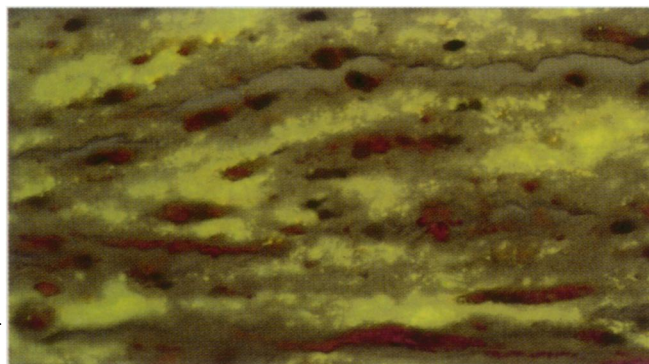


Newest Cholesterol Carriers Isolated

Just when you thought you knew all the players in the cholesterol saga, investigators have isolated and purified two additional particles that may thicken the plot. Normally present in the spaces between cells, these cholesterol-carrying compounds can accumulate into larger deposits that may play a very early role in coronary artery disease — appearing even before the telltale fatty streaks that often precede hardening of the arteries.

This latest twist in the cholesterol story began in the mid-1980s, when pathologist Howard S. Kruth at the National Heart, Lung, and Blood Institute detected two previously unknown types of cholesterol-rich particles in human and animal arteries narrowed by atherosclerosis. One was bound to fatty acids, essentially making it an oil droplet; the other was a multilayered sphere unbound to fatty acids (unesterified).

Although most research had focused on cholesterol inside cells, these particles appeared only in the spaces between cells. In subsequent work, Kruth and his co-workers observed the unesterified



Micrograph of human arterial cells shows elongated clumps (light green) of unesterified cholesterol particles found only outside the cells, as well as the more familiar cholesterol deposits (red) inside cells.

particles accumulating — even before fatty streaks appeared — in the arteries of rabbits fed high-cholesterol diets. As cholesterol-induced arterial damage progressed, the team found higher concentrations of the unesterified cholesterol particles and smaller but increasing amounts of the oil-droplet type.

Kruth says previous studies missed these particles because most investigators did not look for extracellular cholesterol and because the unesterified particle cannot absorb the dye com-

monly used to study cholesterol-carrying compounds.

He and his co-workers report in the January *AMERICAN JOURNAL OF PATHOLOGY* that they have now isolated and purified the two cholesterol-rich particles from human aorta tissue. They have also used electron microscopy and chemical separation techniques to further probe the structure of the compounds, confirming and extending the findings of several research groups that have imaged the particles in arteries.

The team found that the two particle types were similar in size — about 10 times bigger than the familiar high-density and low-density lipoproteins (HDLs and LDLs) that carry cholesterol in the bloodstream. Kruth conjectures that the extracellular particles may serve as storage containers for cholesterol excreted by cells that contain too much of the fatty compound. John Guyton of the Baylor College of Medicine in Dallas, who has performed several electron microscopy studies of the particles, says he is searching for a possible chemical factor linking HDL, LDL and the newly isolated cholesterol-rich compounds.

Kruth told *SCIENCE NEWS* he and his collaborators recently found that HDL dissolves the unesterified particle in the test tube. In other new experiments, he says, his research group has discovered a link between that particle and LDL: When an enzyme robs LDL of its oily core, the LDL swells like a popped kernel of corn until it resembles the unesterified compound in size and structure.

“What’s exciting about this work is that these particles appear before cholesterol accumulates as deposits in cells of the artery wall,” Kruth says. “Our studies suggest that we should look for drugs that facilitate the removal of cholesterol that accumulates outside cells.”

Deposits of these particles may not always lead to atherosclerosis, cautions Russell Ross, a pathologist at the University of Washington School of Medicine in Seattle. “But this is one possible route,” he says.

— R. Cowen

‘Abortion pill’: New data, new markets

In the largest study of its kind, the controversial French pill RU 486 appears safe and effective as a means of terminating pregnancies of less than seven weeks’ duration, its developers say. Moreover, the so-called contraceptive — approved in France in September 1988 — may soon become available in some other European countries, says endocrinologist Etienne-Emile Baulieu of the University of Paris-South, who oversaw the drug’s development.

Researchers and family-planning experts say the new data and the drug’s move beyond French borders will escalate an already-heated debate about RU 486’s potential role in the United States, where doctors perform 1.6 million abortions each year. Despite an estimated \$1 billion U.S. market, no drug company has applied for FDA approval of RU 486, in part because anti-abortion activists have threatened to wreak financial ruin upon any group attempting to sell the drug here.

The new data — which Baulieu says will appear soon in the *NEW ENGLAND JOURNAL OF MEDICINE* — indicate the pill successfully induced abortion in 96 percent of more than 2,000 women studied, and in only one case triggered bleeding severe enough to require a blood transfusion. Previous studies showed about the same success rate but

about twice the rate of serious bleeding. About 40,000 French women have taken the drug regimen, which costs the equivalent of about \$45 and today accounts for about one-third of the abortions performed in France, Baulieu said in Boston this week at a symposium on “New Birth Control in the 1990s.”

The pill blocks the action of progesterone, a sex hormone required for fetal survival. Women must return to their doctor 48 hours after taking the pill for a follow-up dose of prostaglandin, which triggers uterine muscle contractions. Expulsion of the fetus generally follows within a few hours. The new study indicates that pregnancy continued in 1 percent of the women. Most of the remaining failures resulted from incomplete expulsion requiring medical intervention.

“I think this compound is going to enter the USA very soon,” Baulieu says. While some U.S. observers remain skeptical, others say growing demand for such a pill and the lack of any evidence of toxicity virtually ensure its eventual arrival in the United States. According to Baulieu, the drug’s manufacturer will soon apply for permission to market RU 486 in England, Holland and Scandinavia and expects the drug to be available in those countries by the end of the year.

— R. Weiss