Case Studies in Environmental Epidemiology

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Case Studies:
Past: Love Canal
Present: Atrazine in Drinking Water
Future: Biology Century
Love Canal

- 1890’s - William Love’s vision for a canal to connect the Niagara River to Lake Ontario, parts built and then abandoned
- 1942 - Hooker Chemical Company begins dumping of chemical wastes
- 1947 - Hooker Corporation buys the 16-acre dump site
- 1952 - City of Niagara Falls disposes of municipal wastes at the site
- 1953 - Hooker Corporation fills the canal and sells the land to Niagara Falls Board of Education
- 1955 - Elementary school (99th Street) opens
- 1959 - Chemical seepage into basement is reported
- 1974 – Surface begins to collapse exposing barrels of chemicals
- 1976 - NYDEC documents widespread contamination of sewers and sumps in the neighborhood
- 1977 - Local reporter begins investigating possible links to illness
This Indenture,

Made the 26th day of April, Nineteen Hundred and
fifty-two.

Between

RODOX ELECTROCHEMICAL COMPANY

a corporation organized under the laws of the State of New York with its
office and principal place of business on Buffalo Avenue in the City
of Niagara Falls, County of Niagara and State of New York,

party of the first part,

and

THE BOARD OF EDUCATION OF THE SCHOOL DISTRICT OF THE CITY
OF NIAGARA FALLS, NEW YORK,

party of the second part,

WITNESSETH:

That Rodox Electrochemical Company, hereinafter called the Grantee,
for the sum of Ten Dollars, in hand paid, unto the said Board of
Education, the receipt whereof is hereby acknowledged,
transfers and assigns to the said Board of Education, a tract of
real property, together with all appurtenances belonging to and
situated thereon, all of which is more particularly described in
the map and plat heretofore recorded in the books of the County
Recorder of Niagara County, State of New York,

being a certain tract of land lying and being described as
commenced on the north by the right of way of a road,
commenced on the east by a lot owned by the 

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Prior to the delivery of this instrument of conveyance, the grantee herein has been advised by the grantor that the premises above described have been filled, in whole or in part, to the present grade level thereof with waste products resulting from the manufacturing of chemicals by the grantor at its plant in the City of Niagara Falls, New York, and the grantee assumes all risk and liability incident to the use thereof. It is, therefore, understood and agreed that, as a part of the consideration,

Love Canal

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NEW CHEMAGINATION CENTER

A few things you can do now with Hooker products - that couldn’t be done 10 years ago

- Convert coal into chemicals for plastics
- Make new pesticides
- Develop new medicines
- Improve industrial processes
- Find new sources of energy

Among the basic areas of endeavor with which Hooker research is concerned is the chemistry of aromatics, nitrobenzene, polystyrene, polyester, and high polymers. The industrial-strength drugs, and many more, have come about as a result of creative Hooker research on the techniques used in the manufacture of Hooker chemicals.

HOOVER CHEMICAL CORPORATION

Farm

Waste filled canal

Approx. limit of former canal

Path to recreation area

Waste cells

Drainage swales

Dike

Recreational trails

Recreational trails

Recreational trails

Recreational trails

Recreational trails

Circa 1953

1927
Barrels Collected During Clean-up

Love Canal: Community Activism

Lois Gibbs and daughter
April, 1978 - Lois Gibbs, resident and mother of two children, canvasses the neighborhood with a petition to close the 99th Street School located near the center of the dumpsite.

May 19, 1978 - New York State Health Department meets with to explain potential hazards of exposure to toxic chemicals in and around homes.

August 2, 1978 - The New York State Commissioner of Health declared a State of Emergency at Love Canal and ordered the 99th Street School be closed.

August 7, 1978 - The President of the United States declared an emergency and provided funds to permanently relocate the 239 families who lived in the first two rows of homes that encircled the landfill site. Families living in the remaining 10-block area, including Lois Gibbs' family, were told they were not at risk.

October 1, 1980 - President Carter visited Niagara Falls to sign the appropriation bill that provided the funding for permanent relocation for all 900 families who wished to leave.

