2023 GW Epilepsy Board Review & Best Practices

Women's Issues In Epilepsy

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Outline

01

Introduction

02

Hormones, fertility and contraception

- Hormones
- Sexual dysfunction
- Fertility
- Contraception
- Transgender women
- Men

03

Catamenial epilepsy

04

Pregnancy

- Preconception counseling
- ASM management in pregnancy
- Postpartum care

05

Aging

- Bone health
- Menopause

Introduction

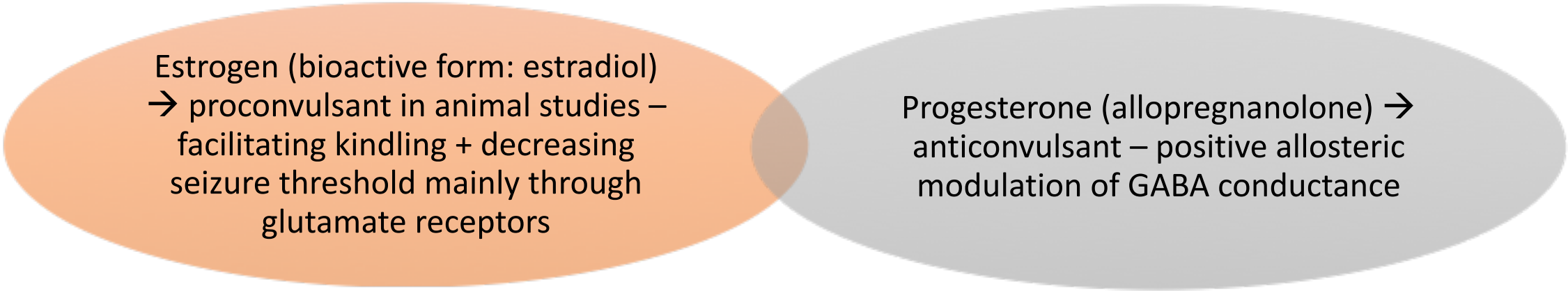
Introduction

- Globally: 15 million women of childbearing age with epilepsy
- Important to understand multidirectional relationship between hormones, seizures and ASMs
- Important concept to keep in mind: distinction between sex and gender
  - Most preclinical research: focused on sex differences
  - Transgender women with epilepsy: stigma and gender affirming medications

Hormones, Fertility and Contraception

Hormones

- 2 key steroid hormones impacting women with epilepsy:



- Higher prevalence of PCOS, amenorrhea, menstrual irregularities, premature menopause in women with epilepsy (especially TLE)
- Hormonal dysregulation can occur in absence of ASMs

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Hormones and ASMs

- ASMs can impact hormones:
  - Enzyme-inducing ASMs → induce hepatic metabolism of sex hormones and increase production of SHBG → decrease available free sex steroid hormones
  - Valproate → inhibits testosterone breakdown, induces weight gain with subsequent insulin resistance, direct antiprogestin effects due to progesterone receptor blockade → PCOS

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Sexual dysfunction

- Multiple factors
  - Poorly controlled disabling seizures
  - Comorbid mood disorders
  - Drug-related

- Topiramate, valproate, pregabalin, gabapentin → can cause sexual dysfunction

  vs. lamotrigine, levetiracetam, oxcarbazepine

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Fertility Issues and Treatments

- Potential causes of fertility issues: stigma, employment status, marital status, choice to not have children
- Potential risk factors for infertility: childhood-onset epilepsy, associated disability, structural or metabolic cause, drug-resistant or severe seizures, polytherapy, older age, lower education
- Associated risks from exogenous hormones → increase estrogen-to-progesterone ratio and interaction with ASMs → increased risk of seizures
- Similar chances as women without epilepsy of conceiving through ART

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Contraception

- Should be discussed starting at menarche
- Up to 50% of pregnancies can be unanticipated
- May become first aware of pregnancy at ~6.5 weeks of gestation
  - After closure of neural tube (4 weeks) and other major fetal development
- Epilepsy Birth Control Registry study:
  - Women with epilepsy on hormonal birth control 6.75 times risk of increased seizures compared with those using the barrier method

Differential impact of contraceptive methods on seizures varies by antiepileptic drug category: findings of the Epilepsy Birth Control Registry. Herzog et. al. 2016

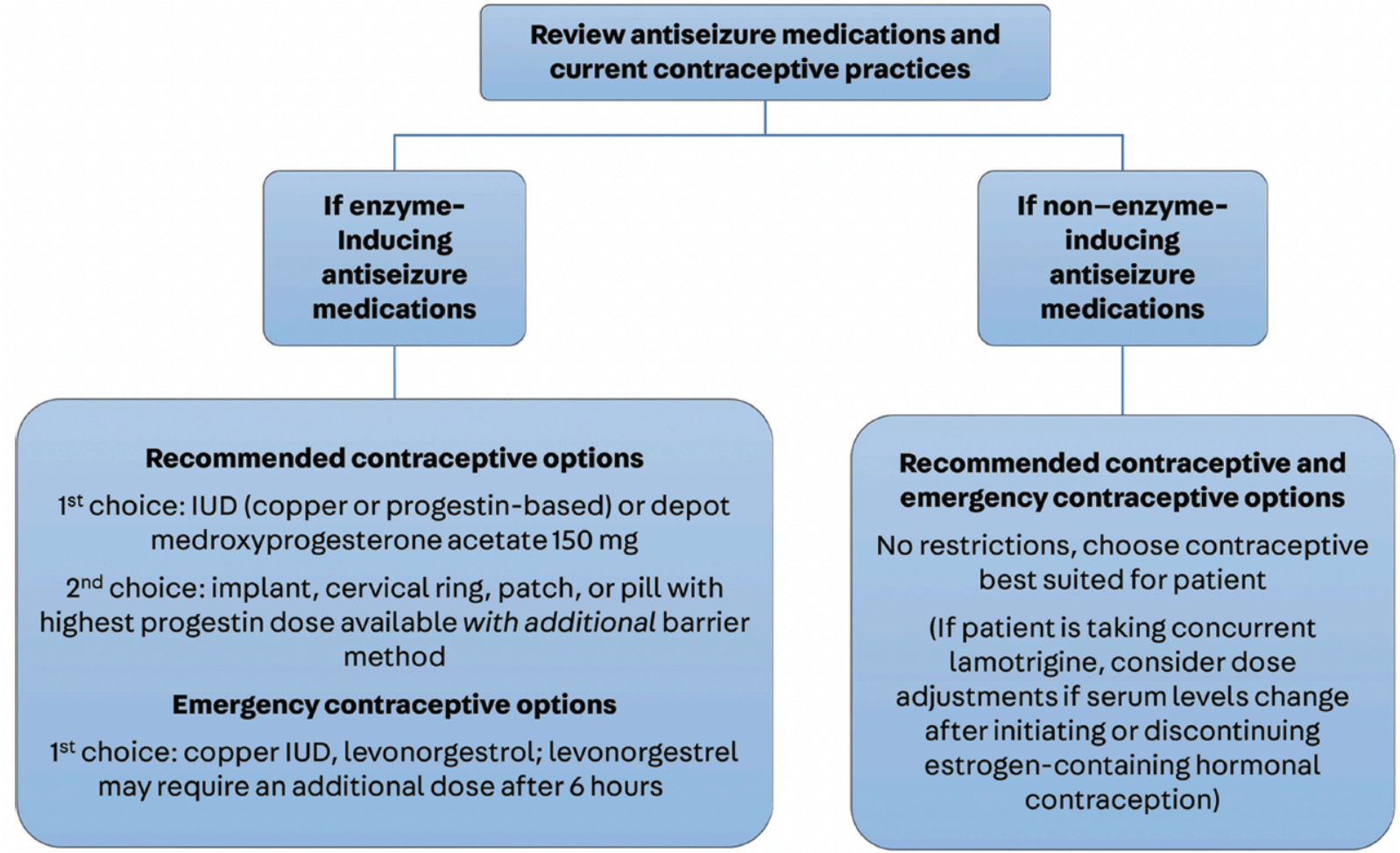
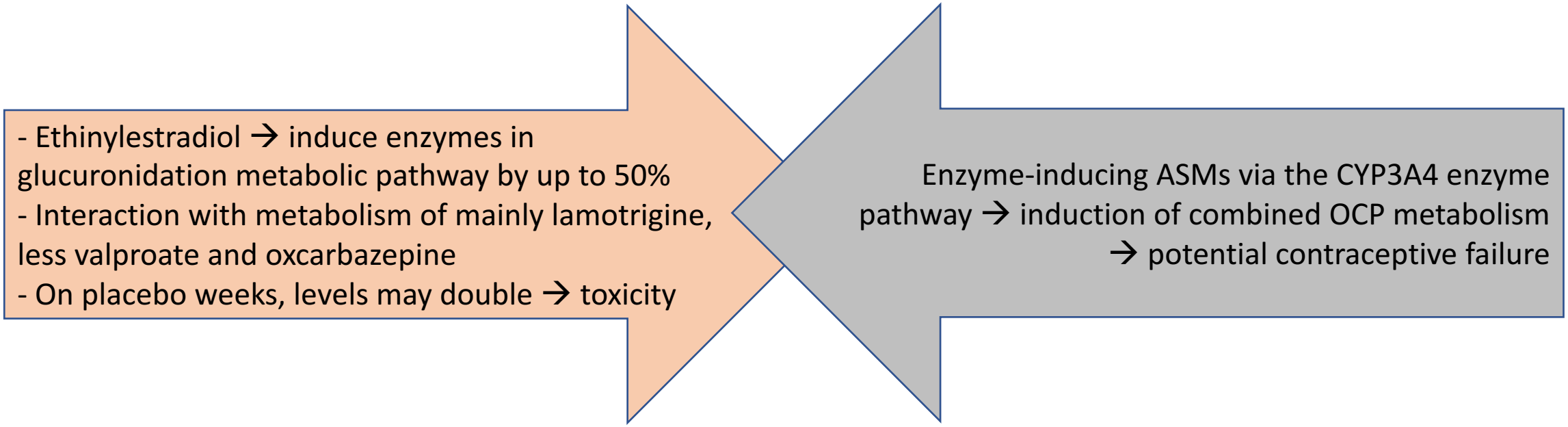


