Letters

Advertising Prescription Drugs

According to Gina Kolata's article "Prescription drug ads put FDA on the spot" (News and Comment, 22 Apr., p. 387), certain manufacturers of prescription drugs have proposed that they be permitted to engage in direct consumer advertising. Their proposal is based on the assumption that direct consumer advertising would prove effective in increasing a company's market penetration. In that regard the proposal is ironic, because its underlying assumption (consumer advertising will be effective) clashes with an assumption that underlies a legal doctrine long championed by the drug industry—the "learned intermediary" doctrine. Under the learned intermediary doctrine a manufacturer of prescription drugs owes no duty to the consuming public to warn the public of a drug's side-effects or contraindications; the manufacturer owes a duty only to the prescribing physician. The doctrine is based on the assumption that the prescribing physician acts as a learned intermediary between the manufacturer and the consumer. Consequently, as a medical expert, the prescribing physician is in the best position to weigh the risks of the drug against the benefits of the drug. The choice that the physician makes is an informed one based on his or her knowledge of the patient and the palliative (*1*). Thus under the doctrine, once the drug manufacturer has adequately warned the medical community, it has discharged its duty.

Drug manufacturers have used this doctrine to shield themselves from liability even in those cases where they have inadequately warned or have failed to warn the medical community. For example, in *Douglas* v. *Bussabarger* (*2*), the prescribing physician failed to read an allegedly inadequate warning and instead relied on his own medical knowledge. The court in ruling in favor of the drug company noted that the company's failure to adequately warn was not the proximate cause of the plaintiff's injury. Since the company owed no duty to the plaintiff, the plaintiff, under the learned intermediary doctrine, had to establish not only that the warning to the medical community was inadequate, but also that the prescribing physician relied on that warning in prescribing the drug. Inasmuch as the physician did not read the inadequate warning, a causal link between the warning and the plaintiff's injury could not be established.

If drug companies are permitted to advertise prescription drugs in much the same manner that they now advertise over-the-counter elixirs, then the rationale underlying the learned intermediary doctrine makes little sense. Direct consumer advertising then should have the effect of not only increasing competition but also of increasing a drug company's exposure to product liability law suits.

ROBERT P. CHARROW
College of Law,
University of Cincinnati,
Cincinnati, Ohio 45221

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2. *Douglas* v. *Bussabarger*, 73 Wash. Rep., 2nd ser. 476; 438 Pac. Rep., 2nd ser. 829 (1968) (en banc).

Antiviral Agents

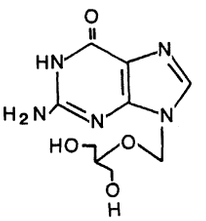
In his article about the antiviral symposium held at the recent meeting of the American Chemical Society (Research News, 15 Apr., p. 292), Thomas H. Maugh II discusses acyclovir and adenine arabinonucleoside (ara-A), two nucleoside analogs that have been approved by the Food and Drug Administration for systemic use as antiviral agents.

Maugh writes that "Acyclovir penetrates the skin more readily but it, like ara-A, is easily degraded by an enzyme called adenine deaminase that is found throughout the body." This statement errs on two counts. Acyclovir has no 6-amino substituent to be deaminated. Furthermore, the enzyme that deaminates ara-A is adenosine deaminase, not adenine deaminase.

Maugh also states that "In the cell, both drugs are activated by a viral enzyme, thymidine kinase, which converts them to a triphosphate ester that inhibits a viral DNA polymerase." Virally induced thymidine kinase does not detectably phosphorylate ara-A (*1*). However, it has been shown to be phosphorylated by two cellular kinases: adenosine kinase (*2*) and deoxycytidine (deoxynucleoside) kinase (*3*). The viral thymidine kinase converts acyclovir to its monophosphate, not its triphosphate as stated. Cellular kinases further phosphorylate this monophosphate to the triphosphate (*4*).

Maugh then says, "Viruses that lack this enzyme are resistant to chemotherapy with these drugs." If "this enzyme" refers to viral DNA polymerase, such resistant viruses have not been reported. Some laboratory-derived resistant strains have a modified DNA polymerase, but none lack this enzyme. If "this enzyme" refers to viral thymidine kinase, the statement is correct for acyclovir, but not for ara-A.

With respect to the compounds that are still at preclinical stages, there is an error in the structural formula for 9-(1,3-dihydroxy-2-propoxymethyl)guanine (DHPG). This compound is a congener of acyclovir, and its correct formula is



THOMAS A. KRENITSKY
LILIA BEAUCHAMP
Wellcome Research Laboratories,
Burroughs Wellcome Company,
3030 Cornwallis Road, Research
Triangle Park, North Carolina 27709

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3. T. A. Krenitsky, J. V. Tuttle, G. W. Koszalka, I. S. Chen, L. M. Beacham, J. L. Rideout, G. B. Elion, *ibid.* **251**, 4055 (1976).
4. W. H. Miller and R. L. Miller, *ibid.* **255**, 7204 (1980); *Biochem. Pharmacol.* **31**, 3879 (1982).

