

Drug firm and FDA suspend IUD sales

A growing number of reports of death and injury associated with the use of the Dalkon Shield, an intrauterine contraceptive device, has caused the manufacturer to suspend sales and distribution until a Food and Drug Administration advisory committee decides on its safety. FDA Commissioner Alexander M. Schmidt is also recommending that doctors not make additional Dalkon Shield insertions until the safety questions are answered.

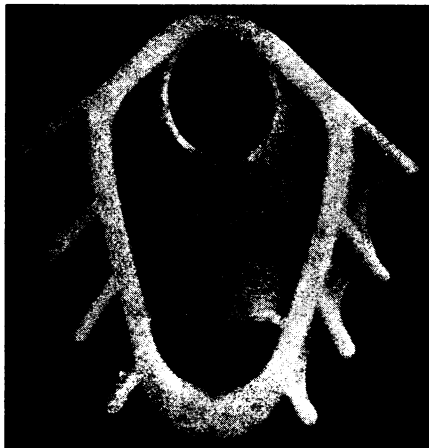
Seven women have died from infected spontaneous abortion (miscarriage) while using the device, and more than 100 nonfatal cases have been reported. Most of the infections occurred during the mid-trimester of pregnancy. The manufacturer, A. H. Robins Co., of Richmond, Va., has received an increasing stream of reports since they issued a "Dear Doctor" letter in May, cautioning physicians about the possible complications if a patient should become pregnant while using the device.

The FDA Obstetrics and Gynecology Advisory Committee, a group of physicians that meets several times yearly to make decisions and recommendations on drugs, devices and medical practices, met June 11 and 15 to hear testimony on the Dalkon Shield. A. H. Robins representative Frederick A. Clark Jr., told the panel that doctors' reports have often been incomplete and inaccurate, and that the device "should not be hastily judged." He said "it is hard to believe" infection could occur with the IUD sitting high in the uterus, and that only low lying IUD's (displaced accidentally or by the wearer herself) would facilitate infection.

A team of FDA physicians from the Center for Disease Control in Atlanta, presented preliminary data behind closed doors. Those data will not be released until August 21 when the Obstetrics and Gynecology Advisory Committee will meet to make final recommendations to Schmidt.

The Dalkon Shield has been inserted in more than 2.2 million American women, and about a million women in 41 foreign countries. The device's effectiveness has also been questioned; an unpublished British study reports a 3.6 percent pregnancy rate in second year users, but a researcher from Beth Israel Hospital in Boston, Johanna Perlmutter, reported a pregnancy rate of 18.5 percent.

The FDA says it will advise physicians through the FDA DRUG BULLETIN about the precautions to be taken in women who become pregnant while using the Dalkon Shield—removal of the device, or possible therapeutic abortion if removal could not be readily accom-



plished. The DRUG BULLETIN will also carry a request for doctors to report all adverse IUD reactions to the FDA. □

Inheritance and high cholesterol

There are different causes for high cholesterol in the blood. One is inheritance. One form of inherited high cholesterol is familial hypercholesterolemia. One in every million persons is a homozygote for this disorder, that is, has received the dominant high-cholesterol gene from both parents. Having a double dose of the gene, the homozygote has six times more cholesterol in his blood than a healthy person and often succumbs to a heart attack before age 20. One in every 500 persons is a heterozygote for this disorder, that is, has received the high-cholesterol gene from only one parent. The heterozygote has two to three times more cholesterol in his blood than a healthy person. He often has a heart attack around the age of 40.

An explanation for why homozygotes have a six times elevation and why heterozygotes have a two to three times elevation is reported in the July 5 SCIENCE by Michael S. Brown and Joseph L. Goldstein, internists at the University of Texas Southwestern Medical School in Dallas.

During the past year or two, Brown and Goldstein have learned that cells called fibroblasts have receptors on them that bind with cholesterol-lipoprotein complexes in the blood. When the complexes bind to the receptors, an enzyme that regulates the rate of cholesterol synthesis is turned off. Then cholesterol production is arrested, until the complexes have dwindled enough in the blood to switch cholesterol synthesis back on.

Brown and Goldstein now report in SCIENCE, that homozygote fibroblasts were able to bind with cholesterol-lipoprotein complexes with about 3.6 percent efficiency of normal fibroblasts. Heterozygote fibroblasts were able to bind with the complexes with about 40 percent normal efficiency. Both homozygote and heterozygote fibroblasts were not deficient in their ability to bind to the complexes, rather, they were deficient in their number of receptor molecules. The heterozygote fibroblasts were able to show 40 percent binding efficiency because they had received a number of normal receptor molecules from the normal cholesterol gene inherited from one parent.

These findings suggest why homozygotes have a sixfold elevation in cholesterol, whereas the heterozygotes have only a two- to threefold elevation. Since cholesterol-lipoprotein complexes are crucial in the feedback regulation of cholesterol synthesis, they have to build up in the blood in order to bind to receptors and thereby turn off cholesterol synthesis. But the fewer receptor molecules there are, the more cholesterol has to build up in order to bind to the molecules and switch off synthesis. That's why a 96.4 percent reduction in receptor molecules on homozygote fibroblasts could well lead to a sixfold rise in cholesterol complexes in the blood, and why a 60 percent reduction in molecules on heterozygote fibroblasts could lead to a two- to threefold rise in cholesterol. □

Soyuz practices for co-op mission

For many months, U.S. and Soviet working groups have been shuttling back and forth coordinating details for next summer's international space spectacular, the Apollo-Soyuz rendezvous in orbit. Last week, cosmonauts Pavel Popovich (veteran of the Vostok 4 flight in 1962) and Yuri Artyukhin (making his first flight after 11 years as a cosmonaut) took off toward a rendezvous with a previously-launched Salyut space station—the first Soviet docking practice since the Soyuz was redesigned following the deaths of three cosmonauts from a pressure leak during the landing of Soyuz 11 in 1971.

The changes made to the Soyuz design were not concerned with docking procedures; they were primarily to refit the spacecraft for use by two cosmonauts in spacesuits as protection against depressurization, rather than by three in shirtsleeves. Nonetheless, docking will be a critical part of the Apollo-Soyuz exercise. An adapter carried by