PSYCHIATRIC MEDICATIONS IN PREGNANCY AND LACTATION

A Clinical Guide to Risk-Benefit Assessment and Safe Prescribing

Evidence-Based Protocols • Pharmacokinetic Remodeling • Prescribing Matrices

THE PARADIGM SHIFT IN PERINATAL PSYCHIATRY

THE PAST: THERAPEUTIC NIHILISM

Driven by the 1960s Thalidomide disaster, leading to an absolute "zero medication" assumption.

Result: Pregnant women left completely untreated, harming maternal and fetal outcomes.

Regulatory Era: FDA Pregnancy Categories (A, B, C, D, X). Often misinterpreted as absolute risk rather than just the quality of evidence.

THE PRESENT: RISK-BENEFIT ANALYSIS

Nuanced clinical assessment prioritizing maternal stability.

Result: Recognition that untreated maternal illness is a severe biological risk to both mother and fetus.

Regulatory Era: The 2015 FDA Pregnancy and Lactation Labeling Rule (PLLR) requires narrative summaries of clinical data instead of simplified alphabetic categories.

THE BIOLOGICAL COST OF UNTREATED ILLNESS

3.7× Increased risk of **preeclampsia**

2.5× Increased **preterm birth** risk

1.6× Increased **low birth weight**

5% **Postpartum psychosis infanticide** risk

Additional impacts: Impaired maternal-infant bonding, compromised breastfeeding.

MEDICATION TERATOGENICITY RISK

Background malformation rate: **~3%** (General population baseline)

Medication absolute risks: Generally low (fractions of a percent for preferred agents).

⚠ The decision to withhold psychiatric medication to avoid fetal exposure is itself a medical risk.

Pregnancy-Induced Pharmacokinetic Changes

CIRCULATORY SYSTEM

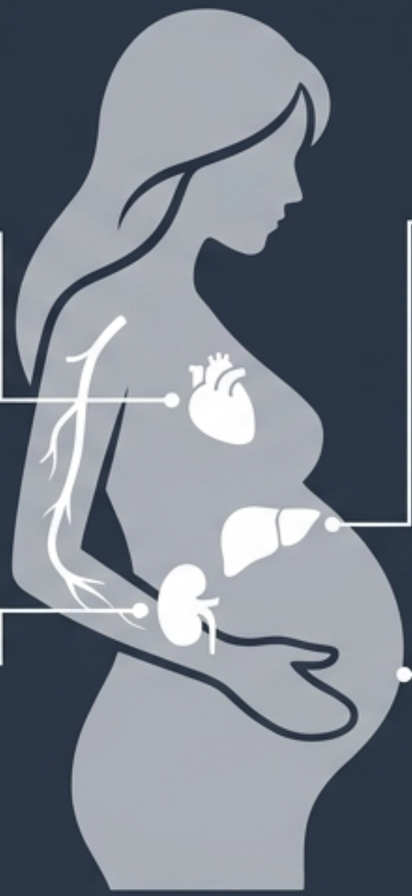
↑ **Blood Volume:** +40–50% (reaches 5.0–6.0 L)

Effect: Dilutes drug concentration.

KIDNEYS

↑ **GFR:** +40–50% (140–180 mL/min)

Effect: Increases renal clearance of medications.



LIVER

↑ **Hepatic Metabolism:** CYP2D6 and CYP3A4 increase 25–60%

Effect: Rapidly metabolizes SSRIs and certain antipsychotics.

