Case report:

Lithium exposure of a prematurely born fetus who became a breastfed infant

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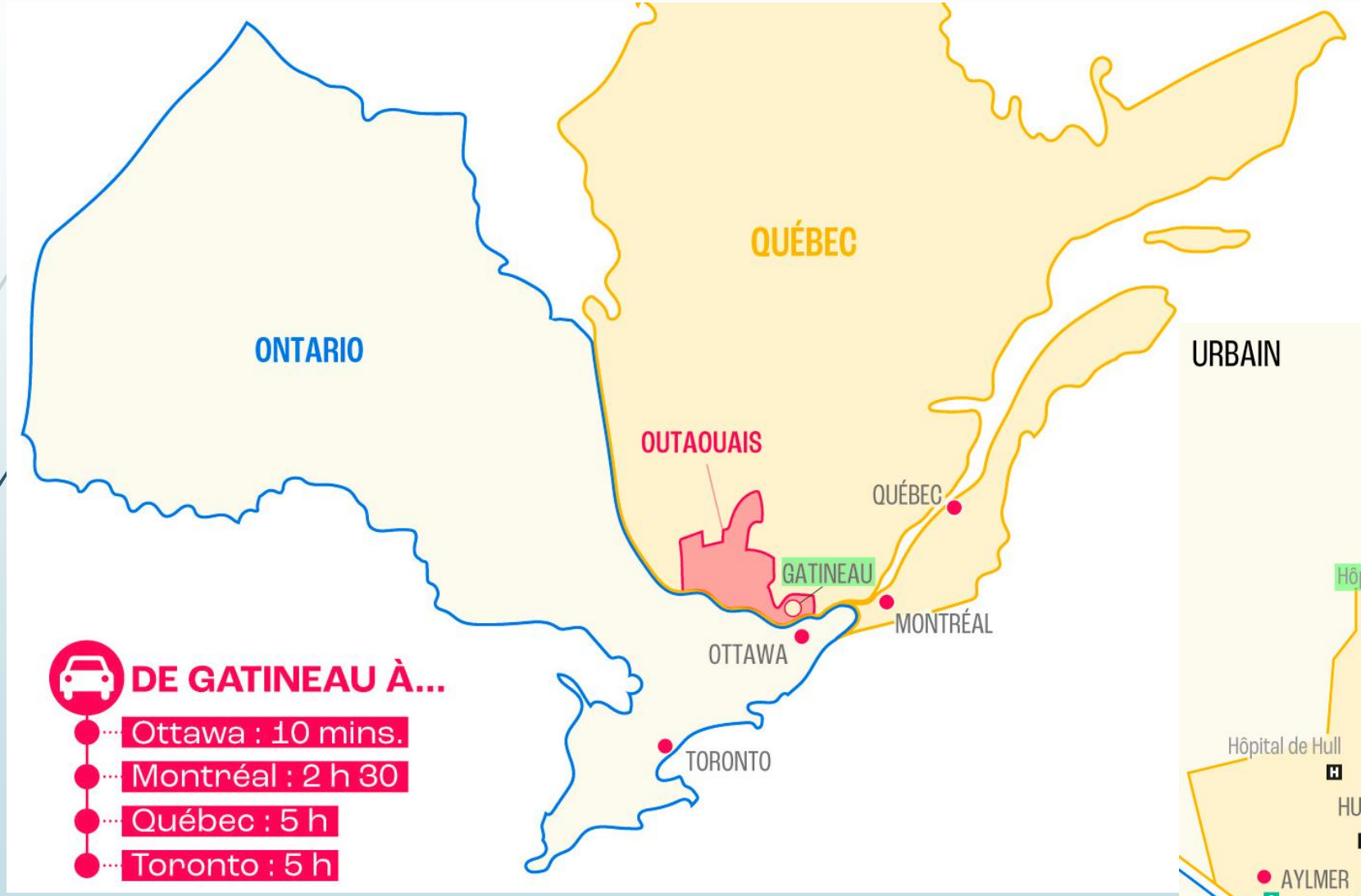
Who am I?

