Neuroblastoma Screening Showed Early Detection Doesn't Always Save Lives

This is part of an occasional series that recalls some of the stories reported 10 years ago in the News section of the Journal.

One of the first indications that neuroblastoma screening was not beneficial came 10 years ago with a report that mass screening of infants in the Saitama prefecture of Japan diagnosed nearly 10 times as many cases as would have been normally diagnosed clinically. Over time, the evidence would mount that neuroblastoma screening was actually harmful, despite the fact that screening diagnosed tumors at early stages.

Screening of infants for neuroblastoma by assessing urinary catecholamine metabolites started in parts of Japan as early as 1974, and mass screening was instituted across the country in 1985. Interest in screening in other parts of the world, including the United States, began in 1984 when a study of the Japanese program appeared in *The Lancet*, said William Woods, M.D., of the Aflac Cancer Center and Children's Healthcare of Atlanta/Emory University in Atlanta.

On the basis of the evidence from Japan, many physicians and pediatric oncologists started advocating for mass screening, but Woods and his colleagues argued instead for a trial to evaluate the method first. "People said, 'Bill Woods, you know this is going to work,'" Woods said, but first "it has to be proven to work."

To try to prove that it works, the Quebec Neuroblastoma Screening Project, a pilot project, was launched and more than 400,000 children at ages 3 weeks and 6 months were screened between 1989 and 1994. The researchers soon saw evidence of overdiagnosis. "We got clues that it wasn't going to work early on; we just didn't have the data," Woods said. And in 1997, they reported that screening had detected 118 cases of neuroblastoma, more than twice as many as the 54.5 cases that would have been expected.

Five years later, the final blow came. The Quebec pilot project and the German Neuroblastoma Screening Project—which screened nearly 1.5 million children at age 1—both reported substantial overdiagnosis that was not accompanied by any change in mortality, the goal of any screening program.

Neuroblastoma screening quickly lost favor around the world. By March 2004, Japan had discontinued its program.

A study published earlier this year in JNCI (*see* Vol. 97, No. 15, p. 1118) found that the Quebec pilot project cost $8.77 million, but by not implementing nationwide screening programs in the United States and Canada between 1989 and 2002, the countries saved $574.1 million in health costs and prevented the unnecessary treatment of 9,223 children and false-positive findings for 5,003 children.

"The Quebec Neuroblastoma Screening Project, from an economics perspective, yielded benefits beyond its costs," said Lee Soderstrom, Ph.D., associate professor of economics at McGill University in Montreal and lead author of the study. The project showed that evaluations of large-scale screening programs before they are widely implemented "can avoid adverse health effects," said Soderstrom. "I think that that's important."

Neuroblastoma screening ended in Quebec in 1994, but "we may have changed forever the incidence in Quebec," said Woods, because of the public's increased awareness of the disease. Also, neuroblastoma incidence in the United States may also be on the rise as more cases are detected before birth due to the increased use of ultrasound, he said.

Although it eventually was shown not to work, neuroblastoma screening did teach an important lesson. "The concept that detecting cancer early on always saves lives just isn't true," Woods said.

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