Selecting AEDs in special situations

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Which medications?

- ลักษณะการชักและประเภทของโรคลมชักของผู้ป่วย
- การบริหารยา
- ผลข้างเคียงของยากันชัก
- Drug interaction กรณีที่ผู้ป่วยได้ยาหลายชนิดพร้อมกัน
- Special situations
  - Reproductive age
  - Elderly
  - Hepatic impairment
  - Renal impairment

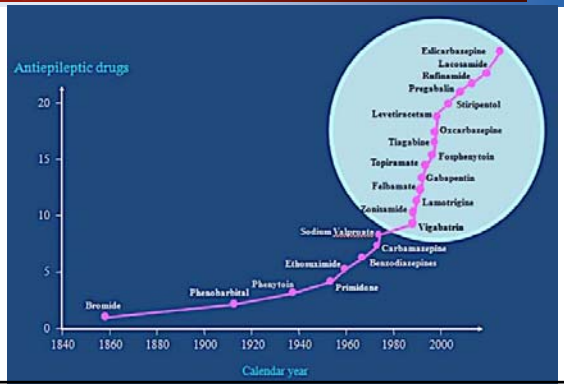
Traditional antiepileptic drugs

- Phenobarbital
- Phenytoin
- Carbamazepine
- Sodium valproate
- Benzodiazepine

New antiepileptic drugs

- Felbamate (1993)
- Gabapentin (1993)
- Lamotrigine (1994)
- Topiramate (1996)
- Tiagabine (1997)
- Levetiracetam (1999)
- Oxcarbazepine (2000)
- Zonisamide (2000)
- Pregabalin (2005)
- Vigabatrin

Antiepileptic drug development



Newest antiepileptic drugs

- Stiripentol (2007)
- Lacosamide (2008)
- Rufinamide (2008)
- Eslicarbazepine (2009)
- Vigabatrin (2009)
- Ezogabine (2011)
- Perampanel (2012)

Hepatic dysfunction

Effects	Older AEDs	New AEDs
Measurable increased in free fraction with hypoalbuminemia	PHT VPA	-
Metabolism affected by renal disease	PB	GBP, LEV, TPM
Metabolism affected by liver disease	CBZ, PHT, VPA	LTG, ZNS, OXC, TGB

Dosing adjustment for patients with impaired hepatic function

- There is insufficient information available to make recommendations on the necessity of dosage adjustment

Patients with impaired hepatic function

- Free fractions of diazepam, PHT, and VPA increase as a result of reduced circulating albumin concentrations. Frequent serum determinations of free fractions and gradual dose regulations are required.

Patients with impaired hepatic function

- Caution should be taken if VPA is used inpatients with liver disease.
- Hepatic dysfunction is less of a concern with PB, gabapentin, levetiracetam, topiramate, and zonisamide.

Renal dysfunction

Effects	Older AEDs	New AEDs
Measurable increased in free fraction with hypoalbuminemia	PHT VPA	-
Metabolism affected by renal disease	PB	GBP, LEV, TPM
Metabolism affected by liver disease	CBZ, PHT, VPA	LTG, ZNS, OXC, TGB

Dosing adjustment for patients with impaired renal function

Creatinine clearance (mL/min)	Dosage (mg)
Gabapentin	
>60	400 tid
30-60	300 bid
15-30	300 od
<15	300 every other day
hemodialysis	200-300* supplement
Levetiracetam	
>80	500-1500 bid
50-80	500-1000 bid
30-50	250-750 bid
<30	250-500 bid
hemodialysis	500-1000*q 24 hr then 250-500 mg supplement

Dosing adjustment for patients with impaired renal function

Creatinine clearance (mL/min)	Dosage (mg)
Topiramate	
>70	Normal dosage
10-70	Decrease dosage 50%
<10	Decrease dosage 75%
hemodialysis	Consider supplement

Transplant patients

Using AEDs in transplant patients

- **CBZ, oxcarbazepine, PB, and PHT may reduce cyclosporine, tacrolimus, and corticosteroid blood levels with a delayed effect of up to 10 days.**
- **Azathioprine, mycophenolate mofetil, and OKT3 metabolism are not significantly affected by AEDs.**

