Antenatal neuroprotective strategy to prevent perinatal brain injury

2016. 4. 2
고려대 산부인과
홍 순 철

아이의 신경 발달과 관련한 연구

- 모유수유와 IQ

-모유수유 아이와 분유를 먹은 아이 사이의 IQ 차이: 4-7 점 모유수유가 높음.

-모유가 아이의 IQ를 증가시키는가

다른 요인이 아이의 IQ를 증가시키는가?

아이의 신경 발달과 관련한 연구

- 모유수유와 IQ

→ 쌍둥이 연구 Der (BMJ 2006)

332쌍둥이 모유수유 여부에 따라

545 쌍둥이 모유수유 기간에 따라 연구

아이의 신경 발달과 관련한 연구

- 엄마의 우울증과 아이의 신경발달

-인지 능력 저하, IQ 저하, 수학 능력 저하, 불안 장애 증가, ADHD.

-우울증 산모가 복용하는 약이 연관이 있는가

우울증이 영향이 있는가?

아이의 신경 발달과 관련한 연구

- 엄마의 우울증과 아이의 신경발달

→ 임산부와 아이 검사: 출생후 3-6세 검사

그룹1: venlafaxine 항우울제 사용

그룹2: 우울증 그룹

그룹3: 정상인

아이의 신경 발달과 관련한 연구

- 엄마의 우울증과 아이의 신경발달

→ 임산부와 아이 검사: 출생후 3-6세 검사

그룹1: venlafaxine 항우울제 사용 FSIQ 104

그룹2: 우울증 그룹 FSIQ 105

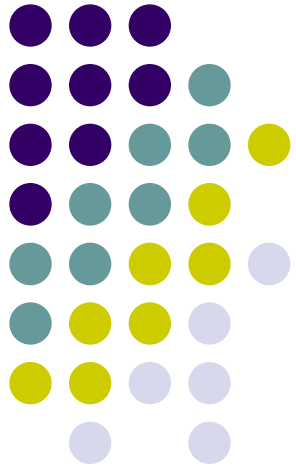
그룹3: 정상인 FSIQ 112

-엄마의 우울증 정도가 아이 행동 결과의 예측인자

Contents

- Introduction
- Antenatal strategy to avoid fetal neurodevelopmental disorder
- Strategy to prevent intrapartum injury
- Summary

Introduction



태아 기형 관련 영역

▪ 태아 이상 ▪ 태아 기형 1-3%;5%;7%	▪ 성장장애	▪ 성장장애 ▪ 기능이상	▪ 신생아"적응장애?" ▪ 생물학적 기능 ▪ 유전학적 이상 ▪ 생식기능
임신 제1삼분기	제2 삼분기	제 3 삼분기	분만후, 장기간의 예후

1st Trimester 2nd Trimester 3rd Trimester

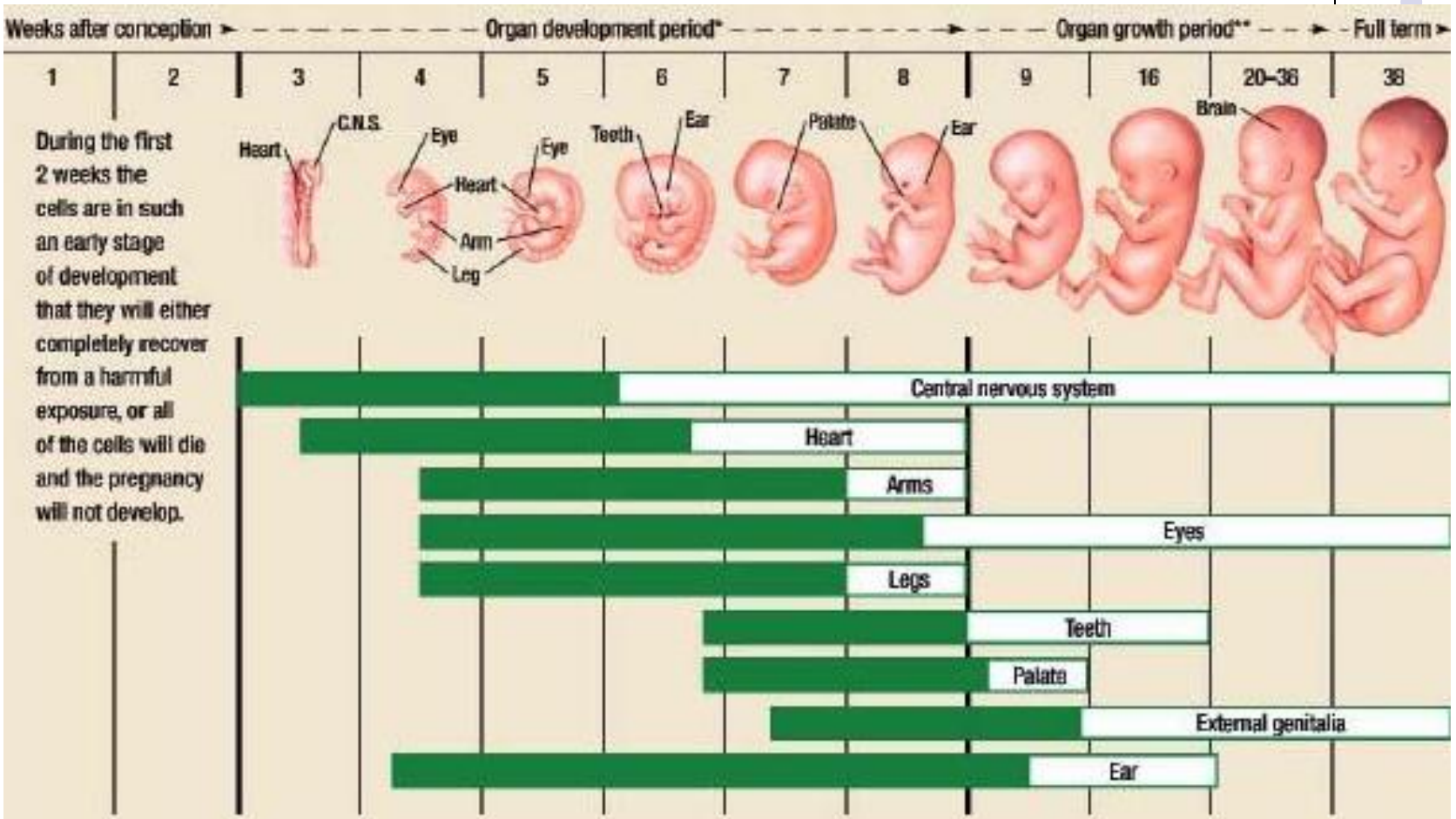
태아사망

1st Trimester 2nd Trimester 3rd Trimester Postnatal

신경계 발달

임신중 신경계 발육 과정

태아의 발육과정

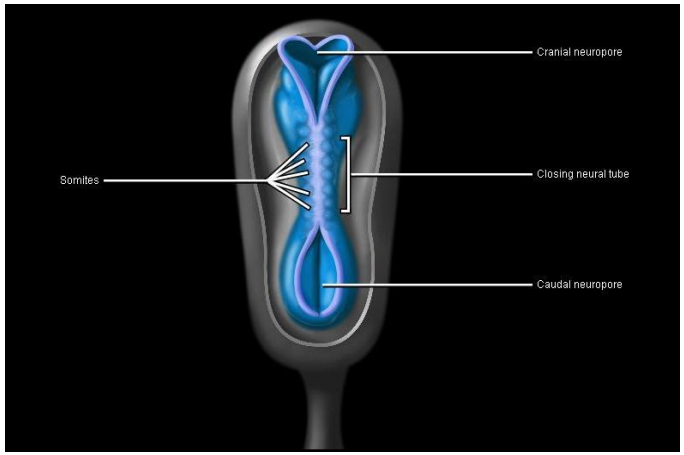


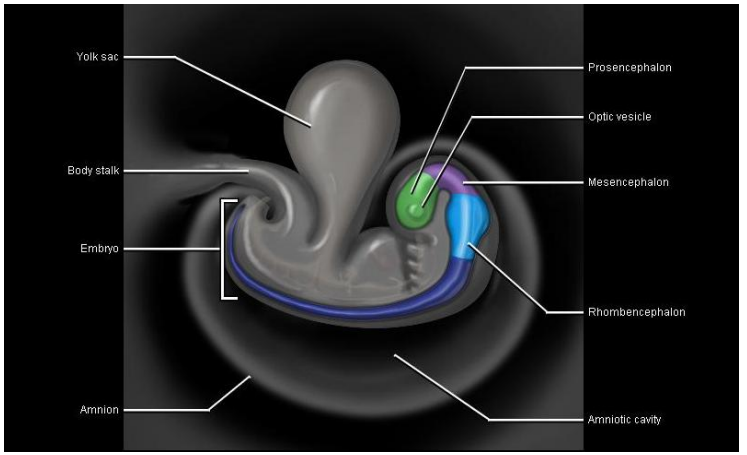
Each bar shows when a baby's organ systems and body parts are forming. The shaded area indicates the most vulnerable time for birth defects.

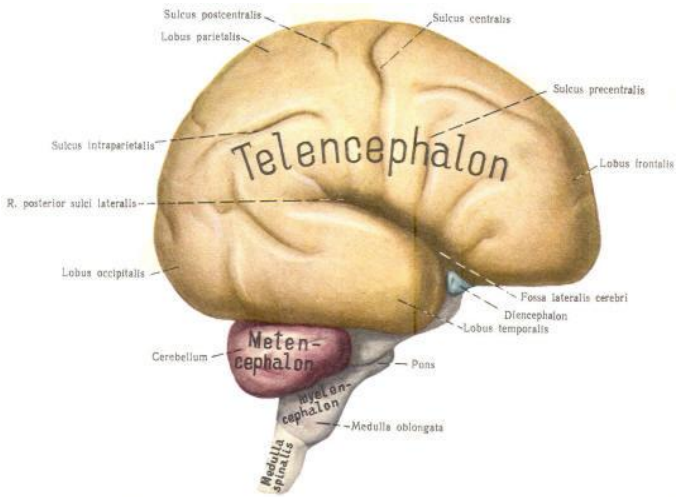
*The period of greatest vulnerability is from 2–8 weeks after conception. During this time, insults could result in abnormally formed organs.
**During the growth period, insults may result in normally formed organs that are unable to function properly.

