

vard Medical School in Boston.

Although some scientists had speculated tPA would prove a superior heart-attack treatment because it dissolves clots faster than streptokinase (SN: 12/12/87, p.376), this trial showed no survival edge for people getting tPA or APSAC. Indeed, the relatively new clot-busters may prove a disadvantage if they are more likely to dissolve beneficial clots in other parts of the bloodstream, such as clots repairing a breach in a brain blood vessel, Hennekens warns.

The new findings also add weight to previously voiced concerns about the high price tag of newer clot-busting agents (SN: 4/8/89, p.214). A course of tPA treatment costs about \$2,200, and the typical tab for APSAC is roughly \$1,700, Hennekens notes. Streptokinase, a drug that has been in use for a variety of purposes for 30 years, costs only about \$200.

The cost and safety advantages may encourage more physicians — especially U.S. clinicians who now favor tPA — to use streptokinase when treating heart attacks, the researchers say. However, Hennekens cautions, physicians should look to tPA for patients previously treated with streptokinase or APSAC.

Because they are derived from bacteria, streptokinase and APSAC are more likely to trigger an allergic reaction than tPA, which is a genetically engineered human protein, Hennekens says.

— K.A. Fackelmann

## Retinoic acid flunks as a master molecule

Two reports published this week question a dominant tenet of developmental biology — that a relative of vitamin A serves as a master control chemical that prompts the formation of such disparate anatomical structures as fingers, legs and toes.

By implanting microscopic beads coated with retinoic acid into the limb buds of unhatched chicks, two independent groups of researchers — one from the University of California, Irvine, and another from three Japanese universities — have shown that retinoic acid, a metabolite of vitamin A, does not directly dictate the pattern of limb formation in developing embryos.

The studies already have stirred two deeply divided camps of developmental biologists: those who believe that a single master chemical, or morphogen, calls the shots during development, and those who believe that a subtle interplay between the embryonic cells themselves determines whether they will become part of a finger or a thumb.

"I don't think the morphogen view works," says Susan V. Bryant, head of the Irvine laboratory. Bryant believes that as-yet-undefined molecules on the surfaces of embryonic cells enable the cells to recognize one another and grow into the precise patterns that lead to limbs and digits.

In their experiment, reported in the March 7 NATURE, Bryant's group put a retinoic acid-soaked bead under the surface of the front edge of a chick-limb bud. They removed the bead, and an hour and a half later cut a tiny wedge of tissue from next to the implant site. When the tissue wedge was grafted onto an untreated limb bud, it made the chick grow an extra set of digits.

Bryant says the effect could not be due to retinoic acid carried over in the tissue wedge, because the chemical breaks down in less than one hour. She believes instead that retinoic acid turns on a set of cells, termed the zone of polarizing activity, which then go on to choreograph development.

The Japanese team, headed by Sumihare Noji of Okayama University Dental School, reports the results of its grafting studies in the same issue of NATURE. They found that grafts taken from an area of the chick-limb bud known to be important in development do not prompt untreated limb buds to make molecular receptors for retinoic acid. Because studies show that retinoic acid causes the expression of retinoic acid receptors, Noji's team concludes that retinoic acid alone cannot cause limb development.

Jeremy Brockes, a developmental biologist from the Ludwig Institute for Cancer Research in London, says in an accompanying commentary that although the new experiments contain some flaws, they do question the role of retinoic acid as a morphogen. But he points out that gradients of retinoic acid have been found across developing limb buds, and researchers have shown that retinoic acid alone can cause newts and salamanders to regenerate amputated limbs. "It's still an open possibility that retinoic acid is responsible" for directing limb development, he says.

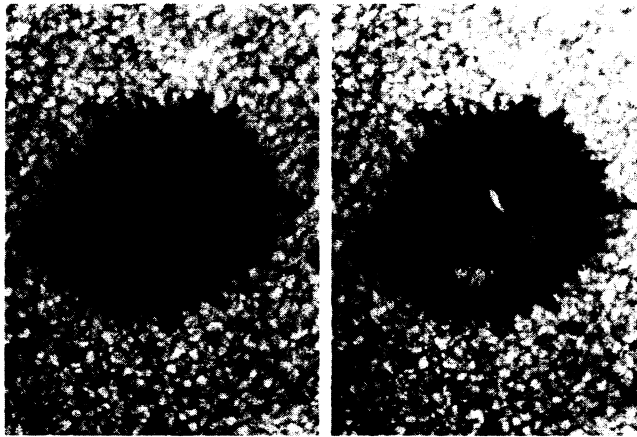
The new work "is not very solid," argues Gregor Eichele from Baylor College of Medicine in Houston. Eichele was one of the discoverers of the retinoic acid gradient in developing limbs, and last year he and his wife, Christina Thaller, found a second potential morphogen, 3,4-didehydroretinoic acid (SN: 7/7/90, p.15). "The only way you can find out what retinoic acid is doing is by finding out what genes it turns on," he says.

Thomas Jessell, a developmental biologist at Columbia University in New York City, terms the new studies "interesting." Jessell, who has collaborated with Eichele and Thaller, says the new reports "will make people slightly less complacent about the identity of retinoic acid as a morphogen." But he still doesn't accept Bryant's theory that cell-to-cell interactions govern development. "You have to invoke some magic to get [it] to work," he says.

— C. Ezzell

### Images reveal greater sunspot structure

Photographs taken with the McMath optical telescope on Kitt Peak near Tucson, Ariz., reveal new details about sunspots, the solar regions where magnetic fields concentrate. The image on the left depicts a conventional view: Filaments of gas — believed to mark the path of magnetic field lines parallel to the solar surface — extend radially from a sun-



spot's outer edge, or penumbra. They do not appear to extend back into the sunspot's darker central region, or umbra. But when astronomer William Livingston of the National Solar Observatory in Tucson took a longer-exposure photo, he detected filamentary "bridges" spanning the penumbra and umbra — an indication that magnetic field lines cross into the central region. The image on the right, a composite of the long and short exposures, delineates the bridging filaments.

Livingston says his images challenge the accepted view that the umbra has a relatively uniform, granular structure. Instead, it contains filaments separated by dark voids where the magnetic field points perpendicular to the solar surface, he asserts. The new umbral detail also indicates that temperatures may vary significantly over the region, Livingston notes. He credits his findings to the Kitt Peak telescope's high resolution and to excellent viewing conditions. But he adds that other observers may have ignored similar evidence because it did not support the granular theory.

Livingston/Natl. Solar Observatory; courtesy NATURE