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The Prospects for Chemical Darwinism

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The ghosts of the Social Darwinists of the nineteenth century and the author of Silent Spring (Carson), published in 1962, must have groaned in their shadowy haunts when they heard Admiral Elmo Zumwalt's poignant interview with the Washington Post (1984). The Admiral's son, who served in the Ca Mau peninsula of Vietnam shortly after his father had ordered the spraying of Herbicide Orange in that area in 1968, has an advanced lymphoma; his grandson has a birth defect. "Even if a causal relationship can be established -- and it hasn't been -- between Agent Orange and the illness," Admiral Zumwalt was quoted as saying, "I would have to conclude in balance, given the tragedy of the war, that many more men are alive today, including possibly my own son, because of Agent Orange."

What political and ethical issues are raised by those few sentences spoken by an anguished father! In the First Inaugural summation, Thomas Jefferson states that "A wise and frugal government which shall restrain men from injuring one another, shall leave them otherwise free to regulate their own pursuits of industry and improvement." (Commager 1951) However, which of these two Jeffersonian ideas is subordinate to the other? Herbert Spencer wrote in his book Social Statics (Knowles 1969) that government should not regulate human activities because "society advances...by survival of the fittest." The great dissenter, Oliver Wendell Holmes, cast an early vote for regulation when he held that constitutional guarantees did not invalidate a law seeking to limit working hours. He noted that "The Fourteenth Amendment does not enact Mr. Herbert Spencer's Social Statics." (Holmes 1905) Rachel Carson's Silent Spring, began with a line from a poem composed by Keats shortly before his death: "The sedge is withered from the lake, And no birds sing." Miss Carson used the imagery of dead grass and silent birds to remind her readers that "in some quarters nowadays it is fashionable to dismiss the balance of nature as a state of affairs that prevailed in an earlier, simpler world." Her warnings of chemical pollution were filled with prophetic emotion but unsupported by solid research.

The conference reported in these pages deals with scientific issues. The conclusions are tentative, the pages full of uncertainties. The widespread use of potentially dangerous material serves as a stark backdrop for the somber message of Dr. Irving Selikoff. Reminding the reader of the lengthy period that elapsed before the risk of asbestos fibers for human health was generally understood, he cautioned against the introduction of new subtances into the general economy before their safety had been assured. Almost twenty years before, President Lyndon Johnson had emphasized the same issue in eulogizing the late Miss Carson as he signed a pesticide bill. "One voice which spoke so often and so eloquently for measures like this is still today -- the voice of Rachel Carson. She would have been proud of this bill and of this moment. We owe much to her and to those who still work for the cause of a safer and healthier America."

Society has probably been undeservedly fortunate in the matter of dioxin. Synthesized by German scientists in the mid-nineteen fifties and known since then to produce an acne-like lesion when applied to rabbit ears, it has been shown to produce all sorts of problems in experimental animals including cancer. Extremely large exposures in man, however, have not produced many lasting illnesses, probably because the insoluble material rarely reaches high tissue concentrations in man or gets into the human food chain. Individual papers analyze the experimental and epidemiologic evidence that 2,3,7,8 TCDD has an adverse effect on human health. While there is little solid evidence that the substance produces substantial chronic disability or premature death in man, a substantial body of experimental evidence for its carcinogenicity makes it likely that a small number of human malignancies might be due to its action. Careful long-term follow-up of Missouri and Vietnam cohorts will be essential in determining the relative risk of cancer in those exposed to the substance.

An important study published after this conference provided important new information regarding the long-term effects of exposure to high concenterations of 2,3,7,8 TCDD (Lathrop et al. 1984). Airborne crews engaged in the aerial spraying of Agent Orange in Vietnam were selected for study in an Air Force study labelled Ranch Hand after the operational name of the military defoliation mission. These crews were selected for study because their almost daily occupational exposure to material containing at least 2000 ppb of TCDD gave them "1000 times more exposure to Herbicide Orange than would an average unclothed man, standing in an open field directly beneath a spraying aircraft." Mortality studies were made on 1274 exposed Ranch Handers and 6,171 unexposed controls who served in Vietnam. Overall mortality rates for the two groups were almost identical. Neither chloracne nor porphyria cutanea tarda were present in the Ranch Hand population. Minor birth defects (usually involving the skin), abnormal peripheral pulses and decreased unstimulated lymphocyte proliferation were more common in the exposed group but other differences were not identified. The absence of an increased mortality from malignant diseases in a study conducted more than fifteen years after the initiation of aerial spraying is reassuring.

The scientific activities identifying the toxicity of TCDD led to chemical process controls that reduced its concentration in commercial herbicide, probably preventing a major public health disaster; however, the means of controlling the introduction of new and even more dangerous materials has not been resolved. The Carsons and Selikoffs of this world have preached mightily but public resolve to control toxic wastes has not been translated into effective governmental action.

Charles Darwin, writing in 1859, had a more natural struggle for existence in mind when he wrote "More individuals are born than can possibly survive. A grain in the balance will determine which individual shall live and which shall die, which variety or species shall increase in number, and which shall decrease, or finally become extinct." Miss Carson suggested that Darwins's doctrine of survival of the fittest was producing natural selection of insects treated with the pesticide DDT: "Out of an original population, the members of which vary greatly in qualities of structure, behavior, or physiology, it is the 'tough' insects that survive chemical attack." The leap from social to chemical Darwinism foretells a misdirected twist for human intelligence.

