The article EM9118 reprinted below and overleaf is of statistical interest in that it illustrates the importance to society of (correct) data-based Answers to Questions.

∗ It also reminds us that differing Answers may be obtained even when analyzing data from investigations involving the proper use of statistical methods.
  ○ In addition, the article indicates possible consequences of differing Answers from the same data.

EM9118: New York Times, December 24, 1991, page C3

MEDICAL SCIENCE: THE DOCTOR'S WORLD

Hidden Discord Over Right Therapy

By LAWRENCE K. ALTMAN, M.D.

A BITTER dispute has erupted among a team of scientists at the University of Pittsburgh over opposite conclusions drawn from a study of middle-ear infection, a common and potentially serious childhood condition.

One side concluded that a widely prescribed antibiotic, amoxacillin, was effective for the condition; the other side said it did not work. But the dissenting report was not published until last week, nearly five years after the original report calling the treatment effective appeared.

The split has provided a rare glimpse into medical and academic politics and how they can converge to influence standard treatments. The conflict has involved two Congressional hearings; investigations by the National Institutes of Health, the Federal agency that paid for the research; inquiries from the sponsoring university, and conflicting reports in rival medical journals.

Middle-ear infection, which can be painful, strikes about two of every three children in the United States by the age of 3. A build-up of fluid in the infected ear can lead to impaired hearing and delayed language and speech development.

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The issue seemed settled in 1987 when Dr. Charles E. Bluestone, who led the study, and members of his team reported in *The New England Journal of Medicine* that amoxacillin was effective for middle-ear infections.

In its Dec. 18 issue, *The Journal of the American Medical Association* published a dissenting report from a group headed by another member of the team, Dr. Erdem I. Cantekin. His report, analyzing data from the same study, had been rejected by *The New England Journal of Medicine* when it was written five years earlier.

In criticizing Dr. Bluestone's study, Dr. Cantekin said it relied too heavily on techniques that were prone to bias in examining an ear. Dr. Cantekin concluded that amoxacillin did not work for middle-ear infections.

> A rare look at how medical politics affects standard treatment.

The data, though several years old, still apply to current practice, and it is up to doctors to decide on the merits of amoxacillin for middle-ear infection, *The Journal of the American Medical Association* said in an unusually long editorial titled "The Cantekin Affair."

The affair exposes the disagreement that often lies hidden behind standard therapies and a greater degree of uncertainty about them than the medical profession is willing to acknowledge.

The extraordinary delay in publishing Dr. Cantekin's report also highlights several important points about medical politics: academia's surprising aversion to dissent; the strong ties between scientific journals, academia and the drug industry; professional jealousies over credentials, and the unresolved issue of how and when critics can use data from publically financed studies in which they participate.

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Academia, scientific journals, practising doctors and industry are heavily interdependent.

Journals are a natural outlet for researchers who want to report advances and new findings, some of which can have strategic importance to practising doctors and patients.

Journals also play a crucial role in academic politics. Faculty promotions in medical schools are often geared to publication in prestigious journals. Editors of journals generally come from the ranks of academia.

Leading scientific journals profit handsomely from drug company advertisements, and the influence of industry on such publications has rarely been studied.

Good editors should welcome controversy because it can be so instructive. But editors tend to consider themselves as professors, not journalists, and they seldom take the iniative in reporting academic disputes like the one in Pittsburgh.

In 1986, both groups submitted separate reports to *The New England Journal of Medicine*. Dr. Cantekin told the journal's editor, Dr. Arnold S. Relman, that his manuscript was a re-analysis and re-interpretation of the paper that Dr. Bluestone had submitted a month earlier.

Journal editors customarily send a submitted manuscript to independent experts for evaluation to help determine whether to publish it. But in the Pittsburgh conflict, Dr. Relman viewed the primary issue as determining which group had the right to publish, and he decided to publish only one version.

"There could be only one responsible investigator or team of investigators officially recognized by the sponsoring institutions," Dr. Relman said.

So Dr. Relman asked officials at the University of Pittsburgh and Children's Hospital, where many of the patients in the study were treated, to decide which group had written the official version. They chose Dr. Bluestone, and Dr. Relman rejected Dr. Cantekin's paper outright in a decision he has since defended.

Dr. Relman was wrong in retrospect, Dr. Drummond Rennie, a deputy editor of *The Journal of the American Medical Association* wrote, because he could have sent both Dr. Bluestone's and Dr. Cantekin's papers out for review. If both were deemed worthy of publication, they could have been published with an editorial outlining the dispute from the start.

Dr. Cantekin refused to give up, and he paid a heavy price for becoming a whistle-blower. A few weeks after submitting his dissenting paper in 1986, Dr. Cantekin saw his career come to an abrupt halt. A decade after Dr. Bluestone recruited him to work with him in Pittsburgh, Dr. Cantekin was dismissed as research director of the university's center for studies of middle-ear infections.

Academia has traditionally boasted about its role in promoting independent thought, challenging prevailing theories, and fostering free speech. Indeed, throughout history, dissent over interpretations of common data has served to clarify scientific issues.

Yet medical leaders have also failed to seize on such disputes as ways to advance science.

(*continued overleaf*)

Instead of serving the public interest, academia sometimes acts to protect its own interest by squelching dissent, stifling criticism and avoiding public contoversy.

"The institution is unlikely to decide a dispute about the matter on the basis of the quality of its science, but on the basis of institutional hierarchy," Dr. Rennie wrote in chronicling the Cantekin dispute.

Until recent decades, scientists tended to work alone and their disputes were generally directed at rivals, not teammates. But the growing complexity of science has led to teams of researchers, headed by a principal investigator, and the creation of teams increases the chances for internal disputes.

The public now pays for most of the scientific work that is carried out in academic centers, even private ones. Yet many universities have developed strong ties to industry, raising the issue of possible conflicts of interest.

This issue emerged in the Pittsburgh dispute because Dr. Bluestone had not declared that he had received $260,000 in honorariums and $3.5 million in grants from drug companies to the middle-ear infection research center. The Federal Office of Scientific Integrity found "the appearance of conflict of interest."

Also, as medical research has become more sophisticated, medical schools have broadened the scope of their faculties to include more scientists from allied fields. Many scientific papers from academic centers include authors who hold degrees other than an M.D.

Dr. Cantekin's degree is in biomedical engineering. It was therefore not unusual that he had climbed the academic ladder to become a full professor in the medical school and that he would have been a co-author of Dr. Bluestone's paper if he had agreed with its conclusions.

In evaluating research results, scientists often say the quality of the data is what is important, not the author's degree. But in the Pittsburgh dispute, Dr. Cantekin's report was criticized on grounds that he was not a medical doctor.

The Pittsburgh affair adds fuel to a call for journals routinely to remove the names and degrees of authors when their manuscripts are sent for independent review as a step to avoid such bias.

Being able to duplicate results is the cornerstone of science. But because most studies are expensive and time-consuming, few are actually repeated.

How teams handle questions and debates among themselves about the organization and analysis of data can have important bearing on the only published conclusions. Also, because there is not space in journals to publish all the data from a study, accessibility to the primary data can be an important issue when public accountability is called for.

But there are few rules on who owns the data from publically financed research projects and how they should be shared.

Scientists have traditionally aired their differences through letters to the editor. But because of their brevity, such letters may not be an adequate way to present additional data. Further, not all journals publish letters or have sections devoted to comment and criticisms.

In the case of middle-ear infections, new studies may clarify amoxacillin's effectiveness – but only if all authors agree on the conclusions.

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The article EM9118 reprinted above and overleaf is used in Figure 1.5 of the STAT 220 Course Materials.

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