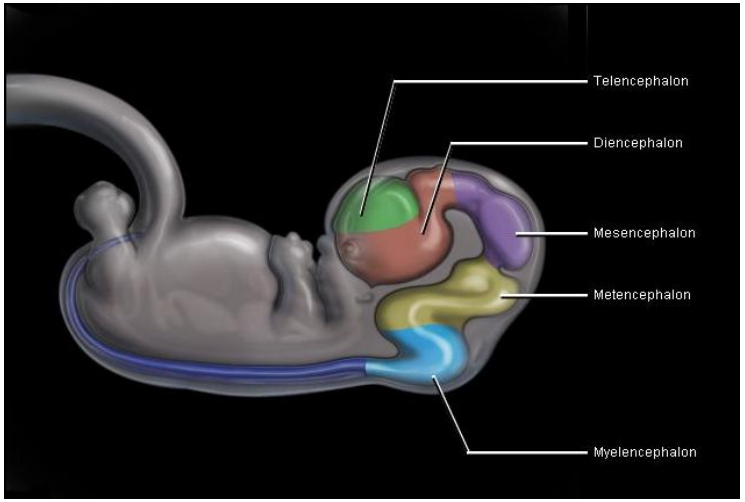
Source: Modified from Moore KL. *The Developing Human: Clinically Oriented Embryology*. Philadelphia, Pa; W.B. Sanders Company:1993. Reprinted by permission, in Mary-K Moos. *Preconceptions Health Promotion*. White Plains, NY. March of Dimes Birth Defects Foundation. 1994:17.

태아 신경 발달 과정

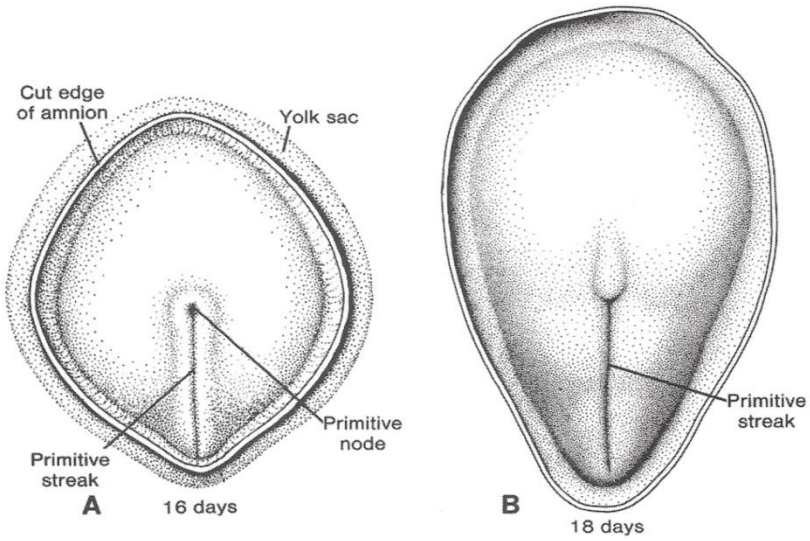

Cranial neuropore
Somites
Closing neural tube
Caudal neuropore

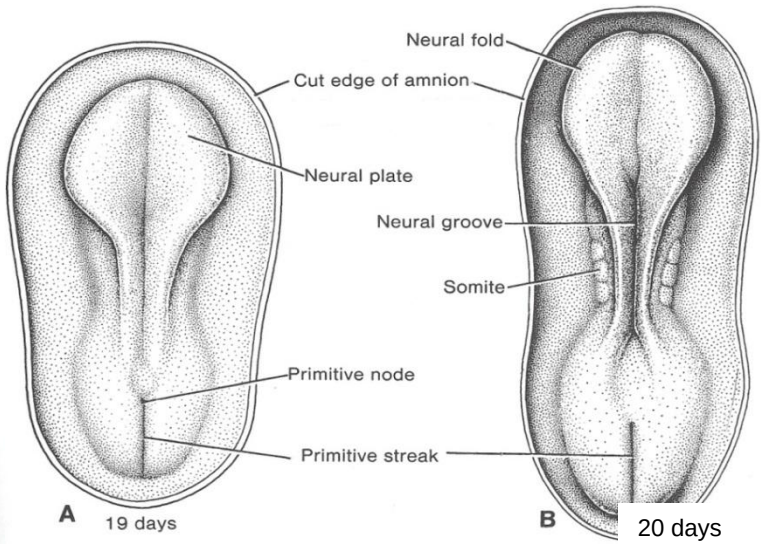

Yolk sac
Prosencephalon
Optic vesicle
Body stalk
Mesencephalon
Embryo
Rhombencephalon
Amnion
Amniotic cavity

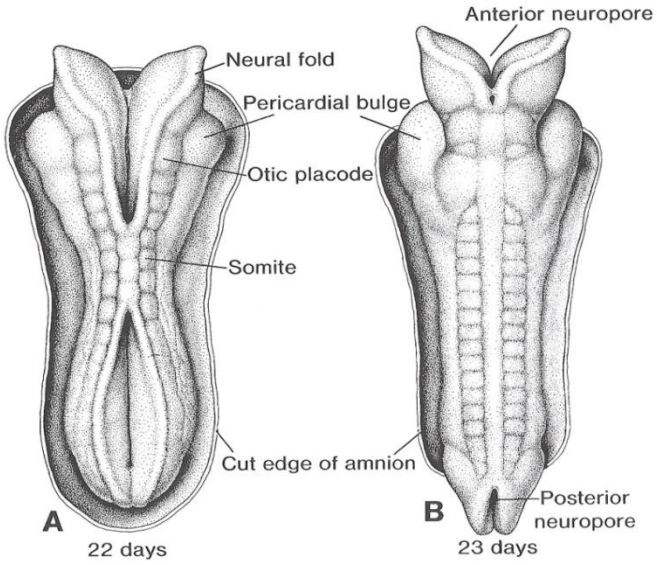

Sulcus postcentralis
Lobus parietalis
Sulcus centralis
Sulcus precentralis
Sulcus intraparietalis
Telencephalon
Lobus frontalis
R. posterior sulci lateralis
Lobus occipitalis
Fossa lateralis cerebri
Diencephalon
Lobus temporalis
Cerebellum
Meten-cephalon
Pons
Myelen-cephalon
Medulla oblongata
Medulla spinalis


Telencephalon
Diencephalon
Mesencephalon
Metencephalon
Myelencephalon

임신 5-6주



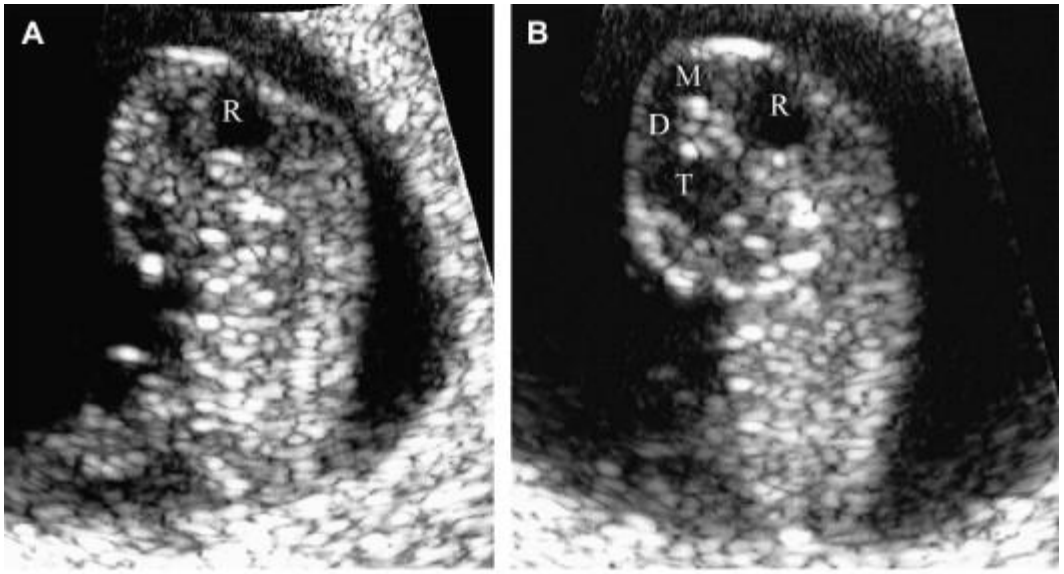


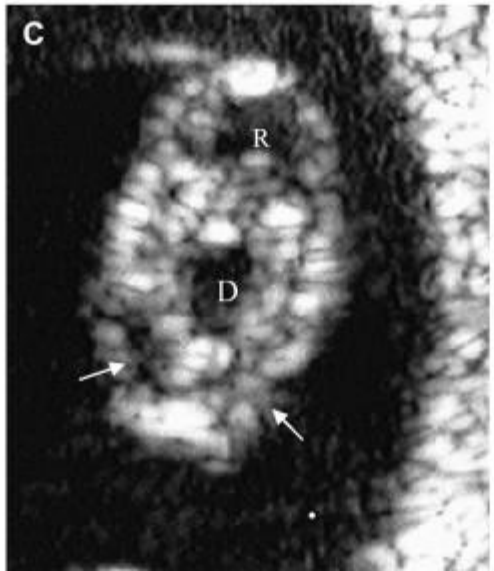


Neurulation

Includes the formation of the neural plate (day 18-19), the neural folds (day 20-21), and the neural tube (day 22-26); the latter will develop into the future brain and spinal cord.

