Urban workout: Sick hearts take a beating

People with coronary artery disease who exercise in air laden with carbon monoxide – a ubiquitous pollutant from auto exhaust and cigarette smoke – may suffer more frequent and more severe episodes of ventricular arrhythmia, a new study indicates. These ill-timed contractions of the heart's ventricles kill an estimated 350,000 people per year in the United States and represent the leading cause of sudden deaths from heart attack.

High-level carbon monoxide already has a reputation as a killer of healthy people – for instance, motorists who leave their engines running when stranded in deep snow or sitting in a closed garage. But the new research focuses on low-level concentrations typically encountered in the most polluted areas of large cities, such as in automobile tunnels and along major highways. A significant increase in ventricular arrhythmias showed up in heart patients who exercised after exposure to the higher of two "low" concentrations of carbon monoxide, the team reports in the September ANNALS OF INTERNAL MEDICINE.

People with coronary artery disease who bicycle, jog or otherwise exercise outdoors "should be cautious when they exercise in areas of potentially high pollution," advises study coauthor David S. Sheps, a cardiologist at the University of North Carolina at Chapel Hill.

Research published last fall found that exercise at low levels of carbon monoxide worsens ischemia, or oxygen deprivation, in hearts with stiff, clogged arteries (SN: 11/25/89, p.342). The toxic gas combines with hemoglobin in red blood cells to form carboxyhemoglobin, preventing the hemoglobin from binding oxygen and delivering it to the body's cells. Together, pollution-linked ischemia and arrhythmias "may have a synergistic effect on the risk for sudden death," write Sidney O. Gottlieb and Sandra M. Walden of the Johns Hopkins University School of Medicine in Baltimore, in an editorial accompanying the new report.

Several studies since the late 1960s have suggested a link between arrhythmia and low-level carbon monoxide, but "there was really no hard look at people with rhythm disturbances," says Bernard R. Chaitman of the St. Louis University School of Medicine, who coauthored last year's ischemia report.

Sheps studied 36 men and five women aged 47 to 77 – all nonsmokers with coronary artery disease, and most with some degree of preexisting rhythm irregularity. Volunteers worked out on exercise bicycles in room air 20 to 30 minutes after exposure to ordinary room air or to air containing enough carbon monoxide to create blood carboxyhemoglobin levels of either 4 or 6 percent. During exercise, the researchers tallied single misplaced beats and multiple beats (two or more beats repeating in quick succession).

The number of single, out-of-time beats rose by almost one-third after the 6 percent exposure compared with room-air exposure. And rapid runs of repeating beats – a particular cause for concern since they pose a risk of sudden death – jumped threefold at the 6 percent blood level. "That's really the more important finding," says Sheps.

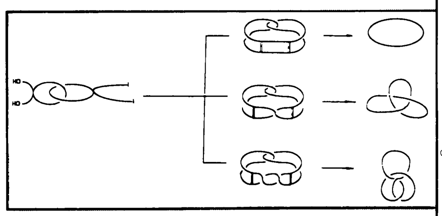
Arrhythmias did not increase, however, at the 4 percent level. Sheps maintains that the data need not show an increase with dose in order to indicate a response, and he suggests that blood levels of the gas must cross a threshold before rhythm effects show up. But Chaitman argues that the lack of a trend of increasing arrhythmia frequency with increasing exposure may mean that the 6 percent effect "might be a spurious finding."

Last April, at the annual conference of the Health Effects Institute in Scottsdale, Ariz., Chaitman reported that his own preliminary and as-yet unpublished findings indicate no rise in arrhythmias among 31 patients with coronary artery disease who exercised after breathing low levels of carbon monoxide, even though these patients displayed "relatively high [preexisting] rates of arrhythmias."

Previous studies exposing cardiac-compromised dogs to low levels of carbon monoxide similarly revealed no rise in arrhythmias, says physiologist Jay P. Farber of the University of Oklahoma Health Sciences Center in Oklahoma City, who conducted one such investigation with cardiologist Emilio Vanoli of the University of Milan, Italy.

The question of carbon monoxide's influence on arrhythmia remains unresolved, Chaitman contends. Nonetheless, he says, "there is a consensus among people working in this field that low levels of carbon monoxide in patients with coronary artery disease are not good for them." *– P.L. Weiss*

Chemists learn to knot their molecules



Zheng Walba

Precursor on left ties into a ring, a trefoil knot or a figure-8 knot.

The quest to make molecules shaped like knots gives flight to chemists' imaginations. It also challenges their molecule-building ingenuity, a basic exercise that can later prove useful for more practical pursuits such as drug design.

After four years of laboratory effort, chemist Qun Yi Zheng of the University of Colorado in Boulder has come up with a "hook and ladder" approach for making knotted compounds. At last week's meeting of the American Chemical Society in Washington, D.C., he reported that his procedure has yielded a candidate molecular knot. Zheng suspects it may have a clover-like trefoil shape, similar to a molecule synthesized last year by French chemists using a different method, or an even twistier figure-8 shape. He is now performing structural analyses to determine the actual conformation.

The making of a molecular knot involves sequences of reactions in which molecular laces thread through molecular loops and then tie together, sometimes with twists, to form finished knots. The same assemblies can tie together with different twists to yield several related structures. Zheng and his supervisor, David M. Walba, refer to these products as topological isomers.

More familiar to chemists are geometric isomers, in which the same atoms arrange in different spatial patterns, and stereoisomers, in which atoms arrange in different orientations around an atomic hub.

Zheng begins his synthesis of molecular knots by constructing a "hook," which looks like a ring with two dangling chemical groups. He temporarily "caps" these to protect them during further reactions. Next, he threads a semicircular molecular segment through the hook's opening and joins it with another semicircular segment, which has a pair of alcohol groups at the far end. He then elongates these with flexible molecular segments.

To set the stage for the final tying of the knot, Zheng tips the elongated segments with iodine atoms and replaces the protective caps on the hook's far end with reactive alcohol groups. The final steps involve linking the sets of iodine- and alcohol-tipped ends and breaking a couple of rigid double bonds, which earlier served structure-directing roles and which look like ladder rungs in sketches of the molecules. The four ends link in any of three possible ways that differ in the number of half-twists the ends make before joining. Molecules with no, one and two twists yield a ring, a trefoil knot or a figure-8 knot, respectively. *– I. Amato*