HIV patients

Drug	Protein Binding (%)	Metabolism
Older AEDs		
Phenobarbital	45	CYP450
Phenytoin	90	CYP450-2C
Carbamazepine	~75	CYP450-3A, 2C
Valproate	90	Gluc
Newer AEDs		
Gabapentin	Minimal	Nil
Lamotrigine	55	Gluc, CYP450
Oxcarbazepine	40	Gluc, CYP450
Topiramate	Minimal	CYP450-3A
Levetiracetam	Minimal	Enzymatic hydrolysis
Tiagabine	96	Hydrolysis
Zonisamide	Minimal	Gluc, CYP450
Pregabalin	Minimal	Negligible
HAART		
NRTI	Minimal to ~38	Gluc
NNRTI	50–99	CYP450
PI	>90	CYP450

SPECIAL REPORT

Antiepileptic drug selection for people with HIV/AIDS: Evidence-based guidelines from the ILAE and AAN

*†Gretchen L. Birbeck, ‡Jacqueline A. French, §Emilio Perucca, ¶David M. Simpson, #Henry Fraimow, **Jomy M. George, ††Jason F. Okulicz, ‡‡David B. Clifford, §§Houda Hachad, and §§René H. Levy for the Quality Standards subcommittee of the American Academy of Neurology and the ad hoc task force of the Commission on Therapeutic Strategies of the International League Against Epilepsy

Epilepsia, 53(1):207–214, 2012

Recommendations

- AED–ARV administration may be indicated in up to 55% of people taking ARVs.
- Patients receiving phenytoin may require a lopinavir/ritonavir dosage increase of approximately 50% to maintain unchanged serum concentrations (Level C: one class II study).
- Patients receiving valproic acid may require a zidovudine dosage reduction to maintain unchanged serum zidovudine concentrations (Level C).
- Coadministration of valproic acid and efavirenz may not require efavirenz dosage adjustment (Level C: one class II study).

Epilepsia, 53(1):207–214, 2012

Recommendations

- Patients may be counseled that it is unclear whether dosage adjustment is necessary when other AEDs and ARVs are combined (Level U).

Epilepsia, 53(1):207–214, 2012

Recommendations

- It may be important to avoid enzyme inducing AEDs in people on ARV regimens that include protease inhibitors or non nucleoside reverse transcriptase inhibitors because pharmacokinetic interactions may result in virologic failure, which has clinical implications for disease progression and development of ARV resistance. If such regimens are required for seizure control, patients may be monitored through pharmacokinetic assessments to ensure efficacy of the ARV regimen (Level C: one class II study).

Epilepsia, 53(1):207–214, 2012

Brain tumors

Patients with brain tumors

- Based on observations from randomized studies, prophylactic use of AEDs is not recommended. After brain surgery, AEDS can be discontinued after 1 week in patients without a history of previous seizure

Glantz MJ, Cole BF, Forsyth PA, et al. Neurology 2000; 54:1886–93.

Potentials interaction between AEDs and chemotherapy

- Enzyme inducing AEDs have been shown to have effects on levels of chemotherapy that metabolite through CYP 450
- Taxanes, vinca alkaloids, methotrexate, teniposide, and camptothecin analogues such as irinotecan

Vecht CJ, Wagner GL, Wilms EB. Lancet Neurol 2003;2:404–9.

Potentials interaction between AEDs and chemotherapy

- In a study of 716 children with ALL, 40 children who were on enzyme-inducing AEDs had worse event-free survival (hazard ratio 2.67 [95% CI, 1.50 to 4.76]), hematological relapse (3.40 [1.69 to 6.88]) and CNS relapse (2.90 [1.01 to 8.28]).
- These children were found to have a higher clearance of teniposide and methotrexate.

Relling MV, Pui CH, Sandlund JT, et al. Lancet 2000;356:285–90

Antiepileptic drugs for treating seizures in adults with brain tumours (Review)

Kerrigan S, Grant R

THE COCHRANE COLLABORATION®

Kerrigan S, Grant R. Cochrane Database of Systematic Reviews 2011, Issue 8: CD008586.

Authors' conclusion

- There is a lack of robust, randomised, controlled evidence to support the choice of antiepileptic drug for the treatment of seizures in adults with brain tumours.
- While some authors support the use of non enzyme-inducing antiepileptic drugs, reliable, comparative evidence to provide clinical justification for this is limited.
- There is a need for further large, randomised, controlled trials in this area.