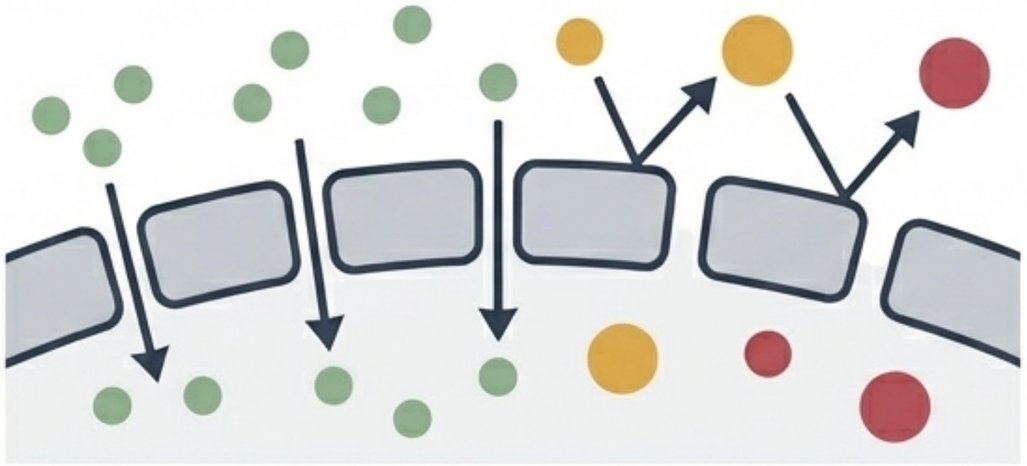
BLOODSTREAM

↓ **Protein Binding:** Decreased serum albumin

Effect: Higher unbound (active) drug fractions.

CLINICAL IMPLICATION: Serum concentrations of many psychiatric medications decline during pregnancy, requiring dose increases to maintain therapeutic efficacy.

THE PLACENTAL FILTER MODEL



PASSES THROUGH EASILY:

- Highly lipophilic drugs
- Molecular Weight <500 Da

BLOCKED / REDUCED TRANSFER:

- Highly protein-bound drugs
- Molecular Weight >1000 Da

NOTE: Weak bases accumulate in acidic fetal circulation (ion trapping).

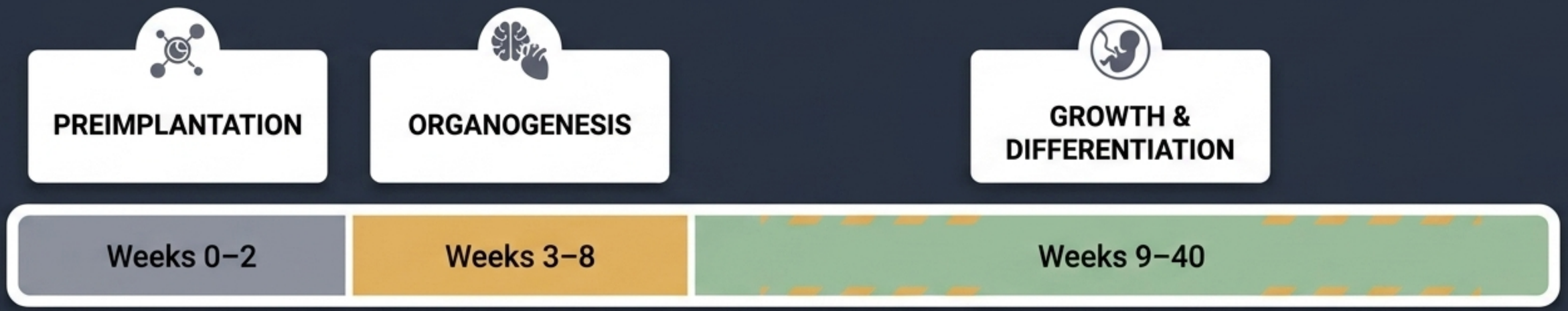
LACTATION RISK PROFILE

$$\text{RID} = \left(\frac{\text{Infant dose via milk}}{\text{Maternal dose}}\right) \times 100$$

