Biological balm via blood vessel growth

A healing wound requires a new network of capillaries to supply blood to tissue under repair. For properly directed blood vessel growth, cells that form capillaries must migrate to the sites where they are needed. Scientists at the University of California at San Francisco now report that in work with rabbits they have discovered and partially purified a chemical that can give such direction to capillary growth.

In preliminary tests on animals, the chemical, called angiogenesis factor, accelerated wound healing. The scientists speculate that the human form of this substance could be of clinical importance for treating burns, speeding acceptance of skin grafts and accelerating healing of surgical wounds. The research also could lead to a material that would be useful in treating types of wounds, such as tendon injuries, that are slow to heal because they have poor blood supplies and in treating people prone to poor healing, such as the elderly and those undergoing chemotherapy.

The healing substance was identified in fluid withdrawn from rabbit wounds. Wound fluid is an extracellular sterile liquid, similar to blood plasma but specially conditioned by the inflammatory cells, especially macrophage, at the wound site. Wound fluid also contains enzymes that break down damaged tissue and that promote cell division to provide material for the repair.

Wound angiogenesis factor was identified by its ability to stimulate new capillary growth in rabbit eyes and in a laboratory assay to cause the rabbit brain cells that give rise to capillaries to migrate across a gelatin-coated filter. Michael J. Banda, David R. Knighton, Thomas K. Hunt and Zena Werb report in the December PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (No. 24) that they have purified the rabbit angiogenesis wound factor almost 10,000-fold, but it is still not homogeneous. The amount of the slightly impure angiogenesis factor required to stimulate capillary growth in the rabbit eye, about one ten millionth of a gram, "approaches biologically active doses of peptide hormones," the scientists say.

From its light-absorbing characteristics, the angiogenesis factor seems to be a protein or polypeptide, not a nucleic acid or polysaccharide. Its size indicates it consists of 20 to 90 amino acids. The factor guides cells but does not cause them to divide, Banda and associates report. They suggest that other factors in wound fluid and blood are responsible for triggering production of capillary-forming cells and scar tissue.

A factor that promotes growth of blood vessels into tumors had previously been described, but it is smaller than the wound angiogenesis factor. Because the tumor factor was purified from lysed cells instead of from extracellular fluid, Banda and colleagues suggest it may not be the form that acts extracellularly in the body. Cancer researchers propose that an antibody against a tumor angiogenesis factor might prevent capillary ingrowth and thereby starve a tumor. The San Francisco scientists say that future investigations with more purified material are needed to compare the angiogenesis factors and determine whether they act on capillary-forming cells in the same way.

—J. A. Miller

Orphan drug bill is signed by Reagan

A bill to provide incentives for the pharmaceutical industry to develop orphan drugs has been signed by President Reagan. Orphan drugs are those that could treat diseases that afflict only a few people, but have not been tested and developed for commercial sale because the profits from the sale of these drugs would not compensate for the high cost of their research and development.

The bill provides tax credits to drug companies developing orphan drugs in amounts equal to the cost incurred by the companies in research and clinical testing. It also authorizes the FDA to grant limited patent rights if the drug is not normally patentable, as would be the case if the drug is found in nature, instead of synthesized in a laboratory. Finally, since there are sometimes too few patients available for several human trials, the bill authorizes the FDA to approve an orphan drug on the basis of just one adequate study furnishing evidence for the safety and effectiveness of the drug. Two such studies are currently required.

Although Congress and the Department of Health and Human Services supported the measure, the bill was in danger because Treasury Department officials did not believe that tax credits provide a sufficient incentive for developing orphan drugs. Bill Corr, counsel for the subcommittee on health and the environment, stated, "We know OMB [Office of Management and Budget] opposed the bill when it was on the floor because of the tax credit." He added that he had heard from sources in the White House that the Justice Department was opposed to the bill because of an unrelated rider introduced by Sen. Orrin Hatch (R-Utah). The measure requires a study on the health effects of radiation exposure, and this might interfere with litigation in the government's case with ranchers in Utah and Nevada over radiation damage to their livestock (SN: 8/14/82, p. 100).

—A. Chen

Government rescues TRIS-pajama makers

During the final days of its lame-duck session last month, Congress passed a controversial bill that allows manufacturers of children's pajamas treated with the carcinogenic, fire-retardant chemical TRIS to file claims for government refunds for losses caused by the ban on such sleepwear. Proponents said the bill will compensate firms that were unfairly forced to shoulder the financial burden of the federal ban on TRIS-treated apparel. Opponents argued it will set a dangerous precedent, paving the way for other industries whose products are banned to demand similar legislation.

The story behind this legislation began more than a decade ago with the growing public awareness of the hazards posed by the highly flammable children's sleepwear on the market at the time. In response, the Department of Commerce in 1971 ordered that infant sleepwear meet specific nonflammability standards. The Consumer Product Safety Commission later extended that order to include larger-sized children's pajamas.

These federal sleepwear standards did not mandate the use of any particular fabric or fire-retardant chemical. Nonetheless, use of TRIS — then produced mostly by Michigan Chemical Co. (now Velsicol) — grew in popularity, partly because that chemical was relatively cheap and left the treated garment with a desirable texture.

However, by 1975, a standard bacterial test, the Ames test, showed TRIS can cause genetic mutations and therefore may be carcinogenic. Animal tests confirmed its carcinogenicity, so the CPSC banned further sales of TRIS-treated pajamas in April 1977. In addition, the commission also initially ruled that manufacturers have the responsibility to buy back all the TRIS-treated clothing they had sold to retailers. A series of subsequent court cases questioned where in fact the repurchasing responsibility should stop: with the manufacturer of TRIS clothing, the fabric maker or the TRIS producer? In the end, the CPSC ruling contained only the ban on further sales of TRIS-treated sleepwear; by not addressing the repurchasing issue, this ruling left the door open for manufacturers who already had bought back TRIS pajamas to recoup losses by suing their suppliers (of the TRIS fabric, for example).

Meanwhile, though, the manufacturers instead had channeled their efforts into pushing for a federal bailout. An intense lobbying effort resulted in the introduction of bailout legislation by Sens. Strom Thurmond (R-S.C.) and Edward Kennedy (D-Mass.). The bill first passed both House and Senate in 1978 but was vetoed by President Jimmy Carter. This time around, however, President Reagan signed it into law.

—L. Garmon