- Pharmacist involved in perinatal and pediatric care since 2007 and offering perinatal and pediatric internship to pharmacy students and residents from Université Laval since 2018
- Volunteer breastfeeding mentor and doula from 2005 to 2011
- Webinars and presentations at various healthcare professional conferences on medications in breastfeeding
- Initiatives on medications in breastfeeding recognized by awards from Ste-Justine hospital Pharmacy Department, Profession Santé (Canadian Healthcare Network) and the Canadian Society of Hospital Pharmacists (CSHP) in 2019
- *Development of pharmacological advice sheets and dissemination via a breastfeeding support organization*, poster recognized by awards at the International Interdisciplinary Congress on Advanced Breastfeeding, Université du Québec à Trois-Rivières in 2023 and at the Association des Pharmaciens en Établissement de Santé (APES) Grand Forum congress in 2024
- Commitment Award at the CISSS de l'Outaouais Distinctions Gala in 2024
- Citizen Merit Award from the City of Gatineau in 2025

Where do I come from?



Background

- Even today, some references state that it is contraindicated for a mother treated with lithium to breastfeed her child.
- However, pregnancy, childbirth and breastfeeding constitute a continuum. Transfer of lithium into breast milk (BM) appears to be lower than through placenta where concentrations on both sides are equivalent. Thus, the breastfed child would never be as exposed to it as during fetal life.
- There are case reports of children exposed to lithium in utero and then breastfed. On the other hand, none mentioned a child born prematurely exposed to combination therapy at the time of this case.

Goal

The healthcare team wanted to respect the mother’s wish to successfully breastfeed exclusively her baby born prematurely while implementing a progression aimed at minimizing, or even eliminating, the occurrence of adverse effects.

Method

The data were obtained prospectively until 2 months old, thanks to the agreement of and interview with the parents and consultation of the clinical file of the mother and her child.

A short interview with the mother was conducted 28 months after birth, thanks to her.

Context

- Premature rupture of membranes (PROM) at 36 weeks of gestation and breech presentation foot first led to cesarean section (CS) birth.
- Baby presented hypotonia at birth.
- APGAR score of 1-4-6. Weight 2.525 kg (4 lbs 6.5476 oz).
- Required temporary respiratory assistance, weaned on day 1.
- Child's "maladjustment to extrauterine life" possibly multifactorial and consecutive to CS, prematurity and the effect of oral maternal medications.

Context

Mom's medications:

- bupropion 400 mg po daily
- lurasidone 40 mg po daily
- lithium 750 mg po daily
- trazodone 50 mg at bedtime as needed

Mom's lithium level the day of the birth: 0.9 meq/L

Results

- On day 2, the mother was informed of the lack of breastfeeding data in a case like her dyad.
- The “slowly but surely” precaution was therefore adopted in a process of shared decision-making with the parents.
- Serum creatinine, TSH and lithium level were ordered for the morning after (67 hours of life):
  - Infant's lithium level (ILL) = 0.5 meq/L
  - Infant’s serum creatinine (ISC) = 44 meq/L (0.5 mg/dL)
  - Infant’s TSH = 5.07 mUI/L

Results

- BM intake was started at 10% of total nutritional needs.
- Upon discharge from the hospital on day 8:
  - ILL below 0.2 meq/L
  - ISC = 34 meq/L (0.38 mg/dL)
  - Weight: 2,555 kg (4 lbs 6.5479 oz)

  and BM administration progressed to 20% of total nutritional needs
- On day 22 with 33% of BM ingested since several days :
  - ILL below 0.2 meq/L
- The pediatrician considered normal his development and authorized exclusive breastfeeding.