Those adherents of Social Darwinism who applied the doctrine of survival of the fittest to politics and economics probably may not have understood that a consequence of their philosophy might be the emergence of true natural selection as newly synthesized chemicals proved toxic to those with certain genetic weaknesses. Only certain individuals, for example, develop cancer when exposed to a carcinogen, perhaps because the enzymatic systems necessary to transform certain subtances into cancer producing agents differs from person to person. This variability in the ability to metabolize exogenous chemical materials is particularly evident with 2,3,7,8 TCDD. Some strains and some species are quite sensitive; others are not. Poland and Glover have shown that 2,3,7,8 TCDD binds to a specific cytosolic receptor which induces an enzyme, aryl hydrocarbon hydroxylase (Poland and Glover 1975). The ability to induce this enzyme is inherited in inbred mice as simple autosomal trait which appears to be controlled by different species. Thus, sensitive mice, or people, might become ill with small doses of a chemical toxin while others without this genetic prediliction might be insensitive to even large concentrations. If such chemicals produced serious illness or death, the survivors would be those favored by the forces of natural selection to survive and multiply. Eventually, sensitivity to that particular chemical might disappear as the trait became a fatal one; a different chemical, however, might select to new weak point in the genetic apparatus of the survivors.

The possibility of chemical Darwinism demands a reasoned societal approach. Public policy has emphasized the protection of the most sensitive members of the population. Unusual consequences limited to genetically pre-determined individuals limits the easy recognition of toxic substances. Exposure studies with multiple species,

development of national occupational exposure registries and more general use of studies that might predict a sub-cellular effects in humans, such as sister chromatid exchanges and lymphocyte proliferation, should be the rule. New molecules must be scrutinized with even more care than at present before acceptance for general use.

No matter how careful the evaluation of a new agent, however, mistakes are inevitable. Rarely, an extremely valuable chemical will prove to have undesirable side effects that were not predictable from animal or limited human evaluation. Government regulation, corporate morality and market sense and product liability litigation are the major safeguards against chemical accidents. While isolated injuries are reasonably well handled by litigation, large-scale personal injury allegations frequently become unmanageable and grotesque as squadrons of lawyers and scientists joust before court and jury. Legal "reasonable certainty" is difficult to equate with statistical significance. Juries simply cannot rationally deal with conditions such as soft tissue sarcoma and uroporphyria or exposure data expressed in parts per billion, million or trillion.

A possible approach to dealing with the uncertainties of cause and effect after an accidental exposure is typified by the recent settlement between seven chemical companies and 15,000 veterans representing a class action suit. Attorneys agreed that the relationship of TCDD exposure to a variety of health effects could not be agreed upon: "Veterans assert that it has caused them cases of cancer, nerve and liver diseases as well as produced birth defects among their children. Chemical companies contend that none of these problems have been conclusively linked to dioxin" (Wall Street Journal, May 8, 1984). The total settlment amounted to $180 million which will swell by $70 million in six years. Compensation from this trust fund will be based on rules established by a court-appointed panel.

Richard J. Mahoney, President of Monsanto, indicated that "We settled this controversial case because, when all the factors were weighed, it was the right thing to do.... Judge Weinstein helped both the plaintiffs and the defendants focus our thinking on these larger issues; in other words, whether it was in the interests of either side for this case to go to trial, regardless of who was right or wrong." For many, the settlement appears to be a precedent-setting method for dealing with issues not resolvable by the usual scientific methods. The settlement appears even more reasonable considering alternative approaches such as prolonged litigation with multiple appeals or thousands of individual trials congesting the court system for years to come.

Readers of these collected papers will need to evaluate the available scientific evidence and decide whether that evidence establishes a case for dioxin-associated illness. They must also ponder the necessity for quick responses following accidental exposures in situations marked by uncertainty. Long term studies may determine the precise risk to exposed individuals but it would seem that vigor-

ous clean-up and compensation for those suffering putative damage should be completed long before any such information is available. Reasonable operational decisions must be made by governmental entities on a timely basis. An entire town in Missouri was condemned, for example, but not all homes in another area of contamination have been bought by the federal government. The ethical and political imperatives of waste control have moved ahead of scientific knowledge. Admiral Zumwalt may be correct in asserting that risks are necessary in battle; they should certainly be minimized for a civilian population!

REFERENCES

Carson R (1962) Silent Spring. Houghton Mifflin Co., Boston.

Commager HC (1951) First Inaugural Address of Thomas Jefferson. In: Living ideas in America. New York, 1951.

Darwin C (1976) The Origin of the Species: By Means of Natural Selection. Avenel, New York.

Dissenting Opinion of Justice Oliver Wendell Holmes, Lochner v. New York, 106 U.S. 45 (1905) "The fourteenth amendment does not enact Herbert Spencer's Social Statistics.

Knowles J (1969) Individualism, social welfare and the frontier in American life. In: Medicine in the Ghetto. Appleton-Century-Crofts, New York.

Lathrop GD, Wolfe WH, Albanese RA, Moynahan PM (1984) An epidemiologic investigation of health effects in air force personnel following exposure to herbicids. Brooks Air Force Base, Texas, USAF School of Aerospace Medicine.

Meier, B and Winslow, R. Seven firms in agent orange case agree to $180 million settlement. Wall Street Journal, May 8, 1984.

National Institute for Occupational Safety and Health (1984) 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, "dioxin"). Current Intelligence Bulletin 40, January 23.

Poland A, Glover, E (1975) Genetic expression of aryl hydrocarbon hydroxylase by 2,3,7,8-tetrachlorodibenzo-p-dioxin: evidence for receptor mutation in genetically nonresponsive mice. Mol. Pharmacol. 11:389-398.

United Press International (1984) Interview of Admiral Elmo Zumwalt by the Washington Post, St. Louis Post Dispatch, May 21.

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