Government/Industry Dispute Brain Tumor Risk

For 2 years epidemiologists have been analyzing a putative link between brain tumors and work in the petrochemical industry; results are conflicting

In July this year William Lloyd, of the Occupational Safety and Health Administration (OSHA), Washington, D.C., made an urgent telephone call to Irving Selikoff at his office in the Mount Sinai School of Medicine, New York. Lloyd's purpose was to argue for the expeditious organization of a conference that would evaluate the risk of brain tumors in workers in the petrochemical industry. Selikoff was persuaded that speed was essential, and he managed to arrange such a conference through the offices of the New York Academy of Sciences, the whole process taking a little over 2 months as compared with the usual 1½ years.

"We wanted to know how much evidence there is suggesting an occupational link with brain cancer," explained Selikoff while introducing the hurriedly convened meeting earlier this month, "we wanted to have the best scientific minds here so that we could evaluate the evidence and see whether or not there is a problem." At the end of the 3-day meeting, which was strikingly polarized between the views of government researchers and those of the petrochemical industry, the verdict was at best equivocal: case not proved, but neither was it dismissed.

The meeting heard four reports from government epidemiologists (from OSHA, the National Institute for Occupational Safety and Health (NIOSH), and the National Cancer Institute) and the same number from industrially supported investigators (Dow Chemical, Gulf Oil, Du Pont, and a consortium of United Kingdom oil refineries). Dow and Gulf facilities were the subject of two of the government surveys. Without exception, the government studies were said to indicate roughly a twofold elevated risk of primary brain tumors among petrochemical workers. The industrially supported investigations just as unanimously failed to detect any increased risk. These disparities provoked lively debate among the protagonists.

To the innocent onlooker the crisp patterns of the fallen chips appeared at first sight to betray blatant gerrymandering. Both sides have a lot at stake: the industry its reputation and its possible capital burden in further cleaning up hazardous pollutants, and OSHA/NIOSH its future as the guardian of the workers' well-being. Selikoff, however, was less cynical: "You don't have to be suspicious about this," he said. "There are too many people involved in the investigations for anyone to think they could get away with bent work." Eula Bingham, a toxicologist and Assistant Secretary for OSHA, also took a sanguine view: "I have never been to a scientific meeting when there was not conflicting data from epidemiologists. There are often many difficulties with this kind of work."

The problems faced by investigators in this particular issue unquestionably are enormous. Numbers of cases are relatively few, making statistical analysis somewhat insecure. The work environments in the studies are many and varied, with people frequently switching from job to job during their working lives. And the task of doing retrospective analyses by tracing work and death records back through 40 and more years is horrendous. All of which makes for less than exact analysis. There are also methodological issues that confound comparisons between different studies.

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The saga that eventually led to Lloyd's telephone call to Selikoff began just 2 years ago, shortly after Thanksgiving. A worker with Union Carbide in Texas City contacted the local OSHA office, to suggest that the brain tumor from which he was suffering might be related to his occupation. A young industrial hygienist at the office began investigating the complaint, and he very soon uncovered five more brain tumor cases. When a report reached the OSHA headquarters in Washington, D.C., the following January, Victor Alexander immediately dropped other work he had in hand and went to the Texas City facility. His precipitous response appeared to be justified, as, with the considerable help of the Union Carbide plant physician, the total soon reached ten. The Texas City Brain Tumor Turmoil—as the plant manager dubbed it—was on.

With the aid of NIOSH research resources, Alexander eventually traced 18 deaths from primary brain tumors among the 6800 white males who had worked at the plant since 1941. According to Alexander's calculations, these cases represent 21 percent of brain tumor deaths in Galveston County during the period under study. By contrast the work force comprises just 10.3 percent of the county's working population. "This indicates a plant-wide doubling of risk of developing a brain tumor in workers at this facility," concludes Alexander. He also points out that if the active agent or agents were localized to one plant process, then the risk at that point would be substantially higher than the global twofold elevation.

The OSHA/NIOSH investigation at Union Carbide led directly to an indication of a similar problem at nearby Dow Chemical. Lloyd had death certificates for Galveston and neighboring counties in his office in Washington in the summer of 1979. Looking through them for brain tumor deaths in Brazoria County, where the Dow plant is located, he noticed that 11 of the 32 in his list showed Dow Chemical as "usual employer." Gordon Reeve, a NIOSH investigator, took up the lead and, with a case-control study, he showed that for residents of the area, the risk of dying from a brain tumor was doubled for those who had ever worked at Dow. Once again, an apparent twofold elevation of risk.

Dow has a long-established and active epidemiological department and as soon as word leaked out of a possible link between brain tumors and the chemical industry, investigators there began their own study. Ralph Cook, director of epidemiology for Dow, adopted a different approach from Reeve's. He asked the question, do the brain tumor victims at Dow show any clustering of job types

