Médicaments dans l'eau

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Drugged Waters

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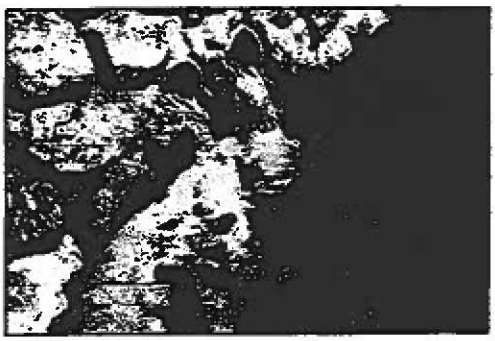
Does it matter that pharmaceuticals are turning up in water supplies?

By JANET RALOFF

Chemists at an agricultural research laboratory run by the Swiss government were screening lake water for pesticide contamination when they ran across a puzzling result. Their instruments turned up a compound that resembled mecoprop, an herbicide they had been looking for, but it wasn't a perfect match.



Treated municipal wastewater entering a Swiss stream. Treatment plants have not been designed to remove excreted drugs before releasing their effluent into public waterways.

Suspecting that they might have found the pesticide in an early stage of degradation, Hans-Rudolf Buser and Markus D. Müller probed further. To their surprise, the pollutant turned out to be clofibric acid, a widely used cholesterol-lowering drug.

Immediately, the pair began scouting for the drug elsewhere -- and they found it everywhere, from rural mountain lakes to rivers flowing through densely populated areas. Concentrations, ranging from 1 to 100 nanograms per liter of water, seemed to correlate with how densely a region was inhabited. While barely detectable, these concentrations resemble those of other, more conventional pollutants found in the environment, Buser notes, such as a persistent, toxic ingredient of the pesticide lindane (SN: 3/15/97, p. 157).

The ubiquity of clofibric acid, which is not even manufactured in Switzerland, argued against the possibility that the contamination stems from some industrial accident or spill, Buser says. The only reasonable explanation, he and Müller conclude in the Jan. 1 Environmental Science & Technology, is that it comes from human wastes.

Though the body tends to break down any medicine it uses, how effectively it

does so can vary widely -- by individual and by drug. As a result, in some cases, 50 to 90 percent of an administered drug may be excreted from the body in its original or its biologically active form. In other cases, partially degraded drugs are converted back into their active form through chemical reactions with the environment.

Seven years earlier, environmental chemists Thomas Heberer and Hans-Jürgen Stan of the Technical University of Berlin had stumbled upon clofibric acid while looking for agricultural chemicals in groundwater beneath a German sewage treatment farm. Heberer suspects that he and Stan would have missed the drug if it hadn't resembled a common pesticide. The drug's structural similarity, he says, "proved the key to its detection."

Like the Swiss team, the Berlin scientists went on to find clofibric acid throughout local waters. It laced some groundwater at concentrations of up to 4 milligrams per liter, or 4 parts per million (ppm), they will report in an upcoming issue of the International Journal of Environmental Analytical Chemistry. It also turned up in all the Berlin tap water they sampled -- at up to 0.2 ppb.

When it comes to waterborne drugs, however, clofibric acid is just the tip of the iceberg. Heberer and Stan are part of a Berlin research team that has found drugs for regulating concentrations of lipids in the blood (such as phenazone and fenofibrate) and analgesics (including ibuprofen and diclofenac) in groundwater beneath a sewage treatment plant. This aquifer serves as a source of drinking water. Other researchers have detected chemotherapy drugs, antibiotics, and hormones in bodies of water that supply drinking water.

What do low concentrations of these drugs in water mean? asks ecotoxicologist Bent Halling-Sørensen of the Royal Danish School of Pharmacy in Copenhagen. Do they pose a health risk to people? Can they harm wildlife or substantially alter aquatic ecosystems? Do they foster the buildup of resistance to antibiotics?

For now, there are no answers, he and his colleagues conclude in the January (No. 2) Chemosphere. After reviewing more than 100 published reports on drug residues in the environment, they found "practically zero" data for gauging the potential toxicity of chronic exposures to low doses of these compounds in the environment.

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Most countries have regulatory agencies explicitly charged with protecting the environment from pesticides and other potentially toxic industrial chemicals.

Drugs, however, have come to be regulated by health departments, which possess little expertise in protecting natural ecosystems and water supplies. Moreover, they tend not to look at pharmaceuticals as potential pollutants -- even though up to 90 percent of a delivered drug may leave the body in urine and feces.

One reason for medicines' low visibility in environmental regulations is their low concentrations in water. Until recently, most drugs in public water supplies would have been undetectable.

Regulators have attempted to cope with this problem by asking manufacturers to model a new drug's projected concentration in public water supplies, based on what was known about company projections for how much of the compound might be sold, the quantities of lake and stream water into which the excreted drug would be flushed, and laboratory information on the rate at which it would break down in the environment. They were also asked to predict its accumulation in wildlife.

