# NEUROLOGICAL DISORDERS IN PREGNANCY

## نوايا الدراسة

.لأجل الله ورضاه

.نفع الأمة وتمكينها والنهوض بها

.نفع نفسي والمسلمين بتفريج كرباتهم

.تحسين صورة الإسلام

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.بر الوالدين بإدخال السرور عليهم

.أن يسهّل الله لنا بالعلم طريقا للجنة

.زيادة خشية الله واستشعار نعمه

.الكسب الحلال والرزق الطيب


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«مادُمتَ تسعى فلا تُذعِن لِمُعضلةٍ
لا بُدَّ ـ من خاضَ دربَ السَّعيِ ـ أن يصِلا»

# HEADACHE IN PREGNANCY

-Headache is defined as a pain, discomfort in the head or scalp or neck.
-Headaches can differ greatly in regard to pain type, severity, location and frequency.

--Most headaches in pregnancy are benign (primary headache e.g. migraine or tension-type headache ) , but the pregnant woman is at risk of life-threatening secondary headaches (headache caused by another condition , e.g. impending eclampsia and cerebral venous thrombosis)

# PRIMARY HEADACHES

**Primary headaches in pregnancy**
**Most headaches in pregnant women have no sinister underlying pathology, and migraine and tension-type headache are the most prevalent diagnoses in early pregnancy.**

**Primary headaches peak in women of reproductive age anyway due to the impact of hormones, however 75% of women who experience benign headaches pre-pregnancy find they reduce in the antenatal period.**

**-Most are migraine and tension-type headaches.**

# MIGRAINE

They are progressive unilateral headache pulsating in character often in the frontotemporal area , worsened by excretion and lasts for 4-72 hours.
-patient often present with nausea,vomoting , photophobia etc.

Migraine is influenced by cyclical changes in the sex hormones, and attacks often occur during the menstrual period, attributed to a fall in oestrogen levels. Migraine often improves in pregnancy, with worsening of headaches occurring infrequently.
Throughout pregnancy around 20% of pregnant women will experience migraine-like headaches, many of whom do not get migraines outwith pregnancy. Obstetric complications are not increased in migraine sufferers. Migraine during pregnancy should be treated with analgesics, antiemetics and, where possible, avoidance of factors that trigger the attack. Low-dose aspirin or beta-blockers may be used to prevent attacks.

-Approximately 60-70% of migraine improve spontaneously during pregnancy. On occasion , the first migraine attack occurs during pregnancy , usually during the first trimester. New onset of aura may occur during the second and third trimesters.

# TENSION HEADACHE

Tension-type headache (TTH) is a primary headache disorder characterized by a bilateral,nonthrobbing (constant pressing tightening) headache of a mild to moderate intensity, typically without other associated features .

it is often gradual in onset and last from 30m-7days

# SECONDARY HEADACHES IN PREGNANCY

**Secondary causes of headache are more serious and often refers to underlying serous problem.**

- **Hypertension**
  - **Subarachnoid hemorrhage**
  - **Drug-related**
  - **Cerebral venous thrombosis**
  - **Arteriovenous malformation (can enlarge/bleed in pregnancy)**
  - **Meningitis**
  - **Enlargement of a pituitary tumor**
  - **Enlargement of a hormone-sensitive tumor , e.g. meningioma**
  - **Bleeding into a pre-existing tumor**

# POST-DURAL PUNCTURE HEADACHE

-CSF leakage from the puncture site
-Decrease in the CSF volume may lead to compensatory vasodilatation of the cerebral vessels that causes severe headache. Also, accumulation of the CSF in the epidural space irritates the meninges
-The headache is usually in the fronto - occipital regions and radiates to the neck. It is characteristically worse on standing , relieved with lying and typically develops 24–48 hours post-puncture.

**Managed by:**

1. Analgesia, bed rest and adequate hydration
2. Epidural blood patch is injected at the site of the meningeal tear
3. Other medications: theophylline and hydrocortisone (vasoconstrictors)

# SUBARACHNOID HEMORRHAGE

-Bleeding in the space between the brain and the surrounding membrane (subarachnoid space).
-Outside pregnancy the commonest cause is a ruptured berry aneurysm , but arteriovenous malformations (AVMs) may dilate in pregnancy due to the effect of estrogen , resulting in a similar incidence.
-The primary symptom is a sudden, severe headache,associated with nausea/vomiting/stiff neck.

# CEREBRAL VENOUS THROMBOSIS

-Distinct neurological emergency caused by occlusion, either partial or complete, of the dural venous sinus and/or the cerebral veins.
-The greatest risk period is the third trimester in Pregnancy and the first few weeks after delivery
-• Headache is the most frequently (80–90%) occurring symptom in cerebral venous thrombosis and often the first symptom reported by patients.
usually acute or subacute in onset , localized , continuous and moderate to severe.other clinical manifestations present at onset or develop during the course of the disease. include papilledema , focal deficits , altered consciousness , seizures

# MANAGEMENT OF HEADACHE IN PREGNANCY

**In the initial clinical assessment of a pregnant or postpartum woman with headache , a history and neurological examination often allows the correct cause for the headache to be identified.**

# HEADACHE HISTORY TAKING

-The vast majority of headache aren’t life-threating ,however in some cases may be the first indication for serous pathology.
-Pain = SOCRATES
-Location
-onset
-Character
-Radiation
-Associates symptoms
-Duration
-Severity

# RED FLAG FEATURES

Thunderclap : rapid time to peak headache intensity (seconds to 5 minutes)

- Focal neurological symptoms (e.g. limb weakness , aura 1 hour)
- Non-focal neurological symptoms(e.g. cognitive disturbance)
- Change in headache frequency , characteristics or associated symptoms
- Headache that changes with posture
- Headache awakening the patient

Headache precipitated by physical exertion or Valsalva manoeuvre

- Jaw claudication or visual disturbance (women over 50 years)
- Fever
- Neck stiffness
- New onset of headache in a patient with a history of HIV infection
- New-onset headache in a patient with a history of cancer

# TREATMENT OF HEADACHE IN PREGNANCY

For treatment of primary and secondary headaches, ACOG recommends acetaminophen 1000 mg orally as initial treatment of acute migraine. For persistent headache in pregnancy, the guideline recommends metoclopramide 10 mg (IV or enteral), alone or in combination with diphenhydramine 15 mg (IV or enteral), as additional treatment. ACOG recommends against the use of ergot alkaloid–containing products (in lactating patients as well) and medications containing opioid narcotics, and recommends cautious use of prednisolone, IV magnesium, or sumatriptan for secondary treatment.

For patients with persistent headache attributed to preeclampsia with severe features, ACOG recommends treatment with magnesium sulfate, blood pressure control, and delivery etc.

medscape , neurological disorders and pregnancy

**Table 35.1** Characteristics of headaches in pregnancy

| Headache type | Onset | Location | Character | Duration | Worsened by | Other symptoms | Course with pregnancy | Diagnosis |
|---|---|---|---|---|---|---|---|---|
| Tension type | Gradual | Bilateral | Constant, pressing/ tightening, mild/moderate | 30 minutes to 7 days | – | Pericranial tenderness, minimal photophobia | No change | Symptomatology and history |
| Migraine | Progressive, may be preceded by aura | Unilateral, frontotemporal | Pulsating, moderate/severe | 4–72 h | Exertion | Nausea, vomiting, photo/phonophobia | Majority improve | Requires at least 5 attacks to fulfill definition |
| Cluster | Sudden, up to 8 times per day | Unilateral, periorbital | Severe, constant | 15–180 minutes | – | Ipsilateral tearing, sweating, congestion, edema, miosis, agitation | Rare | Symptomatology and history |
| Pre-eclampsia/ eclampsia | Gradual | Bilateral | Pulsating | Persists intermittently until delivery | Exertion | Scotomata, right upper quadrant and epigastric pain | Occurs during pregnancy after 20 weeks gestation and up to 7 days post partum | Typically blood pressure >140/90 on 2 instances 6 hrs apart and proteinuria >300mg/24hrs |
| Hypertensive crisis | Gradual | Bilateral | Pulsating | Resolves within 1 hour of normalization of blood pressure | Exertion | – | Increased incidence in women with chronic hypertension | Blood pressure >160/120 |
| Cerebral venous thrombosis | Progressive | Diffuse | Severe | Weeks, until dissolution of thrombus by anticoagulation | – | Neurologic deficits, seizures, loss of consciousness, increased intracranial pressure | Increased incidence | MR or CT angiography |
| Subarachnoid hemorrhage | Abrupt | Unilateral | Incapacitating, worst ever | Days | Exertion | Nausea/vomiting, altered consciousness | Unchanged | CT, MRI, LP |
| Idiopathic intracranial hypertension | Progressive | Diffuse | Constant | Resolves within 72 h of normalization of ICP | Coughing, Valsalva | Papilledema, visual field defects | Unchanged | LP to measure ICP (>200mm H20) |
| Postdural puncture | Progressive within 5 days of dural puncture | Diffuse | Constant | 1 week or 48 h after epidural blood patch | Upright position | Neck stiffness, tinnitus, hypacusia, photophobia, nausea | Associated with epidural and spinal analgesia | Symptomatology and history |
| Neoplasm | Progressive | Localized | Worse in morning | Indefinite, unless surgically resected | Cough or bending forward | Focal neurologic signs | Unchanged | CT, MRI |
| Caffeine withdrawal | Within 24 h of last caffeine intake | Bilateral | Pulsating | 1 h if caffeine ingested, 7 days if not | – | – | Frequent in first trimester | Symptomatology and history |
| Meningitis | Progressive | Diffuse | Constant | Up to months after resolution of infection | – | Fever, stiff neck, nausea, photo/phonophobia | Unchanged | LP |
| Sinus headache | Gradual | Frontal, facial | Constant | 7 days | – | Acute sinusitis | Unclear | CT, MRI |

# CEREBROVASCULAR DISORDERS

**Cerebrovascular disease during pregnancy categorised into:**

**1-stroke**
**2-cerebral venous thrombosis**

# STROKE

Stroke is the third leading cause of death and the primary cause of adult disability in the United States. It may be broadly classified as either ischemic or hemorrhagic.

