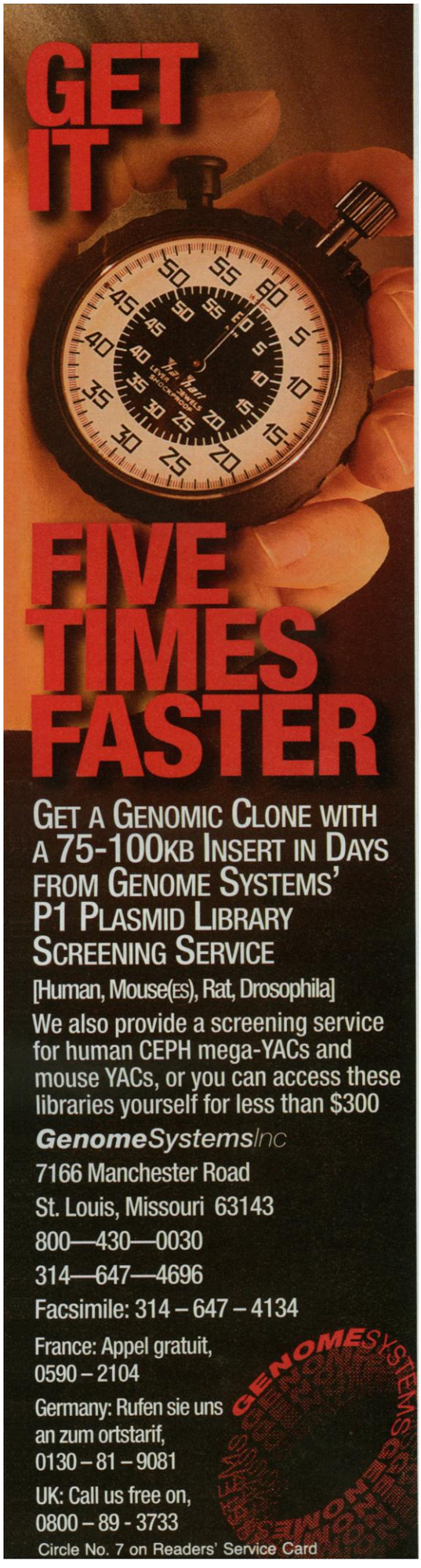

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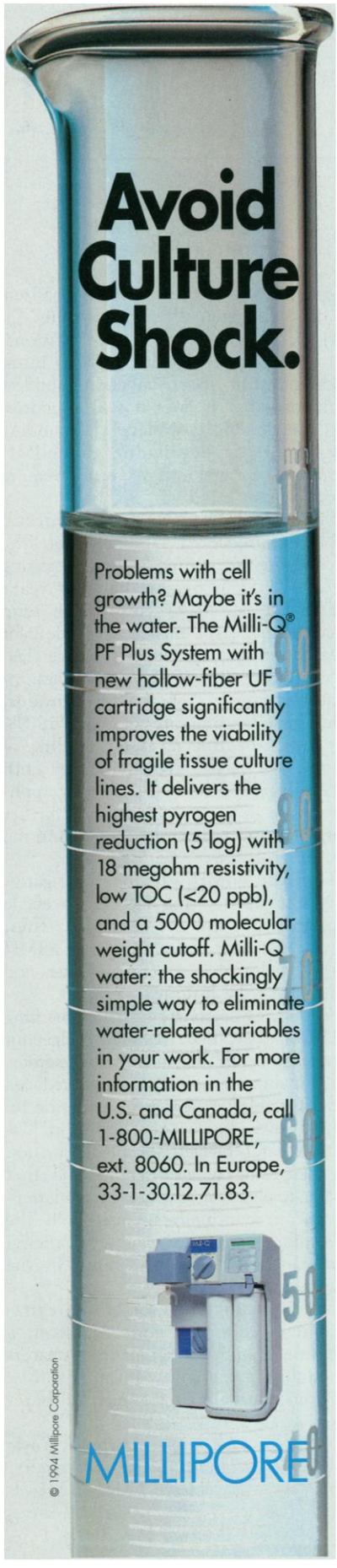

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Carcinogenicity of Chloroform

Philip H. Abelson's 8 April editorial "Chemicals: Perceptions versus facts" suggests that the Environmental Protection Agency's (EPA's) assessment of cancer risk from chloroform in drinking water is based on data for hepatocellular pathology in mice given the maximum tolerated dose (MTD) for chloroform by gavage in corn oil (*1*). The editorial is misleading in several respects.

First, EPA's cancer risk assessment of chloroform ingestion from drinking water is based on a finding of elevated kidney tumors in rats administered chloroform in drinking water (*2*). EPA has calculated that 60 parts per billion (ppb) of chloroform (and not 4.3 ppb, as might be surmised from Abelson's editorial) corresponds to an increase in lifetime cancer risk of 1 in 100,000. (Minnesota policy is that incremental cancer risks of 1 in 100,000 or lower are negligible risks. Therefore, 60 ppb is the Health Risk Limit in rule for chloroform in drinking water in Minnesota.)

Second, rodent data for chloroform administered in drinking water or by gavage indicate elevated tumors at half or less of the maximum tolerated dose (MTD). Abelson does not mention this, again giving the unwary reader the erroneous impression that the EPA consensus opinion on chloroform carcinogenicity from drinking water is based on a pathological response to a single high dose of chloroform administered to mice by gavage in corn oil.