December 20, 1983 - Lawsuit filed by 1328 Love Canal residents was settled for just under $20 million dollars with Occidental Chemical Corporation, a subsidiary of Occidental Petroleum. One million dollars were set aside for a Medical Trust Fund.

August 15, 1990 - Love Canal Revitalization Agency renamed a portion of Love Canal, Black Creek Village, and announced that 9 homes were available for sale to the general public.

December 22, 1995 - Occidental Petroleum agreed to pay $129 million to cover the federal government’s cleanup costs at Love Canal.

August, 1998 – A playground was built on the southern section (not habitable) section area of the neighborhood.
Chemicals from the Love Canal hazardous waste site were found in stormwater off First Avenue near the 10th Street School in Niagara Falls on April 15, 1978. Officials posted signs to keep children and passersby out of the hazard zone. (News file photo)

**Exclusive: Are Love Canal chemicals still making people sick?**

By Don Herbeck (http://buffalonews.com/author/don_herbeck/) | Published: June 1, 2018 | Updated: June 1, 2018
The Toxicological Paradigm

Exposure and Health Risk at Love Canal

- Single or complex exposure? Complex and unknown
- Identity of exposures over time? Not really
- Route of exposures: soil, air, water, food
- Population at Risk: across the whole life-span
- 10,000 people lived within one-mile and 70,000 people lived within three-miles
- If the incidence of a single disease was 20 per 100,000 per year, could you detect a difference by an epi study?
Case Studies:

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Atrazine

- MW 215.68
- Melting point: 175°C
- Boiling point: 200°C
- Solubility in water: 7mg/100 ml
- Herbicide
- Increases crop yield by ~3-5%.
- Mostly used on corn
Present: Atrazine in Drinking Water

- About 76,000,000 pounds were applied in the United States in 2003.
- Half-life in soil is weeks to months.
- US EPA maximal contaminant level 3 ppb (3 μg/liter and solubility is 70,000 μg/liter). *Yearly average or point estimate?*
- The U.S. EPA said in the 2003, "The total or national economic impact resulting from the loss of atrazine to control grass and broadleaf weeds in corn, sorghum and sugar cane would be in excess of $2 billion per year ..."

Toxicology of Atrazine

- Endocrine disrupting compound in experimental models. Increases aromatase, a critical enzyme in estrogen production.
- Epigenetic modifier and transgenerational effects in experimental models.
- Concern about impact on elderly with compromised health status, e.g. Type II diabetics.
- Not shown to be a potent carcinogen in experimental models.
Syngenta agrees to $105M settlement of Atrazine litigation

- Friday, May 25, 2012, - Syngenta AG, the Swiss specialized chemical company has agreed to pay $105 million to settle litigation involving several community water systems and the herbicide Atrazine.
- The proposed settlement agreement was filed with the United States District Court for the Southern District of Illinois on Thursday. Water systems agreeing to the settlement will be eligible for payments from a $105 million settlement funded by Syngenta.
- Plaintiffs had argued that Atrazine, used extensively by Midwestern corn growers to prevent weeds, had leached over time into their water systems.
- “Under the terms of the agreement, Syngenta expressly denied liability and the plaintiffs acknowledged that they are not aware of any new scientific studies relating to Atrazine,” the company said.
- Approximately 2,000 water districts in the U.S. may be eligible to make a claim.
The Toxicological Paradigm

Exposure, Effects and Health Risk of Atrazine

- Single or complex exposure? **Single**
- Identity of exposures over time? **Yes**
- Route of exposures: **water**
- Population at Risk: Between 35-40 million people live in the major contaminant areas.
- Carcinogenic or non-carcinogenic effects: endocrine disrupter.
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Convergence
The Biology Century and Convergence

The Biology Century: At the beginning

- Starting the third generation in the biological revolution.
- The first generation (1953-1970’s) involved intensive studies at the molecular/cellular level.
- The second generation involved genome sequencing and cloning (1980’s-2000’s).
- Convergence is the third generation, merging life, engineering and physical sciences to fundamentally change the approach to disciplinary based strategies in human health at a global scale.
- Public health provides the multidisciplinary training for convergence work. (JDG, 2014)

Science 29 July 2011: 527
What is “Epigenetics”? 

[Images of monarch butterfly's life cycle]
What is “Epigenetics”?  