Kerrigan S, Grant R. Cochrane Database of Systematic Reviews 2011, Issue 8: CD008586.

Expert opinion

First choice AED monotherapy[a]	Add-on AED
LEV	GBP
LTG	LCM
OXC	PGB
TPM	ZNS
VPA	

Maschio M, Dinapoli L. J Neurooncol 2012

Patients with psychiatric diseases

Issues to be considered

- Effects of AEDs on psychiatric symptoms
- Potential drug interaction of AEDs and psychiatric drugs.

γ-Aminobutyric acid (GABA)-ergic AEDs

VGB
TGB
PB
BZD
VPA (multiple actions)

Sedative, anxiolytic, antimanic properties promote depression

Antiglutamatergic AEDs

LTG
FBM
TPM

Activating anxiety-promoting Antidepressive effects

Selecting AEDs in patients with psychiatric comorbidities

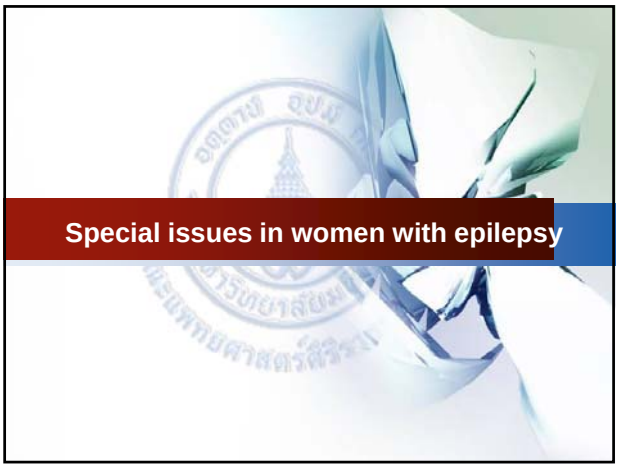
Psychiatric comorbidities	Avoid	Consider
Mood lability/ bipolar disorder	-	LTG, CBZ, OXC, PHT, VPA
Anxiety	FLB, LEV, LTG, TGB	BZD, GBP, PBG
Depression	Barbiturates, LEV, PGB, TGB, TPM, VGB, ZNS	LTG
Psychosis	ETX, FLB, LEV, PHT, TGB, TPM, VGB, ZNS	-

Perucca P & MulaM. *Epilepsy Behav* 2013;26:440-9

Interaction with psychiatric drugs

- Occur mostly with enzyme inducing AEDs
- Reduce level of tricyclic antidepressants
- Reduce level of typical and atypical antipsychotic
- Reduce level of some SSRI and SNRI esp. citalopram, sertraline, mirtazapine, bupropion

CYP1A2	CYP2C9	CYP2C19	CYP3A4	CYP2D6
Substrates	**Substrates**	**Substrates**	**Substrates**	**Substrates**
Amitriptyline	Olanzapine	Amitriptyline	Amitriptyline	Paroxetine
Imipramine	Thioridazine	Imipramine	Imipramine	Fluoxetine
Clomipramine		Clomipramine	Nortriptyline	Venlafaxine
Fluvoxamine		Citalopram	Desipramine	Mianserine
Trazodone		Moclobemide	Clomipramine	Nefazodone
Haloperidol			Sertraline	Amitriptyline
Clozapine			Nefazodone	Clomipramine
Olanzapine			Venlafaxine	Nortriptyline
Ziprazidone			Haloperidol	Imipramine
Chlorazepam			Risperidone	Desipramine
			Clozapine	Trazodone
			Zipradone	Clomipramine
			Quetiapine	Maprotiline
				Haloperidol
				Chlorpromazine
				Olanzapine
				Risperidone
				Quetiapine
AED inducers	**AED inducers**	**AED inducers**	**AED inducers**	**AED inducers**
Phenytoin	Phenytoin	Phenytoin	Phenytoin	None known
Carbamazepine	Carbamazepine	Carbamazepine	Carbamazepine	
Phenobarbital	Phenobarbital	Phenobarbital	Phenobarbital	
Primidone	Primidone	Primidone	Primidone	
			Oxcarbazepine*	
			Topiramate*	
AED inhibitors	**AED inhibitors**	**AED inhibitors**	**AED inhibitors**	**AED inhibitors**
None known	Valproic acid	Felbamate	None known	None known
		Topiramate		