FIGURE 6-4

Approach to contraceptive options for women with epilepsy on antiseizure medications.

Data from Davis AR, et al, Springer[30]; Woodhams EJ and Gilliam M, Anne Intern Med[31]; and Thomas SV, Ann Indian Acad Neurol.[32]

Bidirectional Relationship of Contraceptives and ASMs



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ASMs that may reduce efficacy of hormonal contraceptives	ASMs that do not typically reduce efficacy of hormonal contraceptives
Carbamazepine	Acetazolamide
Clobazam	Brivaracetam
Eslicarbazepine	Clonazepam
Felbamate	Diazepam
Lamotrigine (at daily doses of 300mg or more)	Ethosuximide
Oxcarbazepine (at daily doses of 1200mg or more)	Gabapentin
Perampanel (at daily doses of 12 mg or more)	Lacosamide
Phenobarbital	Lorazepam
Phenytoin	Levetiracetam
Primidone	Pregabalin
Rufinamide	Tiagabine
Topiramate (at daily doses of 200mg of more)	Valproate
	Vigabatrin
	Zonisamide

Special Considerations in the Management of Women with Epilepsy in Reproductive Years. Parekh et al. 2022

Drug-Drug Interactions of Antiseizure Medications and Hormonal Oral Contraceptives[a,b]

Enzyme inducers	Decrease in ethinylestradiol	Decrease in progestin
Carbamazepine	Yes	Yes
Felbamate	Yes	Yes
Lamotrigine[c]	No	Yes
Oxcarbazepine[d]	Yes	Yes
Eslicarbazepine acetate	Yes	Yes
Phenobarbital	Yes	Yes
Phenytoin	Yes	Yes
Topiramate[d]	Yes	No
Perampanel[d]	No	Yes
Rufinamide	Yes	Yes
Clobazam	Yes	Yes
Primidone	Yes	Yes

[a] Data from Reimers A, et al, Seizure[33]; Reimers A, Open Access J Contracept[37]; Dutton C, et al, Contraception in Neurologic and Psychiatric Disorders[38]; and Stockis A, et al, Epilepsia.[39]

[b] Valproate is an enzyme inhibitor. Clonazepam, brivaracetam, ethosuximide, gabapentin, levetiracetam, tiagabine, vigabatrin, zonisamide, and lacosamide have no effect on hormonal contraceptives. It is unknown if pregabalin and stiripentol have an effect on hormonal contraceptives.

[c] Antiseizure drug levels decreased by a combined oral contraceptive pill.

[d] Enzyme-induction effect is dose dependent (eg, topiramate at doses of ≥200 mg total daily, oxcarbazepine at doses ≥1200 mg total daily, perampanel at doses ≥12 mg total daily).

Transgender Women with Epilepsy

- Worldwide: up to 450,000 transgender people with epilepsy

- Risks: discrimination, stigma, reluctance to discuss gender identity with healthcare providers
  - ➡ May impact epilepsy care, choice of ASM, access to social work, patient advocacy

- Unwanted ASM esthetic side effects with some drugs
  - ➡ May impact mental health and choice/dosing of gender-affirming medications

- Gender affirming medications may interact with ASMs:
  - Oral 17beta-estradiol may lower lamotrigine levels
  - Enzyme inducing ASMs may lower drug levels of gender-affirming drugs