Although cerebrovascular disease is thought to be uncommon in pregnancy, it is an important source of maternal and fetal morbidity and mortality, causing 3.5–26 cases of neurologic dysfunction per 100,000 deliveries, and is associated with more than 12% of maternal deaths.

it can be classified into : haemorrhagic or ischemic strok

# STROKE

### Causes of stroke or stroke-like events in pregnancy

| |
|---|
| **Hematologic** |
| Essential thrombocythemia |
| Sickle cell disease |
| Thrombophilias (inherited or acquired) |
| Thrombotic thrombocytopenic purpura |
| **Cardiac** |
| Valvular abnormalities |
| Arrhythmias, especially atrial fibrillation |
| Cardiomyopathy |
| Infective endocarditis |
| Patent foramen ovale |

| |
|---|
| **Vascular** |
| Aneurysms |
| Arteriovenous malformations |
| Vasculopathy (eg, moyamoya disease or syndrome, Takayasu arteritis) |
| Cervical artery dissection |
| Atherosclerotic steno-occlusive cerebrovascular disease |
| Reversible cerebral vasoconstriction syndrome (RCVS) |
| Posterior reversible encephalopathy syndrome (PRES) |
| Cerebral venous thrombosis |
| **Pregnancy related disorders** |
| Preeclampsia, eclampsia, and HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome |
| Peripartum cardiomyopathy |
| Amniotic fluid embolism |
| Air embolism caused by caesarean delivery, uterine manipulation, central venous catheterization, or sexual activity |

# ISCHEMIC STROKE

Ischemic strokes account for 85% of all strokes. [76] Causes of ischemic stroke in pregnancy may be divided into 2 general categories: pregnancy-specific etiologies and stroke-in-the-young factors.

**The first category includes the following:**

Preeclampsia [77] and eclampsia - These are present in 24-47% of ischemic strokes and 14-44% of intracranial hemorrhages [73, 75]

Choriocarcinoma

Amniotic fluid embolism

Peripartum cardiomyopathy

Postpartum cerebral angiopathy - This rare and reversible condition causes narrowing of the blood vessels, which can lead to ischemia (69, 73]

# ISCHEMIC STROKE

**Causes of stroke in a young person include the following:**

**Atherothrombotic etiologies**

**Cardioembolic events**

**Other vasculopathy (eg, fibromuscular dysplasia [FMD], dissection, or arteritis)**

**Hematologic disorders**

**Drugs (eg, cocaine)**

**Migraine**

**Unknown causes**

# HEMORRHAGIC STROKE

Women at risk for intracerebral hemorrhage in pregnancy are those with eclampsia, vasculitis, or an aneurysm or vascular malformation. High blood pressure is the most important risk factor for intracranial hemorrhage in pregnancy.

Prevention is the key.

Blood pressure should be monitored closely during pregnancy.[76]

# CLINICAL MANIFESTATIONS OF STROKE :

:

1) Ischemic stroke ( focal neurological abnormalities) :

- weakness
- sensory changes
- cranial nerve abnormalities

2) hemorrhagic strokes:

- intense headache
- decreased consciousness
- seizures
- nausea and vomiting
- focal neurological abnormalities

# DIAGNOSIS

## History and physical examination

Obtaining a history and performing a physical examination are important aspects of evaluating the type of cerebrovascular event that may have occurred. Important historical points include pain (eg, headache or neck pain), trauma, fluctuating neurologic symptoms, seizures, mental status changes, recent fevers, and drug use.

A complete history should include a medical history of previous stroke or risk factors for stroke, spontaneous abortions, collagen vascular disease, and a family history. In addition, a history of complications that developed during the current and previous pregnancies should be obtained. The patient should undergo a complete physical examination, including funduscopic, cardiovascular, skin, and full neurologic examinations.

# MANAGEMENT OF ACUTE ISCHEMIC STROKE

Intravenous thrombolytic therapy ( alteplase )
Mechanical thrombectomy – it is indicated for selected patients
(for women considered to have a high risk of hemorrhage, such as those with placenta previa or a history of obstetric hemorrhage )
Blood pressure control
Acute antiplatelet therapy — Early aspirin

# CEREBRAL VENOUS THROMBOSIS:

**CVT is rare in the general population but occurs more commonly in association with pregnancy**

**Clinical manifestations:**

- **Headache (severe and diffused)**
- **vomiting**
- **focal or generalized seizure**
- **Confusion**
- **blurred vision**
- **focal neurologic deficits**
- **altered consciousness**

# DIAGNOSIS AND MANAGEMENT

**Diagnosis of arterial and venous infarctions is made based on clinical signs and radiographic abnormalities**

**anticoagulation with heparin**
**which after delivery is switched to warfarin**

# BRAIN TUMORS

- The incidence of primary brain tumors during pregnancy is uncommon. The etiology of these can range from different genetic syndromes such as Li Fraumeni, neurofibromatosis type I, and hormonal associated tumors.

- The incidence of brain neoplasms does not increase during pregnancy, and the types of tumors are similar to those seen in nonpregnant women of the same age.

- The presence of an intracranial tumor during pregnancy can be associated with serious complications, such as increased maternal mortality, intrauterine growth restriction, premature delivery, and emergency caesarian delivery

# CLINICAL MANEFESTATION

**1) Nausea and vomiting:** -tumor-related nausea and vomiting is more likely to arise late in gestation, gradually worsens, and may be accompanied by headache. -pregnancy-related nausea and vomiting occurs very early in pregnancy and tends to improve across gestation

**2) Seizure** : -Tumor-related seizures may be focal and associated with focal neurologic findings. However, secondary generalization may occur rapidly, and the focal onset therefore may be unapparent to observers. -Eclamptic seizures are typically generalize

**3) Dizziness**
**4) Headache**
**5) visual disturbances**
**6) increase of intracranial pressure**

Because of these unspecific symptoms, differential diagnosis from the other complications of pregnancy could be difficult .
**The most common conditions showing similar symptoms are: eclampsia, hyperemesis gravidarum and post-partum psychosis**

## Diagnosis::

1.adequately interpret signs and symptoms
2.proper physical examinations ( proper neurological exploration )
3.imaging studies ( CT and MRI )
4.hormonal assessment

## Management::

The treatment and prognosis of brain neoplasms seen during pregnancy is highly dependent on :
1) upon the particular cell type involved
2) the clinical manifestations
3) the stage of pregnancy If possible, the first choice is close observation until labour

# TREATMENT

## 2 PATHWAYS TO TREAT ::

### 1) SYMPTOMATIC TREATMENT ::

During pregnancy, ideally the treatment is symptomatic, to preserve the fetus, and definite treatment may be performed after birth **anticonvulsants** if they develop seizures or increase in frequency (25-30%) , **corticosteroids** to reduce intracranial edema, but should be used with appropriate caution because ( Long-term steroid use may induce adrenal insufficiency in the fetus BY SUPPRESSING CORTISOL PRODUCTION ).

Maternal **blood pressure and fluids** should be monitored closely
Excessive hydration should be avoided , because it could worsen cerebral edema.

## 2) SURGERY::

Surgery during pregnancy is indicated in patients with malignant tumors or tumors causing severe symptoms (Large , high grade,aggressive ).

Its safer to carry out in the **second trimester** with the continuation of pregnancy, due to vulnerability of fetus during first trimester and higher risk of intraoperative bleeding during third trimester.
**Induction of labor** may be considered **as early as 34 weeks** in asymptomatic patients followed by surgery for brain tumor.

# EPILEPSY

- Epilepsy is a chronic disorder, characterized by recurrent unprovoked seizures.
- Seizure is a temporary dysfunction of the brain in which neurons will produce excessive electrical discharges.
- Most of childbearing potential who have epilepsy expected to become pregnant.
- Epilepsy is not in itself a contraindication to pregnancy
- Approximately 30% of those with epilepsy are woman in their childbearing age years

Approximately 35% of women with epilepsy have more seizures during pregnancy, 10% have fewer 55% remain the same.

## What are major pregnancy related threats to women with epilepsy?

increased seizures rates – risks for fetal malformation because of antiepileptic drugs not because of untreated epilepsy.

The principles of epilepsy management are that while the risks to pregnancy from seizures out weight those from AEDs, Seizures should still be controlled with the minimum possible dose of the optimal drug.
Multiple factors may contribute to worsening seizures. In women who are pregnant, the volume of distribution and the hepatic metabolism of antiepileptic drugs (AEDs) are increased .This, along with decreased compliance with AEDs because of concerns about their effects on the fetus, leads to an increase in seizure frequency.

# TERATOGENIC EFFECTS OF AEDS

1- IUGR
2- Oligohydramnios
3- Stillbirth
4- Eclampsia
5- mental retardation
6-congenital malformations
7- Cleft lip/ palate
8- Cardiac abnormalities
9- Hypoplasia of terminal phalange
10-neural tube defects
11-skeletal problems
12-urinary tract problems.
13-Perinatal mortality is 1.2 to three times higher
14-Prematurity
15-Perinatal death
16-Hemorrhagic diseases of the newborn
17-Intracranial hemorrhage
18-increase chance of epilepsy in offspring of epileptic mother

# Risk of congenital anomaly with epilepsy:

- The principle concern related to epilepsy in pregnancy is the **increased risk of congenital anomaly caused by anticonvulsant medications**, which increase risk **two-three fold ( 5-6 %) compared to general population .**
- Approximately **doubling of the risk in unexposed epileptic mothers.**

# EPILEPSY BEFORE GETTING PREGNANT

- Epilepsy before getting pregnant  managed by Antiepileptic drugs, AEDs work by changing the levels of chemicals in your brain. They do not cure epilepsy but can stop seizures happening. ( to control seizures).