Special issues in women with epilepsy

- **Side effects of antiepileptic medications**
  - Cosmetic side effects
  - Weight issues
  - Osteoporosis
  - Teratogenic effects
- **Contraception**
- **Pregnancy**
- **Lactation**
- **How to advise the patients**

Cosmetic side effects

- **Phenytoin: hirsutism, coarse facies, gum hypertrophy**
- **Sodium valproate: weight gain, alopecia**

Weight issues from AEDs

Weight Gain	Weight Neutral	Weight Loss
Valproate	Lamotrigine	Topiramate
Gabapentin	Levetiracetam (?)	Zonisamide
Carbamazepine	Phenytoin	Felbamate
Tiagabine (?)		
Vigabatrin		

Body weight changes with AEDs

Side effects	AEDs	Time frame	Incidence	Extent
Weight gain	VPA	2-3 months and may be continue	Up to 30-40%	1-3% of BW Up to 8% of BW (with high dose)
	GBP		23%	
	PGB		18%	
	RTG			
Weight loss	TPM	Stabilize after 12-18 months	6-17% in leaflet (upto 60% in review)	Up to 7.5% of BW Dose dependent
	ZNS		3%	
	FBM			
	STP			

Gaitatzis A, Sander JW. CNS Drugs 2013; 27:435–455

AEDs and osteoporosis

- **Enzyme inducing AEDs may interfere with metabolism of vitamin D, therefore can cause increased incidence of osteoporosis with long term use.**
- **Valproate may have effects on increased bone turnover**

All patients: adequate intake of dietary vitamin D and Ca and regular exercise
Institutionalized patients and postmenopausal women: supplement of vitamin D (800 IU) and Ca (1000 mg)
Patients with additional increased risk: supplement of vitamin D (1000–4000 IU) and Ca (1500 mg)
Dual-energy X-ray absorptiometry (DXA) scan 5 years after initiation of antiepileptic drugs (AED) treatment
DXA scan at initiation of AED treatment in postmenopausal women
DXA scan every 2–3 years in high-risk patients (eg. users of valproate or enzyme inducers)
T-scores < −1: supplement of vitamin D (800 IU) and Ca (1000 mg) and weight-bearing exercise
T-scores between −1 and −2.5: supplement of vitamin D (800 IU) and Ca (1000 mg), weight-bearing exercise, new DXA scan repeated after 1–2 years
T-scores < −2.5: referral for the treatment of bone disease, usually with the addition of bisphophanates

Svalheim S, et al. Acta Neurol Scand: 2011; 124 (Suppl. 191): 89–95.

Contraception in epilepsy patients

- **AEDs that cause induction of CYP 3A4 increase metabolism of oral contraceptives resulting in failure of contraceptives.**
- **Potent enzyme inducing AEDs:**
  - phenytoin, carbamazepine, primidone, phenobarbital.
- **Less-potent enzyme inducing AEDs:**
  - oxcarbazepine, lamotrigine
  - topiramate >200 mg.

Contraception in epilepsy patients

- **AEDs that are non-enzyme inducing have no effect on oral contraceptives.**
- **Non-enzyme inducing AEDs:**
  - levetiracetam, gabapentin, tiagabine, valproic acid, zonisamide, pregabalin, vigabatrin, topiramate ≤200 mg.

Contraception in epilepsy patients

- **Oral contraceptives should contain >50 micrograms of estrogen in the combination and external methods to prevent insufficient protection.**

