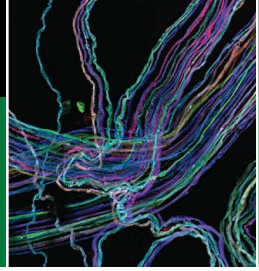

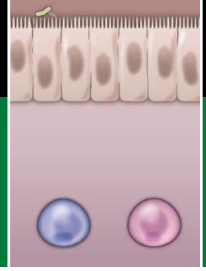

LETTERS

edited by Jennifer Sills

Make a Bid for Bird Biodiversity

ON 7 DECEMBER 2010, THE HAMMER DROPPED AT LONDON AUCTION House Sotheby's auction of James Audubon's *Birds of America*. The final bid: 7,321,250 pounds (US$11.6 million), making this work the most expensive book ever sold (*1*). The book of life-size bird illustrations, painted between 1827 and 1838, is perhaps as rare as some of the birds Audubon himself illustrated—the critically endangered California condor, for example, now consists of fewer than 200 birds in the wild (*2*). This homage to the dwindling avian fauna of the world was predicted to attract the attention of a select group of hedge fund executives, oil billionaires, and retail billionaires, but the final bid was made by a London art dealer.

Pricey pages. James Audubon's *Birds of America* was auctioned off in December for a record-breaking price.

Audubon himself was an avid hunter and taxidermist, shooting his subjects and then wiring them up in life-like poses. Yet the US$11.6 million in proceeds from the sale of his work would surely do a lot for bird conservation. The Royal Society for the Protection of Birds (RSPB), the UK bird conservation charity, is the largest conservation organization in Europe, and its annual expenditure for conservation at RSPB reserves—US$42.8 million in 2010 (*3*)—is just a few times the price of Audubon's book. In other parts of the world where conservation action is more pressing and costs of conservation are lower, one would get a lot more for such a bid (*4*). BirdLife International is "the World's largest partnership of conservation organisations" (*5*), with a total income in 2009 of US$16.7 million, of which $5.2 million was spent on conservation action in 2009.

This is a call to all those billionaires with a penchant for birds: Global biodiversity is dwindling fast, despite global efforts (*6*). Why not make a bid for these birds instead, so future generations might actually see some of them in flight?

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Fighting Liverflukes with Food Safety Education

MORE THAN 45 MILLION PEOPLE IN ASIA ARE infected with liverflukes (trematodes), which cause diseases such as chlonorchiasis and opisthorchiasis (*1*–*3*). *Opisthorchis viverrini*, the parasite that causes opisthorchiasis, is a recognized type one carcinogen that leads to a fatal cancer of the bile duct (*1*). Opisthorchiasis, which affects at least 10 million people in the Thailand and Laos alone (*1*), is not considered one of the major neglected tropical diseases in the Southeast Asia region by the World Health Organization (*4*). Past efforts to control this disease have lacked sufficient funding and institutional backing typically provided to combat well-known maladies such as leprosy, lymphatic filariasis, visceral leishmaniasis, schistosomiasis, and onchocerciasis. Thus, the threat of this condition and the resultant cancer lingers in the region. More important, the threat extends globally through the export of contaminated fish products and through infected tourists and overseas workers residing or visiting regions where intermediate hosts exist (*5*–*7*). Throughout Asia, up to 750 million people are at risk by infection from fish-borne liverflukes (*1*, *3*). Food safety education may be the most expedient way to control the spread of infections because prevalence is inherently linked to human behavior.

Opisthorchiasis persists today largely because raw fish consumption is linked to cultural identity in Southeast Asia. Every day millions of people eat infected fish that have not been cooked properly. The lack of hygienic toilet facilities completes the epidemiological cycle by facilitating the return of *O. viverrini* eggs to waterways, where they are first consumed by *Bithynia* snails and later passed to cyprinid fish species.

Medical interventions have had only limited success in treating *O. viverrini*. Praziquantel, for example, kills the adult worms in the human host, but it does not prevent reinfection (*8*). It may also compromise the immune system or cause liver complications when taken repeatedly after reinfection (*9*, *10*). Rapid land-cover and land-use modifications now taking place in the region, coupled with uncertainties regarding future climate

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change, prevent tackling the problem efficiently at the ecosystem level.

Education has been successful in the past. Between 1981 and 2001, outreach programs that included food safety education in rural communities in northeast Thailand helped reduce *O. viverrini* prevalence from about 35 to 16% (*11*). Unfortunately, outreach was patchy at best, and it lacked the momentum to withstand political administrative changes. Consequently, *O. viverrini* prevalence leveled in the past decade, and continues to remain very high (>80%) in some localized areas.

Similar health education programs are now needed to raise the level of awareness across the region to the dangers of eating improperly cooked fish. Many still believe that the *O. viverrini* parasite can be killed through fermentation, preparation of raw fish with chilies or lime, or consumption with alcohol. In reality, parasites can survive all these strategies, as well as drying, salting, and freezing (*7*, *8*). Some see praziquantel as a panacea, allowing reckless consumption of raw fish. Others simply ignore the health risk—a situation analogous to cigarette smoking.

As with smoking, schoolchildren are an obvious priority. When infected at a young age, the resulting cancer can potentially develop 30 to 40 years later during the prime income earning years (*8*). Given the high prevalence in the region, the projected economic impact is catastrophic. New approaches are also needed to reach the elderly and adult men—two groups that tend to ignore the risks, yet serve as role models for younger generations.

We believe that food and health safety education should be promoted through participatory activities in schools, the lessons of which children will then bring into their homes. The program will thereby have a major influence at the village level. This approach will likely be more effective than relying on national administrative interventions and/or the agendas of international agencies.