Third, Abelson juxtaposes a risk number (1 in 100,000) and concentrations of chloroform (4.3 ppb versus 1,800,000 ppb) in such a way that one is led to believe that the corn oil gavage experiment and the drinking water experiment yield estimates of the carcinogenic potency of chloroform that disagree by many orders of magnitude. The potency estimates from the two experiments differ by a factor of 14.

Risk-assessment bashing may be fun, but *Science* could better serve its public by engaging in a more reasoned dialog. EPA's policies on cancer risk assessment, particularly its methodology for low-dose extrapolation in the absence of convincing evidence of genotoxicity, should be examined, but fairly.

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References

1. *Report of the Carcinogenesis Bioassay of Chloroform* (NTIS No. PB264018/AS, National Cancer Institute, Bethesda, MD, 1976).
2. T. A. Jorgenson *et al.*, *Fundam. Appl. Toxicol.* **5**, 760 (1985).

Response: Messing *et al.* refer to a paper by Jorgenson *et al.* (*1*) which describes experiments that provide the basis on which EPA regulates the level of chloroform in water at 60 ppb. The nature of the experimental findings and their subsequent use in standards provide further testimony of the need for EPA to improve its procedures for risk assessment and management.

While some drinking water potency risk estimates for chloroform are based on the Jorgenson *et al.* 1985 drinking water study in male Osborne-Mendel rats, the risk estimates for airborne chloroform are more stringent and are based on the female mouse liver tumor kidney response (*2*).

In the crucial Jorgenson experiments, chloroform was administered in drinking water at concentrations of 0 (controls), 200,000, 400,000, 900,000, and 1,800,000 ppb, respectively. The animals that received chloroform all lived longer than the controls. At the end of 2 years, only 12% of controls were alive, while 66% of the highest dosed animals survived.

The occurrence of tumors in 10 different tissues was examined. In some tissues, more tumors were found in controls than in the highest dosed animals. For example, there was more than twice the rate of thyroid tumors in the controls. The total rate of tumors was slightly higher in the controls than in the highest dosed animals. However, in animals that were given a dose of 1,800,000 ppb, there were increased kidney tumors (7/50). The excess of kidney tumors was the basis on which EPA estimated human risk.

The significance of kidney tumors at high chloroform doses is doubtful. The incidence of nontumor pathology of the kidney was high in all animals regardless of dose. The incidence of nephropathy was 91% in the control group and 92% in the animals that received a dose of 1,800,000 ppb. Nephropathy includes regenerative hyperplasia. Chloroform is not a genotoxic substance. Thus, formation of the kidney tumors, which were tiny, was probably related to cellular proliferation.

The EPA employed its unproved "conservative" mathematical model to extrapolate to humans from a dose of 1,800,000 ppb in rats and arrived at a regulatory level of 60 ppb. Included is the assumption that humans are sevenfold more susceptible to cancer than are the nephropathy-prone Osborne-Mendel rats.—***Philip H. Abelson***

References

1. T. A. Jorgenson *et al.*, *Fundam. Appl. Toxicol* **5**, 760 (1985).
2. *Report of the Carcinogeneis Bioassay of Chloroform* (NTIS No. PB264018/AS, National Cancer Institute, Bethesda, MD, 1976).

Cotylorhynchus: Not a Mammal

In the Random Samples item "Natural history in New York" (25 Mar., p. 1688), a 250-million-year-old fossil amniote (*Cotylorhynchus*), a mammalian ancestor, is said to be grouped in an exhibit "with more modern mammals." However, this fossil species is not a mammal. Everyone knows what the mammalian characters are—hair, warm-bloodedness, nursing the young with milk, a mammalian jaw and mammalian teeth, and many other characteristics by which mammals differ from ancestral amniotes, usually classified with the reptiles. Indeed, *Cotylorhynchus* has always been classified with that primitive group of reptiles, the *Pelycosauria*.

There are now two systems of ordering organisms in use—Darwinian classification, by which organisms are grouped according to both similarity and genetic relationship, and Hennigian ordering, by which organisms are grouped according to the branch of the phylogenetic tree on which they occur. These two methodologies sometimes come to much the same conclusions, but when a branch is very long, its stem groups are usually very different from its crown groups, and the stem groups are often far more similar to groups on other branches and would be classified with them in a Darwinian classification.

Both systems of classifying are legitimate, the preference depending on what one wants to demonstrate, phylogeny or closeness of relationship. Therefore, Hennigian ordering does not replace Darwinian classification. And even though *Cotylorhynchus* is on the branch that ultimately gave rise to the mammals, it is definitely *not* a mammal.

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■

DNA Handedness

Referring to "A new twist in the tale of nature's asymmetry" by David Bradley (Research News, 13 May, p. 908), I would like to draw readers' attention to the fact that the two DNA helices shown in the figure are both right-handed! As an early observer of left-handed DNA (*1*), I must also challenge the statement that "Only the right-handed DNA helix exists in nature."

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References

1. F. M. Pohl and T. M. Jovin, *J. Mol. Biol.* **67**, 375 (1972).

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