

# Rachel's Environment & Health News

## #758 – From Silent Spring to Scientific Revolution -- Part 2

### December 12, 2002

by John Peterson Myers\*

[Continued from RACHEL'S #757. We are exploring the shifts in scientific thinking about chemicals and health that have occurred since the publication of Rachel Carson's SILENT SPRING in 1962 -- shifts resulting from the discovery that some industrial chemicals in the environment can interfere with hormones and growth factors in plants and animals, including humans. This essay first appeared in SAN FRANCISCO MEDICINE, November 2002. See <http://www.sfms.org/sfm/>. For more documents related to these topics, see <http://www.OurStolenFuture.org> and <http://www.ProtectingOurHealth.org>. --Peter Montague, editor]

#### Low Doses May Be More Potent than High Doses

Another key shift [in scientific thinking] is the acknowledgement that the assumption that the dose makes the poison can be misleadingly simplistic, if it is used to imply that only high dose exposures induce effects. In fact, low exposure levels sometimes cause effects not seen at higher levels [for example, see 12,13,14]. Researchers are now intensely pursuing these non-monotonic dose response curves and the uncertainty about their underlying mechanisms, which likely vary from case to case. [A "non-monotonic dose response curve" means that as the dose of a chemical is raised or lowered, the effect does not necessarily rise or fall in lock step with the dose. In some cases, low doses may cause greater effects than high doses.] One plausible hypothesis [to explain why dose and response do not always move together in lock step] is that at low, physiological levels, the contaminant interferes with developmental signaling but does not activate biochemical defenses against impacts that would be caused by higher exposures. At somewhat higher levels, these defenses are activated and the contaminant is successfully detoxified. At even higher levels, the defense mechanisms are overwhelmed by the toxicant and more traditional toxicological effects are induced.

#### Common Chemicals Can Disrupt Hormone Signals

As scientific research has focused on mechanisms of message disruption, it has implicated a wide array of chemicals. This expansion has involved both ongoing identification of compounds capable of interfering with estrogen, which was the initial focus, as well as research broadening the range of message systems studied. Some of the most troubling discoveries about new actors is that they involve compounds in widespread use in consumer products, including plastic additives like phthalates and plastic monomers like bisphenol A, which leaches from polycarbonate products [for example, see 15,16]. [Polycarbonates are strong plastics, such as Lexan, used in drink bottles, eyeglass lenses and shatterproof windows.]

#### New Studies Reveal Unsuspected Health Effects

That is not to say that we have complete understanding of even the best known contaminants. This reality was highlighted by a study published in 2001 about DDT, in which Longnecker and others[17] report a highly significant association between DDT in maternal serum [blood] and the likelihood of preterm [premature] birth. Their study used birth records and stored serum from the mid 1950s-60s. They concluded that the U.S. had experienced a hitherto undetected epidemic of preterm birth

during this period because of DDT use. Longnecker (personal communication) went further to estimate that because of the close association between preterm birth and infant mortality, up to 15% of infant mortality during that period may have been attributable to DDT use.

#### Chemicals Interfere with Hormones in Unsuspected Ways

Disrupting chemicals have been identified that interfere with [many hormone systems, such as] estrogen, androgen, progesterone, thyroid, insulin and glucocorticoid signaling, among others. The mechanism does not always involve mimicking (or inhibiting) ligand-receptor binding. [Many hormones work like a key fitting into a lock and the scientific name for this is ligand-receptor binding.] For example, as noted above, atrazine appears to enhance aromatase conversion of testosterone to estrogen.

#### Chemicals Can Disrupt Hormones in Several Ways

Signal disruption may also intercede in steps leading to gene activation after ligand-receptor binding. [In other words, after the hormone key fits into one of the cell's locks, other things should happen, but some chemicals disrupt normal events at this stage.] This was established by in vitro [test tube] experiments showing that arsenic selectively inhibits gene activation by the glucocorticoid-receptor complex after normal ligand-receptor binding and subsequent entry into the cell nucleus, at arsenic concentrations far beneath cytotoxic [toxic to cells] levels.[18] While human health impacts have yet to be demonstrated via this mechanism, dysfunctions [interferences] in glucocorticoid action have been linked to weight gain/loss, protein wasting, immunosuppression, insulin resistance, osteoporosis, growth retardation, and hypertension.

#### Mixtures are Important but Not Often Studied

Another important issue raised by emerging science is the powerful interactions that can occur within mixtures of chemicals, even though regulatory toxicology is conducted virtually exclusively on pure single compounds. Two results published in 2002 emphasize the importance of considering mixtures: In the first, Rajapakse and others[19] demonstrated that a mixture of estrogenic compounds, each present at a level beneath that capable of producing a statistically detectable estrogenic response in an in vitro [test tube] system, combined to more than double the response of the system to 17-estradiol [the commonest form of female sex hormone]. In the second, Cavieres and others[14] found that a common off-the-shelf dandelion herbicide mixture strongly reduced fetal implantation [successful pregnancy] rates in mice at one-seventh the concentration considered safe for its principal herbicidal component, 2,4-D, by the U.S. Environmental Protection Agency.

#### Chemicals and Germs Together Increase Disease Risks

The issue of mixtures is complicated further by interactions now known to occur between contaminants and infectious agents [bacteria and viruses]. Large increases in disease risk can be associated with simultaneous exposure to contaminants and infectious agents. For example, Rothman and others[20] reported

a greater than 20-fold increase in relative risk to non-Hodgkins Lymphoma with combined exposure to elevated (but still background) PCBs and Epstein-Barr virus. The mechanism underlying this result is unknown, but is possibly due to well-established immune system impairment by PCBs. If this mechanism is widespread, then current estimates of morbidity and mortality due to contamination are likely to be unrealistically low. Immune system interference by a variety of contaminants is widely reported (for example, Baccarelli[21]).

### **Traditional Regulatory Science May Not Protect Us**

Together these conceptual shifts are also challenging the adequacy of current epidemiology to guide regulatory standards. The patterns underlying these conceptual shifts -- including (1) non-monotonic dose response curves; (2) windows of vulnerability during development; (3) the ubiquity of mixtures; (4) the likelihood that multiple chemicals can induce similar impacts via disruption of developmental processes; (5) the same chemical can cause different impacts depending upon when exposure occurs; (6) long latencies [delays] between exposure and manifestation of impact in a mobile population, etc. -- all increase the likelihood of false negatives [falsely concluding that no harm is occurring] in epidemiology as it is currently practiced.

Thus the revolution in science that Rachel Carson stimulated raises today a series of troubling questions about whether current health standards truly protect public health. Effects of low level, background exposures are likely to be far more widespread than acknowledged, and involve many more health endpoints [health effects] than traditionally considered, yet these new mechanisms of toxicity thwart the epidemiological tools now available to establish human harm.

### **Important Role for Health Professionals**

We are confronting an enormous gap between what science now tells us about the links between contamination and health, and the antiquated approaches still used to safeguard public health. Health professionals will be important contributors to narrowing that gap, first by informing themselves about the underlying science, and then by helping to advance public understanding of the emerging evidence. Carson's scientific revolution can drive a transformation in public health that reinvigorates investments in prevention through exposure reduction.

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\* John Peterson Myers, Ph.D., is co-author of OUR STOLEN FUTURE (paperback: Plume, 1997; ISBN 0452274141), Senior Advisor to the United Nations Foundation and Senior Fellow, Commonweal, Bolinas, California. See <http://www.OurStolenFuture.org> and <http://www.ProtectingOurHealth.org>.

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