Generally Safe | **Caution / Monitor** | **Increased Risk**

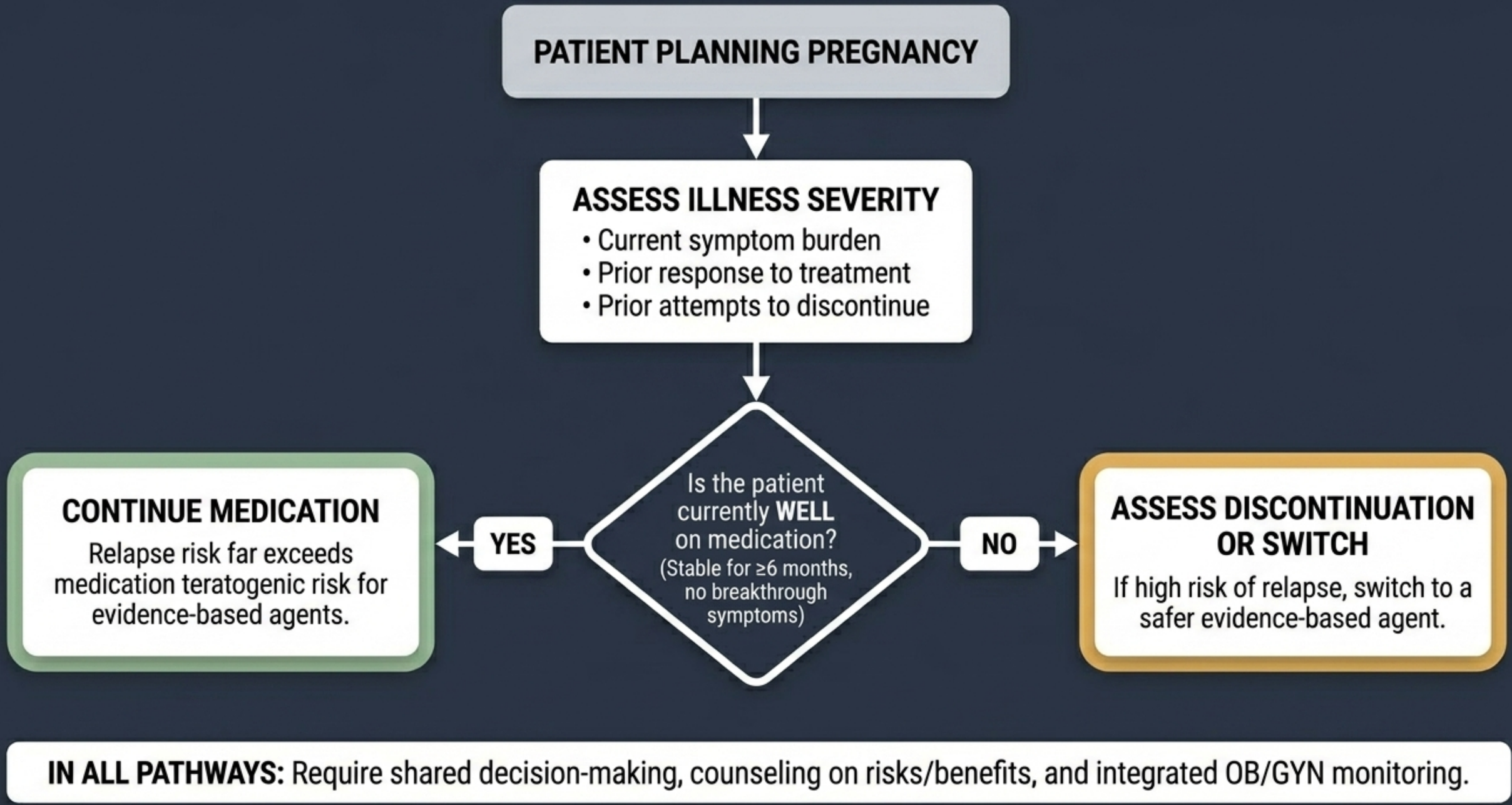
* **Clinical Pearl:** Neonatal CYP450 maturity increases over the first weeks of life, altering metabolic risk dynamically.

Chronological Map of Fetal Vulnerability



GLOSSARY: PNAS

Poor Neonatal Adaptation Syndrome: Jitteriness, poor feeding, and irritability associated with SSRI exposure in the third trimester.


PATIENT PLANNING PREGNANCY
ASSESS ILLNESS SEVERITY
• Current symptom burden
• Prior response to treatment
• Prior attempts to discontinue
Is the patient currently WELL on medication?
(Stable for ≥6 months, no breakthrough symptoms)
YES
NO
CONTINUE MEDICATION
Relapse risk far exceeds medication teratogenic risk for evidence-based agents.
ASSESS DISCONTINUATION OR SWITCH
If high risk of relapse, switch to a safer evidence-based agent.
IN ALL PATHWAYS: Require shared decision-making, counseling on risks/benefits, and integrated OB/GYN monitoring.

