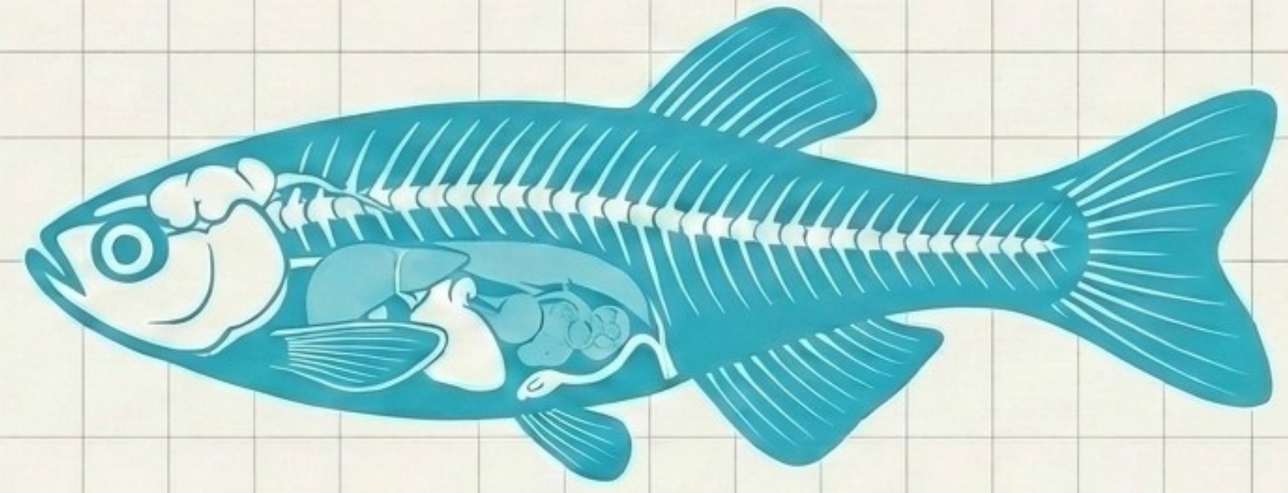
Developmental & Reproductive Toxicology

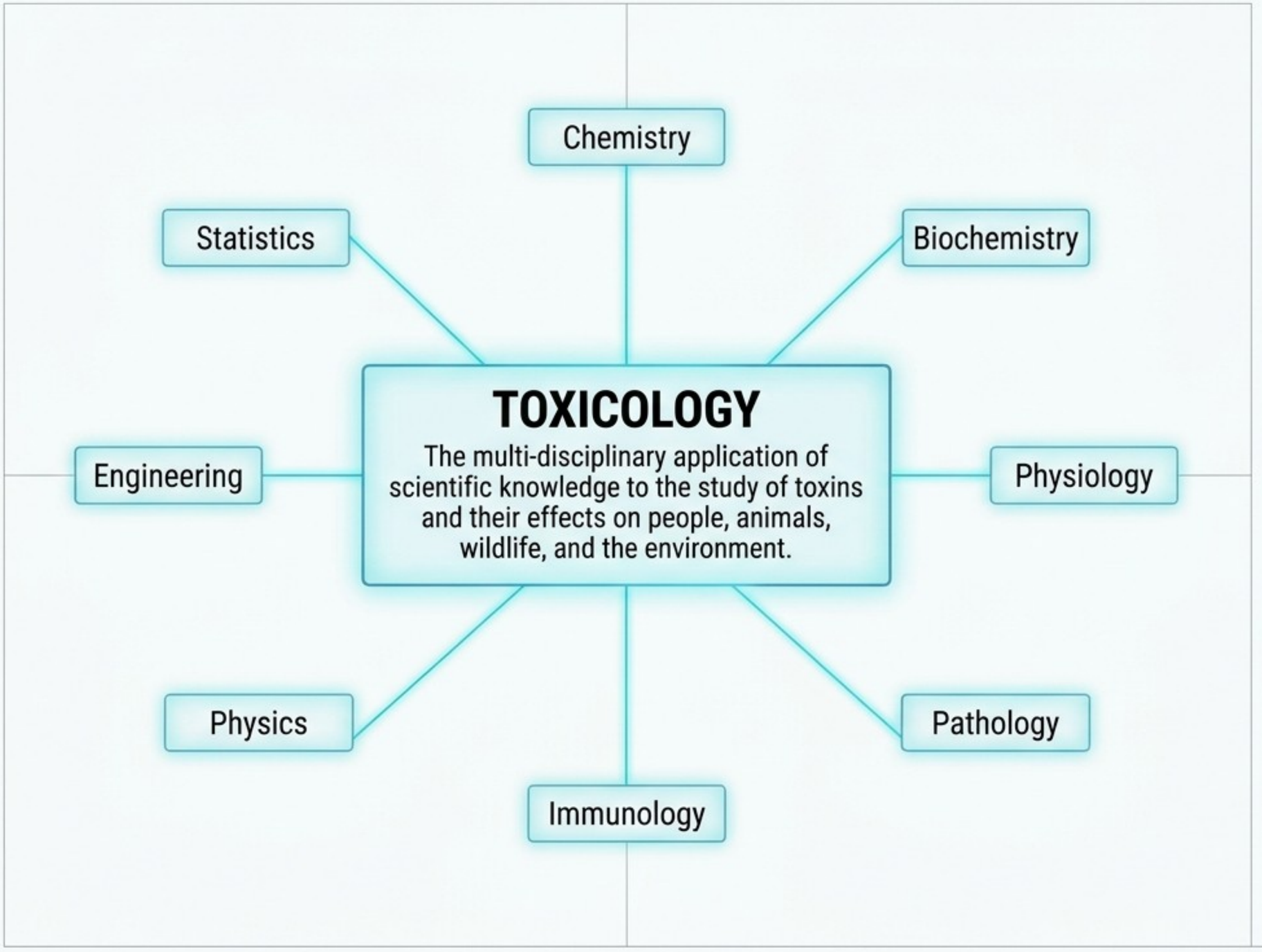
Sources, effects, and critical evaluation of environmental contaminants.