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Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the past 3 months or matters of general interest. Letters are not acknowledged upon receipt. Whether published in full or in part, Letters are subject to editing for clarity and space. Letters submitted, published, or posted elsewhere, in print or online, will be disqualified. To submit a Letter, go to www.submit2science.org.

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HIV Prevention in Women: Next Steps

THE RECENTLY PUBLISHED CAPRISA 004 TRIAL of tenofovir 1% gel used intravaginally to prevent HIV was an impressive success ("Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women," Q. Abdool Karim *et al.*, Research Articles, 3 September 2010, p. 1168). The gel, when used once up to 12 hours before and once up to 12 hours after coitus with a maximum of two doses per 24 hours, was 50% effective at preventing HIV infection, based on a follow-up 12 months later. At 2.5 years, the protective effectiveness was lower (39%), likely due to lower adherence over time. Among those who were high (>80%) adherers, based on counting used and unused applicators, the effectiveness estimate was 54% at 2.5 years. No viral resistance in breakthrough infections was seen, a concern in ongoing oral pre-exposure prophylaxis trials such as iPrEX and PEM-PrEP [see the Research Article as well as (*1*, *2*)].

A confirmatory trial is needed to empower licensure approval by regulatory bodies such as the U.S. Food and Drug Administration, the European Medicines Agency, and the South African Medicines Control Council (*3*). Confirming safety is especially important with a prevention method used by healthy women, given that there is a lower threshold for acceptable side effects compared with the use of antiviral products by HIV-infected persons.

CAPRISA 004 was the first Phase 3 trial of a topical antiretroviral product, providing a proof of concept that the right microbicide could prevent HIV acquisition by women (*4*, *5*). Only one other phase 3 trial of tenofovir gel is ongoing: "VOICE" of the NIH-funded Microbicide Trials Network (MTN 003) (*6*, *7*). VOICE compares five arms: oral tenofovir, oral tenofovir combined with emtricitabine (Truvada™), oral placebo, vaginal tenofovir 1% gel, and placebo vaginal gel. Women in the topical microbicide arms are instructed to use the gel every day, a more laborious and costly strategy than CAPRISA 004's coitally dependent use. Daily use has been thought to be more effective than intermittent use, because it provides higher and more consistent topical drug levels. However, we believe that daily use may be less effective in real-world usage than coitally dependent use because of potential nonadherence to a tiresome daily regimen. If nonadherence is "random," drug levels should indeed at least equal the levels obtained in CAPRISA 004; however, levels may be much less to nonexistent if women (or their husbands) tire of the daily gel and stop its use completely. If VOICE indicates a lower efficacy level than did CAPRISA 004, it will not serve to confirm CAPRISA 004 and would paradoxically retard product licensure.

Two groups plan a response to confirm CAPRISA 004 results with placebo-controlled, randomized clinical trials of tenofovir 1% topical gel: the FACTS 001 group in South Africa and the Microbicide Development Programme MDP 302 protocol. FACTS 001 proposes a two-arm trial to replicate the CAPRISA 004 design, albeit with a lower eligibility age (16 years). The study has garnered partial support from the South African government, USAID (original funders of CAPRISA 004), and the CDC for conduct in six South African sites and one Kenyan site. The MDP-302 seeks to assess the same coitally dependent regimen as CAPRISA 004, as well as a third arm to assess the effectiveness of only one dose per sexual act, a cheaper, simpler approach that might increase adherence. The MDP group will recruit a majority of volunteers outside of South Africa.

We believe that the global donor community should respond aggressively to support one or both of these trial concepts of a coitally dependent dosing approach for tenofovir 1% gel. The trial cost of about $40 million is about 0.1% of the NIH budget. We suggest that this low-risk, high-yield trial will represent an historic investment toward a vital new woman-controlled prevention tool in the fight against HIV/AIDS (*8*–*10*).

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Hopes for Merit-Based Grants in China

IN THEIR EDITORIAL "CHINA'S RESEARCH culture" (3 September 2010, p. 1128), Y. Shi and Y. Rao commented on the plight of research in China. The situation is even worse than that described in the Editorial. Hundreds of thousands of grassroots professors and researchers are struggling, lacking sufficient financial support for research. As an ordinary professor, I have never sensed that "[g]overnment research funds in China have been growing at an annual rate of more than 20%," as claimed by the Editorial. The sad fact is that about 30% of full professors and 70% of associate professors in Sichuan University do not have funds for a single research project left in their charge (*1*). In addition, among those professors with projects, the distribution of funding is extremely biased in favor of officials.

I agree with the Editorial that "[a] simple but important start would be to distribute all of the new funds based on merit, without regard to connections." Without such a change, seeking connections to win grants, either big or small, will by necessity continue to be rampant in China.

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CORRECTIONS AND CLARIFICATIONS

Reports: "Rewiring of genetic networks in response to DNA damage" by S. Bandyopadhyay *et al.* (3 December 2010, p. 1385). On page 1389, in the first column, third paragraph, the notation SQ145-146 (representing Ser^{145} and Gln^{146}) and the word "conserved" were incorrect. The sentence should have been "...Cbf1 is hyperphosphorylated at a serine-glutamine motif (SQ45-46)."

Reports: "Broken-symmetry states in doubly gated suspended bilayer graphene" by R. T. Weitz *et al.* (5 November 2010, p. 812). The *x* axis of Fig. 1D should read "Electric field (mV/nm)" instead of "Electric field (V/nm)."

Reports: "A tricyclic aromatic isomer of hexasilabenzene" by K. Abersfelder *et al.* (29 January 2010, p. 564). The last sentence of the first paragraph is inaccurate because there is at least one isomer, fulvene, which according to reference 4 is only 30.9 kcal per mole higher in energy than benzene.