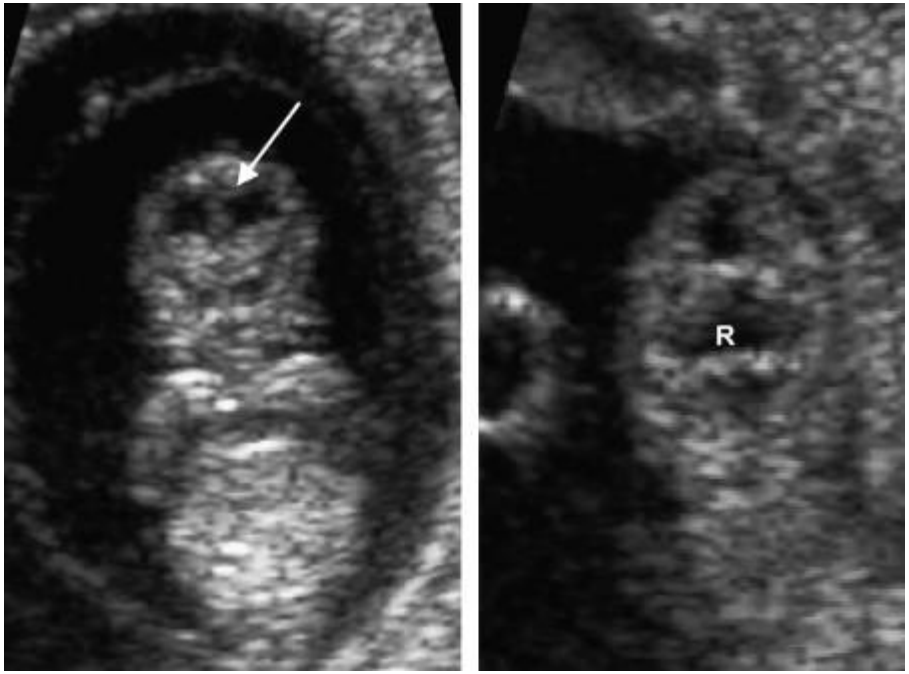
임신 8주





- (A, B): sites of the future brain structures
- The arrows point to the telencephalic vesicle.
- (D, diencephalon;
  M, myelencephalon;
  R, rhombencephalon;
  T, telencephalon.)

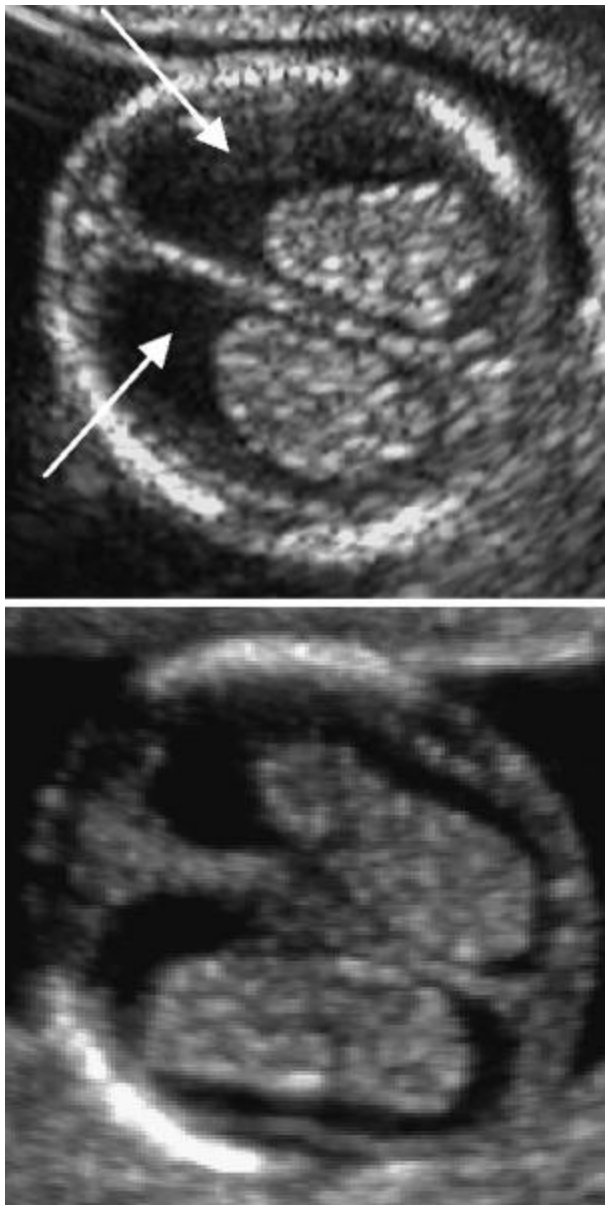
임신 9주



- Coronal and semi-axial planes
- The arrow points to the falx cerebri.

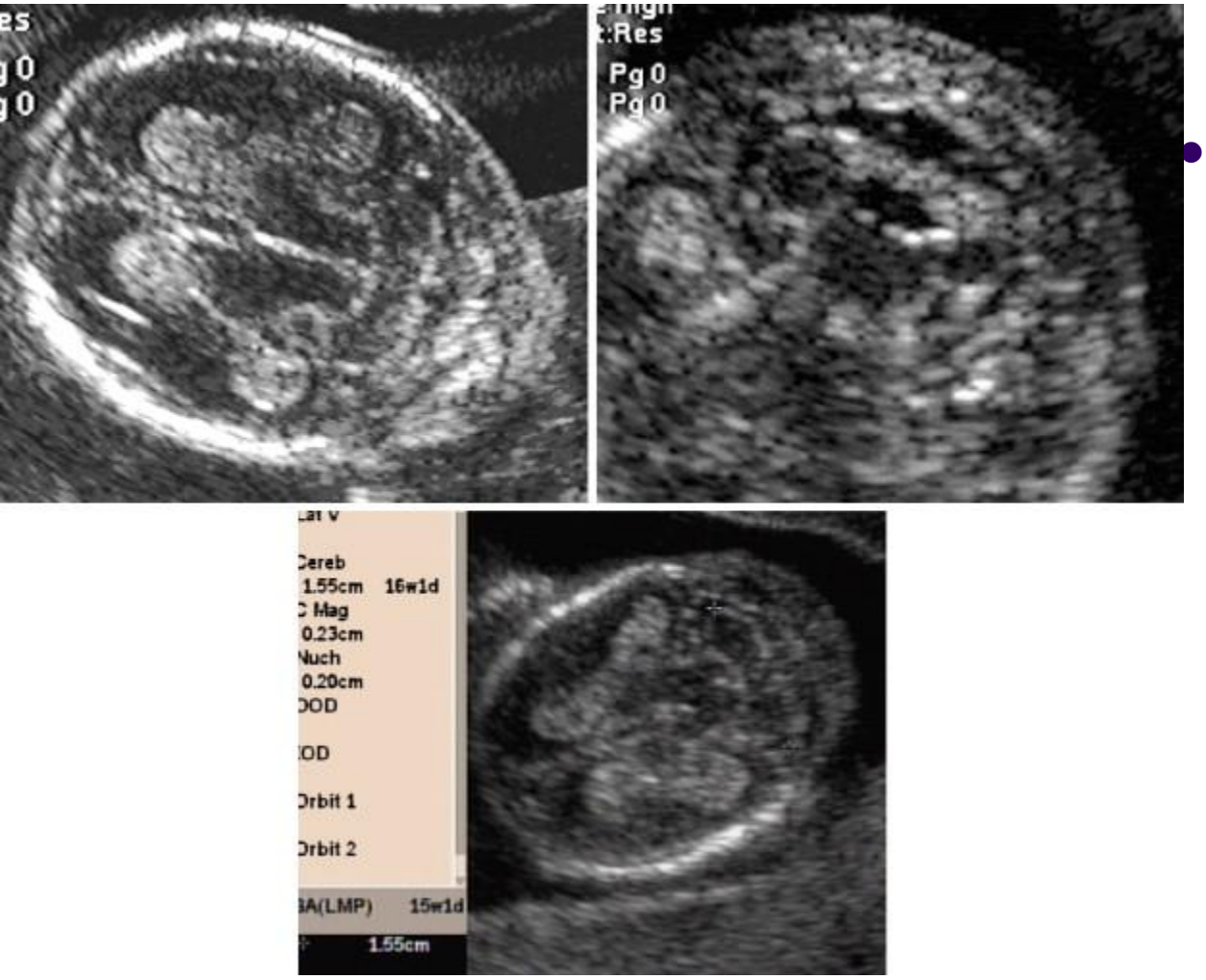
(R, rhombencephalon.)

임신 9-13 주



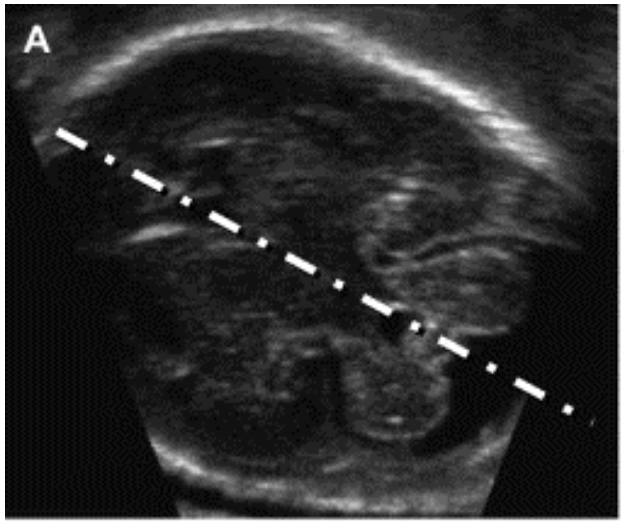
- choroid plexuses do not fill the lateral ventricles, which is normal at this gestational age.