Pregnancy

Epilepsy and pregnancy

- ไม่มียากันชักตัวใดที่ปลอดภัยต่อเด็กในครรภ์มากกว่าตัวอื่นอย่างแท้จริง

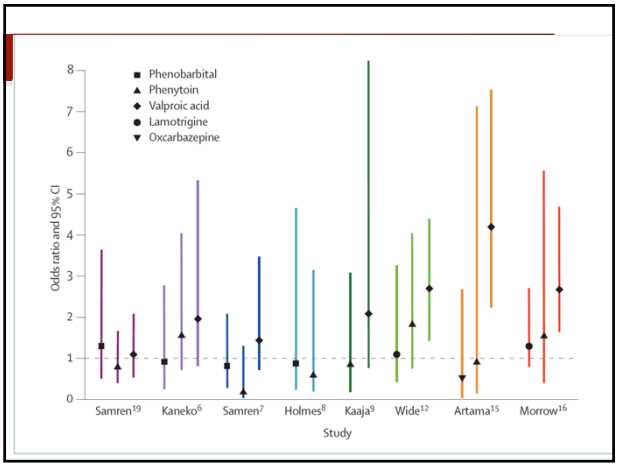
Malformation Risks of AEDs in Pregnancy

❖No AED	2-3%
❖Monotherapy	3.7%-6%
❖Polytherapy	6.1%-15%

AED Specific Malformation Rates in Pregnancy

❖ Carbamazepine	2.1% to 4%
❖ Gabapentin	3.7%
❖ Lamotrigine	2.9% to 3.5%
❖ Phenytoin	4.1% to 6.8
❖ Valproic acid	6.1% 10.7%
❖ Topiramate	?
❖ Levetiracetam	?

UK Epilepsy and pregnancy Registry JNNP 2005
Swedish Medical Birth Registry Acta Paediatr 2004;93:174
International lamotrigine Registry
North America Antiepileptic Drug Pregnancy Registry



Epilepsia, 50(5):1237–1246, 2009
doi: 10.1111/j.1528-1167.2009.02129.x

SPECIAL REPORT

Management issues for women with epilepsy—Focus on pregnancy (an evidence-based review): II. Teratogenesis and perinatal outcomes

Report of the Quality Standards Subcommittee and Therapeutics and Technology Subcommittee of the American Academy of Neurology and the American Epilepsy Society

*Cynthia L. Harden, †Kimford J. Meador, †Page B. Pennell, ‡W. Allen Hauser, §Gary S. Gronseth, ¶Jacqueline A. French, **Samuel Wiebe, ††David Thurman, ‡‡Barbara S. Koppel, §§Peter W. Kaplan, ¶¶Julian N. Robinson, ***Jennifer Hopp, ***Tricia Y. Ting, †††Barry Gidal, ‡‡‡Collin A. Hovinga, §§§Andrew N. Wilner, ¶¶¶Blanca Vazquez, ¶¶Lewis Holmes, ***Allan Krumholz, ****Richard Finnell, ††††Deborah Hirtz, and ‡‡‡‡Claire Le Guen

Risk of congenital malformation using AED in 1st trimester

- AEDs taken during the first trimester probably increase the risk of MCMs in the offspring of WWE (two adequately sensitive Class II studies) but it cannot be determined if the increased risk is from all AEDs or from only one or some AEDs

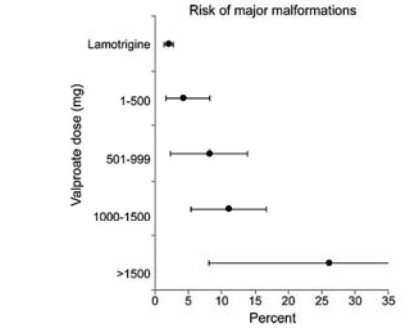
Risk of congenital malformation using AED in 1st trimester

AEDs	MCM risk	Evidences
All AEDs	Prob. increased	2 class II (adeq.sensitive)
VPA monoRx	Prob. increased	1 class II
VPA polyRx	Prob. increased	1 class I
CBZ	Prob. doesnot	1 class I
LTG	Insuff. evidences	1 class I (inadeq.sensitive)
Other specific AEDs	Insuff. evidences	No class III

Risk of congenital malformation using AED in 1st trimester

- If possible, avoidance of the use of VPA as part of polytherapy during the first trimester of pregnancy should be considered to decrease the risk of MCMs (Level B)
- If possible, avoidance of the use of VPA monotherapy during the first trimester of pregnancy may be considered to decrease the risk of MCMs (Level C).

Figure 1 Risk of major malformations by average valproate dose (mg) during the first trimester



North American AED Pregnancy Registry 1997-2011.