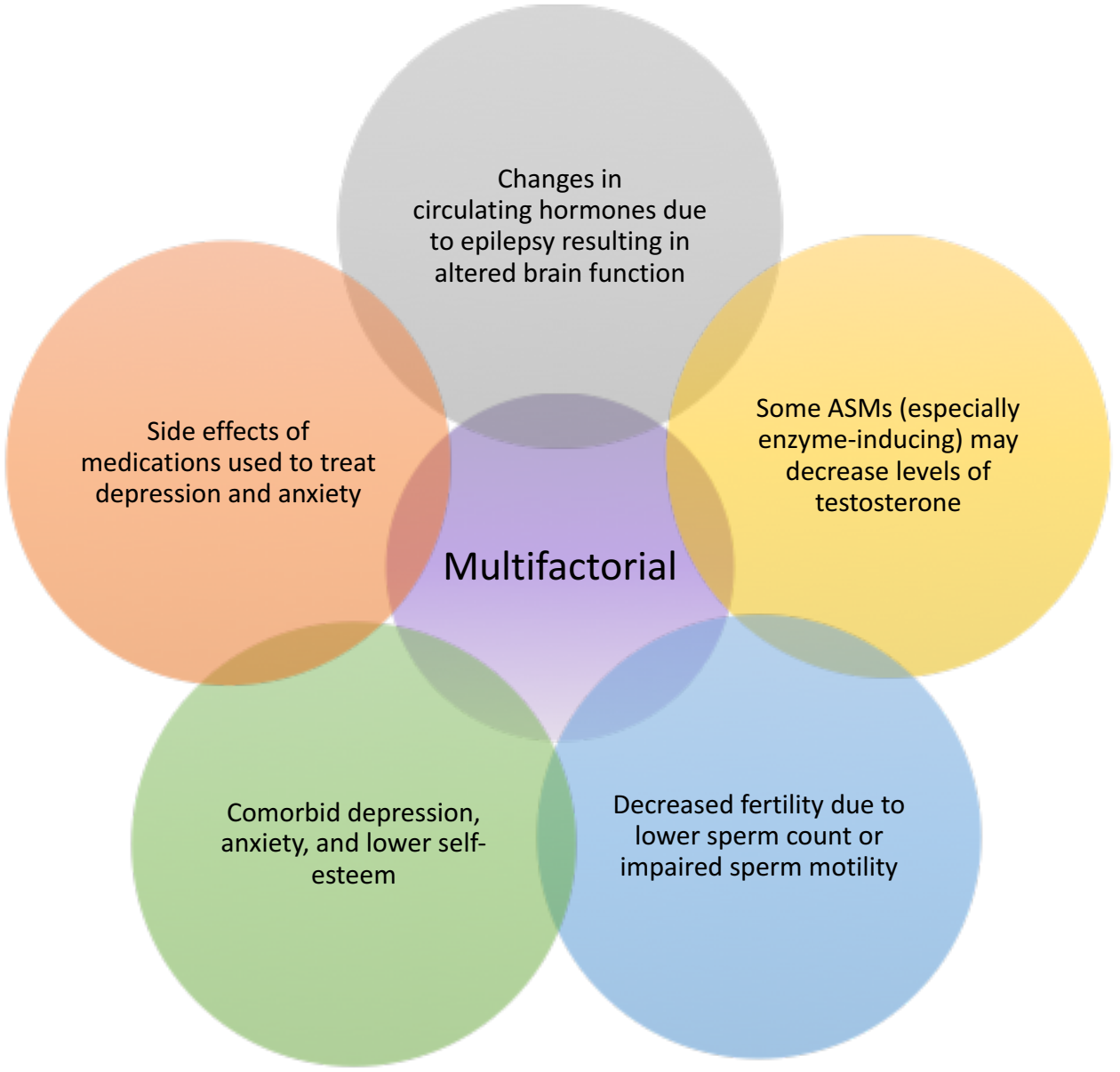
Caring for transgender patients with epilepsy. Johnson et. al. Epilepsia. 2017

Men with Epilepsy

- Seem impacted more than women in terms of lower rates of reproduction

- Sexual dysfunction in men with epilepsy:
  - Decreased libido
  - Erectile dysfunction
  - Decreased ability to achieve an orgasm

https://www.epilepsy.com/specific-populations/men


Changes in circulating hormones due to epilepsy resulting in altered brain function
Side effects of medications used to treat depression and anxiety
Some ASMs (especially enzyme-inducing) may decrease levels of testosterone
Multifactorial
Comorbid depression, anxiety, and lower self-esteem
Decreased fertility due to lower sperm count or impaired sperm motility

Catamenial Epilepsy

Catamenial Epilepsy

- Affects ~1/3 of women
- Doubling of seizures or seizure almost exclusively during specific times of the menstrual cycle
  - vs. menstrual seizure exacerbation – seen in 70% + of women with epilepsy
- Different patterns: Estrogen-to-progesterone ratio at its highest → proconvulsant state

C1	C2	C3
• Exacerbation during menstruation	• Exacerbation during ovulation	• In women with anovulatory cycles • Seizures occur throughout ovulatory, luteal, and menstrual phases

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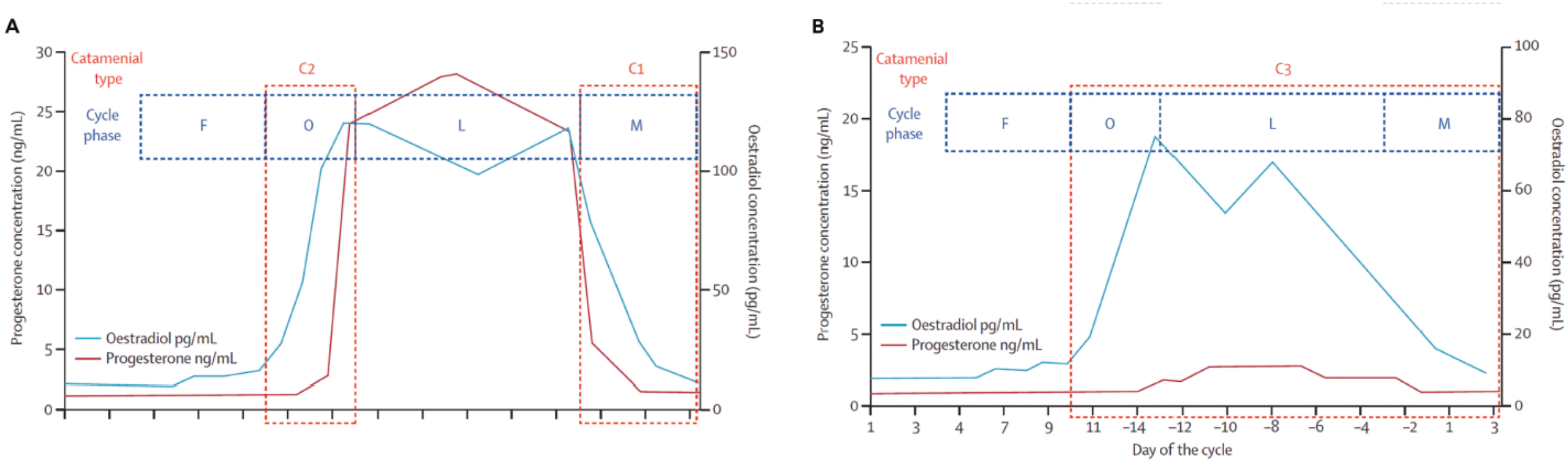


FIGURE 6-2

Types of catamenial epilepsy. Day 1 is the first day of menstrual flow; day -14 is ovulation. *A*, The C1 pattern represents perimenstrual seizure exacerbation, and the C2 pattern represents periovulatory seizure exacerbation. *B*, The C3 pattern represents catamenial epilepsy in anovulatory cycles.

F = follicular phase; L = luteal phase; M = perimenstrual; O = periovulatory phase.

Reprinted with permission from Herzog AG, et al, Epilepsia.[10] © 2013 The International League Against Epilepsy.