임신 15주



- A tilted axial plane demonstrates the choroid plexuses and the forming posterior fossa.

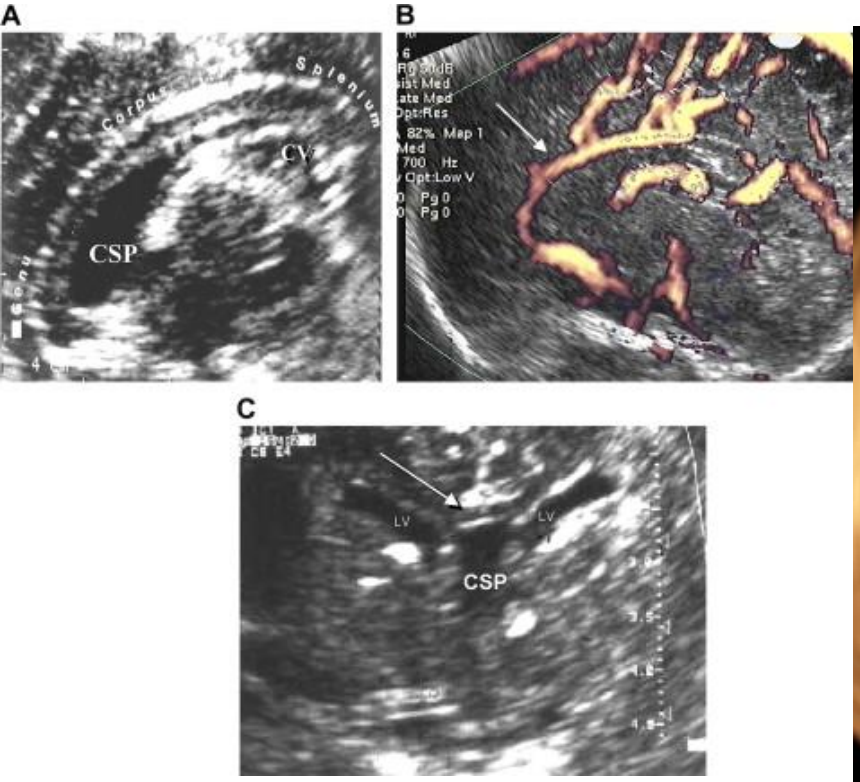
임신 18주



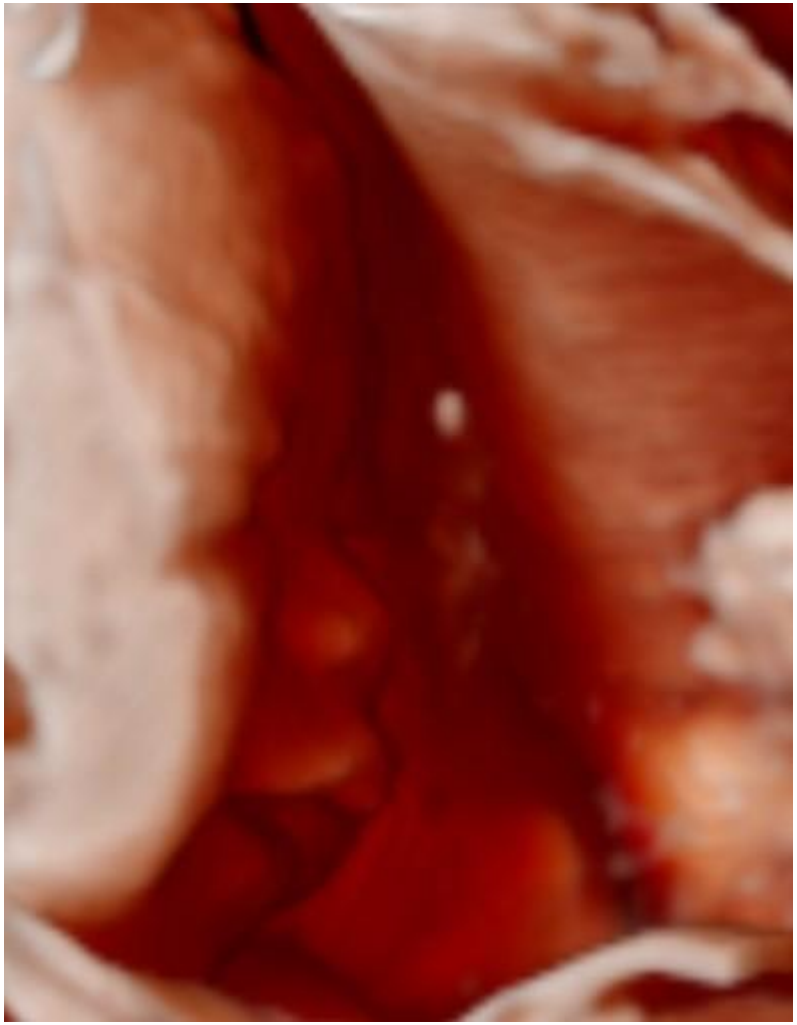
- Cerebellum

임신 19-20 주

- corpus callosum is fully formed.



임신 25-35주



태아 신경계와 감각 기관

- 척수의 발달: 임신 24주 (S1), 출생(L3), 성인(L1)
- 임신 10주: 입벌리기, 불완전한 손가락 운동, 발가락 구부리기, 삼키기 운동
- 임신14-16 주: 호흡
- 임신 24 주: 빨기, 자궁안의 소리듣기
- 임신 28 주: 빛에 반응하기

Antenatal strategy to avoid fetal neurodevelopmental disoder

태아의 신경발달의 위험 요인

- 조산
- 자궁 수축
- 태아 자궁내 감염
- 유전학적 이상
- 모체 감염: CMV 감염, 톡소플라즈마 감염, 풍진, 수두
- 갑상선 기능저하증
- 만성 질환: 당뇨병, 비만, 뇌전증 등
- 방사선
- 고열
- 알코올
- 중금속-수은 등
- 약물-아큐탄, 간질약, 와파린, 미소프로스톨 등

태아 신경 발달을 위해 무엇을 할 것인가?

1. 엽산과 복합 비타민

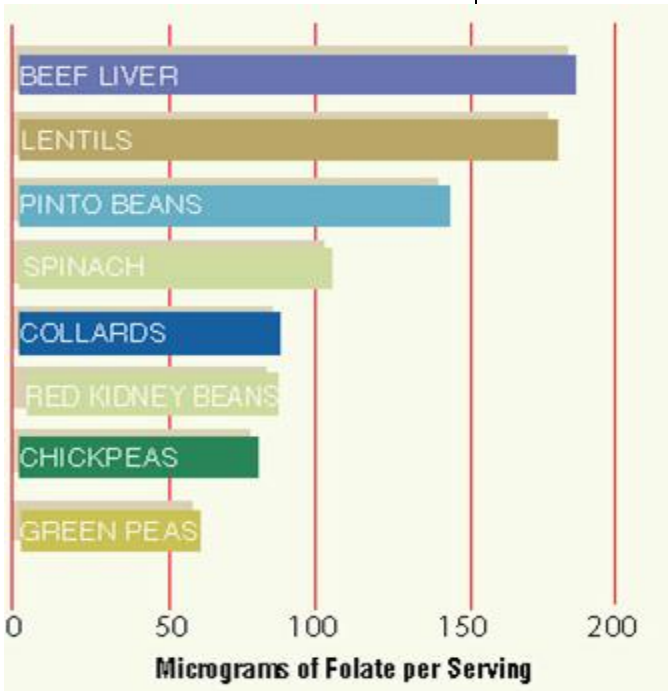
발달에 도움이 되는 영양 성분들(FIGO 2015)

- Folate, Vit B12, Vit B6
- Omega 3, 6
- Vit D
- Ca
- Iodine
- Zinc
- Vit A
- Selenium

엽산 (Folate, Vitamin B_9)

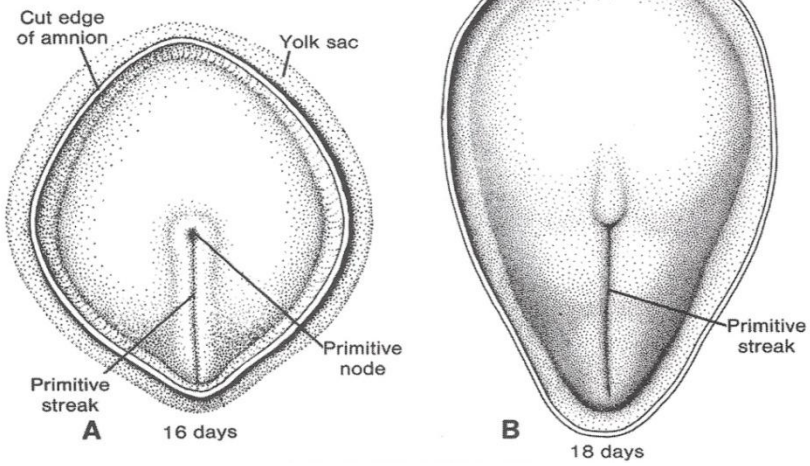
- 수용성 비타민
- 체내에서 합성 불가
- 열(온도)에 약함
- 요리과정에서 50-90% 손실