- AED either monotherapy or polytherapy.
  -polytherapy in pregnancy increase risk of born epileptic fetus (15-25%).

  **-monotherapy is better than polytherapy due to ::**

  1)reduced side effects
  2)absence of drug interactions
  3)better compliance
  4)lower cost
  5)improved seizure control compared to polytherapy

# ANTI EPILEPTIC DRUGS

1.Valporic acid

2.Phenytoin

3. Phenobarbital

4.trimethadione

5.clonazepam

6.carbamazepine

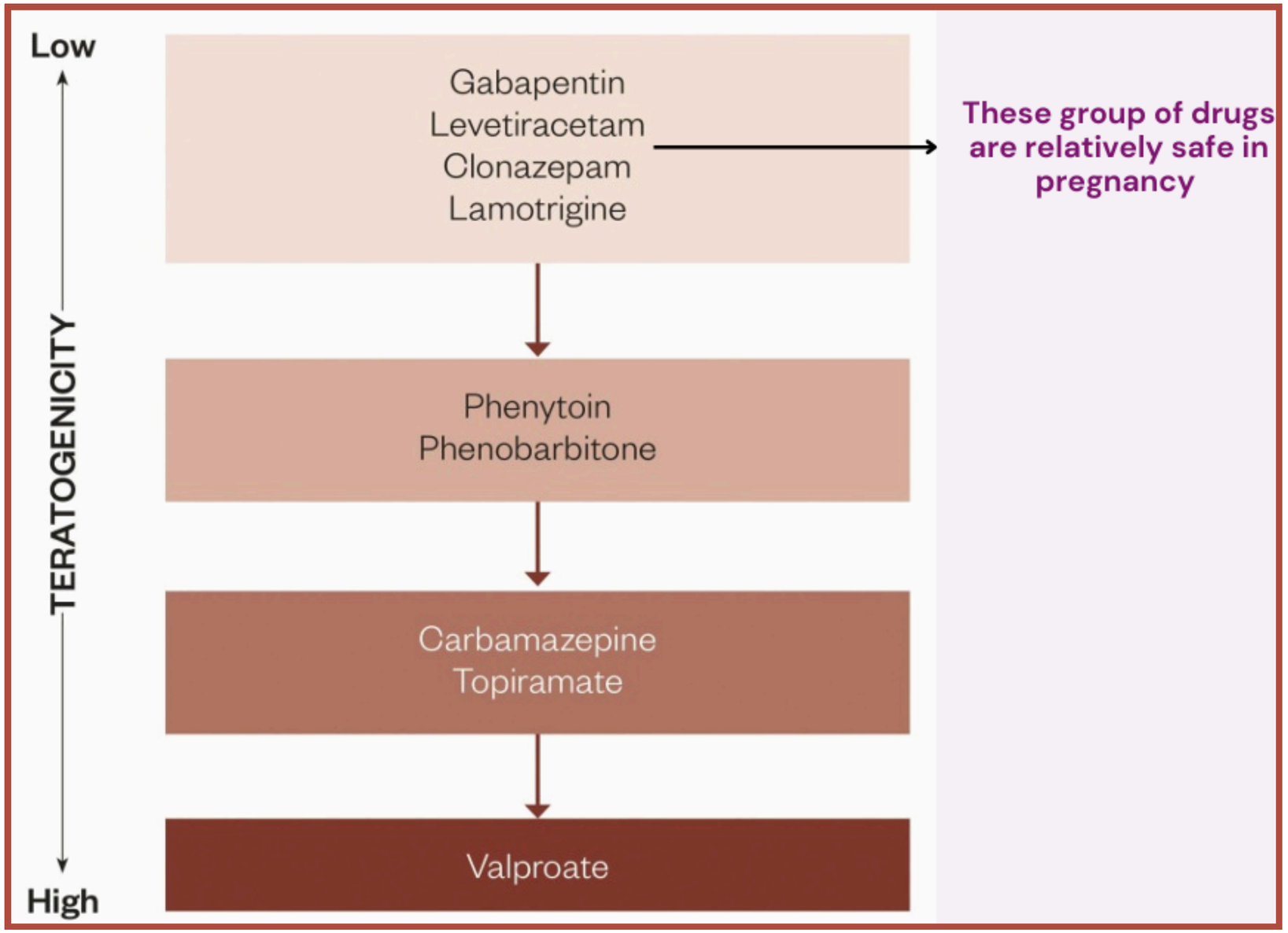
7.Lamotrigine

8.topiramate

9.Levetiracetam.

# ANTI EPILEPTIC DRUGS

- No AED is completely safe to use in pregnancy as the risk of fetal abnormalities are increased.
- The preferred drug is that best control to the patient's seizures. poorly controlled seizures pose a greater harm than the AEDs themselves.
- Prevention seizure provoking stimuli AEDs should be maintained at the lowest dosage associated with seizures control.
- anticonvulsant drugs must be continued during labor and delivery.
- The dose of the anticonvulsant drug may be lowered postpartum, provided that a therapeutic level is maintained.
- Although anticonvulsants are excreted in breast milk in small amounts, breastfeeding is not contraindicated.


Low
TERATOGENICITY
High
Gabapentin
Levetiracetam
Clonazepam
Lamotrigine
Phenytoin
Phenobarbitone
Carbamazepine
Topiramate
Valproate
These group of drugs are relatively safe in pregnancy

## Lamotrigine::

The most safer drug in pregnancy It's level reaches the plateau in 3rd trimester Not increase level of teratogenecity, miscarriage and still birth Daily dose 100–300 mg/d.

Lamotrigine and levetiracetam are safer medicines to take in pregnancy.

## Topiramate and phenobarbital::

They are associated with elevated risks of congenital malformations and neurodevelopmental disorders, though the risks are lower than those of valproate.

# Valproate::

This is the standard broad-spectrum AED (treats all types of seizures).
Rapidly absorption need dose adjustment during pregnancy, Valproate should be avoided during pregnancy because it has the highest risk for major malformations It is not suitable for girls or women who could become pregnant.
Valproate, in monotherapy and polytherapy, has been associated with elevated risk of major congenital malformations and neurodevelopmental disorders in children born to mothers who took it.

For monotherapy, intrauterine exposure to valproate probably **reduces cognitive outcomes**
The use of VPA as a single drug (monotherapy) in the first trimester of pregnancy was associated with significantly increased risks of major and minor malformations, including a **20-fold increase in neural tube defects (NTDs)** such as spina bifida, cleft lip and palate, cardiovascular abnormalities, genitourinary defects, developmental delay, endocrine disorders, limb defects, and autism as compared with no-use of antiepileptic drugs (AEDs) or with use of other AEDs.
should probably not be used in a woman planning a pregnancy, unless other drugs have proven ineffective

## Carbamazepine::

As with valproic acid, exposure during pregnancy is associated with an increased risk for **fetal spina bifida** and is an indication for *amniotic fluid AFP analysis*.
Some studies have reported a specific malformation pattern that includes minor craniofacial defects, fingernail hypoplasia, and developmental delay, which are features that would be unlikely to be detected prenatally
**lower risk of cleft lip, with or without cleft palate**
–Relatively slow absorption –Eliminated by hepatic metabolism.

# Phenytoin::

first-generation AED. The American College of Obstetricians and Gynecologists recommends 4 mg of folate per day for women taking phenytoin (Dilantin) during pregnancy. •Although folate supplementation is recommended for pregnant women taking the drug, the efficacy of folate supplementation in preventing neural tube defects not well proved.
About one third of children whose mothers are taking this drug during pregnancy typically have **fetal hydantoin syndrome**

**(A) hypertelorism, broad nasal bridge, cleft lip and low-set ears.**
**(B) Hypoplastic distal phalanges in the right hand with contractures.**
**(C) Oligosyndactyly.**
**(D) Absent distal phalanges in bilateral feet.**
**(E) Single umbilical artery.**
**IUGR with small head circumference**

