AUTISM SPECTRUM DISORDER: ENVIRONMENTAL FACTORS AND EMERGING RESEARCH METHODOLOGIES

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Recent data from the Centers for Disease Control and Prevention confirms that autism diagnoses in this country are on the rise. We should not assume that these increasing rates reflect only changes in diagnostic criteria and improved detection.

Current scientific evidence supports that autism is fundamentally a multifactorial disorder. We and others in the field are moving to studying multiple genetic and environmental factors and how they may act in concert. Research consistently demonstrates that environmental factors influence individual autism onset and severity risk. Manufactured chemicals could contribute to autism etiology via multiple mechanisms (PMID: 32479765, 39418383).

Aspects of the modern environment require serious consideration in autism research. One critical area is the increasing exposure to manufactured plastic chemicals (PMID 39183960). Plastics are the most utilised manufactured material in daily life; global production (460 M metric tons in 2019) is projected to triple by 2060. A range of chemicals including plastic additives (e.g. bisphenols, phthalates) should be investigated, not only a focus on microplastics. There is no precautionary principle; plastics are assumed safe unless proven otherwise.

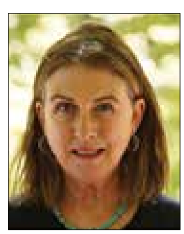
Our work published in *Nature Communications* in 2024 demonstrated that prenatal exposure to bisphenol A (BPA) is associated with autism risk in boys through a mechanism involving aromatase suppression (PMID: 39112449). Boys with low aromatase activity and high prenatal BPA exposure were six times more likely to receive an autism diagnosis by age 11 years. This research revealed that BPA suppresses the aromatase enzyme and is associated with anatomical, neurological, and behavioral changes in male mice consistent with autism. This represents the first identification of a specific biological pathway that might explain the connection between autism and BPA exposure (PMID: 39112449).

Environmental factors such as BPA rarely act in isolation. There is growing recognition that prenatal exposure to neurotoxic mixtures of environmental chemicals—including endocrine disruptors (e.g. bisphenols, phthalates), pharmaceuticals, pesticides, and food additives—may contribute to neurodevelopmental outcomes such as autism. Yet chemical mixtures have rarely been investigated in autism.

Chemical co-exposures through shared pathways can contribute to cumulative chemical effects. However, current exposure science has been constrained by targeted approaches. This limited scope fails to reflect the complexity of real-world exposures: >4,600 chemicals with high production volume (>1,000 tons/yr). A key technical advance is that we can now accurately quantify low-abundance environmental chemicals in human serum.

Research demonstrates significant synergistic interactions between commonly used chemicals, with combinations showing greater neurotoxicity than individual substances alone. A 2024 Science report found that almost all pregnant women have multiple chemicals detectable in their blood, with 90% having more than 38 chemicals, including many with known neurotoxic effects (PMID: 39418383). The top-ranked chemical for inducing cellular neurotoxic effects was a food additive, demonstrating the value of comprehensive untargeted toxicological approaches.

New machine learning techniques are revolutionizing our capacity to comprehensively measure and understand complex pathways and mechanisms underlying autism development and the multifactorial nature of autism. The convergence of epidemiological evidence, mechanistic research, and advanced computational approaches is opening new frontiers in autism research, providing hope for both improved outcomes for individuals with autism and prevention strategies.



Dr. Anne-Louise Ponsonby is an epidemiologist and public health physician. She has extensive experience in the design, conduct, and analysis of population-based studies, and public health translation. Ponsonby has 427 publications, has contributed to three patents, and is on the research committee for the International Paediatric Multiple Sclerosis Study Group.