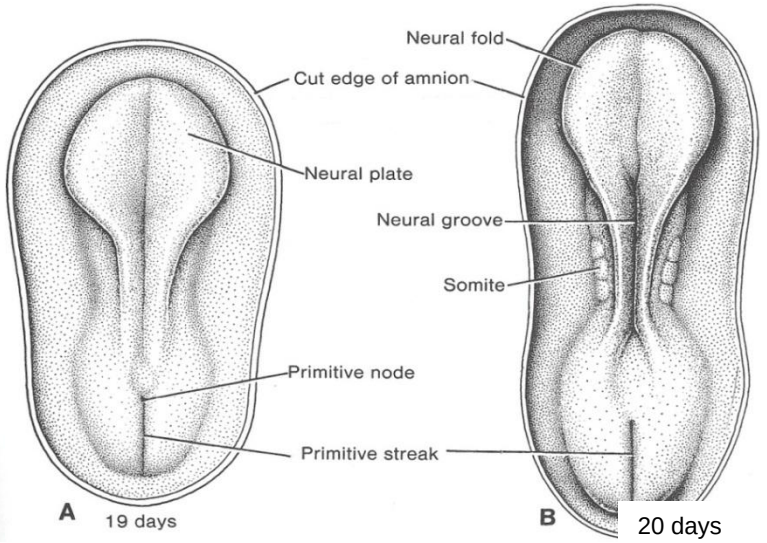
❖ 엽산이 풍부한 음식:

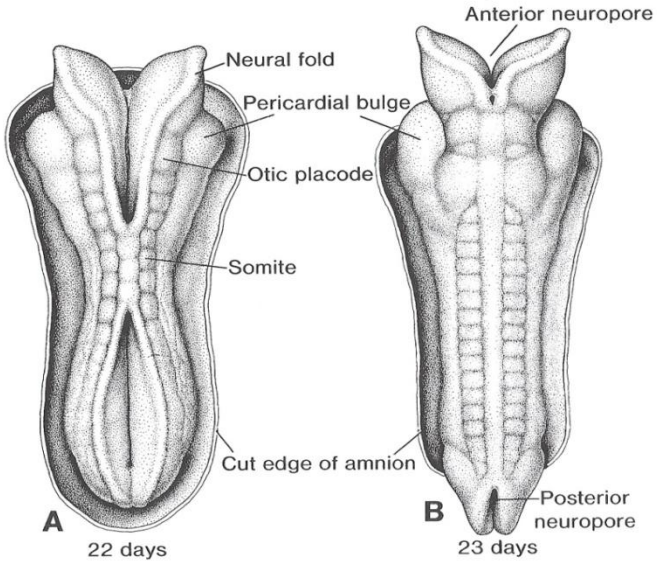


Natural Food Sources of Folate	Serving Size
Beef liver, cooked, braised	3 ounces
Lentils, boiled (not canned)	1/2 cup
Pinto beans, canned	1/2 cup
Spinach, canned, drained	1/2 cup
Collards, boiled, drained	1/2 cup
Green peas, canned	1/2 cup
Chickpeas, canned	1/2 cup
Red kidney beans, canned	1/2 cup

엽산의 태아 기형 예방 효과



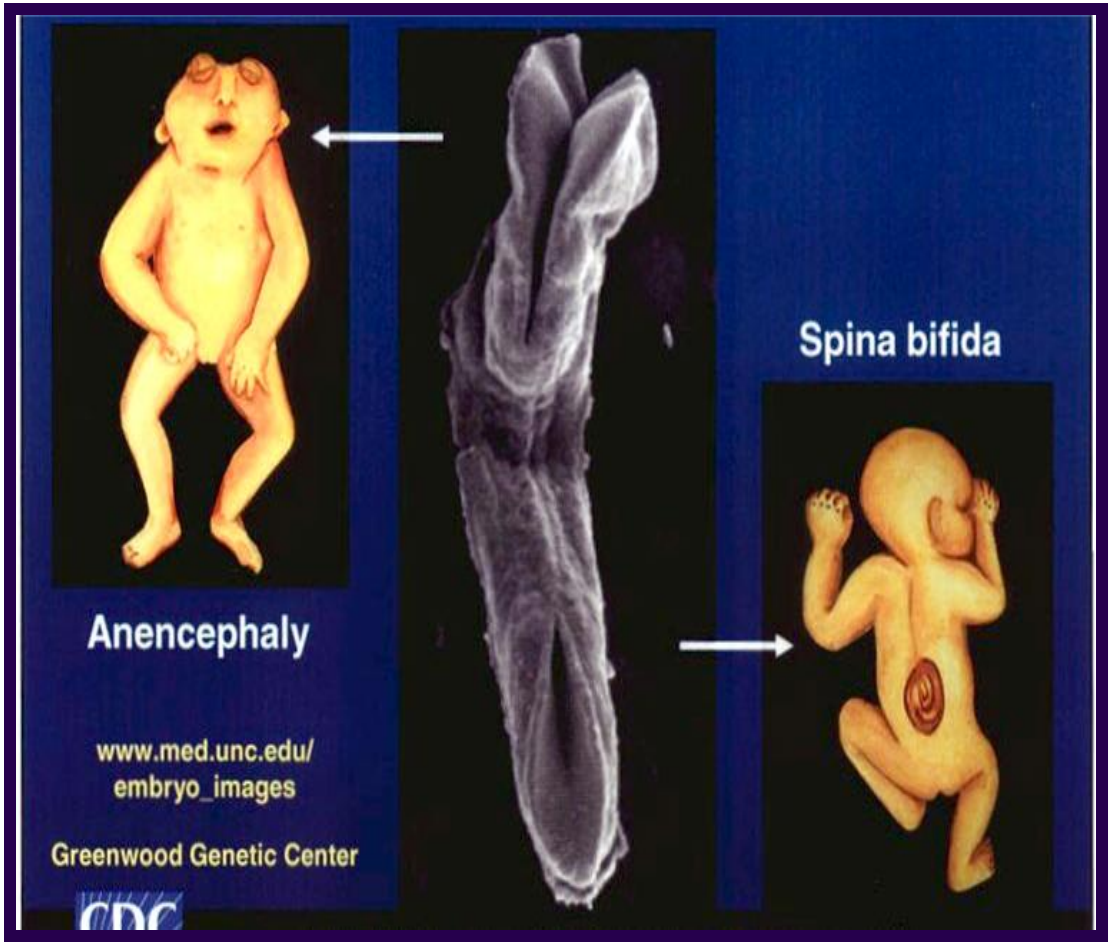




Neurulation

Includes the formation of the neural plate (day 18-19), the neural folds (day 20-21), and the neural tube (day 22-26); the latter will develop into the future brain and spinal cord.

엽산의 태아 기형 예방 효과

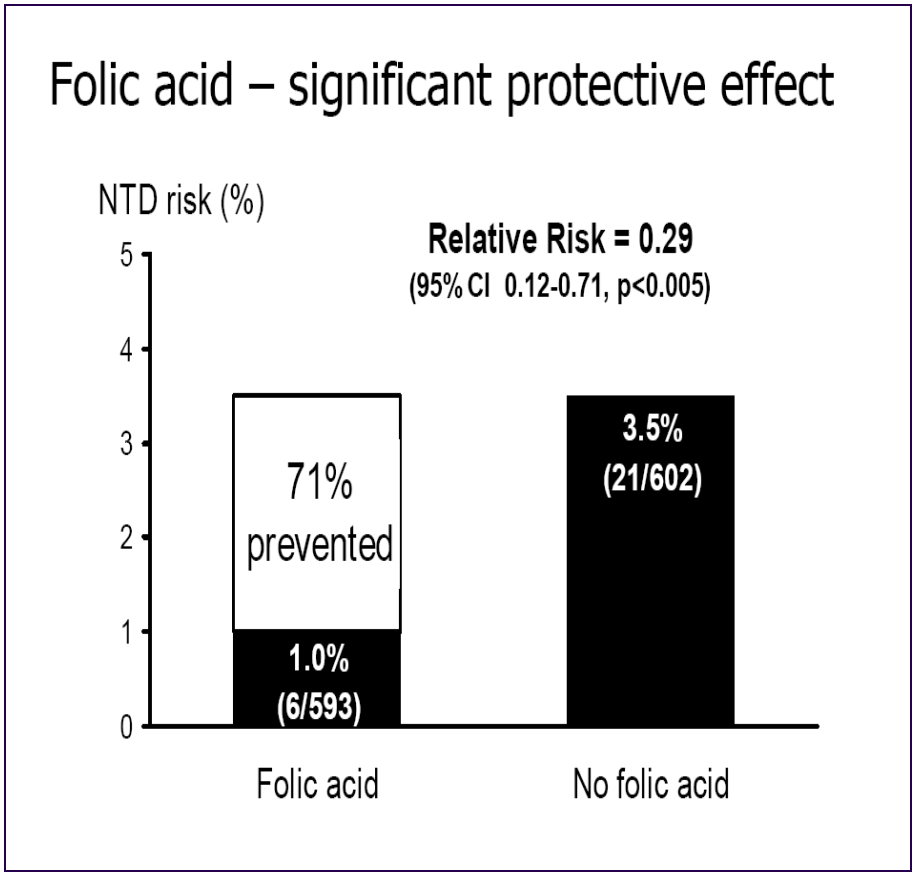


엽산의 태아 기형 예방 효과

임신전 엽산 복용의 중요성

엽산의 태아 기형 예방 효과

엽산과 신경관 결손증



MRC Vitamin Study in UK (1991)

