Biomedicine

NIH limits gene experiments done abroad

Nobody will ever know exactly what happened after researchers inoculated 20 cows with an experimental rabies vaccine in Argentina nearly three years ago. According to the Philadelphia-based Wistar Institute, which conducted the trials with the Pan American Health Organization (an arm of the World Health Organization), everything went according to plan. Cows vaccinated with the genetically engineered rabies-virus protein developed antibodies to the deadly virus as intended, and the cows and handlers showed no ill effects.

But the researchers conducted the experiments without first obtaining permission from the Argentine government. And according to Argentine government scientists and others, some workers and unvaccinated cows became infected with the experimental vaccine—though with no apparent ill effects. The Argentine government halted the experiment, destroyed the cows and provided the impetus for a series of meetings of U.S. scientists and policymakers over the issue of performing U.S.-government-funded genetic engineering experiments in foreign countries. At issue was whether scientists receiving funds or materials from the National Institutes of Health (NIH) must follow the same safety and notification guidelines in foreign countries as they must in the United States when performing experiments with recombinant DNA. The trick lay in ensuring that developing nations would not become cheap testing grounds for controversial experiments, without dictating to other countries what they may or may not do in terms of hosting scientific trials that could benefit them directly.

Now, after more than two years of debate triggered by a petition from the Washington, D.C.-based Foundation on Economic Trends, the NIH has revised its guidelines regarding recombinant DNA research in foreign countries. The new guidelines preclude the foreign testing in humans or animals and the deliberate release into the environment of materials containing recombinant DNA developed with NIH funds unless the experiments comply with the host country's rules regarding such experiments. If the host country has not developed such rules – and many have not – the proposed experiments must be reviewed by an NIH-approved board, then accepted by an appropriate national authority in the host country. In any case, the new guidelines say, NIH-associated researchers in foreign countries must use safety practices "reasonably consistent" with NIH guidelines governing similar experiments conducted in the United States.

Alliterative prescriptions pose problems

A letter in the March 30 NEW ENGLAND JOURNAL OF MEDICINE draws attention to a growing problem among medical professionals as they try to keep current on the many new, chemically related but pharmacologically distinct drugs coming onto the market. Pharmacist Robert Ellis and physician Danny J. Lancaster, both of the Regional Medical Center at Memphis (Tenn.), make special note of drugs related to the antibiotic cephalosporin – including cefotaxime, cefoxitin, ceftizoxime, ceftriaxone, cefotetan and ceftazidime.

"So similar are their spellings that they are frequently referred to as 'cephawhatchamacallums' by physicians and pharmacists, and often it is the pharmacy's best guess that determines which drug the patient receives," Ellis and Lancaster write. Among the many misspelled, nonexistent drugs they've seen ordered by physicians in the past two years are ceftatozine, cefoxitane, cefatotoxin, ceftodzine, cefotatime, ceftrioxime and ceftriazone.

"We can offer no simple solution to the problem," they conclude. But "the institution of mandatory cephalosporin spelling bees in medical schools and residency programs" might help, they say.

Chemistry

Fish oil: New hope in fighting malaria

Malaria afflicts an estimated 500 million people worldwide, killing about 2.5 million of them annually. But a highly effective dietary treatment for routing the single-cell parasites that cause malaria may lie on the horizon.

The omega-3 fatty acids in fish oils are extremely susceptible to oxidative breakdown. Antioxidants – like vitamin E – can protect these fatty acids, necessary for building cell membranes. In their new study, chemist Orville A. Levander with the USDA's Agricultural Research Service in Beltsville, Md., and microbiologist Arba L. Ager Jr., at the University of Miami's Center for Tropical Parasitic Diseases, fed mice a diet high in fish oils but containing no vitamin E. Their animals dined on the special diet one to four weeks before being inoculated with a malarial parasite – either *Plasmodium yoelii* or *P. berghei* – and for another 60 days afterward.

"The parasites multiply for a while. But by three or four weeks, the [mice on the special diet] are free of them," Ager says. Levander says he suspects the actual cause of death is a rupturing of the parasite's cell membrane or that of its red-blood-cell hosts. Infected red cells are more prone to rupture, he notes, because the parasites foster a number of the destructive oxidative reactions to which the diet leaves them vulnerable.

The researchers say they were particularly excited about the diet's devastation of *P. berghei*, a strain resistant to chloroquine, the most widely used antimalarial drug. However, they say this dietary therapy may prove even more effective when used in conjunction with oxidizing drugs, such as the Chinese herbal remedy qinghaosu, now being explored as a malaria treatment by the World Health Organization.

It's not fish oil, but . . .

Preliminary research suggests the body can convert vegetable-derived linolenic acid – an omega-3 fatty acid – into the same fatty acids found in marine fish oils. This finding suggests people may reap the fish oils' benefits from natural constituents of soybeans and other, less costly plants, says Edward A. Emken, the Peoria, Ill.-based Agricultural Research Service chemist who directed the study.

Emken fed four healthy men 10.7-ounce milkshakes whose fats had been tagged with nonradioactive deuterium labels. Then he periodically sampled blood from these volunteers over two days and studied changes in its fatty acid profiles. The tests showed that the two men whose shakes contained linolenic acid converted it through a cascade of reactions into a family of new molecules.

EPA and DHA – the primary omega-3 fatty acids in fish oils – were the main end-products. This transformation, "undoubtedly occurring in the liver," required lengthening linolenic's 18-carbon chain by two or four carbons and adding two or three more double bonds, Emken says.

Although the transformation has been documented in rodents, many researchers suspected the conversion by humans was negligible, largely because tissues sampled from people consuming linolenic-rich diets showed no excess EPA or DHA. Emken's new data offer an alternative explanation for this observation: Humans use newly formed EPA and DHA primarily to replace those same fatty acids already in their tissues, not as a substitute for other fatty acids. In fact, Emken's data show that the turnover of omega-3 fatty acids in human tissue occurs at a rate many times faster than that of the omega-6 fatty acids more typical of vegetable fats.

Emken is now exploring how the presence of other fats affects the linolenic-acid conversion. His provocative findings hint that increasing saturated-fat consumption actually enhances the activity of linolenic-transforming liver enzymes.