SCIENCE NEWS of the week

Ocean Anti-Inflammatory Agents

More than two-thirds of the world is covered by water, so it should come as no surprise that some important discoveries drip. From a Caribbean soft coral, researchers have isolated a novel class of compounds that they say may hold the key to new types of anti-inflammatory drugs. Perhaps equally important, the researchers say, is that the compounds, called pseudopterosins, act in unique ways—raising hopes for a new probe into the processes of inflammation.

In experiments using mice, the pseudopterosins were more potent than indomethacin, a commonly prescribed treatment for arthritis and other inflammatory conditions, the researchers report in the September PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (Vol. 83, No. 17). The pseudopterosins were 100 to 1,000 times more effective, depending on the assay, in blocking inflammation produced by a skin irritant. According to the researchers, that may be because the pseudopterosins act earlier in the inflammatory process.

The mechanisms of inflammation are maze-like; there are many points at which drugs can have a moderating effect. Most anti-inflammatory drugs target the arachidonic acid cascade, which produces two major mediators of inflammatory responses, prostaglandins and leukotrienes. Nonsteroidal drugs can dam only one side of the cascade — they block production of prostaglandins but leave the leukotrienes unaffected. Steroidal drugs block both routes, but their side effects can make them an undesirable, though sometimes irreplaceable, treatment.

Although the pseudopterosins are not steroids, they appear to act early in the arachidonic cascade, damming both inflammatory routes. But unlike the steroids, they also have potent analgesic properties.

The pseudopterosins seem to be relatively free of toxicity, says William Fenical of the University of California in San Diego. Fenical, one of the leaders of the study, has studied the chemical adaptations of soft corals for a number of years.

Courtesy, Fenical/UCSD

A sea whip of the same genus as Pseudopterogorgia elisabethae, *from which the pseudopterosins have been extracted.*

The pseudopterosins may provide a template for the development of an entirely new class of drugs for inflammatory conditions like psoriasis or arthritis, says Fenical. "They certainly do not act like any other drugs," he says. The University of California has applied for a patent on the class of compounds.

Exactly where in the arachidonic cascade the pseudopterosins have their effect, and how, remain mysteries. In a way, that's encouraging, says Fenical. "These compounds are pharmacologically quite unique — so unique that we don't know where to start in pinning down the mechanism of action," he says. "We've been studying them for years and still have no idea. Either we've overlooked something, or when we do find the mechanism, we're going to find out something fundamental about the mechanism of inflammation." — *L. Davis*

Even low lead levels in mom affect baby

Adverse health effects — one striking, another subtle — have been identified among infants whose mothers were exposed during pregnancy to lead in the environment at levels well below what is usually regarded as toxic to children. Preliminary results of an ongoing study involving more than 300 low-income, inner-city families in Cincinnati were reported Monday in Anaheim, Calif., at the American Chemical Society's national meeting. According to Kathleen M. Krafft and her colleagues from the University of Cincinnati Medical Center, the study indicates that exposure to even moderately low levels of lead *in utero* increases the chance not only that a child will be born with a low birthweight, but also that the child's early neurological development will be somewhat slowed.

Women were recruited into this study at their first prenatal health exam. Lead levels measured in their blood at that time are being used as the gauge of fetal exposure. The children's blood-lead levels are being measured at three-month intervals from 10 days after birth through age 6. Since it's assumed the home environment contributes most to a young child's lead exposure, the program also surveys each family's residence for the heavy metal's presence in paint, dust and soil. Finally, because others have linked lead exposure with learning and neurological problems (SN:2/6/82,p.88), Krafft, a neurobehavioral psychologist, is attempting to chart the cognitive and neurological development of the children through frequent behavioral tests.

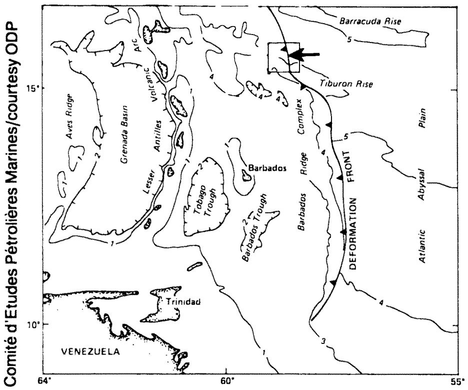
Because so many of these children are quite young, Krafft says statistically significant correlations can be made only for effects in children under 1 year old. One of the strongest of those is the link between a mother's lead exposure and her child's birthweight. Even "relatively low" maternal blood-lead levels of 8 micrograms per deciliter — 25 micrograms per deciliter is usually considered toxic to children (SN:2/16/85, p.203) — correlated with a birthweight 192 grams lower than that of infants whose mothers had no obvious lead exposure. Krafft says this effect is as striking as the link seen between maternal smoking and decreased birthweight (SN:1/19/80,p.37) — a factor that has been taken into account in designing these experiments.

Children whose mothers had the lowest lead levels scored slightly higher on neuromotor development tests given through age 6 months. But this correlation may not hold up beyond that age, Krafft warns, because in lead-laden households, children's exposures begin deviating from their mothers' at about this time — when they begin grasping, putting things in their mouths and crawling. — *J. Raloff*

Growing edge of a Caribbean wedge

Researchers on Leg 110 of this summer's Ocean Drilling Project became the first to drill into the detachment surface of a subduction zone — the surface of contact where one crustal plate burrows beneath another. The international expedition bored nine holes in six sites north of Barbados to better understand how the movement of fluid influences the very early stages of some mountain-building processes. They found that the folding and thrusting of the colliding plates have laced the area with fractures that allow water to seep through submarine rock to the ocean floor. The force of the two converging plates squeezes unusually warm water and sometimes methane out of the rock and up through these cracks, lubricating the plates as they slide past each other.