엽산의 태아 기형 예방 효과

- U.S.: Fortification of cereal grain products: 140 μg/100 g *(- FDA 1998)*

  → ***NTD occurrence decreased by 27% (CDC; MMWR 2004)***

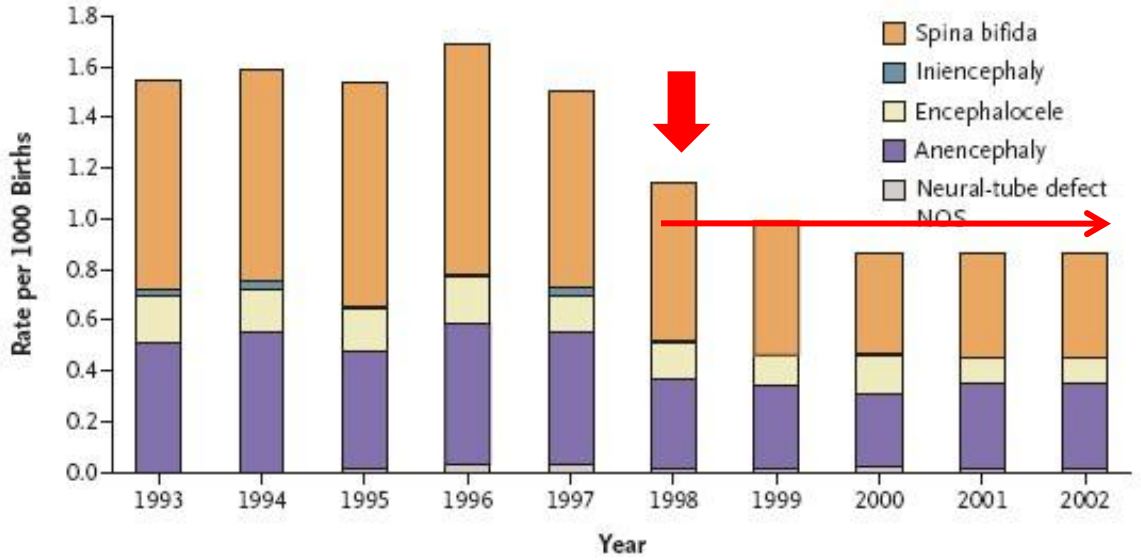
- Canada: Fortification with folic acid of all types of white flour, enriched pasta, and cornmeal:

  150 μg/100 g of flour or cornmeal,

  154-308 μg/100 g of rice *(1998)*

  → ***The prevalence of NTD decreased by 46% (1.58/1000 births → 0.86/1000 births) (NEJM 2007)***

엽산의 태아 기형 예방 효과



All neural-tube defects	1.55	1.59	1.55	1.69	1.50	1.14	0.99	0.86	0.86	0.86
Spina bifida	0.83	0.84	0.89	0.91	0.77	0.62	0.53	0.39	0.41	0.41
Iniencephaly	0.02	0.03	0.01	0.01	0.03	0.01	0.00	0.01	0.00	0.00
Encephalocele	0.19	0.17	0.16	0.18	0.15	0.14	0.12	0.15	0.10	0.10
Anencephaly	0.51	0.55	0.47	0.56	0.52	0.36	0.33	0.29	0.34	0.34
Neural-tube defect NOS	0.00	0.00	0.01	0.03	0.03	0.01	0.01	0.02	0.01	0.01

1993년부터 2002년까지 캐나다 7개 지역의 신경관 결손증 유병율 변화 (1998년 곡류 엽산 강화정책 시행)

한국인의 혈중 엽산 수치와 엽산 복용량의 기대효과

엽산과 신경관 결손증

	Serum folate (ng/mL) concentration (and % risk reduction) expected for given folic acid intake against background serum folate (ng/mL)			
	2·5	5·0	7·5	10·0
Increase in folic acid intake (mg/day)				
0·1	3·4 (23%)	5·9 (13%)	8·4 (9%)	10·9 (7%)
0·2	4·4 (36%)	6·9 (23%)	9·4 (16%)	11·9 (13%)
0·3	5·3 (45%)	7·8 (30%)	10·3 (23%)	12·8 (18%)
0·4	6·3 (52%)	8·8 (36%)	11·3 (28%)	13·8 (23%)
0·5	7·2 (57%)	9·7 (41%)	12·2 (32%)	14·7 (27%)
0·75	9·6 (66%)	12·1 (51%)	14·6 (41%)	17·1 (35%)
1·0	11·9 (71%)	14·4 (57%)	16·9 (48%)	19·4 (41%)
2·0	21·3 (82%)	23·8 (71%)	26·3 (63%)	28·8 (57%)
3·0	30·7 (87%)	33·2 (78%)	35·7 (71%)	38·2 (66%)
4·0	40·1 (89%)	42·6 (82%)	45·1 (76%)	47·6 (71%)
5·0	49·5 (91%)	52·0 (85%)	54·5 (80%)	57·0 (75%)

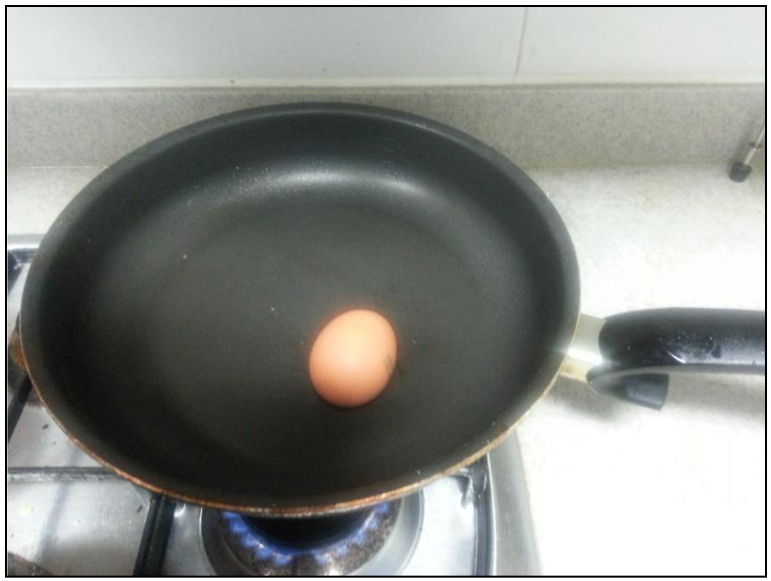
Values are background serum folate (reduction in risk of neural tube defect).

젊은 여성에서 엽산 처방후 혈청내 엽산 농도 변화

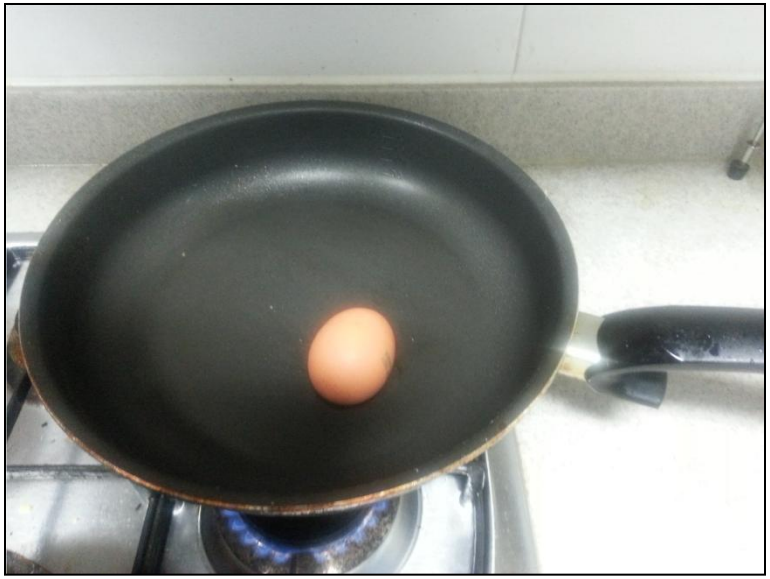
– Wald NJ, et al. Lancet 2001

태아 신경 발달을 위해 무엇을 할 것인가?

2. 고열 피하기



2. 고열



2. 고열

- 모체의 심부 온도 1.5~2.0 도 이상 상승시
  : 태아에 영향 (teratogen)
- 착상 전기 (임신 4주 이전) : 유산 증가
- 배아기 (임신 4주3일-10주)
  : 태아 기형 발생에 가장 민감한 시기

✓ 임신 5-6주: 신경관이 닫히는 시기

2. 고열

- ◆ 고열 경계 수치
- ✓ 실험 동물 :

  2~2.5도의 중심 체온 상승 → 기형 발생

  1.5 도 중심 체온 상승 → 유산
- ✓ 인간 : 38.9 ℃ → 기형 발생 가능성

- ◆ 38.9 ℃ 체온 도달:
- ✓ 온천 39 ℃의 물에서 15분, 40-41℃ 물에서 10분만에 질 내 체온이 38.9 ℃ 도달.
- ✓ 93.3-98.8 ℃ 20분간 사우나 후, 구강 체온이 38.9 ℃ 체온 도달

태아 신경 발달을 위해 무엇을 할 것인가?