II YEARS STUDENTS

Course Dossier	
Credits:	4 CFU
Structure:	2 Units (32 hours total)
Practical Component:	20 hours in Zebrafish Facility
Assessment:	100% Final Examination



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Application Matrix

Medical/Clinical: Diagnosis and treatment of human poisoning.

Veterinary: Wildlife and domesticated animal poisoning.

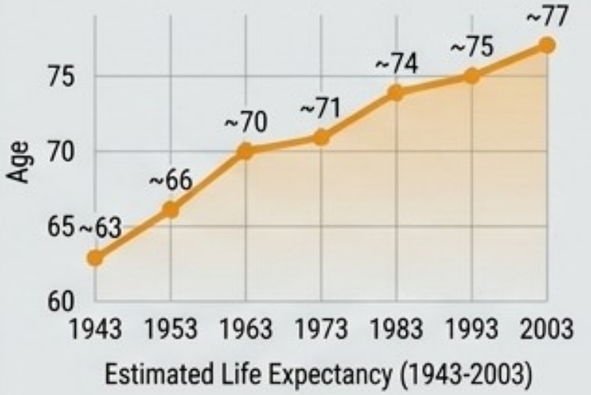
Food: Detection of toxic substances in the food supply.

Forensic: Legal and medical aspects of poisons.

Environmental: Impacts of pollutants on ecosystems.

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Rising Life Expectancy, Hidden Risks



1538: The Foundation

Paracelsus (1493-1541) establishes the bedrock principle: “The dose makes the poison.” All substances are poisons; the right dose differentiates a poison from a remedy.

1960s: The Paradigm Shift (Reproductive Toxicology)

The Thalidomide tragedy shatters the long-held medical myth that the mammalian placenta is an impenetrable shield, birthing modern Developmental and Reproductive Toxicology.

Today: The Trace Dilemma

The focus shifts to low-dose, long-term exposures. While human life expectancy rises, the insidious effects of trace chemicals (endocrine disruptors) on long-term cancer rates and fetal development remain the field’s critical frontier.

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Non dobbiamo dimenticare che ……

. . .