Treatment of Catamenial Epilepsy

- Traditional ASM management – several studies in progress, but no hormonal therapy FDA approved

- Herzog et. al, 2012: *The Progesterone Treatment Trial:*
  - Randomized, double-blind, placebo-controlled trial of natural progesterone supplements for catamenial epilepsy – n = 294
  - No statistically significant reduction in seizures with progesterone
  - Post hoc subgroup analysis: women with C1 pattern and at least a tripling of seizures perimenstrually → statistically significant seizure reduction

- Mattson et. al, 1984: Synthetic progestins may reduce seizures through complete suppression of menstrual cycle

- Anticipatory increases in ASMs could be considered – should be avoided in drugs associated with toxicity

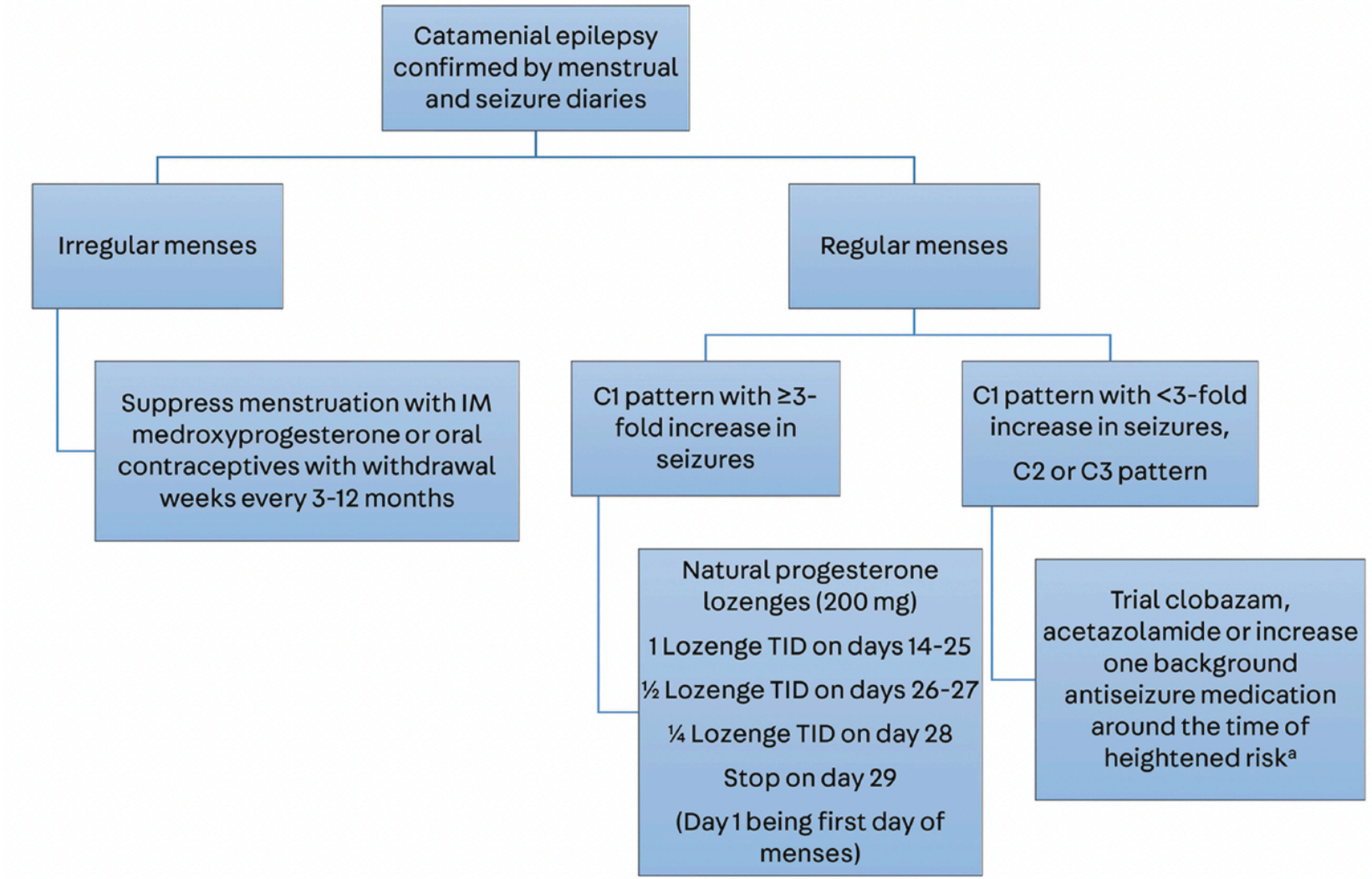


FIGURE 6-3

Approach to the treatment of catamenial epilepsy.

IM = intramuscular; TID = 3 times a day.

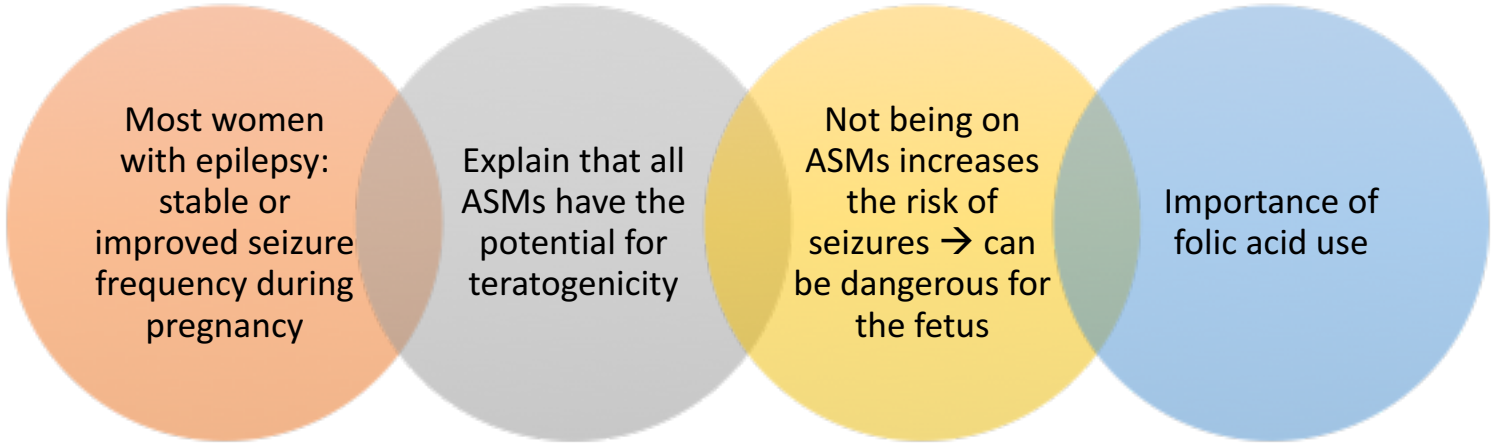
[a] Avoid with drugs prone to toxicity like phenytoin.

Data from Navis A and Harden C, Curr Treat Options Neurol[16] and Vélez-Ruiz NJ and Pennet PB, Neurol Clin.[17]

Pregnancy

Preconception counseling

- Helps address women's concerns and answer questions:



- Predictive factors for seizures in pregnancy: decreases in ASM serum levels, focal epilepsy, polytherapy
  - Best predictor: frequency of seizures 9 to 12 months before conception

- Catamenial epilepsy: may experience seizure improvement

European Registry of Antiepileptic Drugs and Pregnancy (EURAP)

Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD)

Risks of Maternal Seizures to the Fetus

- Convulsive seizures → fetal hypoxia, lactic acidosis, uterine contractions, maternal injuries
- Focal seizures → fetal decelerations or distress

- No evidence suggests maternal seizures associated with major congenital malformations

Harden et. al. Neurology. 2009
Maternal complex partial seizure associated with fetal distress. Sahoo et. al, 2005

Risks of ASMs to the Fetus

- In utero exposure to ASMs associated with teratogenicity – likely dose related
  - Neural tube, cardiac, urogenital, and craniofacial congenital malformations

- **Highest risk ASM:** valproate (10.3% based on EURAP study)
  - FDA warning: avoid use of valproate in women of childbearing age unless other ASMs fail or are contraindicated
- **Intermediate-risk ASMs:** phenobarbital (6.5%), phenytoin (6.4%), carbamazepine (5.5%), topiramate (3.9%)
- **Lowest-risk ASMs:** levetiracetam (2.8%), lamotrigine (2.9%), oxcarbazepine (3%)