3. 알코올 피하기

3. 알코올

Pregnancy

Alcohol

\+

\-

May result in

- 태아 알코올 증후군
- 태아 알코올 스펙트럼장애
- 태아 기형

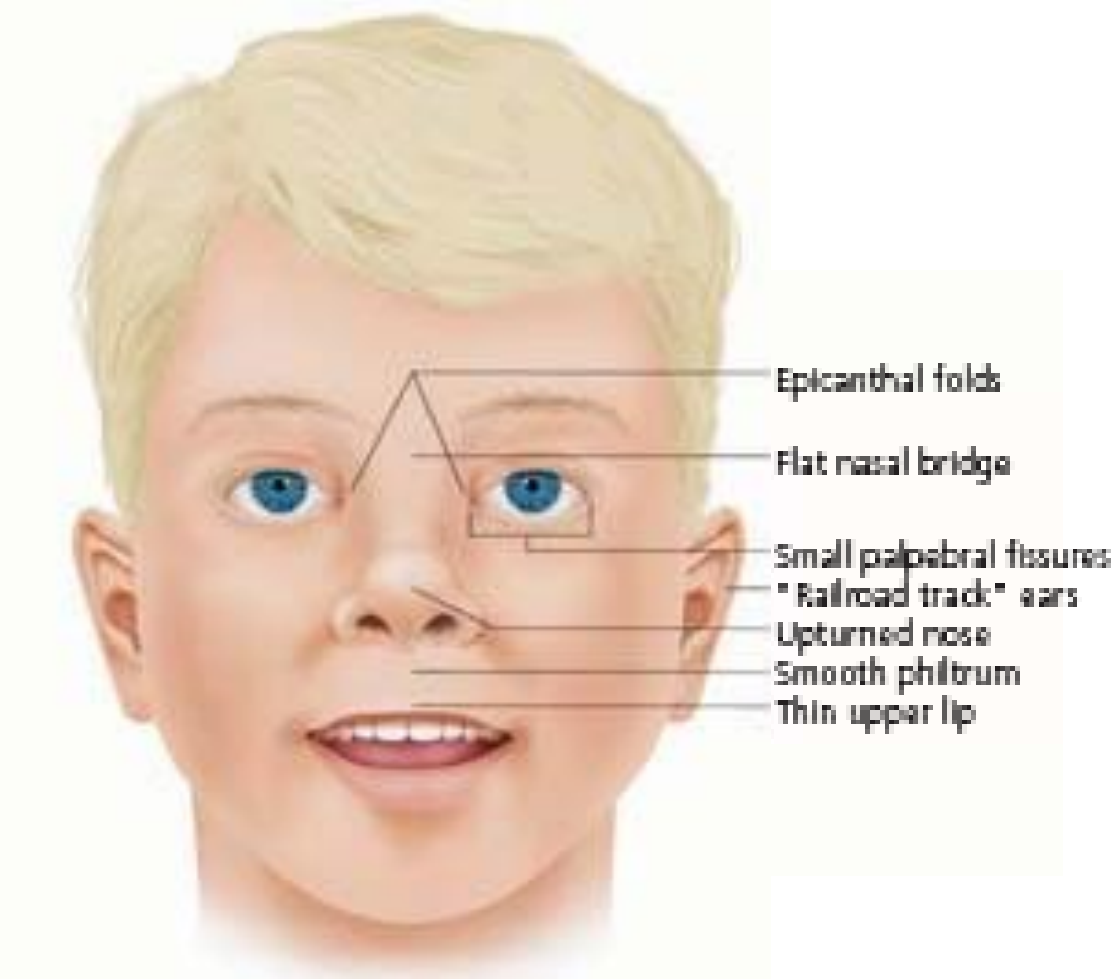
3. 알코올

- 태아알코올 증후군 빈도:
  약 1000명당 1명 (미국)
  아프리카 1000명당 39.2-46.4명

- 태아알코올 스펙트럼 장애:
  약 100명당 1명(미국)

3. 알코올

선천성 태아 알코올 증후군



3. 알코올

선천성 태아 알코올 증후군

3. 알코올

Lip-Philtrum Guide

The smoothness of the philtrum and the thinness of the upper lip are assessed individually on a scale of 1 to 5 (1 = unaffected, 5 = most severe).
The patient must have a relaxed facial expression, because a smile can alter lip thinness and philtrum smoothness.
Scores of 4 and 5, in addition to short palpebral fissures, correspond to fetal alcohol syndrome.

3. 알코올

- 태아 알코올 스펙트럼 장애

- Attention deficit hyperactivity disorder
- Inability to foresee consequences
- Inability to learn from previous experience
- Inappropriate or immature behaviour
- Lack of organization
- Learning difficulties
- Poor abstract thinking
- Poor adaptability
- Poor impulse control
- Poor judgement
- Speech, language and other communication problems

3. 알코올

- ✓ 알코올은 태아 신경 독성 물질
- ✓ 임신중에 알려진 알코올 안전용량 없음
- ✓ 임신중 한잔의 와인도 권장되지 않음.



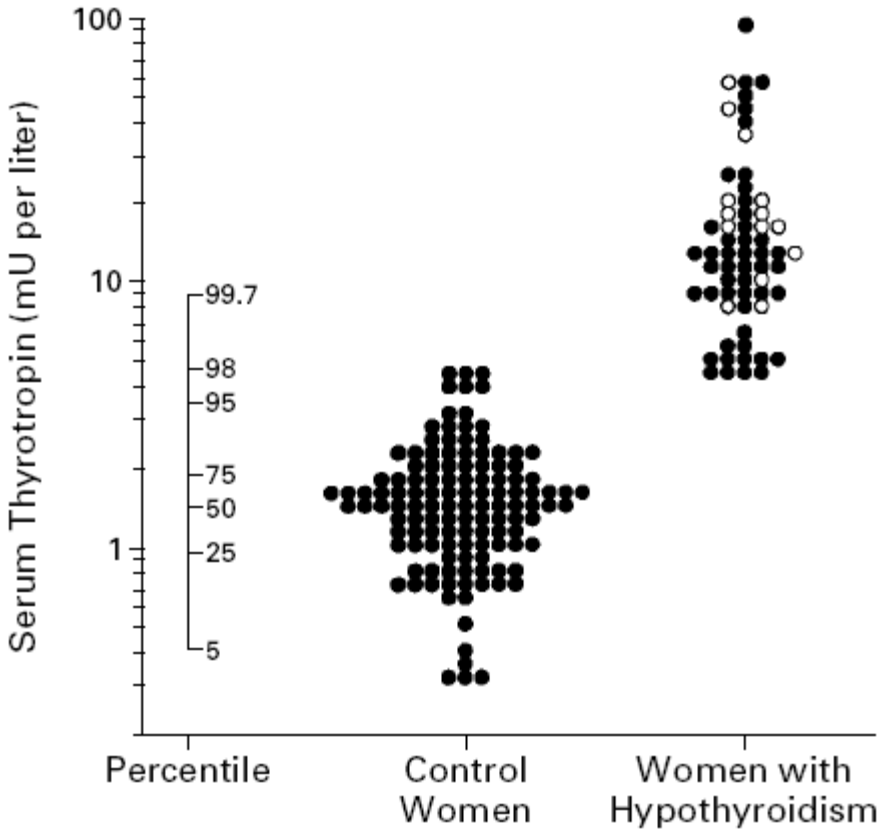
태아 신경 발달을 위해 무엇을 할 것인가?

4. 갑상선 기능저하증 치료

4. 갑상선 기능저하증

- 갑상선 기능저하증은 태아 신경발달 저하의 원인이 될 수 있음.
- 갑상선약(levothyroxine)은 임신중에 안전하게 사용 가능.

4. 갑상선 기능저하증



Maternal hypothyroidism–fetal neurodevelopment study (1999, NEJM)

4. 갑상선 기능저하증

TABLE 4. NEUROPSYCHOLOGICAL TEST SCORES AMONG THE CHILDREN OF WOMEN WITH HYPOTHYROIDISM DURING PREGNANCY AS COMPARED WITH THE CHILDREN OF MATCHED CONTROL WOMEN, STRATIFIED ACCORDING TO WHETHER THE HYPOTHYROIDISM WAS BEING TREATED.*

TEST	CHILDREN OF TREATED WOMEN WITH HYPOTHYROIDISM (N=14)	P VALUE†	CHILDREN OF UNTREATED WOMEN WITH HYPOTHYROIDISM‡ (N=48)	P VALUE§	CONTROL CHILDREN (N=124)
Intelligence					
WISC-III full-scale IQ score	111	0.20	100	0.005	107
WISC-III full-scale IQ score ≤85 (%)	0	0.90	19	0.007	5

Maternal hypothyroidism–fetal neurodevelopment study (1999, NEJM)

4. 갑상선 기능저하증

- TFT in Pregnancy

◆ Reference range for TSH

✓ First trimester 0.1-2.5 mIU/L

✓ Second trimester 0.2-3.0 mIU/L

✓ Third trimester 0.3-3.0 mIU/L

◆ Treated hypothyroid patients who are planning pregnancy should have their dose adjusting TSH <2.5mIU/L preconception

