Riddle of the Nobel Debate

Politics in Stockholm may have forced a would-be laureate off the CAT scanner ticket

Each Nobel Prize has its winners and losers, and this year's award in physiology or medicine is no exception. Several would-be laureates who worked on the early development of computerized axial tomography (or CAT scanning) are quietly wondering just what went wrong.

One such person with an unusually bad case of after-the-fact blues is William H. Oldendorf, a neurologist at the University of California School of Medicine, Los Angeles, and the Brentwood Veterans Administration Hospital. Oldendorf wrote the first paper on the subject of radiographic tomography (1961), received the earliest patent (1963), and shared the 1975 Lasker Award for his "original conception of a scanning system" with Godfrey N. Hounsfield, who along with Allan M. Cormack won the Nobel this year.

"Anybody who goes into science expecting to win the Nobel Prize is about as realistic as a person going to Las Vegas to get rich," Oldendorf says. "But my feeling is that I should be preparing to go to Stockholm."

What makes this feeling especially hard to live with is the fact that many Stockholm watchers, including a previous laureate, say Oldendorf was actually slated to go to the ceremony this year. (Laureates are among the select few who can make nominations for the prize.) One knowledgeable observer says Oldendorf got bumped on the day the prize was announced during a heated debate in the Nobel Assembly.

If true, the incident affords an unprecedented glimpse into the politics of the selection process. Reasons given for the omission of Oldendorf include consideration by the Nobel Assembly of the effect that awarding the prize to two Americans and one Englishman would have on the multimillion dollar litigation over patent rights now under way between U.S. and British manufacturers of CAT scanners. Another is discrimination against a physician-clinician by the basic science faction of the Nobel Assembly.

Such speculation was touched off by what can only be described as an odd event in the otherwise colorless ritual for announcing the prize at the Karolinska Institute in Stockholm. When the official announcement was made on 11 October, it was an hour late, and the press release given to reporters was only in Swedish—not Swedish, German, French, and English as in previous years. "There was no time to check with the translators," Jan Lindsten, secretary of the Nobel Selection Committee, told one reporter after announcing the prize. None of the Assembly members was willing to describe the nature of the difficulty. "I have a lot of comments," Georg Klein, chairman of the Assembly, told the same reporter. "But I can't make them."

The picture eventually pieced together by several reporters in Stockholm to explain these events goes like this. The 5-person Committee recommended that the prize go for work done in immunogenetics. When it came before the 64-member full Nobel Assembly, however, that suggestion was vetoed after some debate, and the award was given instead to the well-known Hounsfield of EMI Ltd. in England, who developed the first practical CAT scanner for the company in the early 1970's, and to the virtually unknown Cormack of Tufts University in the United States, who performed early experiments on scanning and wrote a pioneering paper in 1963.

At first glance this explanation seems plausible. Since there is no separate Nobel Prize in biology or biochemistry, the great majority of the prizes in medicine during the past two decades have gone for fundamental insights into the nature of the genetic code and the mechanisms that control its expression. While these have undoubtedly been exciting developments, they are advances not in medicine but molecular biology. This trend is said to have generated a backlash among some members of the Nobel Assembly who feel that clinical breakthroughs have been neglected, and who would thus be willing to back the CAT scanner. It would also explain why the news releases, always printed in advance by the Committee, were not used by the Assembly and impromptu ones substituted.

On closer inspection, however, this explanation is probably wrong, and wrong on several counts. Although it is not popularly appreciated, the Nobel Committee usually recommends more than one team of researchers to the full Assembly and has press releases prepared for each group. "The recommendation to the full Assembly could be for two, three, or even more," Jan Lindsten recently told *Science*. "Of course, it is practical to have as few as possible. As with any democratic process, it is difficult if you come with too many proposals."

These multiple submissions are the result of an 8-month process in which Committee members sift through hundreds of nominations and check the qualifications of candidates. It is unlikely that the full Assembly would substitute its own, unresearched candidate in the closing minutes. It is also clear that the CAT scanner was among the submissions this year. For more than a decade, no radiologist has been part of the 5-person Nobel Selection Committee—until this year, when Ulf Rudhe of the Karolinska Institute joined it. "This is the biggest breakthrough since the invention of the x-ray," Rudhe told a wire-service reporter after the award for the CAT scanner had been announced.

