Intersex wildlife as sentinels for human health and endocrine disruption near Superfund sites: A Systematic Review

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**Study Question**
Do wildlife in contaminated waters near Superfund sites have a higher prevalence/severity of intersex compared to the same wildlife farther away from Superfund sites?

**Scope & Introduction**

Intersex in wildlife is often used as sentinels for human health.

Intersex is the occurrence of sexual characteristics that are not exclusively female or exclusively male. It is a spectrum of conditions that involve the occurrence of both male and female reproductive tissues, including abnormalities in gonadais, sex chromosomes, and ambisexual gonads. Intersex is a significant public health concern because of the potential health impacts associated with endocrine disruption caused by exposure to certain chemicals, such as those found at Superfund sites.

**Superfund Chemicals**
- Endocrine disrupting chemicals (EDCs) are long-lasting and known to have reproductive and endocrine issues, even at low doses.
- EDCs are widespread throughout US watersheds at both high and low doses and are often present in ecosystems.
- Often emitted Superfund Sites (EPA designated toxic waste sites)

**Methods**

**Study Search**
- Search PubMed, Scopus, ProQuest, Web of Science, Google Scholar databases
- Exposure: "Superfund" or "CERCLA"
- Outcome: "intersex" or "gonad histology" or "hormone disturbance"
- "intersexuality" or "gonadal disorder"

**Study Selection**
- Multiple passes with abstract read then full read
- Inclusion: gonad histology or histopathology done on Superfund site in title or abstract, wildlife animals
- Exclusion: not original research, book section, toxicological studies, human outcomes, outside US, not English

**Risk of bias**
- Possible ratings of "low", "probably low", "probably high", "high", or "not applicable"
- Each study evaluated pre-specified factors: sampling strategy, bias, confounding, comparison group, exposure assessment, incomplete outcome data, etc.

**Quality of evidence**
- Upgraded or downgraded full body of evidence
- Started at "moderate quality" and were upgraded (+1, +2), downgraded (-1, -2) or neutral for a value of 0.
- Prespecified factors: risk of bias, inconsistency, imprecision, inapplicability, etc.

**Strength of evidence**
- The possible rating was "sufficient evidence", "limited evidence", "inadequate evidence", or "evidence of a lack of toxicity"
- Considers quality of evidence, direction of effect, confidence of effect, other compelling attributes of the data

**Results**

**Quality of evidence:**
- Low
  - Lack of control sites, high risk of confounding and biasing
  - Strength of evidence: Limited Evidence
  - Overall small positive relationship trend, no inverse

**Discussion**

**Knowledge Gaps**
- No standard definition for proximity to a Superfund site
- Unknown background levels of intersex for each species
- Long-term impacts of climate change on intersex
- Lack of control sites with surveillance papers

**Recommendations**
- Standardize methods: gonad histology, severity rankings, etc.
- Establish confounders
- Meta-analysis with current studies by species
- Examine links with certain EDC chemicals from Superfund sites
- Look for studies with human health concern: ex. breast cancer risk in the Great Lakes

**Conclusions**

**Limitations of the systematic literature review**
- First looking at this body of evidence
- Only English and in US

**Strengths of the systematic literature review**
- Multiple animal species
- Strong sampling of evidence

**Ecological application of Navigation Guide**

- Limited overall strength of evidence: small positive trend of higher intersex near Superfund sites
- Implications for an indicator of ecological health, watershed health, and human health
- More research needed: meta-analysis with data from this review, species-specific studies
- Address limitations like adding other disruption indicators and multiple chemical exposures

**References**


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