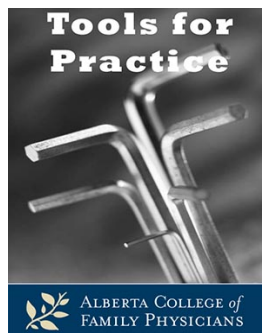


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## **Acetaminophen in pregnancy and future risk of ADHD for the unborn.**

**Clinical Question: Does acetaminophen in pregnancy increase the future risk of Attention Deficit Hyperactive Disorder (ADHD) for the unborn?**

**Bottom-Line: Two well-done cohort studies suggest an association between acetaminophen use in pregnancy and an increased risk of ADHD or similar behaviours in children. While cohort studies cannot prove causation and we need further confirmation, there may be a possible small risk of prolonged use of acetaminophen – especially late in pregnancy. Study limitations prevent specifics.**

### **Evidence:**

- Three cohort studies:
  - Danish prospective cohort of 64,322 pregnancies.<sup>1</sup> Acetaminophen use in pregnancy associated with statistically significantly:
    - Higher scores for behavioural problems on the Strengths & Difficulties Questionnaire (at seven years): Risk Ratio 1.13 (1.01-1.27).
    - From a government central registry (over ~11 years):
      - Diagnosed hyperkinetic disorder: Hazard Ratio 1.37 (1.19-1.59).
      - Prescription of  $\geq 2$  ADHD medications: Hazard Ratio 1.29 (1.15-1.44).
  - Norwegian prospective cohort of 48,631 pregnancies.<sup>2</sup> Focus on 2,919 same-sex sibling pairs:
    - Acetaminophen use  $\geq 28$  days in pregnancy correlated significantly with maternally-assessed child behaviour at three years for:
      - Reduced gross motor skills, delay in walking, increased activity, reduced communication skills, attention/aggression behaviours.
      - Correlation Beta-coefficients around 0.2-0.26, approximately equivalent to a 50-60% relative increase.
    - Strength: Sibling pairs (eliminating differences in mother/families).
    - Weakness: Shorter duration and only maternal assessment.
  - Both studies suggest (results inconsistent) longer use and use later in pregnancy may have stronger association.<sup>1,2</sup>

- Older cohort of 355 children found no association between maternal use of acetaminophen in the first five months of pregnancy and attention testing at age four.<sup>3</sup>

**Context:**

- Cohort studies show associations (things happening together) but not causation. They are subject to ‘confounding’ risk.
  - Women who used acetaminophen may be different: having more pain or headaches and perhaps this contributes to ADHD.
- Based on 5.3% worldwide prevalence of ADHD<sup>4</sup> and a possible 13-37% relative increase,<sup>1</sup> absolute increase might be 0.7%-2%, if real.
- Acetaminophen is used by 55-65% of pregnant women.<sup>1,5,6</sup>
- Acetaminophen is generally felt to be safe in pregnancy<sup>7</sup> (not teratogenic) and recommended first-line for pain due to safety.<sup>8,9</sup>
  - These statements precede this recent research.

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**Disclosures:**

Authors have no conflicts to disclose.

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