So what took place during the debate? According to one scenario, the Committee recommended that the CAT scanner as well as other research reflecting a more basic approach receive the award. In the Assembly, the usual bickering over the merits of applied or basic research broke out. One strong backer of the CAT scanner in the Assembly is said by several sources to have been Torgny Greitz, director of the Karolinska Institute for Neuroradiology. A deadlock developed that was only broken when backers of the CAT scanner nomination agreed to a concession—that the least "basic" of the three scientists named in the award be eliminated. (According to the code of statutes for the Nobel Foundation, a prize may in no case be divided between more than three persons. In the past decade, trios have received the award in physiology or medicine on eight occasions.) Elimination of a third name also explains the last-minute corrections that held up the news release.

If this is the case, the name sacrificed was in all likelihood William H. Oldendorf, who approached the scanning problem in the 1950's as a clinician troubled by the hazards, morbidity, mortality, and generally poor results of cerebral angiography and pneumonencephalography—techniques for taking x-rays of the brain that require the injection of ra-

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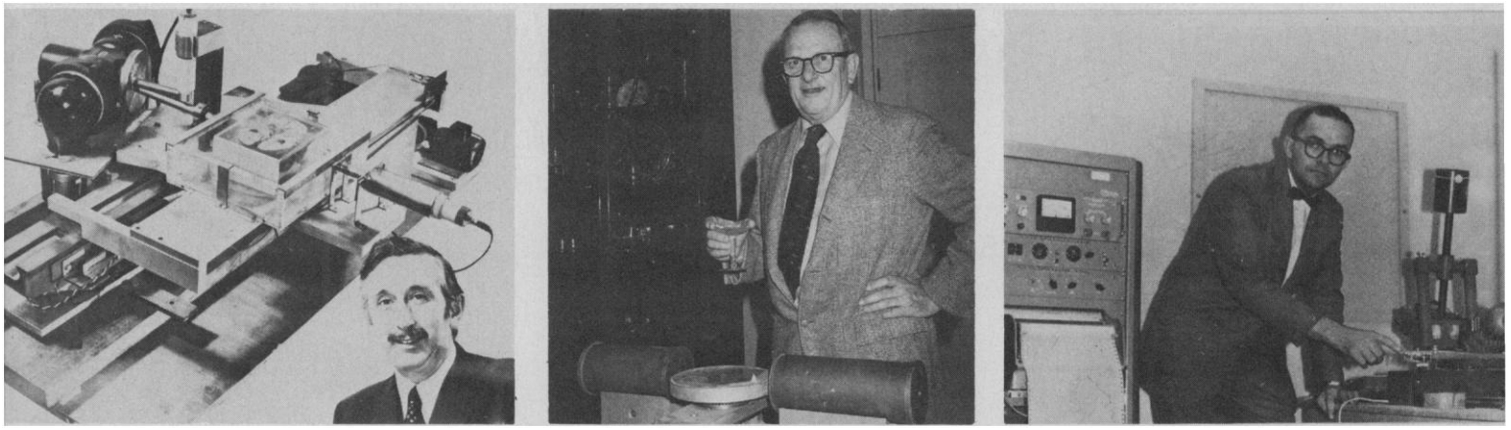

Designers of the scanner with their original machines. Pictured (left to right) are Godfrey N. Hounsfield, Allan M. Cormack, and William H. Oldendorf. Photos are recent, except the one of Oldendorf, which was taken in 1960.

diopaque dye or gas. Oldendorf looked for a better way. Eventually he worked out a tomographic method and built a model in which the beam from a gamma-ray emitter encountered iron and aluminum nails on its way to a crystal detector. After Oldendorf patented the device in 1963, he approached several medical x-ray manufacturers in the hope that they might develop it into a clinically useful system. They figured the machine would cost $250,000—and that ended it. No one was willing to risk the capital.