- ASMs have variable malformation profiles

European Registry of Antiepileptic Drugs and Pregnancy (EURAP)

Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD)

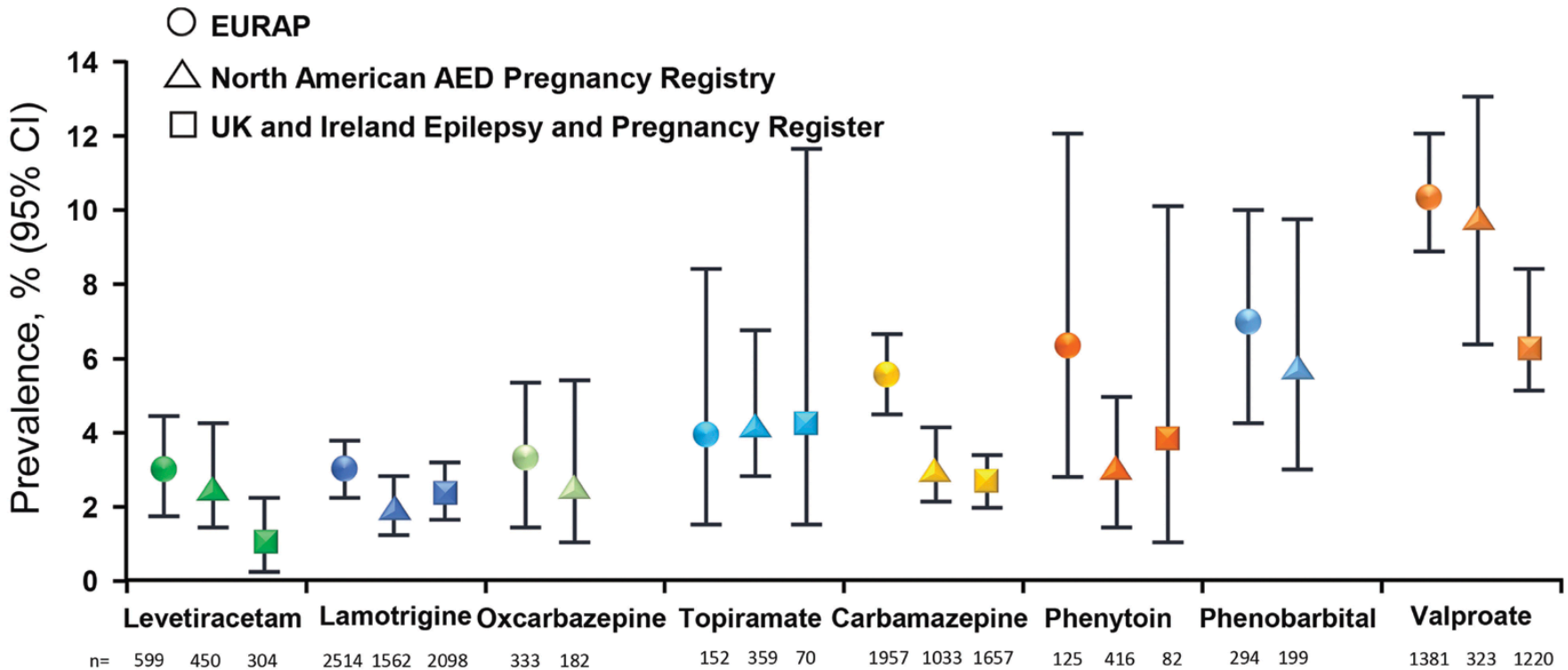


FIGURE 6-6

Prevalence of major congenital malformations of eight antiseizure medication monotherapies from three prospective pregnancy registries.

CI = confidence interval; EURAP = European Registry of Antiepileptic Drugs and Pregnancy.

Reprinted with permission from Tomson T, et al, Curr Opin Neurol.[51] © 2019 Wolters Kluwer Health, Inc.

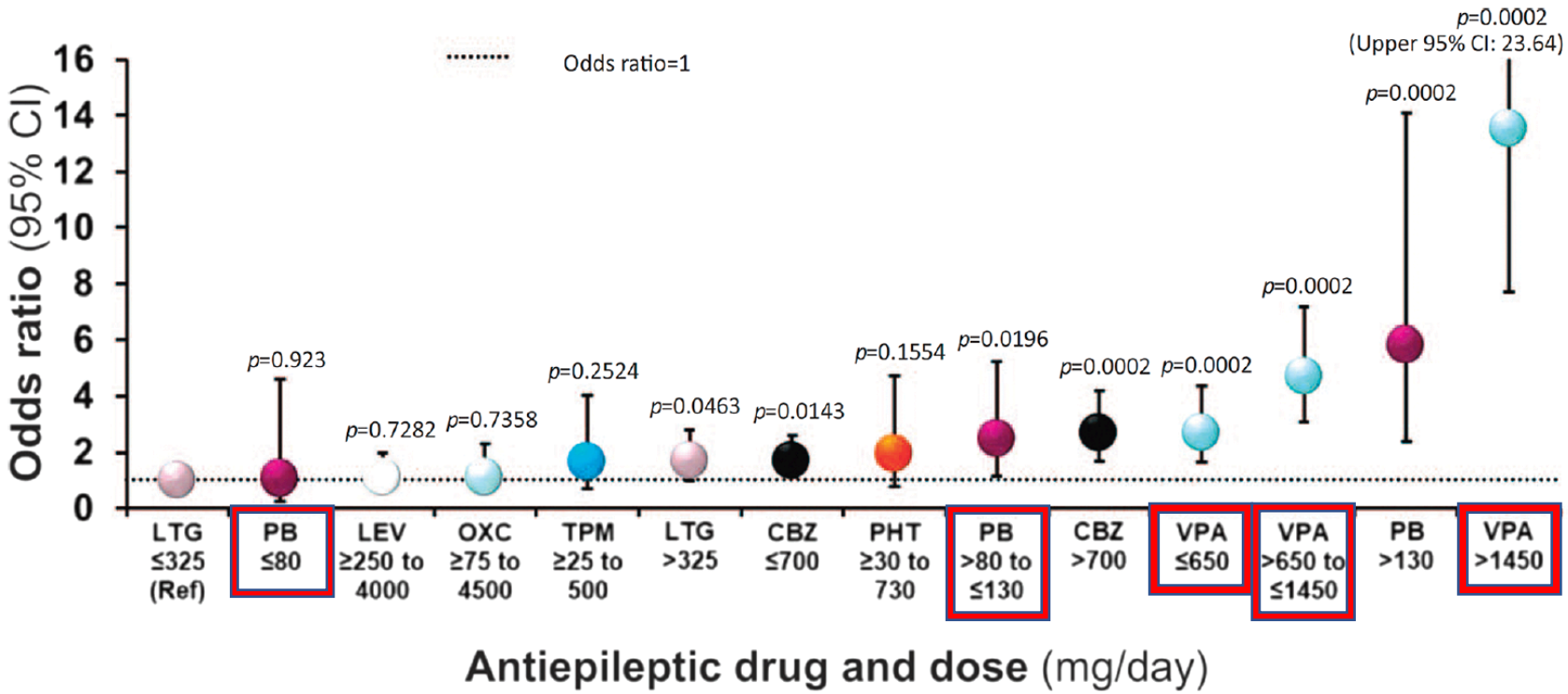


FIGURE 6-7

Prevalence of major congenital malformations of antiseizure medication compared with lamotrigine ≤325 mg/d.