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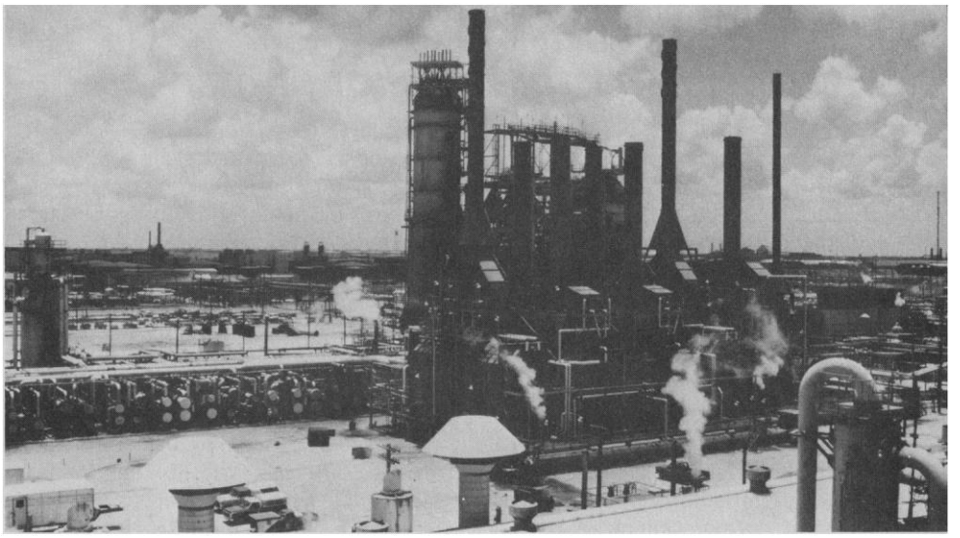
or occupational histories? This project would have both confirmed elevated risk and given an indication of the source of the hazard. The results of this case-control study on 24 brain tumor deaths were, however, negative. "Preliminary calculations suggest that the brain tumors observed to date may not exceed the number one might expect based on U.S. population mortality statistics," reported Cook.

Meanwhile, studies were under way at Du Pont and Gulf Oil. Bruce Karrh, corporate medical director for Du Pont, told the New York meeting that the results of his company-wide survey indicate that "the incidence of brain tumors in the company is essentially the same as in the general population." The study involved 134 brain tumor deaths from 2,224,972 person years observed, as against 132.5 expected, according to Karrh. And Chai-Pang Wen, from the Medical and Health Resources Division of Gulf, reported on a cohort study of all employees who worked at the Texas refinery between 15 June 1935 and December 1979. "The current study represents the largest retrospective cohort study of refinery workers reported to date in North America in terms of the length of observation (44 years) and person-years of observation (408,073)," said Wen. "The results do not support an increased risk of brain tumor among refinery workers as reported elsewhere," he claimed, pointing out that the 25 brain tumor deaths observed compared favorably with his estimate of 27.3 expected.

The Gulf site was the subject of the second direct contradiction of results presented at the meeting. Terry Thomas, of the National Cancer Institute, has examined the records of active members of the Oil, Chemical, and Atomic Workers Union (OCAW) in three oil refineries in the Beaumont-Port Arthur area of the Texas Gulf Coast, one of them being the Gulf facility. With the caveat that her results cannot be seen as conclusive, Thomas claimed that her study "suggests an association between brain cancer risk and exposures in the oil refinery industry." The other two facilities in the study were Texaco and Mobil, and the detected excess of brain tumors in all three sites was 33 cases observed against 15.6 expected.

The last contribution from the government contingent was from NIOSH investigator Richard Waxweiler, and he too used OCAW records as a source of data. In the Amaco refinery he examined he counted four deaths from brain tumors, which compares with the 1.8 that would be expected in the population: the two-fold elevation emerges once again. This, incidentally, gives an indication of the small numbers with which some researchers are forced to deal.



An oil refinery in the Texas Gulf Coast region

Department of Labor Assistant Secretary for OSHA Eula Bingham describes petrochemical plants and oil refineries as "carcinogen-rich environments."

These, then, are the results, the striking disparities presumably resulting in part from the use of different data bases and different methods of analysis. How is this conflict to be resolved? One way—the industrialists'—is simple.

Because data on workers past and present are typically not readily available, some preliminary epidemiological studies automatically inflate the apparent risk of death from conditions such as cancer. All epidemiologists are aware of this problem, but the measure—known as the proportionate mortality ratio (PMR)—can be used as a quick and rough test for illuminating possible hazards. When full data for the population at risk are at hand, a more reliable measure—the standardized mortality ratio (SMR)—can be made. In remarks at the end of the conference, Michael Utidjan, of Union Carbide, said, "What we have seen over the past few days is a series of government PMR-type studies that are suggestive of a problem and a series of industrial SMR-type studies that are essentially negative." In other words, Utidjan is implying that when the preliminary studies are refined, the built-in bias of PMR measures will vanish, and with it may go the putative brain tumor risk. Utidjan is not saying the apparent risk will disappear, just that it may.

The OSHA/NIOSH response to the disparity is, as might be expected, the reverse of this scenario. "You've seen a consistent indication of elevated risk from a number of sites," argues Alexander. Of his Union Carbide study, Alexander claims that it is "100 percent solid." Lloyd agrees that this one is "screwed down pretty tight." And early SMR figures from NIOSH do apparently confirm the preliminary findings at this plant. The government researchers are also sharply critical of the negative studies. First of all because negative epidemiology is always less secure than positive results. But second, and more important, because the industrial surveys were on large populations, often including clerical and other staff who are not necessarily at risk. Such "dilution" can obscure real increases in cancer risk, especially if the incidence is relatively low, as it is with brain tumors. This criticism applies particularly to the U.K. study in which data from eight refineries throughout the country were pooled.

Cook, Karrh, and Wen nod acknowledgment in this direction, but to the evident annoyance of the OSHA/NIOSH investigator the industrialists downplay its impact on their results.

For the workers at potential risk in the petrochemical plants, 2 years of epidemiological research must seem a very long time, but it is clearly insufficient for the investigators in which to assemble and analyze data so that their results can unequivocally evaluate the magnitude of the hazard, if any exists. If the risk proves to be real, then the scale of the problem is likely to be small (brain tumors are an uncommon form of cancer). Unless, as seems possible from some incidental comments at the meeting, brain tumors turn out to be a signal of a wider problem: there are indications of raised incidences of skin and gastrointestinal cancers, for instance, at oil refineries and petrochemical plants currently being studied. This would not be so surprising because, as Bingham said, "Such places are carcinogen-rich environments."

—ROGER LEWIN