birth to more sons than daughters. Struggling, underfed moms should bear extra females.

In decades of searching for this effect, "there have been a lot of contradictory results," says Loeske E.B. Kruuk at the University of Edinburgh. In the June 3 NATURE, she and her colleagues report that the Trivers-Willard effect once seen among red deer on the Isle of Rum disappeared in one area where culling stopped and the population tripled. Crowding and harsh weather, argue the scientists, killed more male than female fetuses, canceling the predicted effect—that top moms would conceive extra sons.

The mechanism could be simple. Perhaps demands of the bigger, faster-growing male fetuses are more likely to overwhelm the resources of an already overstressed mom than the smaller demands of a female fetus are. Kruuk speculates.

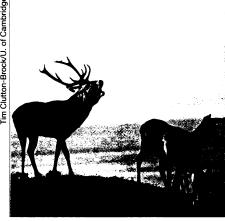
Whatever the cause, this male vulnerability could be confounding studies of the Trivers-Willard hypothesis, Kruuk suggests. The only documentation for its effects come from populations not stressed by overcrowding, she points out.

The Trivers-Willard hypothesis applies to species in which a mother's condition affects her sons' breeding success more than her daughters'. Among red deer, for example, a female in glowing health tends to bear robust sons that grow into big males defending large harems. These sons reproduce more prolifically than daughters, who bear one calf a season, even when in the best of health.

If a weak female produces a runty son, he may not mate at all because the big guys monopolize the females. For fit moms, sons offer a bonus. For frailer moms, a daughter is a safer bet.

Just what internal mechanism could skew sex ratios has fueled considerable speculation. Current views suggest that the mother's hormonal state affects whether more male or female zygotes implant in her uterus, Kruuk says.

In the same issue of NATURE, Andrew Cockburn of the Australian National University in Canberra praises the "superb long-term data" from Rum. Fully demonstrating the Trivers-Willard hypothesis in wild animals has been "pretty difficult," he told Science News. He notes that the first success was on Rum, where biolo-



Prime red deer moms on the Isle of Rum bore extra sons—until life got tough.

gist Fiona E. Guinness of the University of Cambridge in England learned to recognize hundreds of deer by sight.

The idea that bad times slam sons more than daughters "has been widely seen as an alternative to the Trivers-Willard hypothesis," Cockburn says. Researchers had mused that the factors emphasized by the two views might work together, but teasing out interactions seemed as daunting as proving the original hypothesis. "That was an area that inspired a bit of hopelessness," he says.

After the latest analysis, Cockburn predicts, "people will see the two hypotheses can be married."

—S. Milius

## Rooting out dormant HIV-infected cells

Current AIDS treatments can kill off virus to nearly undetectable concentrations. Nonetheless, scientists have been unable to wholly eradicate HIV, the virus that causes AIDS, in any patient.

HIV infects immune cells called CD4 T cells. In a CD4 cell that the immune system hasn't called into action, HIV can lie dormant for years, hiding from anti-AIDS drugs while retaining the potential to replicate.

In an effort to drag these hibernating cells out into the open, where medication or healthy immune cells might destroy the virus, scientists have now employed interleukin-2 (IL-2). In some patients, this immune-system protein that activates CD4 cells appears to flush the infected cells from hiding, report researchers led by a group at the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Md.

The scientists gave 26 HIV-infected patients a combination of anti-AIDS drugs; 14 also received IL-2. Because IL-2 can cause nausea, fatigue, and headaches, physicians gave patients their doses of that protein intermittently over a period of 16 to 51 months. Nearly all the patients had previously received some anti-AIDS therapy, and all started the study with

low viral blood concentrations, or counts.

After treatment, the researchers cultured patients' blood cells to increase the number of CD4 cells. No virus turned up in three of the patients treated with IL-2, even though more than 100 million CD4 cells were examined in each, the scientists report in the June NATURE MEDICINE. Although the virus remained detectable in the other IL-2 patients, they had lower viral counts than the 12 participants not getting the protein.

The scientists obtained lymph node tissue samples from two of the people in whom the virus was undetectable. The CD4 cells collected, even after being cultured, also seemed to harbor no virus.

However, when these two patients later went off anti-AIDS medication, the virus showed up again, says coauthor Tae-Wook Chun, a virologist at NIAID. The third patient who had no detectable virus stayed on anti-AIDS medication and still shows no virus.

While encouraged, Chun remains cautious. "Just because you knock the reservoir [of virus] down to a low level, it doesn't mean you have eradicated it," he says. Rather, these findings support evidence that HIV is lurking in other immune cells or in CD4 cells in hard-to-

reach places in the body, Chun says.

The brain, the eye, and the testes all have barriers that keep out many blood-borne immune cells and proteins. Anti-AIDS drugs "don't penetrate those regions very well," says Roger J. Pomerantz, a virologist at Thomas Jefferson University in Philadelphia. Semen can harbor HIV capable of replicating, even as tests show that HIV in the blood has fallen below detectable concentrations in response to anti-AIDS drugs, he says. Such compartmentalization could thwart IL-2, which is carried in the bloodstream.

"We clearly need some approach to purging these [HIV] reservoirs," says Warner C. Greene, a molecular virologist at the University of California, San Francisco. The new study "represents the first promising effort," even though it doesn't indicate how IL-2 might work in people carrying a lot of virus, he says.

"My concern is that, in the future, it may be difficult to find [patients with] such low viral burdens, even on medication," Greene says. He and his colleagues have already begun to observe HIV resistance to drugs in San Francisco patients. In response, viral counts may soar. "I think we're in a window of time, a honeymoon, where the drugs remain quite effective throughout the population." —N. Seppa

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