- "Tutte le sostanze sono dei veleni; non ne esiste una che non sia un veleno. La giusta dose differenzia un veleno da un rimedio"



"E' la dose che fa il veleno"

- Paracelsus 1493-1541

Principles of Toxicology

Any synthetic or natural chemical can be harmful if ingested in large enough quantity.

THE DOSE MAKES THE POISON

Critical questions: what is the lowest level that will cause harm?



The Safety Illusion

Toxicity: The inherent ability to cause harm or adverse effects.
Safety: Merely the absence of evidence of toxicity. Safety is relative; there is no absolute safety.

The Agents

Drugs / Pollutants / Contaminants: Any substance that, when inhaled, injected, smoked, consumed, or absorbed via skin, causes a physiological change in the body.

The Sources

Natural Sources: Naturally occurring toxins (e.g., wildfires, cyanobacteria).

Anthropogenic Sources: Human-made pollutants (e.g., industrial emissions, synthetic chemicals).



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[HAZARD] + [EXPOSURE] = [RISK]

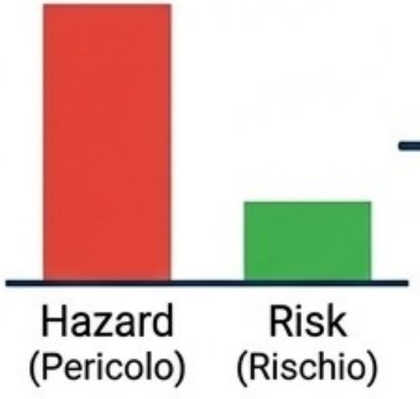
Hazard
The inherent potential of something to cause harm (e.g., a toxic chemical).

Risk
The probability (high or low) that the hazard will actually cause harm to somebody.

Analogy Matrix: Impact of Exposure

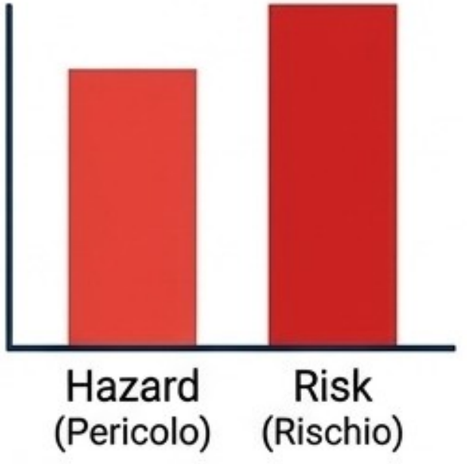
Closed Bottle in a Cabinet





Scenario 2: Bottle Poured into Coffee





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The Golden Rule

Any synthetic or natural chemical can be harmful in large enough quantities.
The critical question: What is the lowest level that will cause harm?