Improved Weather Prediction

Richard A. Kerr's article "The race to predict next week's weather" (Research News, 1 April, p. 39) is an excellent review of the present state of the science of large-scale numerical weather prediction (NWP). Several of its implications, however, deserve further discussion. Kerr emphasizes that resolution differences are helping the European Center win the prediction "race." He writes that "the race . . . may close . . . as NMC [the National Meteorological Cen-

ter] brings on its Control Data CYBER 205." Later he hints that the European Center may well jump ahead again when they get their next-generation computer. One source is quoted as suggesting that this added computer power "would be to increase the model's resolution."

The "race" for bigger computers should not be simply a matter of increasing model resolution. Using a bigger computer to increase resolution is analagous to using a bigger hammer on a small nail just to drive it in further or faster. Brute force! A better approach might be to redesign the nail in order to better match it to both the wood and the hammer. In the case of NWP, resolution (the hammer) is only part of the problem. Data quantity and quality and model physics (the nails) are equally important. The outcome of the race will depend not only on who has the best computer but on who uses it best.

Kerr implies that the race centers on lengths of usable forecasts and states that the ultimate length is about 10 to 12 days. Most users of weather forecasts would prefer that accuracy be improved on all time scales. Improvements in short-range forecast accuracy are just as important as extending the length of present skill from 6 to 12 days.

Finally, Kerr implies that all improvements in weather forecast accuracy are tied to NWP. Surely NWP is important, but so are making sensible inferences from the numbers, displaying the forecast well, and making good use of the prediction. Without parallel improvements in these less glamorous aspects of weather prediction, the winners of any race for the best NWP may find they are only ahead at the first lap.

ALAN I. WEINSTEIN
Naval Environmental Prediction Research Facility, Department of the Navy, Monterey, California 93940

Metric System in Britain

I hope you will permit a native of the United Kingdom and visitor to your shores to comment on Edward Leete's letter (29 Apr., p. 462) about the lack of use of the metric system in the United Kingdom.

The whole metric system is very firmly established in Britain, but its introduction, as prudence would dictate, involves a long changeover period during which imperial and metric measures coexist. Nevertheless, most prepacked domestic goods are now sold by metric weight (our 2-pound bag of sugar weighs 1 kilogram) and volume (the gallon can actually contain 5 liters); even booze comes in 75-centiliter bottles. Petrol is sold by the liter, and distances are beginning to be given in kilometers.

The clincher is that imperial measurements are simply not taught in school. Within a short time of my 10-year old daughter's first exposure to her American school she confidentially asked me if this "yard" that Americans talked about was something like a meter.

Leete's suggestion that we might be enamored of the mile because of Roger Bannister's athletic achievement a generation ago takes no account of the fact that the British currently have world-ranked athletes who compete at distances of 100, 200, 400, 800, 1500, 5000, and 10,000 meters.

Of course, London still has the Mile End Road, Blackpool its Golden Mile, and if you give someone an inch they're bound to take a yard; but I suppose some things will never change.

DAVID MOORE*
Department of Biology, University of North Carolina, Chapel Hill 27514

*Present address: Department of Botany, Manchester University, Manchester, England M13 9PL.

Organometallic Clusters

So far as I am aware, attempts to prepare practical catalysts by depositing organometallic clusters on supports have been unsuccessful, and the effort could now be likened to an aging, promising young man who keeps on promising for too long. The article by Thomas H. Maugh II (Research News, 6 May, p. 592), reports this sentiment, but it may not be clear that my opinion applies to the preparation of useful catalysts and not to matters of scientific interest. Indeed, I have been involved in a small way in two projects using metal clusters, one in collaboration with D. F. Shriver and the other with J. B. Butt and J. B. Cohen.

ROBERT L. BURWELL, JR.
Ipatieff Laboratory, Department of Chemistry, Northwestern University, Evanston, Illinois 60201

Erratum: In Thomas H. Maugh II's Research News article "New agents active against herpesviruses" (15 Apr., p. 292), Raymond Shinazi was incorrectly reported to have found that 2'-fluoro-5-iodoarabinosylcytosine (FIAC) is "the most potent and effective drug known to date" against herpes encephalitis in mice. Shinazi found that 2'-fluoro-5-methylarabinosyluracil (FMAU) is the most effective drug against this disease.