Hernández-Díaz S, et al. Neurology 2012;78;1692

Polytherapy VS monotherapy

- Polytherapy probably contributes to the development of MCMs in the offspring of WWE as compared to monotherapy (one Class I study)
- To reduce the risk of MCMs, avoidance of the use of AED polytherapy during the first trimester of pregnancy, if possible, compared to monotherapy should be considered (Level B).

Lamotrigine

TABLE V. Epidemiological Studies Concerning Lamotrigine Monotherapy During Pregnancy and the Risk of Birth Defects

Authors	Study methodology	n	Rate of MCM (%)	OR/RR (95% CI)
Morrow et al. [2006]	Prospective	647	3.2	OR 1.44 (0.77–2.67) RR 0.92 (0.41–2.05)
Vajda et al. [2006]	Prospective and retrospective	61	0	NA
Vajda et al. [2007]	Prospective	146	1.4	OR 0.37 (0.06–2.26)
Meador [2008]	Systematic review and meta-analysis	1337	2.9	NA
Holmes et al. [2008a]	Prospective	684	2.80	RR 1.4 (0.9–2.3)
Hunt et al. [2009]	Prospective	1.151	2.4	NA
Mawer et al. [2010]	Controlled, observational	40	5.4	OR 2.66 (0.52–13.68)
Vajda et al. [2012]	Retrospective	231	5.2	NA
			1.4-5.2%	OR 0.37-1.44

RR, relative risk; OR, odds ratio; CI, confidence interval; NA, data not available.
Updated from [Hill et al., 2010].

Wlodarczyk BJ, et al. Am J Med Genet 2012

Levetiracetam

TABLE VI. Epidemiological Studies Concerning Levetiracetam Monotherapy During Pregnancy and the Risk of Birth Defects

Authors	Study methodology	n	Rate of MCM (%)	OR/RR (95% CI)
Long [2003]	Case series	3	0	NA
ten Berg et al. [2005]	Prospective	2	0	NA
Morrow et al. [2006]	Prospective	22	0	NA
Hunt et al. [2006]	Prospective	39	0	NA
Holmes [2008]	Prospective	197	2.0	NA
Vajda et al. [2012]	Retrospective	22	0	NA

RR, relative risk; OR, odds ratio; CI, confidence interval; NA, data not available. Updated from [Hill et al., 2010].

2%

Wlodarczyk BJ, et al. Am J Med Genet 2012

Topiramate

TABLE VII. Epidemiological Studies Concerning Topiramate Monotherapy During Pregnancy and the Risk of Birth Defects

Authors	Study methodology	n	Rate of MCM (%)	OR/RR (95% CI)
Morrow et al. [2006]	Prospective	28	2.0	OR 7.1 (2.0–22.6)
Vajda et al. [2007]	Prospective	15	0	NA
Ornoy et al. [2008]	Prospective	29	3.5	NA
Hunt et al. [2008]	Prospective	70	4.8	NA
Holmes [2008]	Prospective	197	4.1	NA
Hernandez-Diaz et al. [2010]	Prospective	289	3.8	2.8 (1.0–8.1)
Vajda et al. [2012]	Retrospective	31	3.2	NA

RR, relative risk; OR, odds ratio; CI, confidence interval; NA, data not available. Updated from [Hill et al., 2010].

2-4.8%

OR 2.8

Wlodarczyk BJ, et al. Am J Med Genet 2012

Gabapentin

TABLE VIII. Epidemiological Studies Concerning Gabapentin Monotherapy During Pregnancy and the Risk of Birth Defects

Authors	Study methodology	n	Rate of MCM (%)	OR/RR (95% CI)
Montouris [2003]	Prospective and Retrospective	17	5.9	NA
Morrow et al. [2006]	Prospective	31	3.2	OR 1.33 (0.17–10.20)
Vajda et al. [2007]	Prospective	11	0	NA
Holmes [2008]	Prospective	127	0.8	NA
Vajda et al. [2010]	Retrospective	14	0	NA

RR, relative risk; OR, odds ratio; CI, confidence interval; NA, data not available. Updated from [Hill et al., 2010].

0.8-5.9%

OR 1.33

Wlodarczyk BJ, et al. Am J Med Genet 2012

Are there specific MCMs associated with specific AEDs?