Conspicuously absent from Oldendorf's original paper is mention of mathematics. Instead of a computer, he used a circuit to reconstruct internal points from the hypothetical patient's head. A Nobel Laureate in physiology or medicine (1977) who is familiar with Oldendorf and his work says he is basically an inspired machine-maker. "He's always building all sorts of gadgets," says Rosalyn Yalow, who won the award for the development of radioimmunoassays. "He is not a physicist. He is a tinkerer, a good all-round tinkerer."

This lack of mathematics did not put off the Lasker Awards jury, which in 1975 said Oldendorf "first envisaged a revolution in diagnostic radiology."

In contrast, this year's Nobel Assembly said in its press release that "the problem was basically a mathematical one," and gave the award to Cormack, a physicist, and Hounsfield, a computer expert. Their work dealt with the problem of scanning in a highly mathematical manner (Cormack's original paper contained 26 separate equations).

It is ironic, but the Nobel Assembly's emphasis on the mathematical aspects of CAT scanning may have done a disservice to EMI Ltd., the company that displayed the first practical CAT scanner. EMI is currently suing General Electric and Pfizer Medical Systems, both of whom manufacture CAT scanners, for infringement of the basic patent rights held by Hounsfield. EMI sued Pfizer in 1977 and GE in 1978. One defense of the Pfizer attorneys has been that the basic mathematics of the machine, or the computer software, cannot be patented. They cite a U.S. Supreme Court ruling (Parker *v.* Flook, 1978) that says "a claim for an improved method of calculation, even when tied to a specific end use, is unpatentable." EMI attorneys, on the other hand, argue that this is not a significant issue, and that the whole machine must be taken into consideration.

Then came the Nobel Prize. Now the Pfizer attorneys are pointing to the Nobel Assembly and saying that here is proof that the CAT scanner is essentially an x-ray machine combined with a fancy computer. This has not gone down well with the EMI attorneys. "Your honor," pleaded one in a Delaware court this past November, "I think that the Pfizer position is, to be charitable, simplistic, and it is simplistic because the Nobel Assembly did not award its prize because somebody invented an algorithm. It eventually awarded that prize because for the first time someone devised a machine which produced a visual representation of a cross-section of the human body."

For EMI, the situation was a bit simpler before the pronouncement of the Nobel Assembly. In 1978, for example, it settled out of court after suing another CAT manufacturer, Ohio Nuclear, for patent infringement. Settlement was for more than $15 million.

The fact that litigation over patent rights has already been influenced by the Nobel Assembly has led some lawyers to speculate that the Assembly tried to take the potential impact of its decision into consideration. EMI's claim to the scanner, for instance, would have been considerably weakened if the Nobel Prize has been awarded to two Americans, Oldendorf and Cormack, and one Englishman, Hounsfield. Since both Americans did work before Hounsfield, an American manufacturer could point to the august opinion of the Nobel Assembly and use it to back up a "prior art" argument in court. As it turned out, however, the convenient symmetry of giving the award to one Englishman and one American diminishes this problem.

The lawyers admit that the foregoing is speculative, and one evidence of this is that they are eager to hold out other solutions to the riddle of the Assembly debate. Some EMI lawyers, for instance, suggest that the Committee originally picked only Hounsfield and that the full Assembly then added Cormack. Pfizer attorneys picture just the opposite.

What is clear in all this is that something unusual did occur at this year's Nobel Assembly, and no one is absolutely certain just what it was. Members of the Assembly, who have their national pride at stake, are not talking. Many knowledgeable observers in the United States and Sweden say the "something" was Oldendorf. Though admitting he does not know for sure, Oldendorf too feels he was on the ticket. He notes that Greitz, who is said to have lobbied extensively this year for the CAT scanner, wrote him in the early 1970's regarding the 1961 paper on tomography, saying "this is evidently the principle of the EMI scanner—I didn't know about it."

Not everyone is that certain. Yalow, who once nominated Oldendorf for the prize and is now upset that he didn't get it, says she is at a loss to know what really happened. "The only thing that will make it up is if he gets another money award," she says and then pauses for a second. "But you don't go down in history with money. You go down with a Nobel."—WILLIAM J. BROAD