CBZ = carbamazepine; CI = confidence interval; LEV = levetiracetam; LTG = lamotrigine; OXC = oxcarbazepine; PB = phenobarbital; PHT = phenytoin; Ref = reference; TPM = topiramate; VPA = valproate.

Reprinted with permission from Tomson T, et al, Curr Opin Neurol.[51] © 2019 Wolters Kluwer Health, Inc.

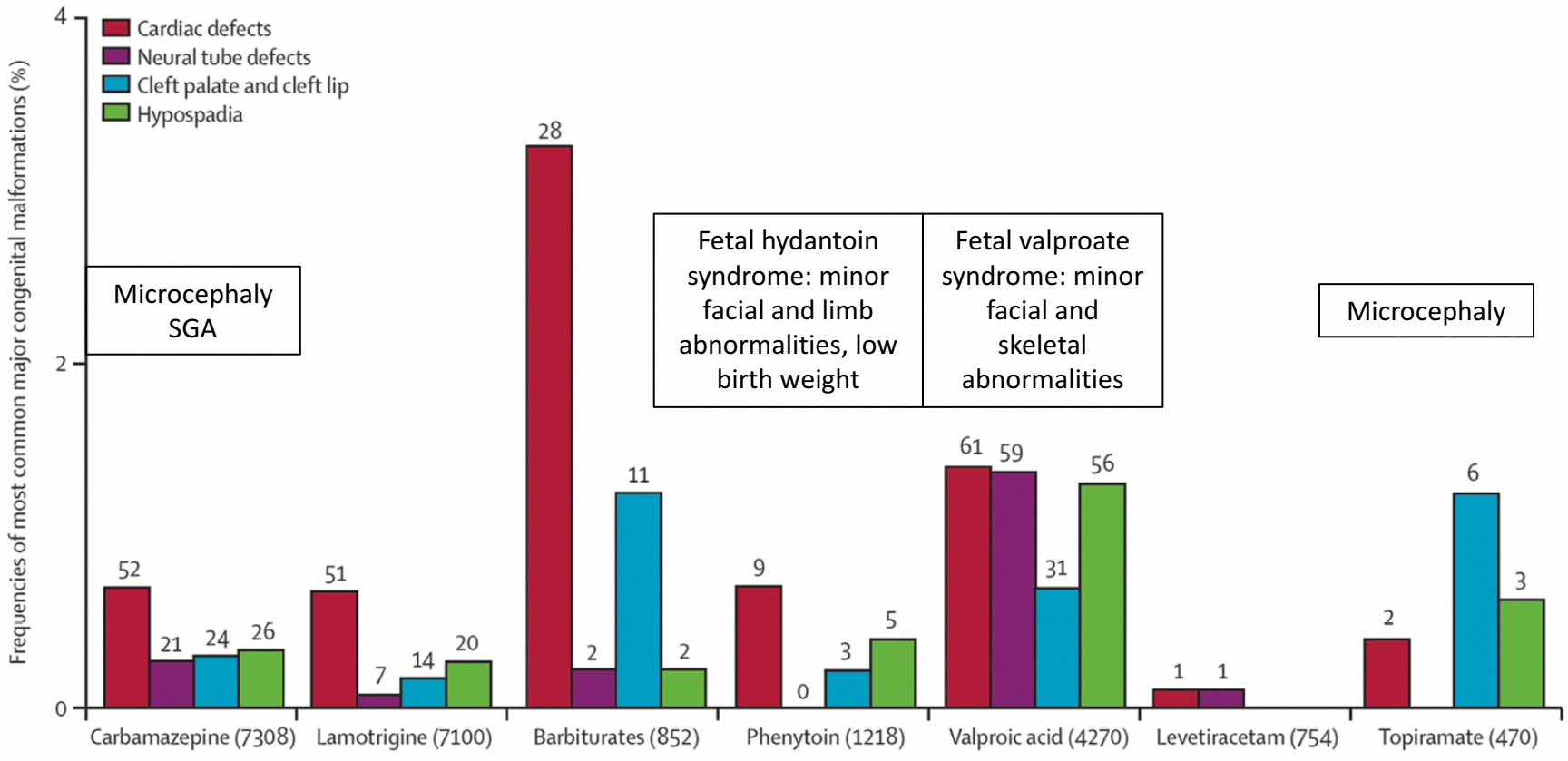


FIGURE 6-8

Common major congenital malformations associated with in utero monotherapy exposure. Total number of exposed fetuses or infants are shown in parentheses with the number of those with specific malformations shown on top of the bars.

Reprinted with permission from Tomson T, et al, Lancet Neurol.[52] © 2016 Elsevier Ltd.

Newer ASMs and Polytherapy

- Data on newer ASMs limited → insufficient to draw conclusions
- Important for physicians to encourage all eligible women to enroll in a pregnancy registry to maximize data collection
- Polytherapy including valproate or topiramate → higher major congenital malformation risk
- Low- to moderate-dose valproate plus another ASM → lower observed major congenital malformation rate vs. high-dose valproate monotherapy (EURAP registry)

Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) Study – Meador et. al, 2013, Cohen et. al, 2019

- Impaired cognitive and behavioral outcomes at significantly higher rate with valproate exposure

- Children exposed to valproate assessed at ages 3 and 6:
  - Lower IQ (6 to 9 points) compared with those exposed to carbamazepine, lamotrigine, and phenytoin
  - Dose-dependent relationship

- Increased risk for developmental delay in cognition, psychomotor, language skills, ADHD, lower performance in the Children's Memory Scale

Anti-seizure medication and risks for major congenital malformations (MCMs)..

	Prevalence % (95% CIs)	Prevalence % (95% CIs)	Prevalence % (95% CIs)	Prevalence *n/n* (%)	OR (95% CrI)	Specific MCMs
ASM	EURAP [56]	NAAPR	UKIEPR [1]	Others	Veroniki *et al.* [5]	
BRV				0,[a,51] 0[b,51]		
CBZ	5.5 (4.5–6.6)	2.7 (1.9–3.8) [96]	2.6 (1.9–3.5)		1.37 (1.10–1.71)	Microcephaly [57]
CLB				2/9 (22.2), [67] 5/96 (9.4) [67]	3.48 (0.52–13.84)	
CLZ		1.6 (0.41–6.5) [96]			1.13 (0.59–2.02)	Hypospadias [5]
ESL				a,81		
ETX				2/13 (15.4) [86]	3.04 (1.23–7.07)	Cleft palate, [5] club foot [5]
FBM				0[b,91]		
GBP		1.1 (0.37–3.5) [96]		2/9 (22.0) [97]	1.0 (0.47–1.89)	Cardiac [5]
LCM		0.0 (0–7.4) [96]		0,[a,92,105] high[b,105]		
LEV	2.8 (1.7–4.5)	1.8 (1.2–2.7) [96]	0.7 (0.2–2.4)		0.72 (0.43–1.16)	
LTG	2.9 (2.3–3.7)	1.9 (1.5–2.6) [96]	2.3 (1.8–3.1)		0.96 (0.72–1.25)	