Concentration Units

ppm (1 part per million)
= 1 mg/Kg

ppb (1 part per billion)
= 1 µg/Kg

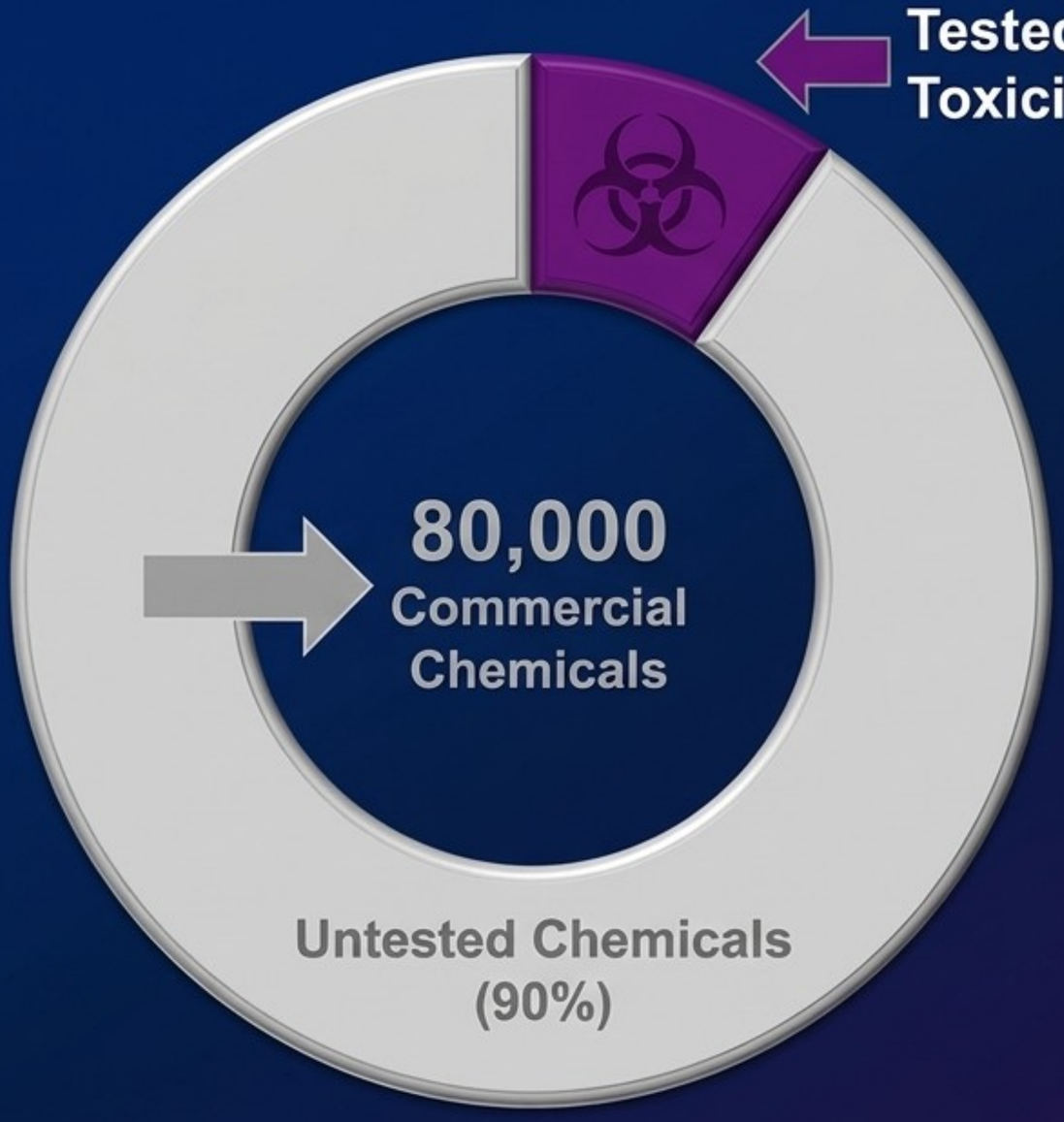
ppt (1 part per trillion)
= 1 ng/Kg

Biological Half-Life

The time required for the concentration in the body to reduce by half.

DDT: 15 years
Lindane: 2 years
Parathion: 130 days
Malathion: 11 days

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The Legal Framework: "Innocent until proven guilty." Chemicals do not require pre-market testing.

The Bottleneck: Lack of funds, lack of personnel, extreme expense, and the nearly impossible task of testing complex chemical interactions.



Toxicologists know a great deal about a few chemicals, a little about many, and nothing about most.

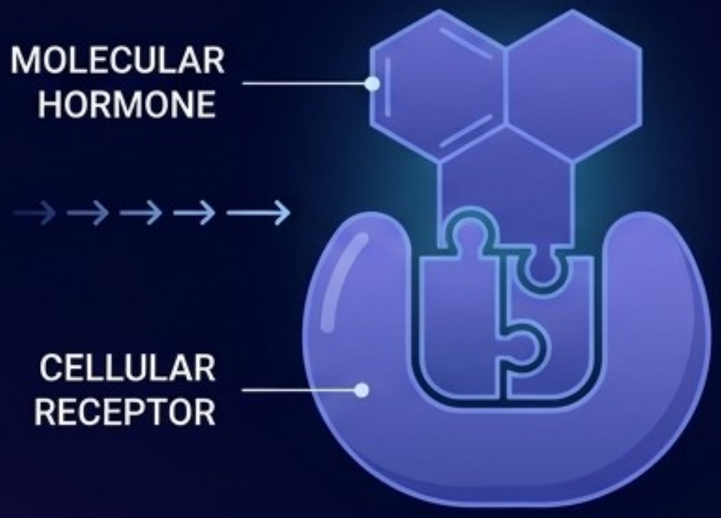
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☁️ AIR (Inhaling 5000 gallons/day)	💧 WATER (The Fluid Vector)	🍽️ FOOD (The Dietary Chain)
Toxins: 4.7 Billion lbs released in US (72M lbs are carcinogens). Sulfates, nitrates, mercury from coal plants. Airborne toxins traveling the global jet stream (1460 metric tons).	**Toxins:** Chlorinated chemicals, cyanobacterial toxins, persistent persistent organics (DDT, PCBs, dioxin, PBDEs), MTBE, protozoa.	**Toxins:** Mercury in freshwater fish (47 states with advisories). DDE found in 63% of surveyed foods. C8/PFOA from non-stick cookware.
Impact: >20,000 premature deaths/year. NYC urban air linked to infant chromosomal abnormalities.	**Impact:** 7M illnesses/year (US). Chlorinated water linked to breast cancer risk.	**Impact:** Strongly immunotoxic, linked to various cancers.