"Hydrogeology is really, really important to geology," says Casey Moore, the project's co-chief scientist, from the University of California at Santa Cruz. "The movement of water through rock controls all kinds of things, and we as geologists have just been studying the rock, the solid material, and not paying any attention to the fluid."



Comité d'Etudes Pétrolières Marines/courtesy ODP

The subduction zone and Ocean Drilling Project site north of Barbados.

As sediment accumulates at the bottom of the ocean, Moore says, it traps ocean water like the pores of a sponge. As the Caribbean plate moves over the Atlantic crust, some of the sediment piles atop the edge of the plate to form an accretionary wedge that is gradually growing eastward; in some places, the wedge is thick enough to create the rolling hills of Barbados. Some of the sediment, however, stays on top of the Atlantic crust as it slides under the Caribbean plate. The pressure of the overriding plate cracks the underlying rock and squeezes out the entrapped ocean water. The water seeps up the cracks into the detachment surface between the two plates. Says Moore, "The water allows [the plates] to slip without building up a lot of strain and therefore [reduces] the potential for a large earthquake."

Because the Atlantic crust sediment lies so deep, the water it releases is much warmer than normal ocean-bottom water. The heat also warms organic matter trapped in the sediment pores, converting it to methane that seeps at least 25 kilometers along the detachment surface up to the ocean's floor, the researchers found. This same mechanism, says Moore, may explain the plumbing network that creates mud volcanoes near Trinidad and feeds the rich biological communities living near submarine vents off the coast of Oregon (SN: 12/15/84,p.374).

As the water squirts out of the sediments, it alters the character of the rock it leaves behind, exchanging minerals in solution for minerals in the rock. "What we're starting out with," says Moore, "are sediments that are on their way to becoming rocks, and we see all these subtle transformations along that path."

– T. Kleist

Knocking the lead out of gasoline

Now that tetraethyl lead is being phased out as an antiknock additive in gasoline, researchers are beginning to pay closer attention to how lead does its job inside a car engine. Although lead additives have been used for about 60 years, the detailed chemistry of the reactions that take place to eliminate engine knock has remained elusive. Recently, two scientists each proposed a somewhat different theoretical mechanism that may account for lead's effectiveness and could lead to a suitable substitute.

Engine knock occurs when unburnt gases in a car engine's cylinder ignite too soon. Normally, a spark plug initiates a flame that rapidly sweeps through the chamber. But the mixture of air and gasoline at the end of the chamber farthest from the spark plug also gets heated and compressed by the moving flame. As a result, sometimes these "end" gases explode before the flame actually reaches them, upsetting the gasoline's orderly burning. This produces engine knock and a loss of power.

"But if you speed up the flame or slow down the ignition of the gas that's farthest away, then you won't get knock," says physicist Charles K. Westbrook of the Lawrence Livermore (Calif.) National Laboratory. Westbrook and his colleagues have been using a computer to model the chemical reactions that may be going on when a lead compound is added. "If we can understand why lead works," he says, "then maybe we can find something else that will do the job as well."

Lead additives appear to slow combustion mainly by removing hydroperoxyl radicals, highly reactive molecules that form during combustion. Westbrook suggests that microscopic particles of lead oxide, about 50 to 100 angstroms across, form within an engine cylinder after tetraethyl lead breaks down. When active molecules like hydroperoxyl radicals hit these solid particles, they are absorbed and no longer contribute to gasoline combustion.

Chemist Sidney W. Benson of the University of Southern California in Los Angeles, however, contends that the key reactions for removing active molecules occur when all of the species, including lead, are present as gases. He proposes a three-step sequence of elementary reactions that reduces the number of both hydroperoxyl radicals and hydrogen atoms, which are released during the breakdown of gasoline hydrocarbons.

Experiments are needed to settle which of the two proposed mechanisms is dominant. "The problem," says Benson, who has been studying combustion reactions for many years, "is that most of what lead does happens in such a short time that it's hard to get convincing evidence."

Westbrook says previous experiments show that a mist of lead oxide particles does form within a car engine just before it knocks. However, the crucial question of exactly when that happens has not yet been answered. Benson argues that the particles probably form too late to be effective.

"The answer almost certainly is that both [mechanisms] are taking place," says Westbrook. "It's a question of their relative importance."

Nevertheless, both theoretical predictions point to the effectiveness of hydroperoxyl removal for preventing engine knock. "You've got the dossier of the character you're searching for," says Westbrook, "but now you've got to find something that fits that profile."

Based on his results, Benson says, "there should be a lot of metals and a lot of metals in various combinations with other things that could play the same role as lead." The ideal candidate, while preventing engine knock, also would be volatile so that deposits don't build up in cylinders, and it should not affect catalytic converters by poisoning the platinum catalyst.

Presently, petroleum refiners and fuel producers blend a variety of hydrocarbons with gasoline to prevent engine knock. Organic compounds like benzene, toluene and isooctane burn in such a way that premature ignition doesn't occur readily. However, these blending agents are expensive.

Moreover, the occurrence of knock limits how much the gasoline-air mixture in a cylinder can be compressed. A higher compression ratio would increase an engine's fuel efficiency.

Because of the cost- and energy-saving potential of an effective means for preventing engine knock, the Department of Energy (DOE), in cooperation with industry, has for the last few years been sponsoring a research effort to help solve the problem. By using sophisticated instruments and facilities at several national laboratories and elsewhere, DOE-sponsored researchers hope to provide fundamental information about the chemical and physical processes that take place during gasoline combustion. That information, says Marvin E. Gunn of DOE's conservation and renewable energy office, should someday allow fuel producers and engine designers to develop better energy-conserving products.

– I. Peterson