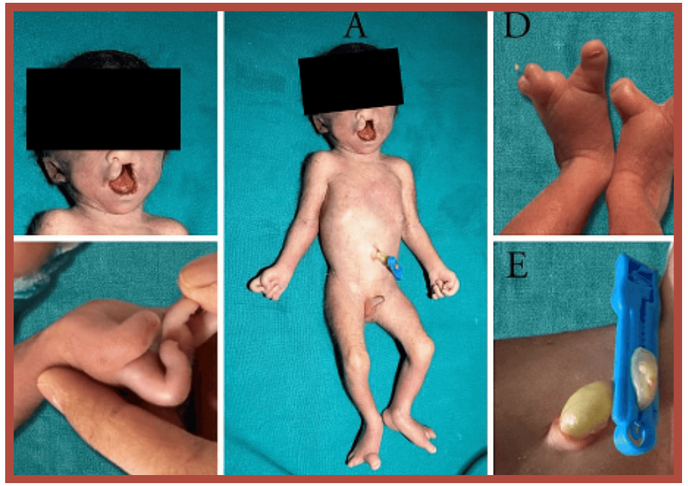


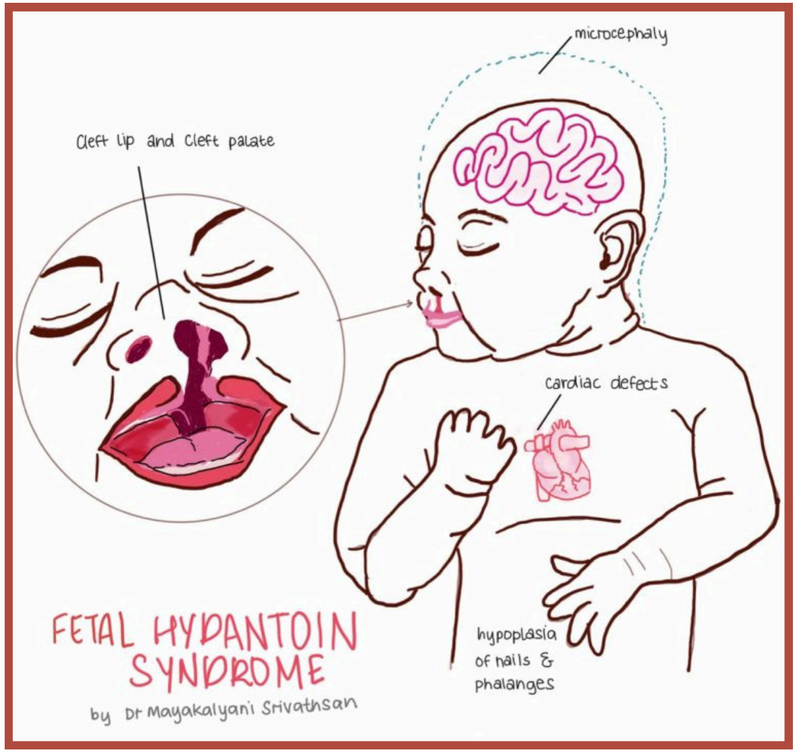
**TABLE 14-5.** Teratogenic Effects of Common Anticonvulsant Medications

| Drug | Abnormalities Described | Affected | Pregnancy Category |
|---|---|---|---|
| Valproate | Neural-tube defects, clefts, skeletal abnormalities, developmental delay | 1–2% with monotherapy, 9–12% with polytherapy | D |
| Phenytoin | Fetal hydantoin syndrome: craniofacial anomalies, fingernail hypoplasia, growth deficiency, developmental delay, cardiac defects, clefts | 5–11% | D |
| Carbamazepine | Fetal hydantoin syndrome, spina bifida | 1–2% | D |
| Phenobarbital | Clefts, cardiac anomalies, urinary tract malformations | 10–20% | D |
| Lamotrigine | Inhibits dihydrofolate reductase, lowering fetal folate levels. Registry data suggest increased risk for clefts | 4-fold with monotherapy, 10-fold with polytherapy | C |
| Topiramate | Registry data suggest increased risk for clefts | 2% | C |
| Levetiracetam | Theoretical—skeletal abnormalities and impaired growth in animals at doses similar to or greater than human therapeutic doses | Too few cases reported to assess risk | C |

From Cunningham (2005), Holmes (2008), Hunt (2006, 2008), Morrow (2006), UCB, Inc. (2008), and all their associates.

# FETAL HYDANTOIN SYNDROME

Mental and physical birth defects that results from maternal use of drug phenytoin (Dilantin) during pregnancy. The range and severity of associated abnormalities will vary greatly from one infant to another



# The characteristics of fetal hydantoin syndrome include :

## P

Cleft **P**alate , Cleft li**P** ( orofacial cleft )

## H

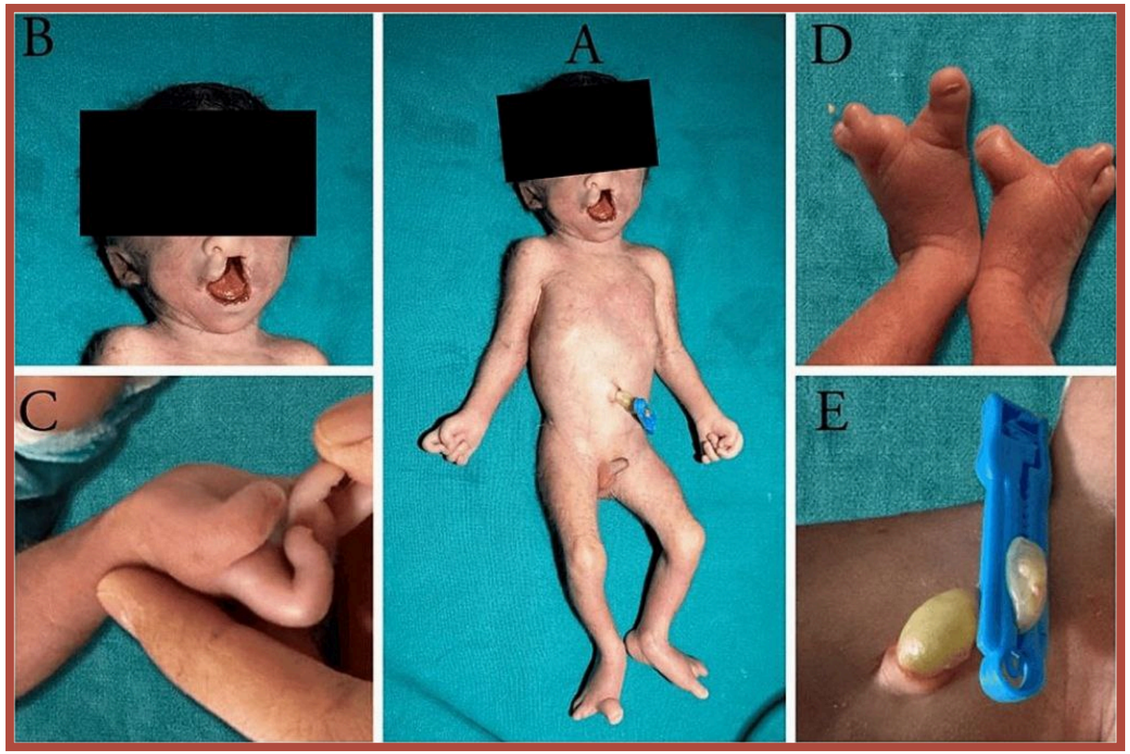
Small **H**ead circumference
**H**ypoplastic face ( dysmorphic face )
**H**irsutism
**H**eart defects

## E

**E**mbryopathy
Anti **E**pileptic use

## N

Hypoplastic **N**ails and distal digital hypoplasia
**N**eurological defects
**N**eonatal growth restriction (IUGR )