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Endocrine Disruptors: The Gender Benders

NORMAL HORMONE



ENDOCRINE DISRUPTOR (SYNTHETIC)



The Mechanism: Exposure to even low levels of certain synthetic chemicals (Hormonally Active Agents) can trick the body by mimicking or blocking natural hormones.

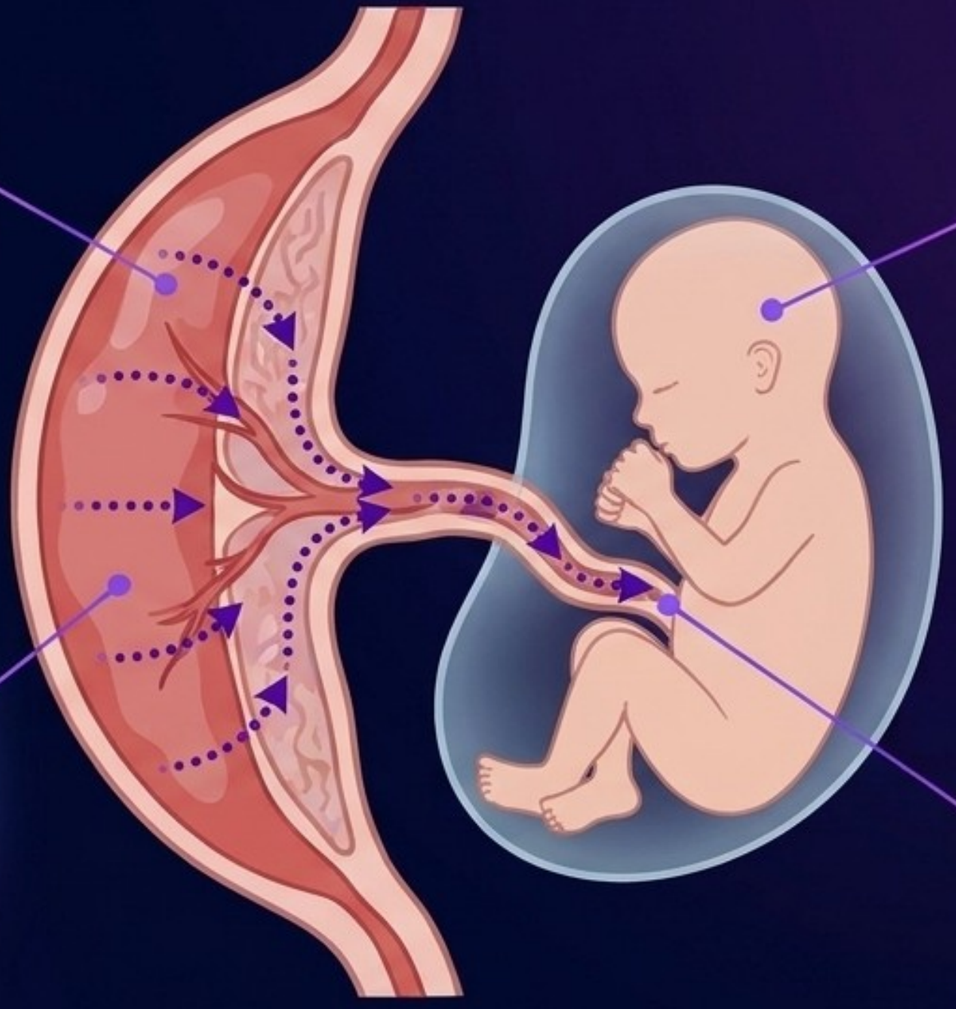
Systemic Impacts: Beyond the endocrine system, environmental chemicals severely impact the **Immune System** (arsenic, dioxins) and the **Nervous System** (neurotoxins affecting the brain and spinal cord).