Prescribing Guide: Depression, Anxiety & PTSD

PREFERRED: SSRIs (Sertraline)

- **Status:** First-line for MDD, GAD, and PTSD.
- **Profile:** Extensive safety data. High protein binding limits milk transfer (RID 0.4–2.2%).
- **Risk Note:** PNAS risk is ~2–5% with third-trimester exposure; vast majority resolves in 48-72 hours.

ALTERNATIVES: Fluoxetine, Bupropion, Buspirone

- **Fluoxetine:** Good safety, but long half-life complicates dose adjustments.
- **Bupropion:** No teratogenic risk identified; useful alternative if weight gain is a concern. Avoid in seizure disorders.
- **Buspirone / Hydroxyzine:** Safe, non-habit-forming alternatives for anxiety.

AVOID: Benzodiazepines

- **Status:** Reserve for acute crisis only. Avoid in pregnancy.
- **Risks:** First-trimester exposure linked to orofacial clefts (RR ~2-3x). Third-trimester exposure causes 'floppy infant syndrome' (hypotonia, poor feeding, withdrawal).

The Mood Stabilizer Matrix

AGENT	TERATOGENIC RISK	MONITORING/ACTION
LAMOTRIGINE (Preferred)	Lowest risk. Fetal effects minimal.	Serum levels decline heavily during pregnancy. Often requires dose increase by 25-100%. Target 4–20 µg/mL.
LITHIUM (Highly Effective)	Ebstein's anomaly. Modern studies show actual absolute risk is only ~0.05–0.1%.	Fetal echocardiography at 16-20 weeks. Check levels q2-4 weeks. Target 0.6–0.8 mEq/L.
CARBAMAZEPINE (Intermediate)	Orofacial cleft risk ~0.5–1% (2-3x baseline).	Baseline screening, 4-5 mg/day folic acid supplementation.
VALPROATE / DIVALPROEX (Absolute Contraindication)	Neural tube defects 1-2% risk (20-50x baseline). Documented neurodevelopmental impairment and autism spectrum.	**Action:** Transition prior to conception. Urgent Maternal-Fetal Medicine consult if pregnant.

Psychosis & Insomnia Interventions

Psychosis & Schizophrenia (Antipsychotics)

- **Principle:** No clear teratogenic signal for major agents. Benefits far outweigh risks.

PREFERRED AGENTS:

- **Haloperidol**: Most studied 1st-gen. Avoid depot near delivery.
- **Quetiapine**: Broad-spectrum, reassuring data, less weight gain.
- **Aripiprazole**: Favorable metabolic profile (RID < 1%).

CAUTION:

- **Olanzapine**: Highly effective but significant metabolic risk. Gestational diabetes screening is mandatory.

Insomnia Interventions

FIRST-LINE:

- **CBT-I** (Cognitive Behavioral Therapy for Insomnia)
- Sleep restriction, stimulus control.

PHARMACOLOGIC OPTIONS:

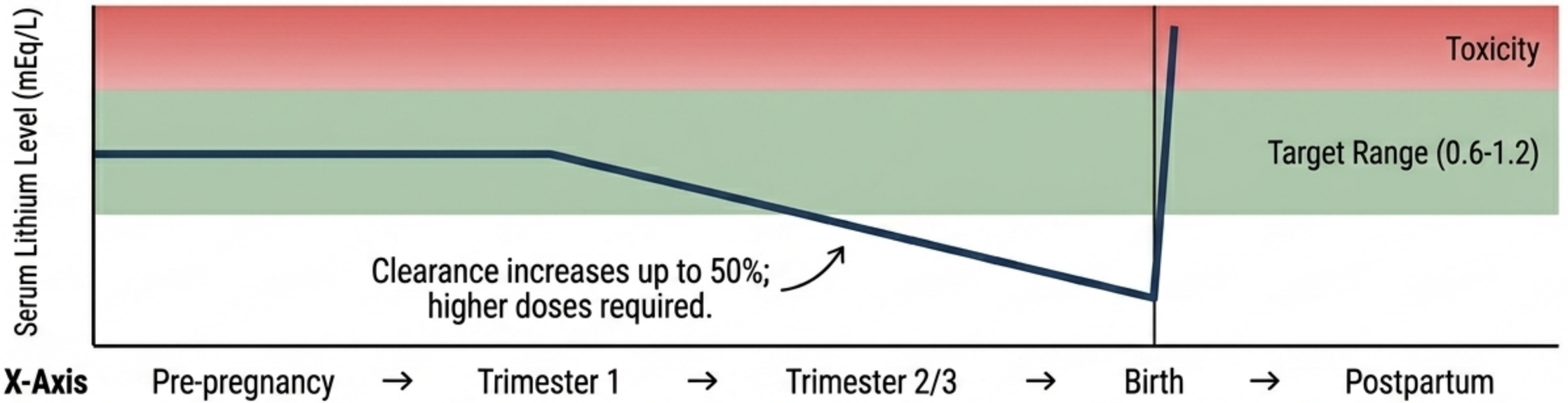
- **Diphenhydramine**: Extensive safety data, RID 0.3-1.5%.
- **Low-dose Doxepin**: 3-6mg.