B
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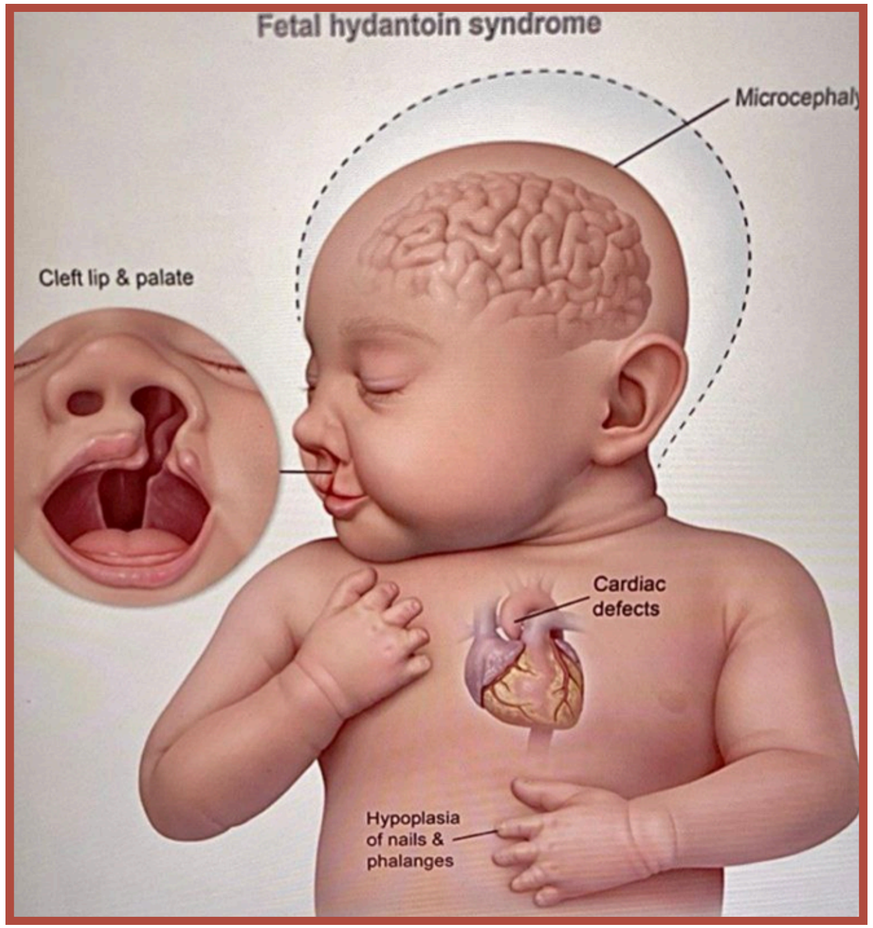
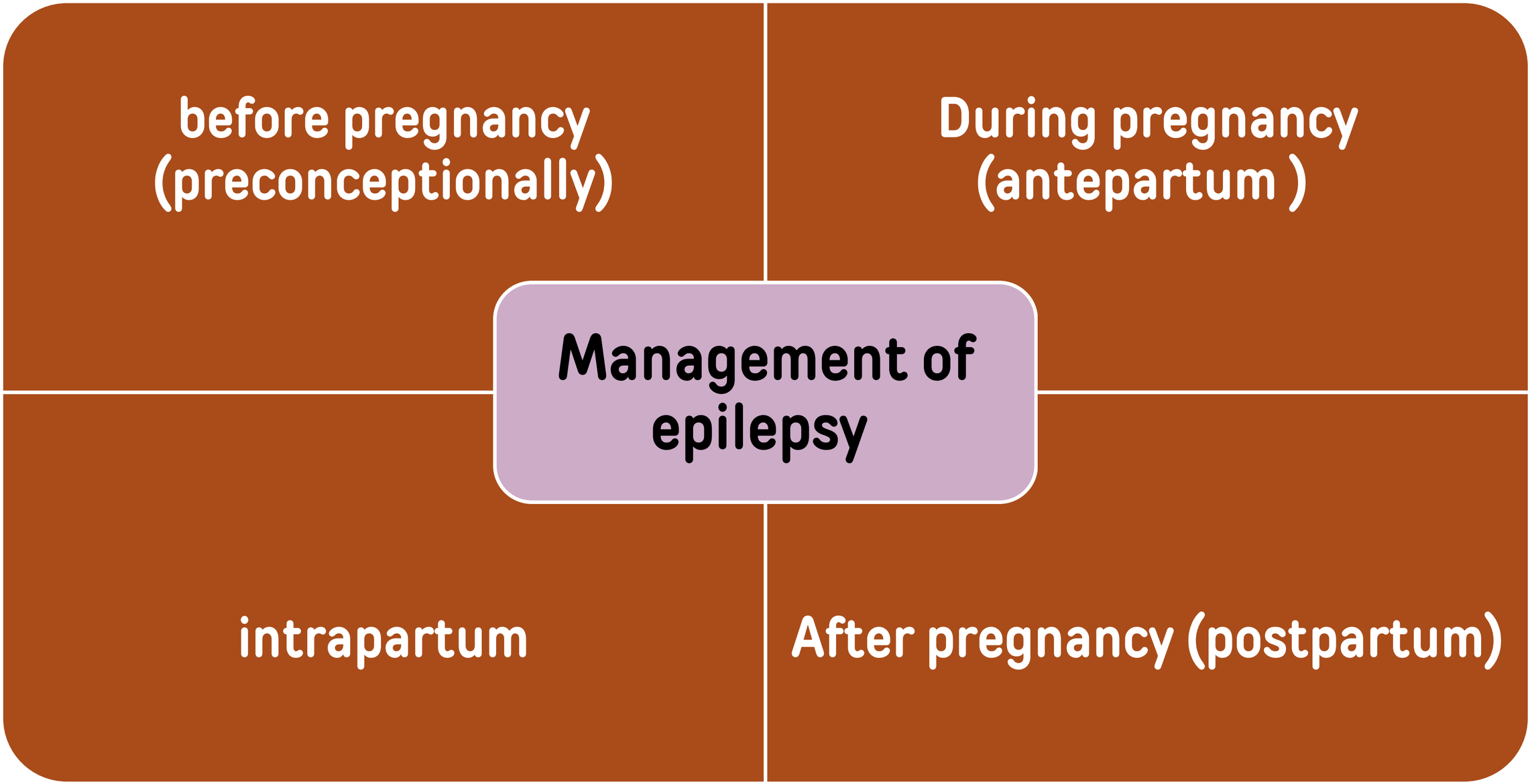
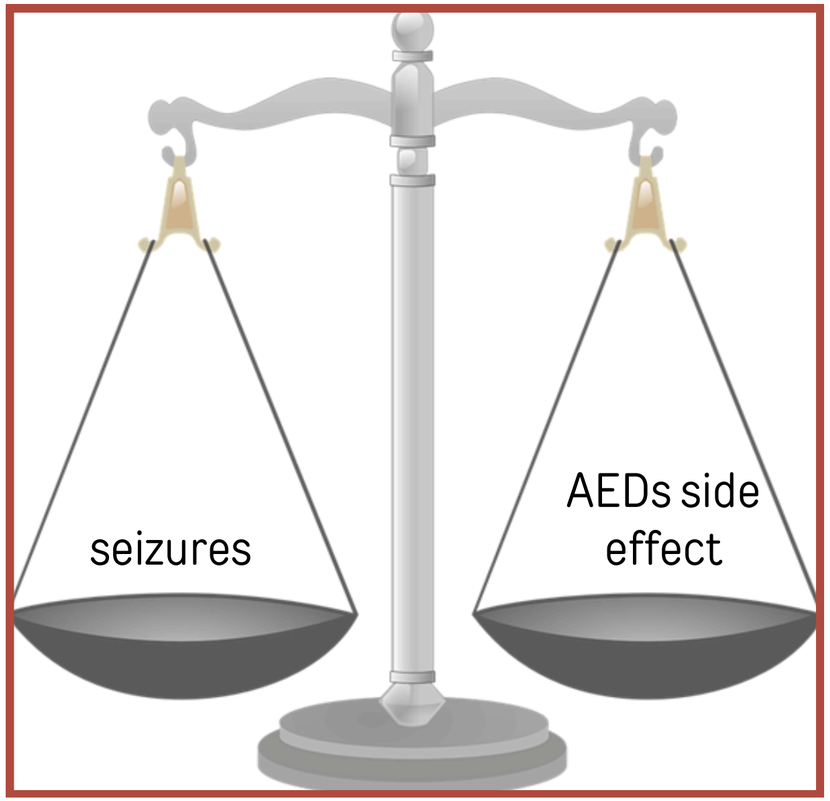

Fetal hydantoin syndrome
Microcephaly
Cleft lip & palate
Cardiac defects
Hypoplasia of nails & phalanges


before pregnancy (preconceptionally)
During pregnancy (antepartum )
Management of epilepsy
intrapartum
After pregnancy (postpartum)

- There is no ideal anticonvulsant for use in women intending to become pregnant or during pregnancy, and all AEDs should be considered potential teratogens
- During seizures there is fetal hypoxia due to poor uteroplacental circulation. When circulation is restored, there is increased oxidative stress, which can trigger teratogenicity
- Seizures in labour may lead to maternal hypoxia (due to apnoea during the seizure), and fetal hypoxia and acidosis secondary to uterine hypertonus.
- Seizures should be controlled with the minimum possible dose of the optimal drugs



- **Antiepileptic drugs (AEDs) that induce cytochrome P450 and related enzymes**
  - can decrease the efficacy of hormonal contraception.
  - Decrease folic acid efficacy
  - increase the rate of vitamin K degradation
  - may increase their metabolism of corticosteroids, with reduced therapeutic effectiveness.
- **Sodium valproate (VPA) interferes with folate transport and metabolism.**

| *Enzyme-inducing AEDs* | *Nonenzyme-inducing AEDs* |
|---|---|
| Phenobarbitone | Valproate |
| Phenytoin | Lamotrigine |
| Carbamazepine | Clonazepam |
| | Ethosuximide |
| | Gabapentin |

AEDs: Antiepileptic drugs

# PRECONCEPTIONAL MANAGEMENT

- Preconception counseling and care are important.
  - Explain risk from recurrent seizures
  - Explain risk of congenital malformation

- Supplement the diet with folate at 5 mg/d daily
- Attempt to decrease pharmacotherapy to monotherapy
- Taper dosages of AEDs to the lowest possible dose
- In women who have not had a seizure for 2–5 years, attempt complete withdrawal of pharmacotherapy
- If a decision is taken to stop treatment, drug should be withdrawn slowly to reduce the risk of withdrawal associated seizures
- Consider preconceptual genetic counseling

# ANTEPARTUM MANAGEMENT

## Major goal is ?
## seizures prevention

- Check total and free levels of AEDs monthly
- Consider early genetic counseling
- Check maternal serum alpha-fetoprotein (MSAFP) levels and perform a level II fetal survey and ultrasonography at 19-20 weeks' gestation
- Vitamin K supplementation (10-20mg/d) in late trimester (36 weeks)to reduce the the risk of postpartum bleeding
- Consider amniocentesis for alpha-fetoprotein

# Antepartum management

- Women of childbearing age who suffer from epilepsy and are on maintenance therapy must have their treatment reviewed and **monotherapy is recommended if at all possible.**
- **Antiepileptic drugs can cause teratogenicity and folic acid 5 mg daily through out the pregnancy** is generally prescribed in view of the relative folate deficiency of many mothers on antiepileptic therapy.

- It is important that control of seizures is achieved to minimize maternal morbidity (**fits can be fatal**) .
- **Patients must be monitored during pregnancy to ensure that dose adjustments are made as appropriate.**

**Sodium valproate is the major cause for concern in these condition .**

# Antepartum managements

- All patients should receive **anomaly ultrasound** assessment to exclude specific abnormalities associated with their medication.
- These are specifically **orofacial clefts, neural tube defects** and **craniofacial dysmorphism.**
- **Vitamin K is recommended to be given from 36 weeks onwards to prevent neonatal bleeding disorders.**

the risk of developing a seizure during labour is nine times that during the rest of pregnancy

## Intapartum management

- Epileptic seizures may occur during labour and as such may confuse the diagnostic situation that includes eclampsia.
- **Epileptic seizures should be treated in these circumstances as they would be normally**
- Vaginal delivery is recommended **unless there is obstetric complication.**

## Postpartum management:

- **Post-partum drug doses may need to be adjusted if doses have been increased during pregnancy.**
- Specific advice must be given to epileptic women about childcare, for example, *not bathing the baby on their own.*
- **Breast feeding can be encouraged.**
- **Contraception** advised: combined oral contraception pill better not used with anti epileptic medication

*Delivery, puerperium and lactation*

1 Recommend hospital delivery
2 Continue usual drug regimen during labour
3 Ensure infant receives vitamin K at birth (1 mg intramuscularly)
4 Observe neonate for drug-withdrawal symptoms
5 Observe breast-fed infant for adverse drug effects
6 Perform paediatric examination
7 Perform clinical genetic analysis in case of congenital malformations