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Mothers Give More Than Love (And More Than Nourishment)

The Maternal Load: 10% of women carry mercury concentrations high enough to cause fetal damage.

Placental Transfer: Pregnancy actively mobilizes fat-soluble Persistent Organic Pollutants (POPs) like Dioxins, DDT, PCBs, and PBDEs.
Heavy metals (Lead, Methylmercury) are actively transported.



Fetal Sequestration: Because the fetus has an immature metabolism, toxins are sequestered directly into the developing fetal brain.

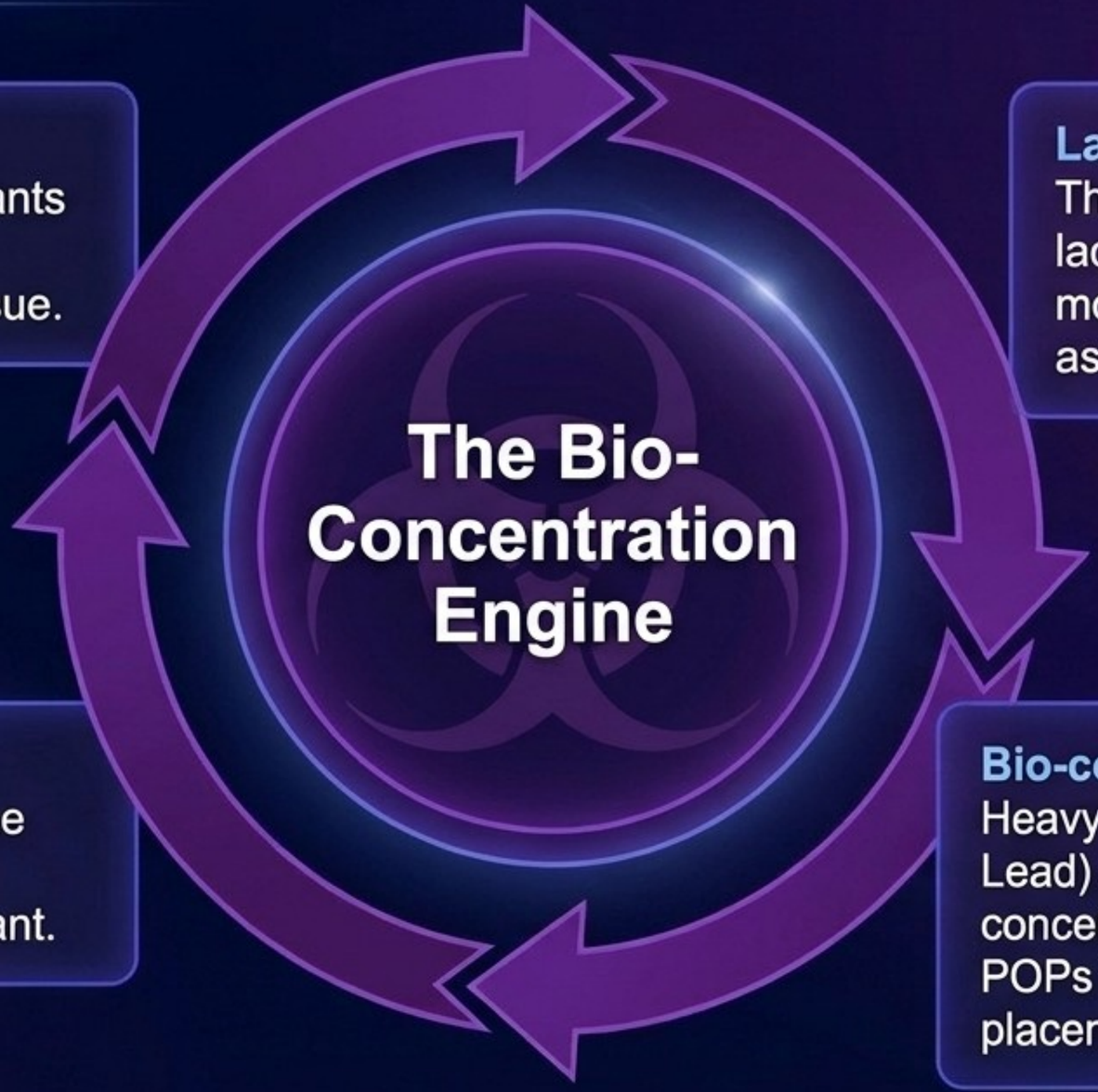
The Result: The average newborn has >200 different industrial chemicals, pollutants, and pesticides in their cord blood.

