Allergy mechanisms: Learning and itching

An artificial flower triggers a full-fledged asthma attack in a patient allergic to roses. Since this puzzling event was reported by physicians in 1886, there have been many anecdotal reports indicating that learned associations may activate allergic reactions. Now scientists at the University of California's Brain-Behavior Research Center in Eldridge demonstrate in animal experiments that learning can enhance immunological activity, and they propose a mechanism for this nervous system-immune system link.

The intermediate between learning and immunity appears to be histamine, an immune system-mediating chemical found in most tissues. Michael Russell, Harmon V.S. Peeke and colleagues report in the Aug. 17 SCIENCE that guinea pigs increase their blood histamine levels when presented with an odor — either fishy or sulfurous — that had been paired in an earlier training situation to a substance (the allergen) provoking an immunological reaction. The rise in blood histamine in response to the odor alone is similar to that observed after animals are actually exposed to the allergen.

The guinea pigs were made allergic to a protein called bovine serum albumin (BSA) by an injection of the protein in a special solution. A month later they began their training, which followed the general procedures developed by psychologists to demonstrate the type of learning called classical conditioning. In 10 training trials, a cotton-tipped swab was placed on each animal's nose for 3 seconds. The swab contained one odor paired with BSA or the other odor paired with a salt solution to which the animal has no immunological response. In test trials that followed, only the odor that had been paired with BSA in the training trials caused a dramatic histamine response. A second exposure to that odor produced a reduced response.

"Through learned associations between allergic reactions and environmental stimuli, a specific allergic response may be generalized to a number of environmental elements," Russell and colleagues conclude. "Associative learning should be included in understanding the development and treatment of allergies."

In a separate study, researchers have also linked the histamine response to a common childhood rash, called atopic dermatitis. This disorder occurs in up to 4 percent of pediatric patients and is most frequently observed in preschool children. Physicians have disagreed whether allergies cause, or even contribute to, the condition. Now, in the Aug. 9 NEW ENGLAND JOURNAL OF MEDICINE, Hugh A. Sampson and Patricia L. Jolie of Duke University Medical Center in Durham, N.C., present evidence that atopic dermatitis can be a food allergy. Specific foods, most often eggs, milk and peanuts, trigger both the itchy rash and a more than threefold rise in blood histamine levels in some pediatric patients, the investigators report.

Among 33 atopic dermatitis patients, aged 1.5 to 24 years, 24 showed evidence of food allergies. Within 10 to 90 minutes of receiving dehydrated food samples either in opaque capsules or in a broth or juice, these patients showed one or more symptoms. Nearly all of the "positive" responses to these food challenges involved itching and rash. Other symptoms included nausea, abdominal pain, vomiting, diarrhea, stuffy noses and wheezing. Nineteen patients responded to eggs, six to milk, five to peanuts and one each to wheat, fish, beef, peas and rye. Placebos — capsules or liquid containing no suspected food allergen — did not produce any symptoms in the patients.

Blood histamine levels rose sharply only in the patients showing symptoms after a food challenge. There was no significant increase in histamine concentration after negative challenges or after placebos. Sampson and Jolie propose that intermittent, and often frequent, ingestion of a specific food allergen leads to release of immune system mediators, including histamine. This histamine production, especially by skin cells, results in the itchy rash, they suggest.

Patients who are examined with food-challenge tests and then are put on appropriate restricted diets generally have a marked improvement in skin symptoms, Sampson and Jolie say. Therefore they conclude that immediate hypersensitivity to food-specific allergens should be considered as one factor underlying atopic dermatitis. — *J.A. Miller*

Skin by the yard covers massive burns

An accident in Casper, Wyoming, last year left two school-aged brothers with severe burns over 97 percent of their bodies, and prompted a team of Boston burn specialists to push ahead with an experimental treatment sooner than they had planned. They succeeded in covering more than half of each boy's body with grafts of healthy skin tissue grown in laboratory dishes.

The pioneering work by Howard Green, G. Gregory Gallico III and colleagues at Shriners Burns Institute in Boston is reported in the Aug. 16 NEW ENGLAND JOURNAL OF MEDICINE. In an accompanying editorial, Jack C. Fisher of the University of California at San Diego says the Boston group's achievement "cannot be overstated." The ability to quickly produce large amounts of high-quality tissue that can be used to seal off even massive wounds before infection sets in marks a milestone in burn treatment, he says.

"The goal is to get the wound closed fast. If you've got a big open surface on your body, you're a setup for sickness," Fisher told SCIENCE NEWS. "For too many decades, burn care has been oriented toward critical care, topical antibacterials and simply keeping the patient alive rather than using every conceivable method of getting the wound grafted as soon as possible."

Usual methods of treating the wounds — covering them with synthetic dressings or cadaver skin for days or weeks until the damaged tissue regenerates or grafts of the patient's own healthy skin can be performed — were valuable, but inadequate for the brothers, their doctors decided. There simply were not enough uncharred areas on the boys' bodies to serve as donor sites. As a last resort, the Boston team used the same techniques they had used to cover smaller wounds in six previous patients (SN: 3/14/81, p. 167), and this time cultivated for each child a square yard of cells from a plug of healthy skin the size of a postage stamp. Each boy served as his own donor.

Today, one year after the accident, the resulting skin remains in place, and is pliable enough to permit the boys to move freely. One child has returned to home and school, and the second awaits additional skin grafting.

Although the quality of tissue seems similar to that produced through conventional grafting, there are some structural differences that may prove important in the long run, Gallico says. Healthy, normal skin consists of two layers: the underlying dermis, a fibrous bed that contains the nerve endings, sweat glands and hair follicles, and the epidermis, a thinner layer of protective outer cells. "Split-thickness" grafting, the most common method used, slices off a thin portion of the dermis along with the epidermis; the lab-grown grafts developed in Boston contain almost exclusively cells from the epidermis. Previous work has indicated that some components of the dermis are involved in creating skin that can stretch and snap back, a particularly important feature around joints, on the face or on other areas of a growing body.

"We believe a dermis may develop under the new covering, but in fact, the dermis may not be absolutely necessary," Gallico says, though he agrees with Fisher that a longer follow-up of the patients will be needed to determine exactly how flexible and durable the new skin really is.

The ultimate skin substitute should probably contain a dermis, and be ready for grafting even faster, Fisher says, but the success of Gallico and co-workers validates the importance of quick grafting. "Burn care," Fisher says, "has been lost in ointments and salves for centuries." — *D. Franklin*