Figure 1

# Pregnancy & Anti-seizure Drugs

Women who take anti-seizure drugs need to plan well ahead for pregnancy

## 1-2 Years Before Pregnancy

**Avoid valproate**
- Valproate has the highest risk of birth defects
- Change it to a safer anti-seizure drug

**Minimize the number and doses of anti-seizure drugs**
- Use the lowest effective dose
- Use only one anti-seizure drug if possible

**Start up to 5mg of folic acid daily**

**Aim to be seizure-free for at least 9 months before pregnancy to lower risk of seizures during pregnancy**

## During Pregnancy

**Avoid stopping or switching anti-seizure drugs during pregnancy**

**Check serum drug levels if there are more seizures**
- Especially with lamotrigine and levetiracetam
- Adjust phenytoin doses using free concentrations, not total concentrations

**Watch for new drug interactions**
- Folic acid may decrease phenytoin serum concentrations
- Antacids may decrease phenytoin absorption

## After Delivery

**Doses of anti-seizure drugs may need to be adjusted**

**It is generally safe to breastfeed with anti-seizure drugs**

Watch baby for side effects such as:
- Poor suck
- Poor weight gain
- Drowsiness
- Hyperexcitability

Developed by: Kelly Grindrod, PharmD; Tejal Patel, PharmD. Design by Adrian Poon, BA; Allysa Misola.
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# ECLAMPSIA

Occurrence of one or more generalized convulsions and/or coma in the absence of other neurological conditions

seizures preceded by frontal or occipital headache, visual disturbances, RUQ pain or epigastric pain

Cerebral vasospasm , leading to ischemia and cerebral edema

# ECLAMPSIA MANAGEMENT:

- Airway :Maintenance of airway latency
- Breathing : supplemental oxygen 8–10L/min via face mask
- Circulation
- left lateral position
- Anticonvulsant:
  - Mg sulfate (loading dose 4–6g then maintenance 1g/hours)
  - Should continued at least 24H after last convulsion .
- Definitive treatment is delivery

## Magnesium sulfate toxicity

- Patella reflex absent
- Decreased urine output
- Decrease respiration

## Antidote calcium gluconate

# ECLAMPSIA COMPLICATIONS:-

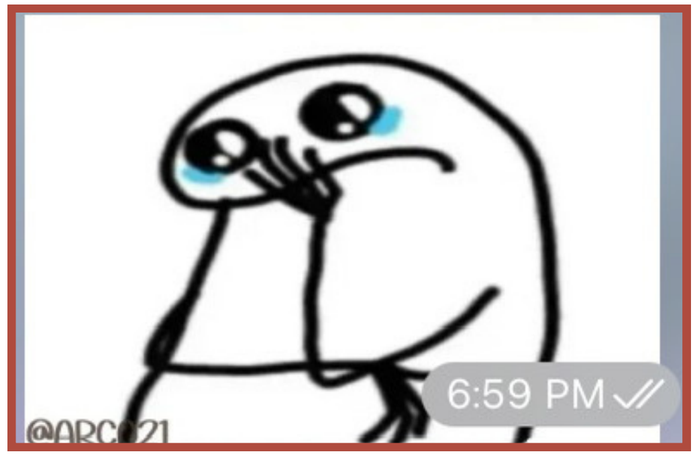
- Placental abruption
- Acute renal failure
- Cerebral Hg
- Hepatic rupture
- DIC
- Fetal growth restriction
- Prematurity
- RDS
- Intraventricular hg
- NEC

## Eclampsia Prevention :-

**Low dose**
**81mg/day**
**Begin at the end of 1st trimester**

**Aspirin**

**Calcium**

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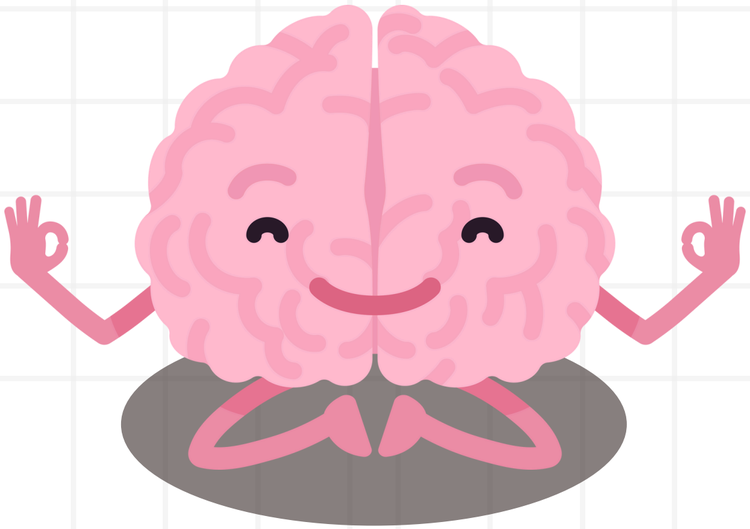

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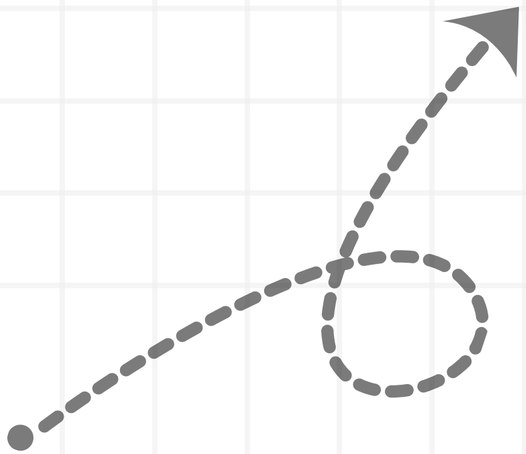
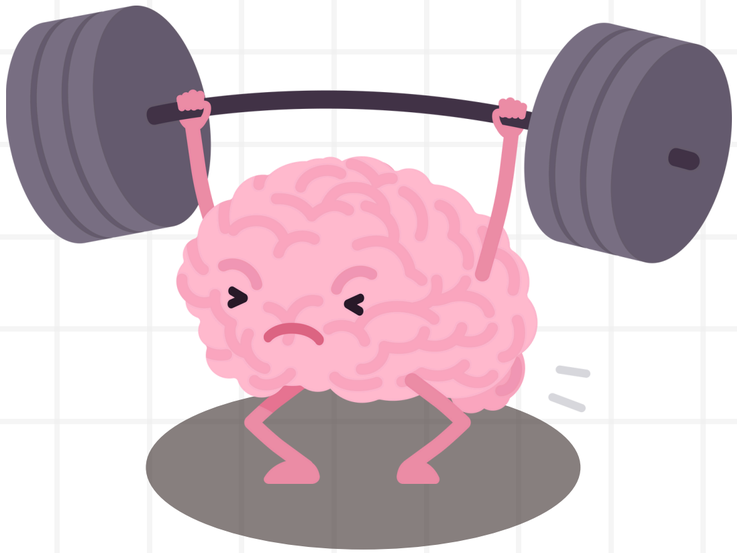
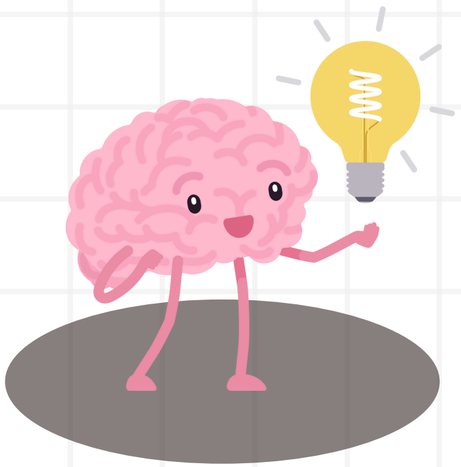




# MULTIPLE SCLEROSIS



Is a relapsing, remitting disease causes disability through demyelination of nerves, leading to weakness, lack of coordination, numbness in the hands or feet, blurred vision, tremor, spasticity and voiding Dysfunction•

MS is usually diagnosed between 20 and 50 years old, and so women with MS will therefore become pregnant relatively early in the course of their illness and usually have little associated disability

# MUTIPLE SCLEROSIS ON PREGNANCY OUTCOMES

## Pregnancy

- Lower birth weight.
- Higher incidence of assisted VD, CS.
- No significant effects higher risk of obestetrical and neonatal complications

## Fertility

- No direct effect.
- Sexual dysfunction delay conception.
- Prior cytotoxic chemotherapy agents as cyclophosphamide will impair the fertility

**The course of MS during pregnancy changes :**

**Lower relapse rate** **has been shown during 3rd trimester**

**Higher rate of relapse** **during the first 3 months postpartum**

# COMPLICATIONS OF MS ON PREGNANCY

Spontaneous abortions

Congenital malformations

Stillbirth

Preeclampsia , premature delivery not increased

Number of planned cesarean deliveries increased,

Women delivering vaginally had an increased incidence of slow labor progression necessitating interventions.

This result may have been partly due to perineal weakness and spasticity and fatigue related to MS.

# Management of exacerbation during pregnancy

- Steroid as (Methylprednisolone) 500mg/day for 3-5d
- IVIG

## Interferons

Interferons beta-1a + Interferons beta-1b-

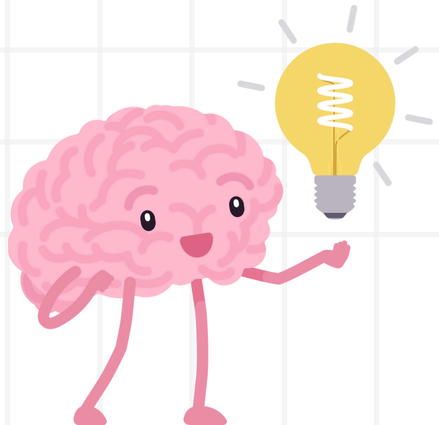
- There are no concerns that IFN use in pregnancy causes birth defects, miscarriages, or low infant birth weight.
- There are some studies have shown that women taking IFN more likely to have PTL.

