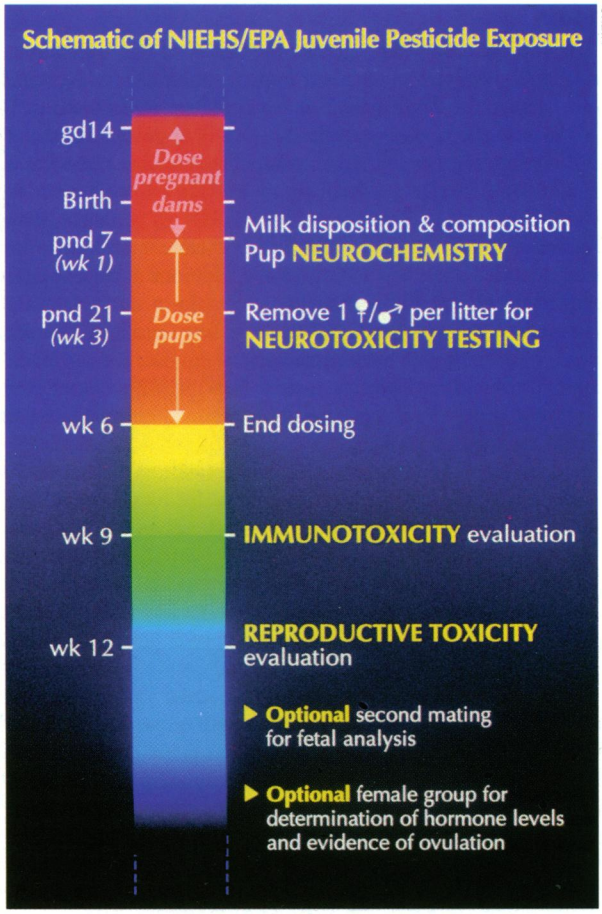
will be evaluated for both general behavior and for learning capability while they are maturing. As adults, they will undergo a series of complex learning/relearning trials to probe for subtle changes in integrated brain function. Reproductive toxicity will be evaluated using a number of indices of sexual development and puberty and, in adult animals, a thorough assessment of reproductive function and structure. Exposed animals will be paired with untreated mates to identify which gender is affected. Hormone and ovulation studies may be conducted if there is evidence that ovulation was impaired in the exposed females. A subset of animals in immunotoxicity studies will be exposed to evaluate their immune responses *in vivo*, while others will provide tissues for *in vitro* evaluation of various immune cellular functions.

Study chemicals were chosen to represent a variety of structures and classes of pesticides. In the first study, methoxychlor will be used as a positive control based on data from Earl Gray and colleagues at EPA. They have shown that methoxychlor has significant reproductive effects in animals exposed as juveniles. Tebuconazole is representative of a widely used class of antifungal compounds that exhibit reproductive and developmental toxicities. The organophosphates are represented by chlorpyrifos, a relatively long-acting organophosphate, and parathion, a relatively short-acting organophosphate. Carbaryl will represent the carbamates, another neuroactive class that may have reproductive effects. Atrazine will be evaluated based on its heavy use in the United States, its prevalence in groundwater supplies, and its reported reproductive activity. Finally, trichlorfon, another organophosphate, is included because it has been reported to be associated with adverse reproductive outcomes in humans.

Because the organophosphates and carbaryl alter neurochemical enzymes in known ways, the degree of these effects will be monitored in animals sacrificed both during and after exposure. Acetylcholinesterase inhibition will be evaluated at EPA and also by Mohammed Abou-Donia at Duke University. This will allow a correlation between a known amount of enzyme inhibition and subsequent behavioral and cognitive function.

By comparing the effects and effective doses in these young animals with those from adults, researchers will be able to tell if there are significant differences between these age groups and will have some appreciation for the degree of the problem, if one exists. If the data suggest that the health risks from juvenile exposures to pesticides has been underestimated, these studies will be the first step in a larger evaluation of the problem.



NIEHS

Testing timeline. NIEHS researchers are designing a study to look at the effects of pesticide exposure on the nervous, immune, and reproductive systems of juveniles.


NIEHS

Glinda Cooper

Frontiersman of Science

Stanley Cohen, who shared the Nobel Prize in 1986 in physiology and medicine for his pioneering discoveries of growth factors, was the keynote speaker at the April "Frontiers of Science Mini-Symposium" sponsored by NIEHS. Cohen's symposium was titled "Growth Factors and Related Signaling Pathways." At the symposium, presentations outlining recent, exciting findings were given by prominent scientists from UNC-Chapel Hill, Duke University, Glaxo Research Institute, and NIEHS.

Growth factors are small proteins that are produced by nearly all tissues and provide potent, local signals that affect behavior of nearby cells or even cells that produce the factor. The various cellular activities regulated by growth factors are extensive and include such events as cell growth and maturation, cell repair, and transport of ions. Specific receptors at the surface of cells determine whether a cell will recognize a particular growth factor.

In his keynote address, Cohen detailed the large body of his research, giving a context for the symposium's other presentations. He reviewed his pioneering Nobel Prize-winning work of 30 years ago on the purification of epidermal growth factor (EGF). His subsequent work has led to the characterization of the response of cells and organisms to EGF stimulation, while his recent work has focused on the specific biochemical changes induced by EGF binding to its receptor in the cell membrane. This binding activates the receptor's enzymatic activity, leading to its interaction with other cellular proteins which lead to metabolic changes in the EGF-stimulated cell.

Since Cohen's pioneering work in growth factor research, hundreds of growth factors have been discovered. The function of many of these factors, however, remains elusive. Many researchers are currently attempting to learn more about the large number of biochemical changes that occur in cells following interaction of growth factors with complementary receptors. Understanding these regulatory circuits in cells might provide insight into the origins of some diseases. Cancer cells, for instance, exhibit changes at nearly every level of some growth factor pathways and many investigations are currently attempting to link specific changes in these pathways with the capacity of cells to change into cancer cells.

Goldstein on Risk Assessment

Bernard D. Goldstein spoke at the Risk Assessment Research Seminar Series on April 22 at NIEHS on comparative risk assessment. Goldstein is the director of the Environmental and Occupational Health Sciences Institute and chair of the Department of Environmental and