In the United States, an environmental assessment containing such estimates would be submitted to the Food and Drug Administration as part of the approval process for a new drug. If such an assessment suggested that worrisome levels of a drug might build up, a manufacturer would have to prepare a more detailed investigation. Such an environmental impact statement might even explore possible mitigation measures, explains Daniel C. Kearns of FDA in Rockville, Md.

So seldom did an environmental assessment for a new drug suggest a hazard, however, that the FDA decided last July to reduce a manufacturer's environmental reporting requirements. The agency concluded that excreted drugs "are probably not having a significant environmental effect," Kearns says. "So unless modeling data suggest a drug's concentrations would reach 1 ppb, a manufacturer no longer must submit an environmental assessment.

"We've never seen a situation where we believe you would have an actual impact upon the environment if [drug] concentrations were under that," he told Science News.

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Though modeling provided a useful surrogate for water monitoring when laboratory analyses were too crude to detect low drug concentrations in the environment, chemists today routinely detect parts per trillion (ppt) of many waterborne pollutants.

When asked whether FDA requires any monitoring of water supplies to see whether concentrations in the real world match the predictions of drug manufacturers' models, Kearns said no.

If they had, many German chemists now believe, regulators might have received a rude awakening -- as Thomas A. Ternes did.

A chemist with the municipal water research laboratory in Wiesbaden, Ternes realized that tons of medicines are prescribed each year in Germany, "but nobody knows what happens to those compounds after they are excreted." So a few

years ago he launched a water-monitoring project to look for drugs in sewage, treated water, and rivers.

He expected to find a few medicinal compounds. Instead, he detected 30 of the 60 common pharmaceuticals for which he tested. These included lipid-lowering drugs, antibiotics, analgesics, antiseptics, and beta-blocker heart drugs. He has even found residues of drugs to control epilepsy and ones that serve as contrast agents for diagnostic X rays. A report of his findings will appear later this year in Water Research.

Ternes detected parts-per-billion concentrations of these drugs in both raw sewage and the water leaving treatment plants. "We also found these compounds in nearly all streams and rivers in Germany," he says. Though concentrations in streams usually fall in the parts-per-trillion range, he notes that for some compounds "you can have maximum concentrations of up to 3 [ppb]."

The highest concentrations tended to show up in the smallest rivers, where 50 percent of the water could be sewage treatment effluent. Residues of up to 10 different drugs have been found in such water at concentrations totaling 6 ppb.

Ternes notes that finding these drugs "is very hard work." For instance, chemists usually identify a compound by comparing it against a standard sample of that compound. These standards often are not available for sale, he finds.

Adding to the problem, Heberer observes, is that almost all excreted drugs dissolve easily in water. Because conventional methods of separation take advantage of differences in the effectiveness of several solvents, it is difficult to segregate the drugs for analysis. That's a problem Shane Snyder at Michigan State University in East Lansing has been wrestling with in his study of estrogens in sewage effluent.

While analyzing Las Vegas wastewater flowing into Lake Mead, Snyder found that "all of the estrogenicity was coming out of the very water-soluble fraction." To isolate the chemicals responsible, he had to repeat the separation procedure 30 times or more. Though estradiol, the primary natural female sex hormone, appears to be the major estrogenic compound in this water, there is evidence that a synthetic hormone in birth control pills may also be a contributor. Further investigation of that possibility is now under way.

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These findings are not all that surprising," observes James F. Pendergast, acting director of the Environmental Protection Agency division that regulates what comes out of sewage treatment plants. For quite a while, he notes, water quality engineers have recognized that one of the highest-volume contaminants emerging in effluent -- especially early in the morning -- is caffeine, a drug excreted by all those people who down a cup or two of Java to jolt their bodies awake.

Although he was unfamiliar with the new European studies documenting drugs in water, Pendergast says that he has no reason to doubt their findings or the possibility that they might herald what could be found in U.S. waters, if anyone were to look.

He's also not surprised that European chemists have stumbled onto the issue before U.S. scientists. A number of environmental issues -- from methyl mercury buildups in acidified lakes to reproductive risks from hormone-mimicking pollutants -- became hot research topics in Europe before U.S. researchers jumped on the bandwagon, he says.

The issue of drugs in water, he concludes, "is certainly an area where we could use a lot more science." The critical issue is whether existing concentrations pose any hazard to wildlife or to people. To date, he notes, "information on hazards at the nanogram level just hasn't been developed."

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A few laboratories stand poised to try. Snyder's assays, for instance, indicate that estradiol in water can reach 20 ppt -- a concentration that can cause some male fish to produce an egg-making protein normally seen only in reproductive females. In upcoming experiments in Lake Mead, he plans to cage fish within a plume of effluent from an upstream sewage treatment plant.