## glatiramer acetate

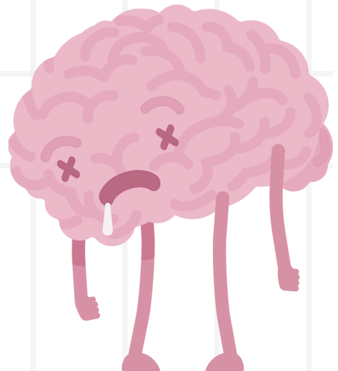
-Brand name: Copaxone

-Evidence suggests that glatiramer acetate might be safe in pregnancy and breastfeeding.

- It reduces the frequency of relapses but not for reducing the progression of disability



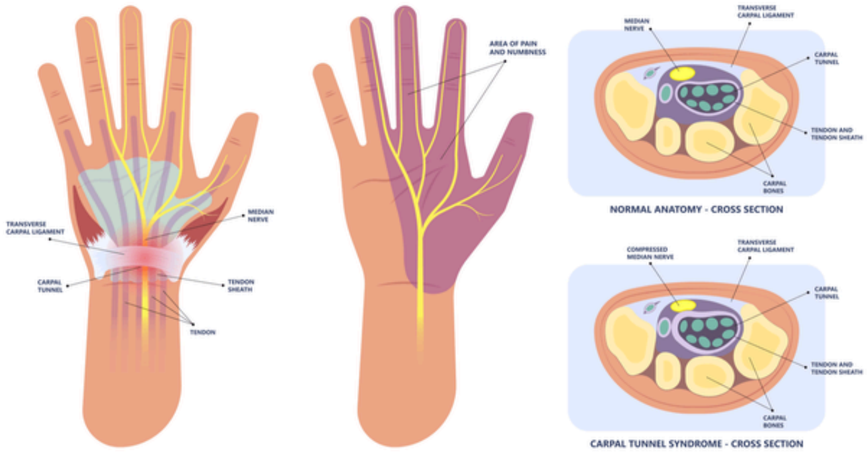
# CARPEL TUNNEL SYNDROME

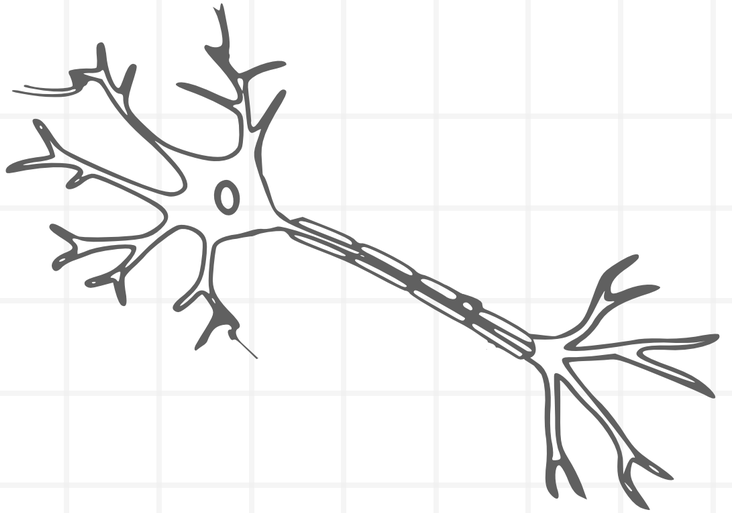


The carpal tunnel is a passage in the wrist that contains tendons and a nerve, called the median nerve, that run through the base of the hand. The carpal tunnel can swell and press against this sensitive nerve, causing pain.

Carpal tunnel syndrome is a condition that occurs as a result of swelling around the nerves of the wrist. It can cause numbness, tingling or pain in one or both of the hands.

Pregnant women are particularly susceptible to this disorder. Around 5 out of 10 pregnant women develop carpel tunnel syndrome .





# HOW DOES PREGNANCY CAUSE CARPAL TUNNEL SYNDROME?

During pregnancy hormones cause fluid retention, they also soften the ligament that forms the roof of the tunnel. When this happens, the nerve running through the tunnel may become squashed which can cause symptoms like pins and needles, numbness and stiff painful hands.

The condition is more common in the third trimester, but it can also happen in the first and second trimesters or after delivery . In most cases, symptoms will go away after delivery.

# SYMPTOMS

•pain, numbness, tingling, or weakness of your hand

• difficulty with hand coordination

• pain spreading to your arm or shoulder

• Patient will feel the symptoms in thumb, index finger and middle finger.

Symptoms can get worse at night.

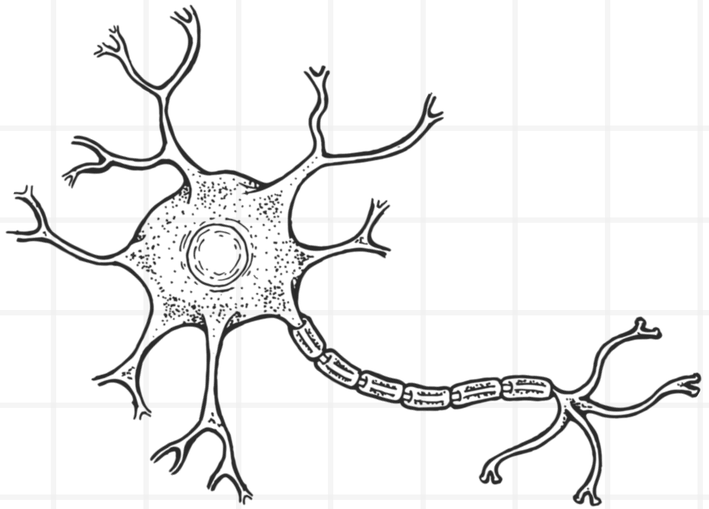
# MANAGEMENT

- Keep your hands elevated as much as you can.
- Keep your wrists in a neutral position (not bent forwards or backwards), as much as you can.
- Maintain good posture in your arms and wrists while working at a desk and take breaks every 20 minutes.
- Sleep on the side of your less affected hand.
- Put an ice pack on your wrist or run cold water over your hand.
- Wear a wrist splint, especially at night, to keep your wrist neutral.
- Perform regular fluid drainage massage and gentle exercises

# CTS IN BREASTFEEDING

- Some women will continue to have symptoms after giving birth or may even develop them after giving birth.

- So we advise her while breastfeeding sit up straight in a supportive chair and have a pillow underneath baby to support them. Once baby is attached to your breast support their head with your forearm rather than with your hand.



# MYASTHENIA GRAVIS

•Myasthenia gravis is an autoimmune neuromuscular disease characterized by weakness and fatigue of the skeletal muscles of the face and extremities.

• It affects people of both sexes and all ages, but twice as many female patients are affected as male patients.

• Myasthenia gravis usually strikes in women in their third decade of life, but the elderly are increasingly affected.

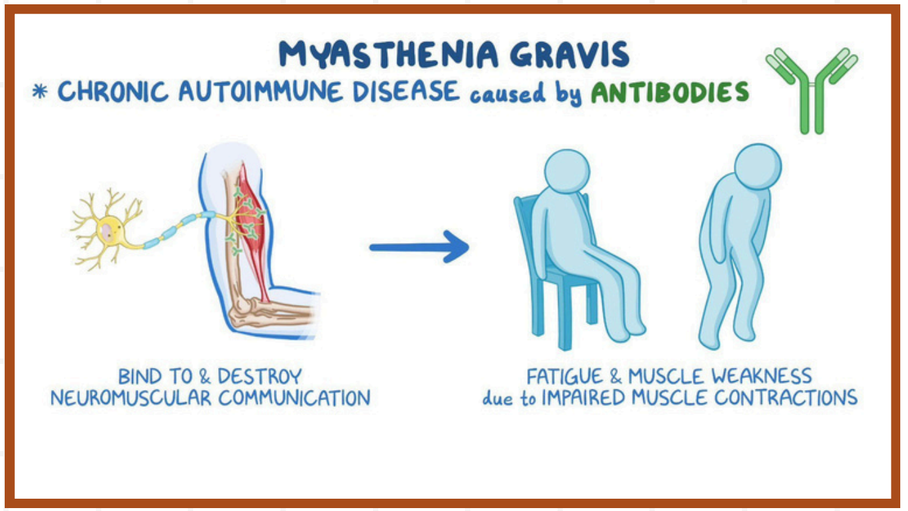
• Although the disease course is variable, pregnant patients face risks of exacerbation, respiratory failure, adverse drug response, crisis, and death.

• The course of myasthenia gravis during pregnancy is hard to predict

• Because the severity of symptoms, as well as maternal mortality, is highest in the first 2 years following onset of myasthenia gravis, it is advisable for women to delay pregnancy for at least 2 years following diagnosis.

.• Severity of symptoms and risk of maternal mortality is lowest 7 years after onset of the disease.

Hypoventilation is a risk during pregnancy, because respiratory muscles are weakened from myasthenia gravis. Also, the lungs do not become fully inflated, because the diaphragm is elevated during pregnancy. Approximately 20% of patients experience respiratory crises that require mechanical ventilation. This is one of most severe complications



•Infections due to decreased immunity play a very important role in the exacerbation of myasthenia gravis during pregnancy.

• Labor may be complicated. Although smooth muscle is not affected by autoantibodies and the uterus is not compromised, the second stage of labor involves striated muscle. The patient may become exhausted during labor and may require assistance. Operative vaginal delivery has been recommended.