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Clinical Dossier: The Increaing Concentration of Toxine

Maternal Fat Stores:
Persistent Organic Pollutants (POPs) bio-concentrate specifically in adipose tissue.

Lactation Mobilization:
The physiological process of lactation aggressively mobilizes fat stores and their associated chemicals.

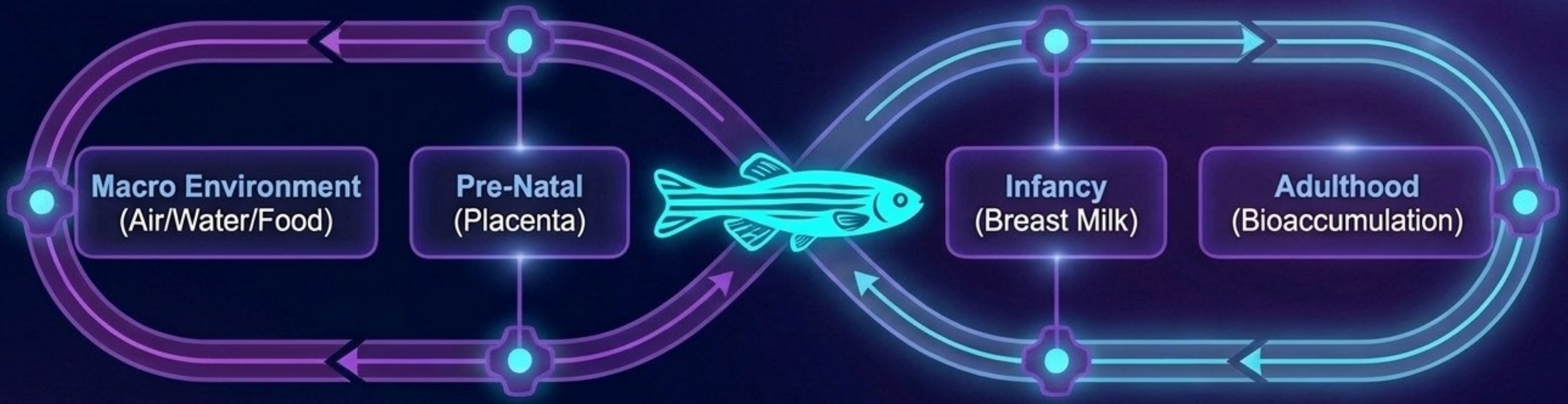


Infant Ingestion:
Dramatically increasing the toxic load on the highly vulnerable developing infant.

Bio-concentration in Milk:
Heavy metals (Mercury, Cadmium, Lead) and POPs aggressively concentrate. Milk transmission of POPs is much greater than placental transmission.

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Clinical Dossier: Synthesis – The Cycle and the Solution



The Lifelong Cycle of Exposure

Environmental and reproductive toxicology are inseparable. Systemic environmental pollutants inevitably become biological burdens, passing from the macro-environment into the most intimate stages of human development.

The Analytical Imperative & Next Steps

To evaluate this cycle, we require robust biological models. We will now enter the Zebrafish Facility to utilize fish anatomy and the Fish Embryo Acute Toxicity test to practically analyze these developmental threats.

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