Results

Still exclusively breastfed on day 51

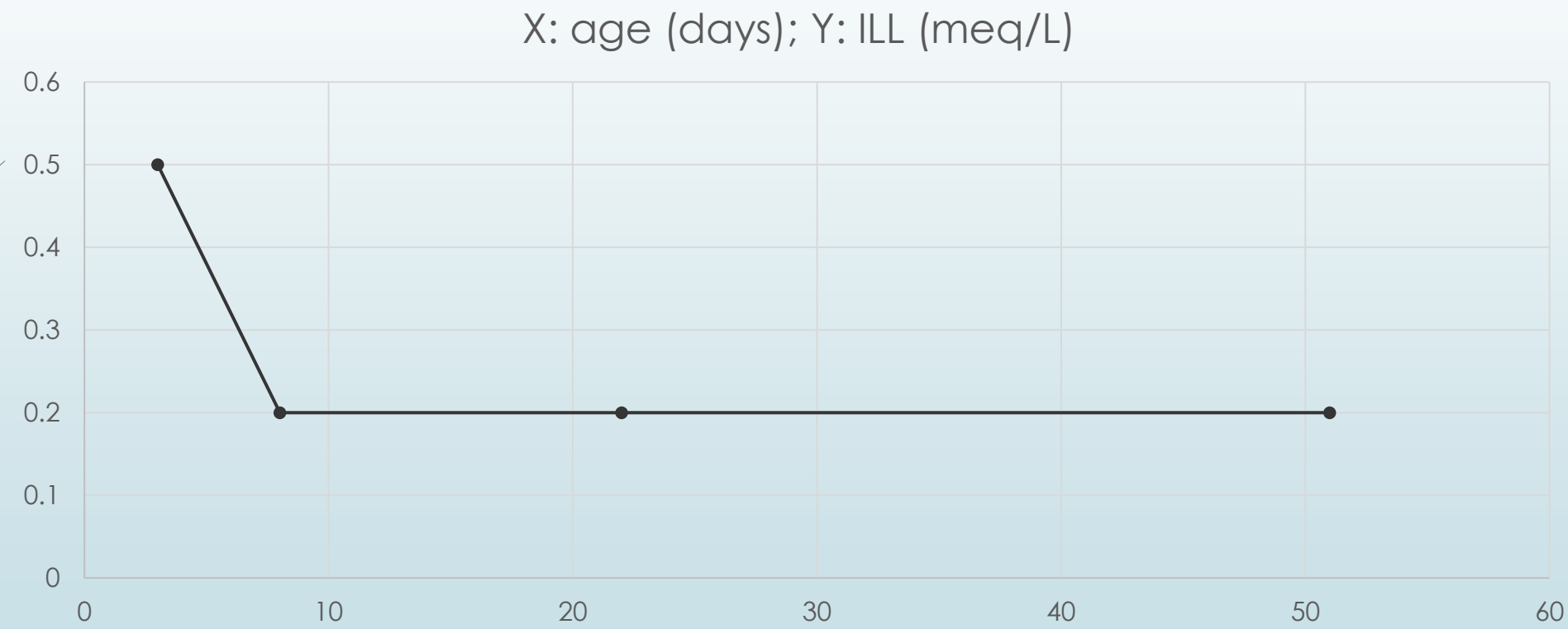
- ILL below 0.2 meq/L
- ISC = 15 meq/L (0.17 mg/dL), normalized
- TSH = 1.49 mUI/L, normalized
- Exclusively breastfed since day 22 and development considered normal by the pediatrician

Mom’s lithium level at day 66 stable at 0.9 meq/L

Discussion

- Lithium has **complete placental passage**, with **an ion equilibration** across placental barrier that is remarkably **uniform** across a wide range of maternal concentrations.
- Lithium is **eliminated** primarily through the **kidneys**. Its **half-life** in **term** newborns is estimated at approximately **3 to 4 days**.
- Serum lithium concentrations in the **first week postpartum may reflect transplacental passage** rather than intake via breast milk.
- Previous systematic reviews have **failed to address clinical symptoms of lithium toxicity** in infants for **levels inferior or equal to 0.3 meq/L**.

