Nutrition guides to cover health, safety

Traditionally, recommended dietary allowances, or RDAs, of numerous vitamins and minerals have embodied only what was necessary to replenish daily losses and to prevent nutrient deficiencies. Beginning this year, however, the RDA will be redefined to reflect amounts needed for optimum health. Expanded nutritional guidelines will also include maximum safe intakes.

The National Academy of Sciences' Institute of Medicine (IOM) plans to release the first set of updated guidelines for vitamins and minerals related to bone health—such as calcium, magnesium, and vitamin D—later this year, says Janet C. King, director of the U.S. Department of Agriculture's Western Human Nutrition Research Center in San Francisco and a member of IOM's Food and Nutrition Board.

King announced the new evaluation system this week at a meeting of the American Chemical Society in San Francisco.

The guidelines are "very important from the standpoint of public policy," says Marion Nestle, a nutritionist at New York (N.Y.) University, because of their widespread use in food planning. For example, food fortification, school lunch, and food assistance programs all rely on the RDAs. A single number for each nutrient isn't sufficient to serve all these functions, King says.

The new standards, to be known as dietary reference intakes, will consist of three numbers: the redefined RDA, an estimated average requirement, and an upper limit for safe intake. The average requirement meets the needs of half of the population, while the RDA, as before, encompasses 97 percent.

To determine these values, seven panels of scientists appointed by IOM will consider the roles nutrients play in preventing disease, something current RDAs don't account for. The lack of such information caused a "huge furor" among nutritionists when the most recent set of guidelines came out, in 1989, Nestle says.

The panels will also look at substances that do not fit the traditional definition of an essential nutrient but may be important for maintaining good health, such as the antioxidant beta carotene.

The popularity of dietary supplements spurred IOM to identify upper safe limits. Supplements and fortified food can add up to high intakes for certain nutrients, King says, and there may be only a narrow range of tolerance for those substances. The trace metal selenium, for example, can reduce the risk of certain cancers, but too much is toxic.

Although few substances are known to have any direct toxicity, Nestle says, some may upset the overall dietary balance—by inhibiting the absorption of another nutrient, for instance.

Some nutrients, such as thiamine and riboflavin, are so benign that an upper limit may not exist, says Annette Dickinson, director of scientific and regulatory affairs for the Council for Responsible Nutrition in Washington, D.C., a trade association of dietary supplement manufacturers. However, for many nutrients, scientists have almost no information on effects of high doses, she adds.

This lack of data is forcing the panels to make "informed guesses" on upper limits, King says. As a guide, the scientists are using amounts established by the Environmental Protection Agency to have no adverse effects and then building in a safety factor.

The seven panels, each responsible for a different group of nutrients, plan to release their recommendations over the next 4 years. The panel examining the B vitamins, folic acid, and choline has begun its review; the next to be convened will look at fat-soluble vitamins, such as vitamins A and E, and related substances.

"We've moved into a new era of nutritional sciences," King says, but one harkening back to the 1930s, "when we were simply trying to determine what the essential nutrients are." — *C. Wu*

Evolutionary origins of fish antifreeze

Nature has a surefire way of keeping cold-blooded fish alive in ice water: antifreeze. All fish in polar regions produce special blood proteins that bind to ice crystals and keep them from growing. The fish, it turns out, have taken different evolutionary routes to the same end point.

For the perchlike notothenioids, the dominant group of fish in Antarctica, the starting point was the gene for a digestive protein. In the April 15 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, researchers from the University of Illinois at Urbana-Champaign describe the evolutionary transformation of this gene and report that convergent evolution in other fish has produced the same antifreeze from a different starting point.

Biologist Arthur L. DeVries discovered antifreeze proteins in the 1960s and continues to study how they have allowed fish to colonize the freezing Antarctic waters (SN: 11/22/86, p. 330).

The notothenioid adaptation seems to have come about by an unusual reworking of the gene for trypsinogen. DeVries and his Illinois colleagues Liangbiao Chen and Chi-Hing C. Cheng had first searched a database of sequenced genes for any similarity to the DNA sequence of the gene for the antifreeze protein. When they found a close match to the end of a fish gene for trypsinogen, they did a detailed comparison of the antifreeze DNA to the trypsinogen DNA of a notothenioid and found an even better match.

"The signatures of trypsinogen in the antifreeze are quite clear at the two ends," says DeVries. More than 90 percent of the nucleotide bases making up the DNA there are identical, indicating a close evolutionary relationship.

In the middle of the gene, they found another match—nine DNA bases coding for the three amino acids that do the ice-binding work of the antifreeze protein. This sequence of bases from trypsinogen seems to have been copied and strung together many times in the antifreeze gene.

This evolutionary scenario is different from the previously known methods of crafting new genes, says molecular evolutionist John M. Logsdon Jr. of Dalhousie University in Halifax, Nova Scotia. New genes can arise, for example, when a whole gene sequence is duplicated, then gradually altered over time to perform a new function.

In this case, says Logsdon, part of a working protein arose from a bit of the trypsinogen gene that does not code for protein. "[The new gene] evolved from a gene duplication at some point, but then it did something special. It created this new functional segment out of the middle of the trypsinogen gene."

The use of a digestive protein makes sense from a design standpoint, the researchers write. The reorganized protein could go to work on any freezing seawater ingested with food in the intestine—at least in Antarctic fish.

In the Arctic cod, in contrast, the researchers' analysis of the antifreeze protein doesn't show the same sequences of bases from the trypsinogen gene, even though the protein is made up of the same three ice-binding amino acids. "It's clearly convergence," says Logsdon.

The researchers found another convergence—between the estimated age of the notothenioid antifreeze gene and the geophysical estimate of the time of cooling in the Antarctic Ocean, about 14 million years ago. Even though it's based on the rate of genetic change in salmon mitochondrial DNA, the estimated antifreeze age of 5 million to 14 million years "is right in the ballpark," says Chi-Hing Cheng.

"Demonstrations of this sort . . . are rare and noteworthy," say Logsdon and Dalhousie colleague W. Ford Doolittle in an accompanying commentary. This story may become "a textbook example of molecular evolution." — *C. Mlot*