• Classic genetics alone cannot explain the diversity of phenotypes within a population (not to mention phenotypic differences in monozygotic twins)

• Epigenetics = “above the genetics”

• Heritable changes in gene expression that are not due to any alteration in the DNA sequence
  – Heritable = inherited mitotically in somatic cells and/or inherited transgenerationally

• Best known epigenetic marker = DNA methylation (e.g., hypo-methylation of DNA in human tumors and hyper-methylated tumor-suppressor genes)
Proof of Concept: Agouti Mice

Coat color in Agouti mice varies from black to yellow due to stochastic methylation of CpG motifs

Folate and B12 have transgenerational effect on decreased expression of the Agouti gene


Folate and B12 have transgenerational effect on decreased expression of the Agouti gene

Waterland and Jirtle. Mol Cell Biol 2003; 23:5293
Epigenetics and Human Disease

Epigenetics is the study of inherited changes in phenotype or gene expression caused by mechanisms other than changes in the underlying DNA sequence.

Environmenal Stress $\rightarrow$ Gene Expression $\rightarrow$ Inherited Adverse Health Outcome

Genomic Editing, Engineered Synthetic Cells and Self Healing Materials
RIDING THE CRISPR WAVE

Biologists are embracing the power of CRISPR/Cas9 to edit and improve genomes.

CRISPR Corrects Blood Disorder Gene

RNA-directed nucleic acid biosensors that can detect cancer cells in blood.

Editing Of Human Embryo Genes Raises Ethics Questions

Biotechnology: Sciences and technologies are now also aimed at human germline.
Gene Editing Spurs Hope for Transplanting Pig Organs Into Humans

by GINA BOLATA, AUG. 10, 2017

NY Times, Aug. 10, 2017

Genetic Engineering to Make New Materials and Public Health

OR

Biologically directed nanoengineering, cells are good bioreactors.
• About 500 million years ago organisms started growing hard materials like calcium carbonate and ... bone...These organisms evolved to make exquisite nanostructures like shells.

• Now evolving simple organisms using directed evolution to .... grow and assemble materials ... for solar cells, batteries, and for medical diagnostics...

• Capitalized on ... properties of biology--using only non-toxic materials, employing self-repair mechanisms, self-assembling precisely and adapting and evolving to become better over time.

http://web.mit.edu/be/people/belcher.shtml
Biological engineering occurs at lower temperatures, pressures and with biologically non-toxic materials.
• Cellulose and chitin are the two most common structural biological materials on Earth
• Both biologic materials are 70-80% as strong as Kevlar

Sequential self-assembly of DNA functionalized droplets

- DNA nanotechnology and self-assembly of crystal structure, drug delivery to brain
- DNA devices at the nanoscale that move
- DNA as “hard-disk” for information storage.
- Moving past 0 and 1 binary units.
Self assembly of complex shapes designed using a molecular canvas of DNA strands

Each image is 150nm x 150nm in size.

Researchers can also design small DNA motifs that self-assemble into lattices. Shown below is a “tensegrity triangle” motif with three double helical edges (represented as cylinders) that contain complementary sticky ends along one, two, or all three of its.
Race Horse First Film Ever 1878 Eadweard Muybridge
CRISPR–Cas encoding of a digital movie into the genomes of a population of living bacteria

Seth L. Shipman¹,²,³, Jeff Nivala¹,², Jeffrey D. Macklin² & George M. Church¹,²

Nature, 2017
Engineered Nanobiosensors and Public Health

Epidermal Electronics
MIT chemists, led by Timothy M. Swager, designed this wireless badge to detect chemical-warfare-like molecules at parts-per-billion levels. The device is based on carbon nanotubes that are immersed in an ionic liquid and that change their resistance in the presence of the electrophilic target molecules. (Angew. Chem. Int. Ed. 2016, DOI: 10.1002/anie.201604431).
The Exposome Project: Opportunity for Citizen Science and Public Health

Characterizing the exposome. The exposome represents the combined exposures from all sources that reach the internal chemical environment. Functionally important cases of exposome chemicals are shown. Signatures and biomarkers can detect these agents in blood or serum.

S M Rappaport, M T Smith Science 2010;330:460-461