OXC	3.0 (1.4–5.4)	1.6 (0.7–3.8) [96]			1.32 (0.72–2.29)	Hypospadias[5,92,134]
PB	6.5 (4.2–9.9)	5.5 (3.1–9.6) [96]			1.83 (1.35–2.47)	Cleft palate [5]
PER				Possible[a,151]		
PGB		1.9 (0.28–13.6) [96]		1/30 (3.3), [57] 28/477 (5.9) [170] 1/13 (7.7), [97] 7/116 (6.0) [171]		
PHT	6.4 (2.8–12.2)	2.6 (1.5–4.5) [96]	3.7 (1.2–10.2)		1.69 (1.30–2.17)	Cleft palate, [5] club foot [5]
PRM					1.22 (0.65–2.12)	Cleft palate, [5] club foot, [5] hypospadias [5]
TPM	3.9 (1.5–8.4)	4.4 (2.9–6.3) [96]	4.3 (1.5–11.9)		1.9 (1.17–2.97)	Cleft palate, [5] microcephaly [57]
VGB					2.27 (0.49–7.93)	
VPA	10.3 (8.8–12.0)	9.2 (6.5–13.0) [121]	6.7 (5.4–8.3)		2.93 (2.36–3.69)	NTD, [133] cleft palate, [5] club foot, [5] hypospadias [5]
ZNS		0.9 (0.46–1.8) [96]	13.0 (4.5–32.1)	3/26 (11.5) [194]		

Anti-seizure medication	Use in WWE
Brivaracetam	[a]
Carbamazepine	With caution
Clobazam	Avoid [a]
Clonazepam	Avoid [a]
Eslicarbazepine-acetate	[a]
Ethosuximide	Avoid [a]
Felbamate	Avoid [a]
Gabapentin	[a]
Lacosamide	[a]
Levetiracetam	Recommend
Lamotrigine	Recommend
Oxcarbazepine	With caution
Phenobarbital	Avoid
Perampanel	Avoid
Pregabalin	[a]
Phenytoin	Avoid
Primidone	Avoid
Sulthiam	Avoid [a]
Tiagabine	Avoid [a]
Topiramate	With caution
Vigabatrine	Avoid [a]
Valproate	Avoid
Zonisamide	[a]

[a] Insufficient data

Treatment and care of women with epilepsy before, during, and after pregnancy: a practical guide. Nucera et. al. 2022

Use of Folic Acid

- Recommended for all women of reproductive age with epilepsy
- Decreases major congenital malformation risk in general population
  - However: no high-quality data specific to women with epilepsy
- Optimal dose not known
- Current guidelines for women with epilepsy:
  - 0.4 mg to 5 mg folic acid daily starting at least 3 months before conceiving
  - Higher doses preferred for highest-risk groups:
    - High dose valproate, polytherapy with valproate or topiramate, women with personal or family history of prior pregnancy with MCM

Management of epilepsy in pregnancy: a report from the International League Against Epilepsy Task Force on Women and Pregnancy. Tomson et. al. 2019.

During Pregnancy

- Balance between best chance of seizure freedom and minimizing fetal exposure to ASMs → use lowest, most effective, tolerated dose
- Levels can fall due to physiologic changes:
  - ≥50% increased renal clearance → levetiracetam and topiramate clearance increased
  - Glucuronidation enhanced by estrogen →lamotrigine > valproate, oxcarbazepine clearance increased
- Specific times during pregnancy associated with more dramatic changes in clearance rates:
  - Levetiracetam and lamotrigine → greatest in **first** trimester
  - Oxcarbazepine and topiramate → greatest in **second** trimester
- Some drugs remain stable/minor decreases:
  - Carbamazepine, carbamazepine-10,11-epoxide, lacosamide

Antiepileptic drug clearances during pregnancy and clinical implications for women with epilepsy. Voinescu et. al. Neurology 2018

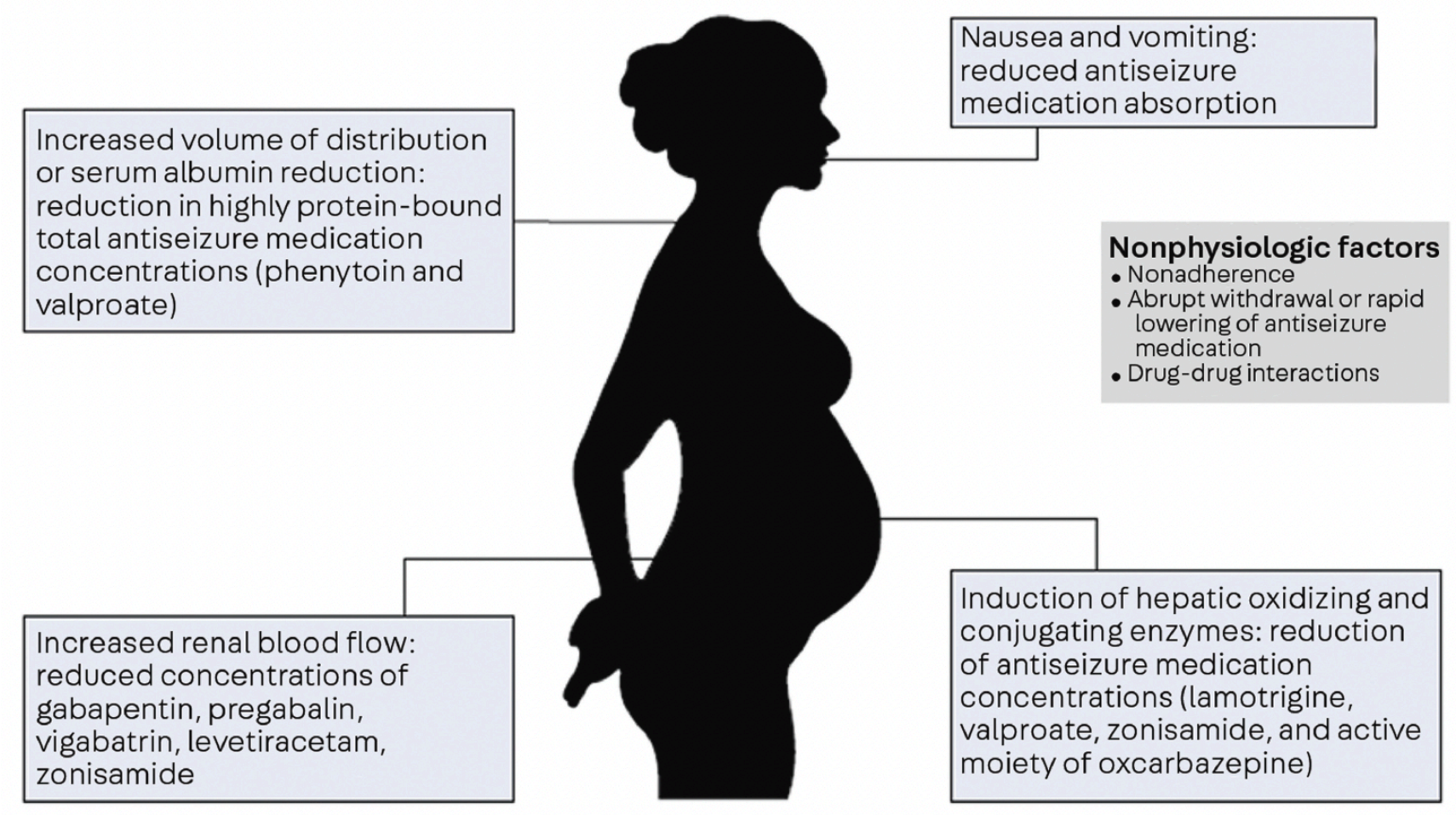


FIGURE 6-5

Changes in antiseizure medication levels in pregnancy for women with epilepsy.

Modified with permission from Stephen LJ, et al, Lancet Neurol.[41] © 2019 Elsevier Ltd.