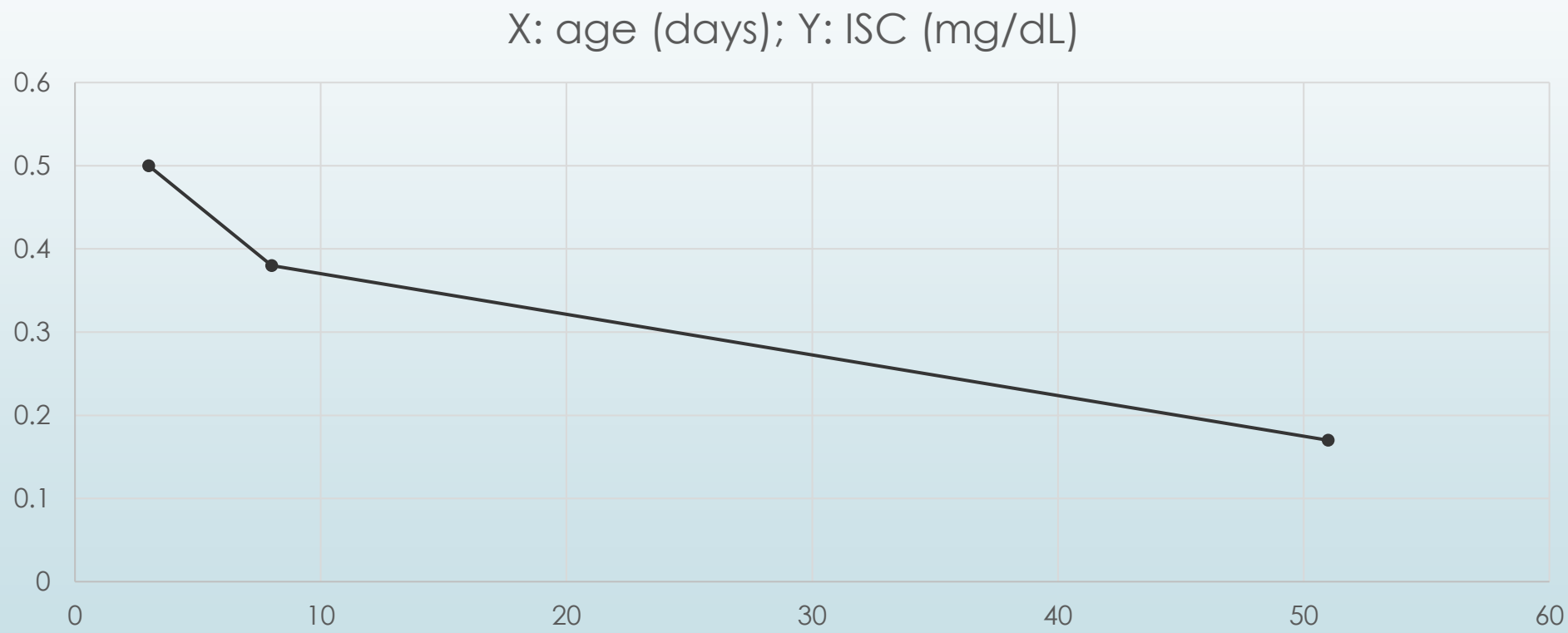
Infant's Lithium Levels (ILL) values



Discussion

- In full-term neonates, **serum creatinine levels are normally elevated at birth**, **reflecting the mother's kidney function** due to **fetal-maternal placental equilibration** (usually 0.70 mg/dL), and this **progressively decreases** over several weeks to reflect the **infant's true kidney function.**