AEDs	MCMs	Evidences
PHT	Cleft palate	1 Class II study
CBZ	Posterior cleft palate	1 Class II study
VPA	Neural tube defects, facial cleft	1 Class I study
PB	Cardiac malformations	2 Class III studies

PHARMACOKINETIC OF AEDS DURING PREGNANCY

Changes in AEDs clearance or levels

AEDs	Level changes	Evidences
LTG	↓ >35%	1 class I, 2 class II
CBZ	↓ Up to 12%	1 class I
PHT	↓ Free PHT up to 16%	1 class I
OXC	↓ MHD conc. up to 36-61%	2 class III
LEV	↓ Up to 60%	1 class II
PB, VPA, ETX	Insufficient data	

Changes in AED level or clearance

- Monitoring of lamotrigine, carbamazepine, and phenytoin levels during pregnancy should be considered (Level B)
- Monitoring of levetiracetam and oxcarbazepin levels during pregnancy may be considered (Level C)
- There is insufficient evidence to support or refute a change in phenobarbital, valproate, primidone, or ethosuximide levels related to pregnancy (Level U)

Breast milk penetration

- Valproate, phenobarbital, phenytoin, and carbamazepine may be considered as not transferring into breast milk to as great an extent as primidone, levetiracetam, gabapentin,lamotrigine, and topiramate (Level B when compared to primidone and levetiracetam and Level C when compared to gabapentin, lamotrigine, and topiramate).

Epilepsy and pregnancy

- ควรมีการให้ความรู้เกี่ยวกับโอกาสและความเสี่ยงที่จะเกิดความผิดปกติของเด็กในครรภ์สำหรับหญิงวัยเจริญพันธุ์ที่ต้องรับประทานยากันชัก เพื่อผู้ป่วยจะได้สามารถวางแผนและตัดสินใจเรื่องการตั้งครรภ์ล่วงหน้าได้

Epilepsy and pregnancy

- ควรวางแผนล่วงหน้าก่อนการตั้งครรภ์เนื่องจาก
  - ในกรณีที่มารดาไม่มีอาการชักนานเกิน 2 ปีอาจพิจารณาหยุดยากันชักได้
  - ในกรณีที่คุมอาการชักได้ดี และมารดารับประทานยากันชักมากกว่า 1 ชนิดอาจพิจารณาลดขนาดยาหรือลดยาเหลือ 1 ชนิด เพื่อลดโอกาสการเกิดผลข้างเคียงต่อทารกในครรภ์

Epilepsy and pregnancy

- ควรวางแผนล่วงหน้าก่อนการตั้งครรภ์เนื่องจาก
  - ควรหลีกเลี่ยงการใช้ยากันชักที่มี teratogenic effect สูง เช่น sodium valproate ในช่วงการตั้งครรภ์หากสามารถทำได้

Epilepsy and pregnancy

- ในขณะที่ผู้ป่วยตั้งครรภ์ไม่ควรปรับหรือเปลี่ยนยากันชัก เนื่องจากโอกาสที่จะเกิดอันตรายต่อมารดาและทารกในครรภ์หากผู้ป่วยเกิดการชักมีมากกว่าโอกาสการเกิดผลข้างเคียงต่อทารกในครรภ์
- ควรมีการตรวจคัดกรองความผิดปกติของเด็กในครรภ์มารดา โดยเฉพาะ malformation ที่พบได้บ่อยและรุนแรง เช่น neural tube defect

Epilepsy and pregnancy

- ในผู้หญิงวัยเจริญพันธ์ควรได้รับ folic acid supplementation ในขนาด 4-5 mg/d ซึ่งจากการศึกษาที่ผ่านมา อาจช่วยลดโอกาสการเกิด neural tube defects ได้บ้าง
- ในผู้ป่วยที่ได้รับ enzyme inducing AEDs เด็กแรกคลอดควรได้รับ vitamin K supplement หลังคลอดเช่นเดียวกับเด็กอื่นๆ

Which medications?

- ลักษณะการชักและประเภทของโรคลมชักของผู้ป่วย
- การบริหารยา
- ผลข้างเคียงของยากันชัก
- Drug interaction กรณีที่ผู้ป่วยได้ยาหลายชนิดพร้อมกัน
- Special situations
  - Reproductive age
  - Elderly
  - Hepatic impairment
  - Renal impairment