Summary of Antiseizure Medication Changes in Serum Levels Observed in Pregnancy (If No Dose Changes Are Made)[a]

TABLE 6-3

Antiseizure medication	Decrease in serum concentration	Decrease in serum free (unbound) concentration	Recommendations to perform therapeutic drug monitoring, if available
Phenobarbital	Up to 55%	Up to 50%	Yes
Phenytoin	60-70%	20-40%	Yes, free concentration
Carbamazepine	0-12%	None	Optional
Valproate	Up to 23%	None	Optional free concentration if done
Oxcarbazepine monohydroxy-derivative	36-62%	Not applicable (NA)	Yes
Lamotrigine	77% of the population: 69% decrease; 23% of the population: 17% decrease	NA	Yes
Gabapentin	Insufficient data	NA	Yes
Topiramate	Up to 30%	NA	Yes
Levetiracetam	40-60%, with maximal decrease reached in first trimester	NA	Yes
Zonisamide	Up to 35% but little data available	NA	Yes

[a] Reprinted from Tomson T, et al, Epileptic Disord.[2]

Therapeutic Drug Monitoring

Important to guide drug-dose optimization during pregnancy:

- Preconception level
- At least every 4 weeks
- Establish postpartum reduction plan
- For some drugs: monitor total and free level
- If drug serum levels decrease (esp. ≥35%) → consider dose adjustments

If drug level not available:

Consider 30-50% dose increase after first trimester if:

- Taking ASM with known pregnancy-associated drop in levels
- Taking lowest, effective dose at start of pregnancy
- Prior severe or injurious seizures
- Prior breakthrough seizures with missed doses

Post partum ASM dose adjustments:

- ASM metabolized through glucuronidation (lamotrigine)
  - Taper as early as postpartum day 3
  - Return to pre-pregnancy dose by 10-21 days postpartum
- ASM metabolized through renal clearance (levetiracetam):
  - Within 2-3 weeks postpartum
- ASM metabolized through cyt P450 pathways (carbamazepine):
  - Slower → 4-8 weeks
- Can maintain slightly increased dose for anticipated sleep deprivation

Management of epilepsy in pregnancy: a report from the International League Against Epilepsy Task Force on Women and Pregnancy. Tomson et. al. Epileptic Disord 2019
Antiepileptic drug therapy in pregnancy I: gestation-induced effects on AED pharmacokinetics. Pennell et. al. Int Rev. Neurobiol 2008

Breastfeeding

- Benefits:
  - For infants: better neurodevelopmental outcomes, decreased obesity, allergies, infections, blood cancers, SIDS
  - For mothers: decreased postpartum bleeding, involution of the uterus, weight loss, delayed ovulation, reduced risk of breast and ovarian cancer

- Breast milk transmission observed with primidone, levetiracetam, gabapentin, lamotrigine, and topiramate
  - Not significant with valproate, phenobarbital, carbamazepine, and phenytoin

⇒ Concentrations low compared with maternal serum drug concentrations

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Breastfeeding

- Counsel mothers to monitor babies for sedation

- NEAD study: no adverse effects on IQ, verbal/nonverbal memory, or executive function
  - Potential **positive** cognitive outcomes at age 6 of adjusted IQ scores: 4 points higher in breastfed children

- Evidence to date provides reassurance on the **relative safety** of breastfeeding while taking ASMs

Changes in anti-seizure medication serum levels during pregnancy and breastfeeding safety profile.

ASM	Levels	%	sz	Adaption	Breastfeeding
BRV					a
CBZ	↔ 1			No	2 199
CLB					4 199
CLZ					4 199
ESL			Yes 82	Likely a	a
ETX	↓ Possible 87	61 87			a
FBM					4 199
GBP	↓ Likely a			Likely a	3 199
LCM	↔ 52 /↓ 106		No 106	a	a
LEV	↓ 1	40–60 1		Yes	3 199
LTG	↓ 1	<69 1		Yes	3 199
OXC	↓ 1	36–62 1	Yes 140–142	Yes	3 199
PB	↓ 157	70 157			4 199
PER					a
PGB	↓ Likely a			Likely a	3 199
PHT	↓ 116	56 116			2 199
PRM					4 199
TGB					3 199
TPM	↓ 1	<30 116		Likely	3 199
VGB					3 199
VPA	↔ 1			No	2 199
ZNS	↓ 198	<35 198	Yes 198	Yes	4 199

'2 – safe'
'3 – moderately safe'
'4 – possibly hazardous'
a – insufficient data

Treatment and care of women with epilepsy before, during, and after pregnancy: a practical guide. Nucera et. al. 2022

Counseling of WWE who are pregnant or are contemplating pregnancy should reflect:

There is probably no substantially increased risk (greater than two times expected) of cesarean delivery for WWE taking AEDs (Level B). However, there is possibly a moderately increased risk (up to 1.5 times expected) of cesarean delivery for WWE taking AEDs (Level C).

There is probably no substantially increased risk (greater than two times expected) of late pregnancy bleeding for WWE taking AEDs (Level B).

There is probably no moderately increased risk (greater than 1.5 times expected) of premature contractions or premature labor and delivery for WWE taking AEDs (Level B).

There is possibly a substantially increased risk of premature contractions and premature labor and delivery during pregnancy for WWE who smoke (Level C).

Seizure freedom for at least 9 months prior to pregnancy is probably associated with a high likelihood (84%–92%) of remaining seizure-free during pregnancy (Level B).

There is insufficient evidence to support or refute an increased risk of preeclampsia, pregnancy-related hypertension, spontaneous abortion, a change in seizure frequency, or status epilepticus (Level U).

Practice Parameter update: Management issues for women with epilepsy—Focus on pregnancy (an evidence-based review): Obstetrical complications and change in seizure frequency Report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society.
Harden et. al. Neurology. 2009

Aging

Bone Health

- ASM use associated with accelerated bone loss in men and women
  - Osteoporosis 4 times more common in women – lower overall bone density, younger age of onset, faster rates of bone loss

- More prominent with enzyme inducing ASMs:
  - Significant bone loss in young women after only 1 year of phenytoin monotherapy
  - Could be due to cP450 enzyme induction → acceleration of vitamin D metabolism
  - Also seen with phenobarbital, primidone, oxcarbazepine >> carbamazepine

- Non–enzyme-inducing drugs (gabapentin, topiramate, valproate) also associated with increased fracture rate or bone loss
  - Poorly understood mechanisms

Bone health in women with epilepsy: clinical features and potential mechanisms. Pack et. al. Int Rev Neurobiol 2008

Gender disparities in osteoporosis. Alswat. J Clin Med Res 2017

Recommendations for Bone Health

- Check bone density 5 years after start of ASM
- Before treatment in postmenopausal women

- Testing includes:
  - Vitamin D, calcium, phosphate levels
  - Baseline BMD

- Preventive measures: exercise, nutrition, calcium and vitamin D supplementation
  - May need higher doses than recommended vitamin D intake of 600 IU daily

Special issues in epilepsy: the elderly, the immunocompromised, and bone health. Carlson et. al. Continuum 2016

Menopause

- Women with epilepsy may experience early menopause
- Perimenopause does not significantly alter seizure frequency in most cases
- Women with catamenial epilepsy:
  - Perimenopause: fluctuations may be associated with seizure exacerbation
  - Menopause: may experience seizure improvement
- HRT may worsen seizures
  - Consider non–estrogen-based therapies: clonidine, SSRIs, SNRIs, and vaginal lubricants for symptomatic treatment
  - If hormonal therapy required: simplified estrogen with natural progesterone

The effect of menopause and perimenopause on the course of epilepsy. Harden et. al. Epilepsia 1999
Epilepsy and menopause. Erel et. al. Arch Gynecol Obstet 2011

THANK YOU!