Using a bacterial test that gauges a pollutant's potential to damage DNA, Andreas Hartmann of the Swiss Federal Institute of Technology in Zurich has been studying effluent from hospitals and municipal wastewater treatment plants. In the March Environmental Toxicology and Chemistry, he reports finding fluoroquinolones, a class of broad-spectrum antibiotics, to be the leading source of a hospital wastewater's toxicity to DNA.

"We're finding 0.5 microgram per liter of fluoroquinolone antibiotics in sewage treatment plant water," Hartmann told Science News. Tests have tentatively identified the drug as ciprofloxacin. Once the antibiotic is more firmly identified, he plans to study "whether it -- alone or in combination with other antibiotics -- has an influence on the developing resistance to these compounds that we're finding in pathogenic organisms in the environment."

"If [he's] finding fluoroquinolone antibiotics at that level in water and they're not breaking down, that would be a problem," says Stuart Levy, who directs the Center for Adaptation Genetics and Drug Resistance at Tufts University in Boston. Parts-per-trillion concentrations of these drugs can affect Escherichia coli and other bacteria, he notes. The 1,000 times higher concentrations reported in German wastewater suggest to Levy that "these antibiotics may be present at levels of consequence to bacteria -- levels that could not only alter the ecology of the environment but also give rise to antibiotic resistance."

Halling-Sørensen is also studying waterborne antibiotics, though his focus is their potential toxicity to algae, crustaceans, and other aquatic residents. By quantifying the potential ecological effects of individual compounds, he says, "we may get information that's useful for decision making.

"For instance, if we have five medicinal compounds that can treat the same disease, we might now identify which is most friendly to the ecosystem -- and choose to use that one."

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References:

Buser, H., M.D. Muller, and N. Theobald. 1998. Occurrence of the pharmaceutical drug clofibric acid and the herbicide mecoprop in various Swiss lakes and in the North Sea. *Environmental Science and Technology* 32(Jan. 1):188.

Halling-Serensen, B., *et al.* 1998. Occurrence, fate and effects of pharmaceutical substances in the environment–a review. *Chemosphere* 36(January):357.

Hartmann, A. In Press. Identification of fluoroquinolone antibiotics as the main source of *umuC* genotoxicity in native hospital. *Environmental Toxicology and Chemistry* 17:3.

Hartmann, A., *et al.* 1997. Determination of the fluoroquinolone antibiotic ciprofloxacin in hospital and municipal water. *Society of Environmental Toxicology and Chemistry*. San Francisco. November.

Heberer, T. 1997. Determination of clofibric acid and N-(phenylsulfonyl)-sarcosine in sewage, river and drinking water. *Journal of Environmental Analytical Chemistry* 3:1.

Heberer, T. *et al.* 1997. Detection of drugs and drug metabolites in ground water samples of a drinking water treatment plant. *Fresenius Environmental Bulletin* 6:438.

Snyder, S., *et al.* 1997. Toxicant identification and evaluation (TIE) of endocrine disrupters in aqueous mixtures. *Society of Environmental Toxicology and Chemistry*. San Francisco. November.

Steger-Hartmann, T., K. Kummerer, and A. Hartmann. 1997. Biological degradation of cyclophosphamide and its occurrence in sewage water. *Ecotoxicology and Environmental Safety* 36:174.

Temes, T.A. In press. Occurrence of drugs in German sewage treatment plants and rivers. *Water Research*.

Further Readings:

1997. National Environmental Policy Act: Revision of policies and procedures. *Federal Register* 62(July 29).

Burhenne, J., *et al.* 1997. Chemotherapeutic agents: Primary photoproducts and half-lives. *Environmental Science and Pollution Research* 4:10.

_____. 1997. Chemotherapeutic agents: Isolation and structural elucidation of polar photometabolites. *Environmental Science and Pollution Research* 4:61.

Knepper, T.P., and K. Haberer. Auftreten von phenylsulfonamiden in kläranlagen–,oberflächen– und trinkwässern(Occurrence of phenylsulfonamides in sewage–, surface–and tap waters). *Vom Wasser* 86:263. (Abstract in English).

Renner, R. 1998. Human estrogens linked to endocrine disruption. *Environmental News* 32(Jan. 1):8.

Sallustio, B.C., *et al.* Genotoxicity of acyl metabolites formed from clofibric acid and gemfibrozil: A novel role for Phase-II mediated bioactivation in the hepatocarcinogenicity of the parent aglycones? *Toxicology and Applies Pharmacology* 147(December):459.

Schlett, C., und B. Pfeifer. 1996. Bestimmung von steroidhormonen in trink–und oberflächenwässern. (Determination of steroidal hormones in drinking and surface water samples.) *Vom Wasser* 87:237. (Abstract in English).

Stan, H.J., and T. Heberer. Pharmaceuticals in the aquatic environment. *Analusis* 25:20.

Stumpf, M., *et al.* 1996. Nachweis von arneimittelruckständlagen und flieb gewässern. (Determination of pharmaceutics in sewage plants and river water). *Vom Wasser* 86:291.

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