# FETAL EFFECTS

•Neonatal MG may result from passive transplacental transfer of antibodies to the nicotinic acetylcholine receptor from the myasthenic mother to the fetus. However, not all infants with detectable levels of antibodies to acetylcholine receptor develop neonatal MG.

• The severity of symptoms varies, ranging from mild hypotonia to respiratory distress. Clinical symptoms develop in the first few hours after birth and usually resolve within 2–3 weeks

.• Children of mothers with MG require careful observation in the first few days after birth, and symptoms may respond to anticholinesterase medication.
Women with MG should deliver in a facility with a neonatal ICU

# MANAGEMENT

• An international consensus guidance for the management of myasthenia gravis included the following recommendations for myasthenia gravis in pregnancy :

• Planning for pregnancy should be instituted well in advance to allow time for optimization of myasthenic clinical status and to minimize risks to the fetus.

• Multidisciplinary communication among relevant specialists should occur throughout pregnancy, during delivery, and in the postpartum period.

• Provided that their myasthenia is under good control before pregnancy, the majority of women can be reassured that they will remain stable throughout pregnancy. If worsening occurs, it may be more likely during the first few months after delivery.

• Oral pyridostigmine is the first-line treatment during pregnancy. IV cholinesterase inhibitors may produce uterine contractions and should not be used during pregnancy.

• Thymectomy should be postponed until after pregnancy as benefit is unlikely to occur during pregnancy

# Drug therapy for myasthenia gravis

✓ The mainstay of treatment in MG includes drugs:

(pyridostigmine and neostigmine)
with inhibit acetylcholinesterase enzyme for symptomatic relief as well as corticosteroids and alternate immunosuppressant drugs (methotrexate, azathioprine, mycophenolate, cyclosporine, cyclophosphamide as well as pulse intravenous immunoglobulins).

✓ Severe exacerbations or myasthenic crisis require either :

plasma exchange or intravenous immunoglobulin with supportive care including ventilator support if required.

✓ The choice of treatment is dictated by clinical severity of MG and risks of therapy

## Anticholinesterase inhibitors (pyridostigmine and neostigmine)

• several studies have shown that pyridostigmine is safe during pregnancy in recommended doses (30–60 mg every 4–8 h).This drug crosses placenta freely and achieves good concentrations in amniotic fluid. Dose and frequency of administration often need to be changed during pregnancy due to changes in blood volume and renal clearance and should be adjusted according to the clinical status of MG.

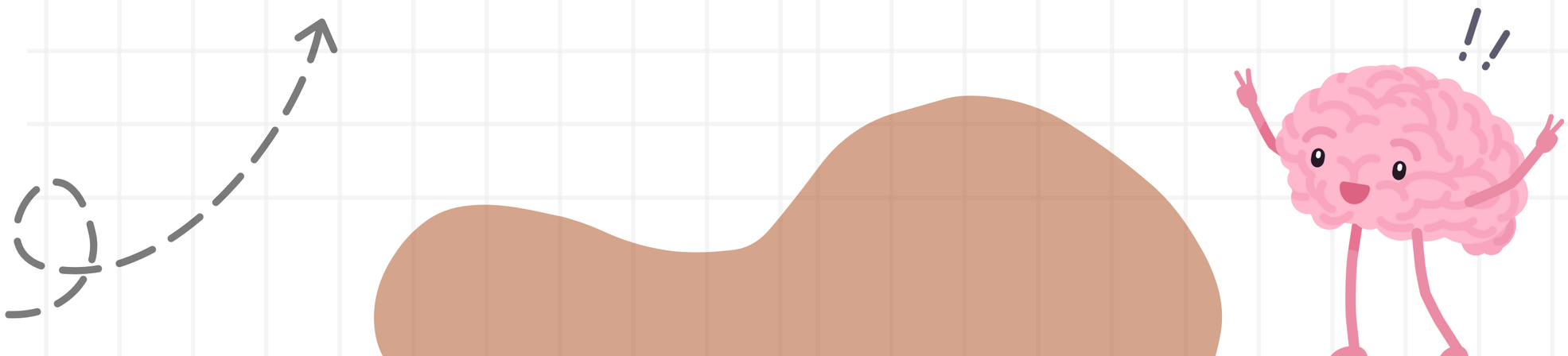
• Prednisone is the IS agent of choice during pregnancy

• Current information indicates that azathioprine and cyclosporine are relatively safe in expectant mothers who are not satisfactorily controlled with or cannot tolerate corticosteroids. Current evidence indicates that mycophenolate mofetil and methotrexate increase the risk of teratogenicity and are contraindicated during pregnancy.

• Spontaneous vaginal delivery should be the objective and is actively encouraged.

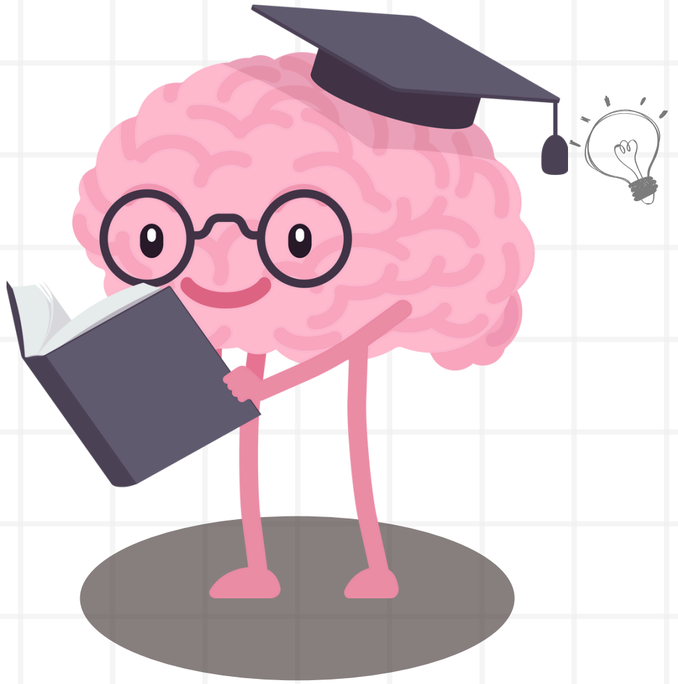
• Magnesium sulfate is not recommended for management of eclampsia in MG because of its neuromuscular blocking effects; barbiturates or phenytoin usually provide adequate treatment.

• All babies born to myasthenic mothers should be examined for evidence of transient myasthenic weakness, even if the mother's myasthenia is well-controlled, and should have rapid access to neonatal critical care support.



# MENINGITIS

Meningitis is an infection and inflammation of the fluid and membranes surrounding the brain and spinal cord. These membranes are called meninges.

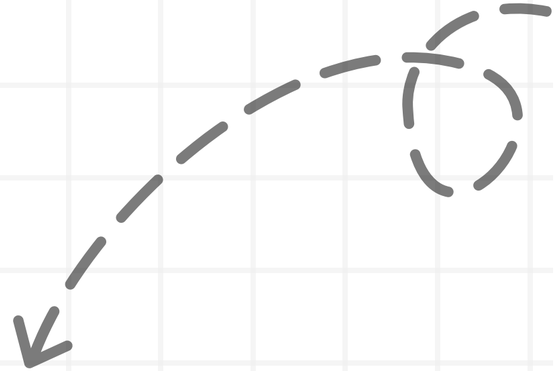


• Pregnancy increases the risk of an infection caused by listeria bacteria, which also may cause meningitis. The infection increases the risk of miscarriage, stillbirth and premature delivery.

• pneumococcal meningitis during pregnancy can be rapidly fatal and is associated with foetal death, especially in the first trimester. L. monocytogenesmeningitis was associated with a high rate of neonatal deaths.

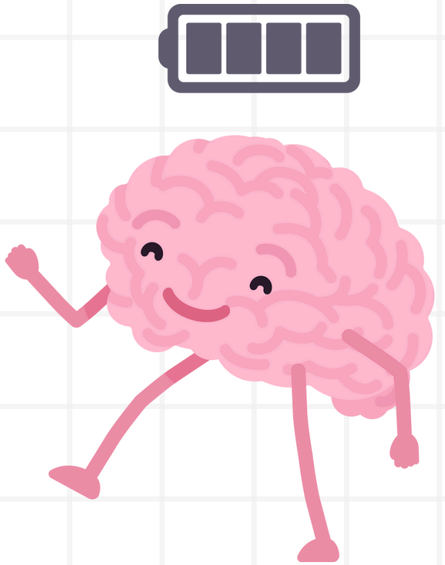
# TREATMENT

1. antibiotics given directly into a vein.
2. fluids given directly into a vein to prevent dehydration.
3. oxygen through a face mask if there are any breathing difficulties.
4. steroid medication to help reduce any swelling around the brain, in some cases



- The type of antibiotics used to treat meningitis during pregnancy can vary depending on the specific cause of the infection. Commonly used antibiotics may include penicillin, ceftriaxone, or ampicillin.

- These type of antibiotics considered to be safe in pregnancy



# THANK YOU

إذا كنت تحب غزة، فانظر إلى أعظم عمل قمت به لوجه الله في حياتك، ثم استجمع قلبك، وارفع يديك إلى السماء خاشعاً متذللاً، وقل: اللهم إن كنتُ فعلت هذا العمل لأجلك، وابتغاء مرضاتك، ففرج عن أهل غزة ما هم فيه من ضيق وكربة، قلها بثقة ويقين، لعل الله يرى من قلبك صدقاً وإخلاصاً، فيفرج عنا كربنا ويطفئ حربنا!!

-جهاد حلس

اللهم عجل بالفرج لعبادك المستضعفين آمين