CONTRAINDICATED:

- **Benzodiazepines**: Teratogenic risk and withdrawal.

The Pharmacokinetic Remodeling Cycle

The Postpartum Lithium Rollercoaster



CRITICAL POSTPARTUM TRANSITION

Delivery triggers rapid normalization of GFR and blood volume. Doses that were therapeutic yesterday are toxic today.

MANDATORY: Reduce Lithium dose by 30-50% immediately postpartum to prevent severe toxicity (tremor, ataxia, seizures).

Neonatal & Postpartum Monitoring Timeline

Hour 0-6 (Birth)

- **ACTION:** Assess Apgar scores. Alert neonatal team to all maternal medication exposures.
- **LITHIUM SPECIFIC:** Obtain neonatal lithium level immediately (normal <0.1 mEq/L).

Day 1-3 (The PNAS Window)

- **ACTION:** Monitor for **Poor Neonatal Adaptation Syndrome** (SSRI exposure).
  - **SYMPTOMS:** Jitteriness, high-pitched cry, poor temperature regulation.
  - **CLINICAL TRUTH:** Vast majority resolve spontaneously within 48-72 hours. Manage with supportive care.
  - **RULE-OUT:** If severe tachypnea (>60 breaths/min), obtain CXR/Echo to rule out rare PPHN.

Day 3-7

ACTION: Recheck maternal lithium levels (clearance should normalize).

ACTION: Screen mother for immediate psychiatric relapse. The immediate postpartum period is the **highest-risk window** for bipolar and psychosis recurrence.

Perinatal Screening Toolkit

EPDS (Edinburgh Postnatal Depression Scale)

Domain: Postpartum Depression

Specs: 10 items. Gold standard. Cutoff ≥10 suggests depression.

PHQ-9 (Pregnancy Version)

Domain: Perinatal Depression

Specs: 9 items. Excellent for tracking symptom change with treatment over time.

PASS (Perinatal Anxiety Screening Scale)

Domain: Perinatal Anxiety

Specs: 31 items. Specifically captures panic, GAD, social anxiety, and OCD variations unique to pregnancy. Cutoff ≥20.

PRIME Screen

Domain: Rapid Mood/Anxiety Screen

Specs: 5 yes/no questions. Best for primary care and fast obstetric triage settings.

Psychiatric Medication Safety in Pregnancy: Traffic Light System

Psychiatric Conditions	Preferred	Caution	Contraindicated
Depression (MDD)	SSRIs (Sertraline, Fluoxetine)	-	-
Generalized Anxiety	SSRIs, Buspirone, Hydroxyzine	-	Benzodiazepines
PTSD	Sertraline (First-line)	-	-
Bipolar Disorder	Lamotrigine	Lithium (intense monitoring)	Valproate (CONTRAINDICATED)
Schizophrenia / Psychosis	Antipsychotics (Haloperidol, Quetiapine)	Olanzapine (metabolic risk)	-
Insomnia	CBT-I (Non-pharm)	Diphenhydramine	Benzodiazepines

TAKEAWAY: MOST psychiatric conditions have evidence-based, relatively safe pharmacologic treatment options in pregnancy. Individualized risk-benefit assessment is always warranted.