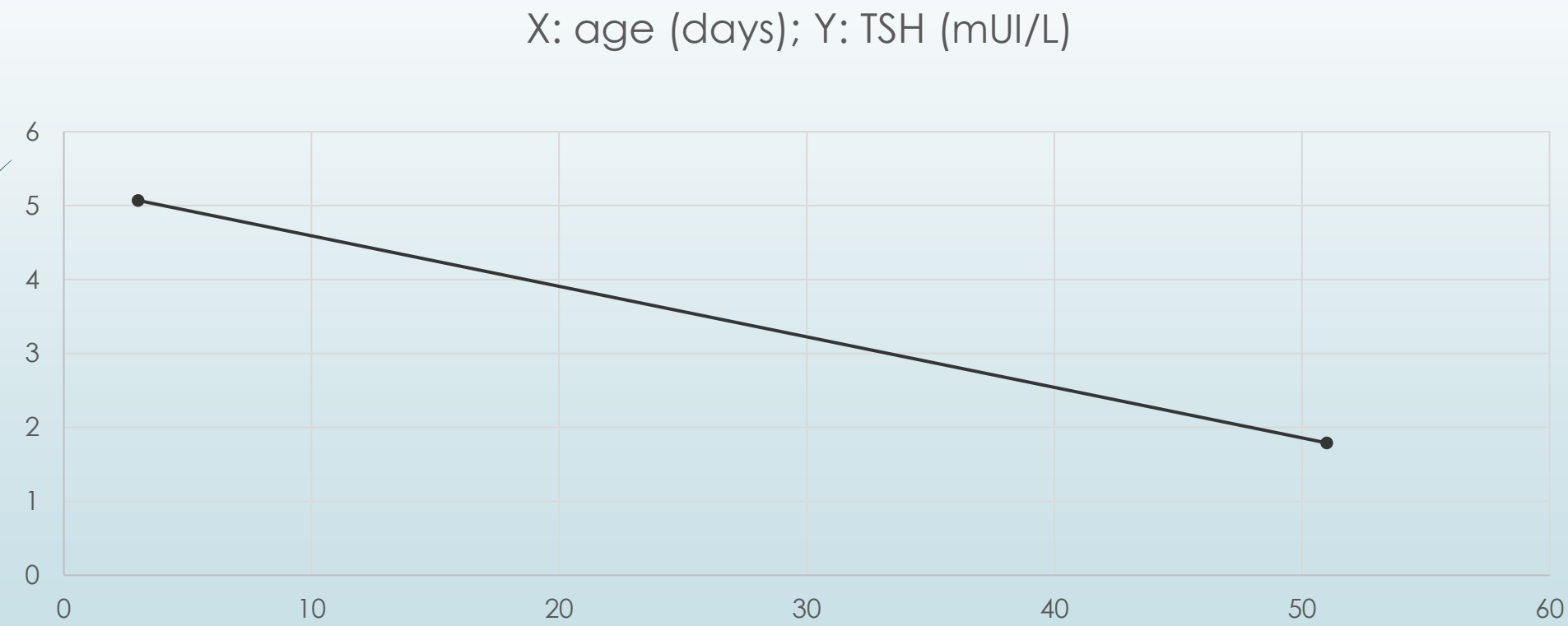
Infant’s Serum Creatinine (ISC) values



Discussion

- **Rare, reversible neonatal effects** have been observed when treatment is continued until delivery. These mainly include: **hypotonia, thyroid dysfunction** (hypothyroid or euthyroid goiters, etc.), cardiac arrhythmias (bradycardia, etc.), heart failure, diabetes insipidus. When they occur, these effects **appear within the first few hours of life** and **resolve within about ten days (or longer for the thyroid)**.

Thyroid stimulating hormone (TSH) values



Discussion

- **The possibility of these neonatal effects** occurring must be **weighed against the risk of decompensation** that could be incurred by the mother **if her treatment was reduced or even stopped**, particularly during the fragile period of late pregnancy and postpartum.
- To date, taking into account all published data, no specific **neurodevelopmental effects** have been reported in children exposed in utero to lithium (children aged approximately 2 to 10-11 years).

Discussion

Only one case of premature baby found in a retrospective cohort…

Mild prematurity (35 2/7 weeks); needed CPAP for one day; breastfed partly at birth and follow-up (11 days old); mother on lithium, SSRI and anxiolytics (which one…?)

Maternal lithium concentration: 0.8 at delivery and 0.6 meq/L at follow-up

Infant's lithium concentration: 0.9 in umbilical cord, 0.6 at 2 days of age 0.7 meq/L at follow-up

"Poor weight gain at 11 days of age" means that baby has not regained its birth weight

"Initial weight loss of 15%": what does it mean? On what day after birth?

Considered "large for gestational age": what weight was used for comparison: at birth or after 24 hours? Did mom receive lots of fluids during birth?

Explanation: combination of exposure to lithium and other drugs, lower kidney function due to prematurity and dehydration due to large initial weight loss

Limits

Of course, the follow-up was very short. The pediatrician who was looking after the baby stopped following him and transferred him to a general practitioner; his clinical record was therefore no longer available.

Follow-up news

At 28 months old (may 2025):

Daycare since last september:

- 5 monthly otitis media infection (september to january)
- Language delay (caused by repeted otitis media?), sign language (Baby signs)
- mild sleep apnea (saturation taken 3 consecutive nights)
- Waiting for speech therapy evaluation and adenoidectomy + tympanostomy (ear tube placement)
- Still breastfed at night

Conclusions

- Similar reported cases on which to rely to outline the decision-making process were lacking when baby was born.
- Caution was required to achieve this mother's ultimate objective, either to exclusively breastfeed her child, without adverse effects.
- A shared decision-making process was conducted with the parents.
- Although initially fed mainly by infant formula, the proportions were reversed to finally meet nutritional needs exclusively by breastfeeding at 3 weeks of life with a stable ILL since day 8, remaining below 0.2 meq/L, without any adverse effects and with a normal development.

Conclusions

This case is one of the few on this topic. It is therefore very important.

As we know the importance of breast milk for premature infants (reduced risk of necrotizing enterocolitis, antibodies to protect against infections, etc.), case reports of other premature babies exposed to lithium in utero and breastfed by their mothers stabilized on lithium are essential to help healthcare professionals and parents in decision-making.

Conclusions

As healthcare professionals, we have a responsibility to:

- Provide objective, complete, and up-to-date information for free and informed decision-making.
- Balancing the risks of the drug in the milk to the child WITH the risks of not treating or changing treatment to the mother and the risks of not breastfeeding to the mother and her child.

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