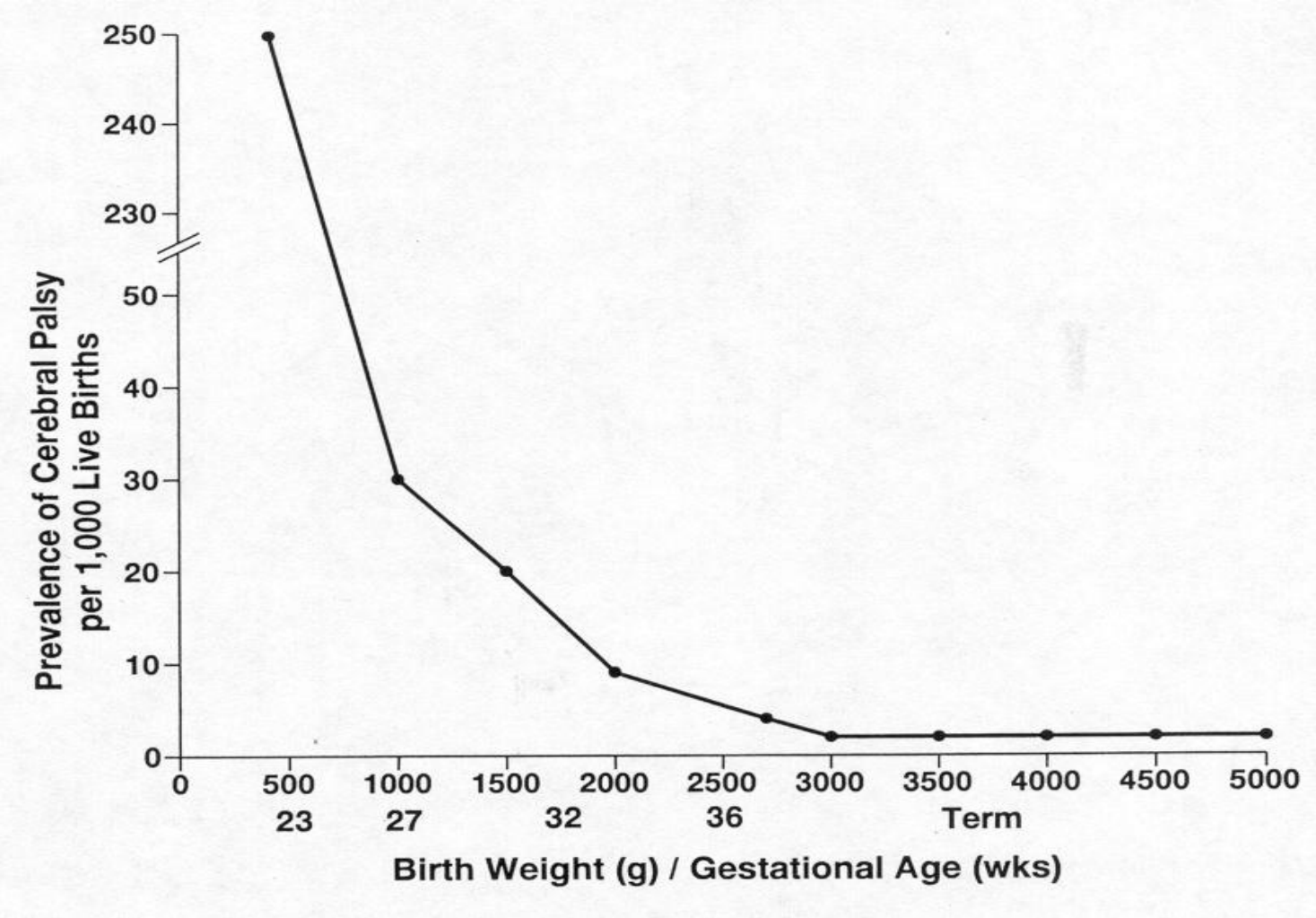
TABLE 1. Recommended patient profiles for targeted thyroid disease case finding in women seeking pregnancy or newly pregnant

Women over age 30 yr
Women with a family history or autoimmune thyroid disease or hypothyroidism
Women with a goiter
Women with thyroid antibodies, primarily thyroid peroxidase antibodies
Women with symptoms or clinical signs suggestive of thyroid hypofunction
Women with type 1 DM or other autoimmune disorders
Women with infertility
Women with a prior history of miscarriage or preterm delivery
Women with prior therapeutic head or neck irradiation or prior thyroid surgery
Women currently receiving levothyroxine replacement
Women living in a region with presumed iodine deficiency

태아 신경 발달을 위해 무엇을 할 것인가?

5. 조산 예방

태아체중/임신주수에 따른 뇌성마비 빈도



임신주수와 뇌성마비(CP)

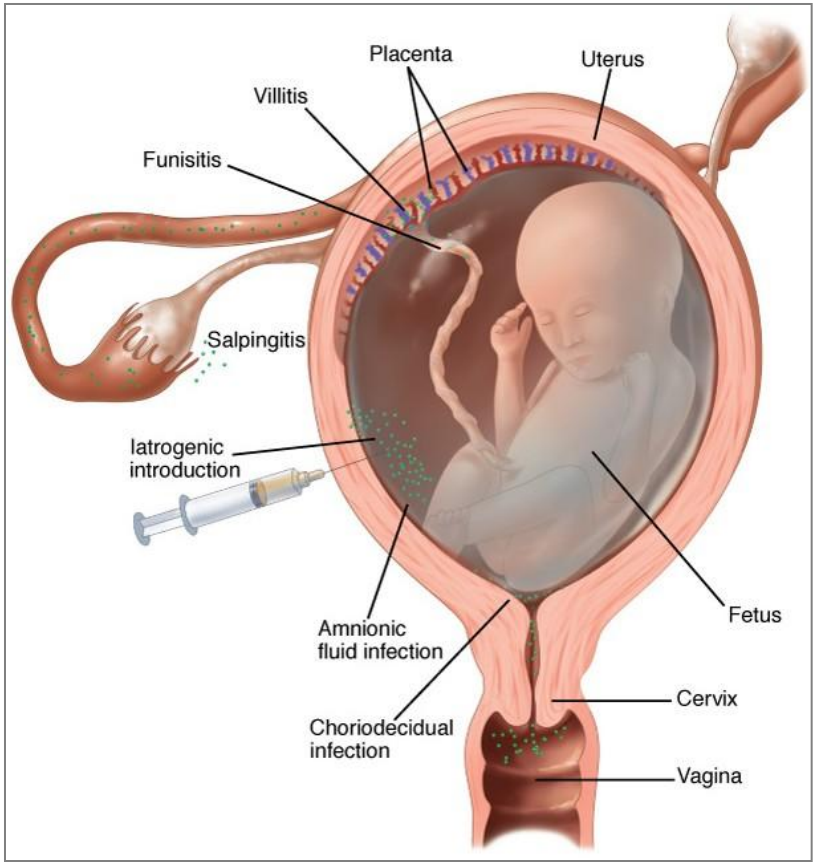
Gestational Age / Birthweight	Prevalence of CP
23 – 25 Weeks / 500 – 600 grams	25%
All infants < 1000 grams	5 – 10%
27 – 28 Weeks / 1000 grams	3%
36 Weeks	5 / 1000

5. 조산 예방

- ◆ 조산의 위험 요인
- ● 감염

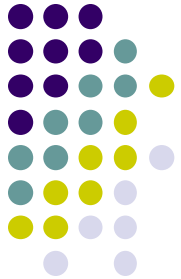
✓ Ureaplasma urealyticum and mycoplasma hominis, have emerged as important perinatal pathogens

✓ Bacterial vaginosis:
adverse vaginal flora, such as in bacterial vaginosis, is associated with spontaneous preterm birth



자궁내 감염 경로

5. 조산 피하기

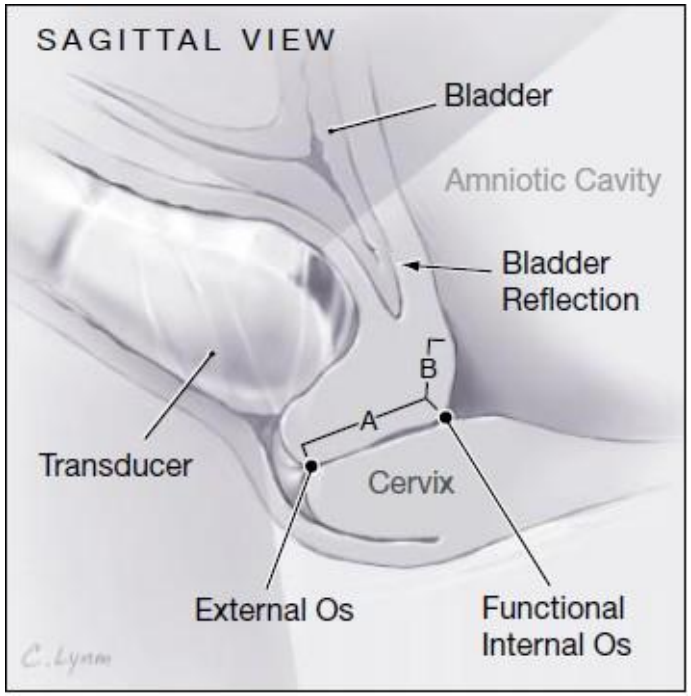


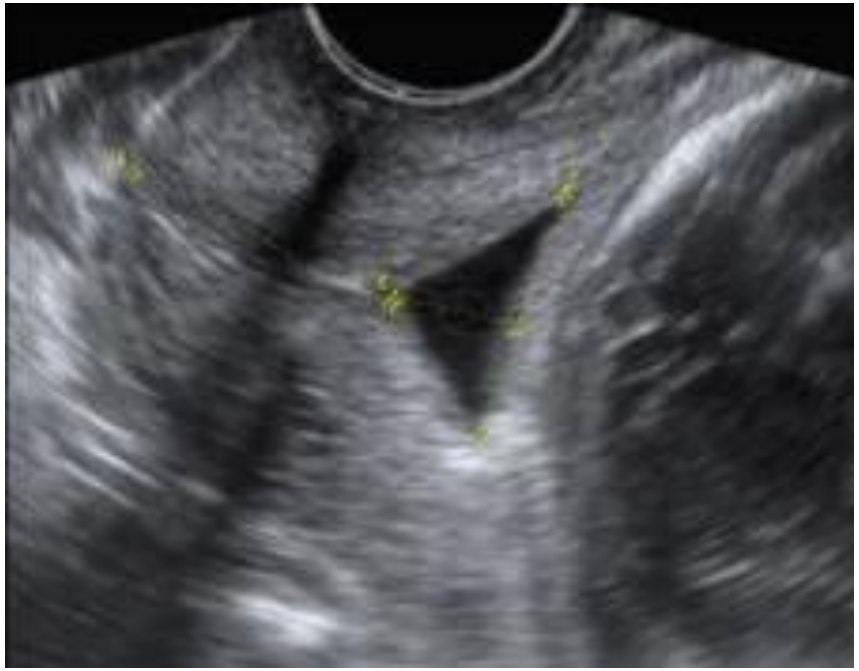
➢ 조산의 위험 요인

: alcohol, smoking, drugs, inadequate maternal weight gain, advanced maternal age, poverty, short stature, occupational factors, psychological and physical stress, periodontal disease, lower genital infection (e.g, bacterial vaginosis), multifetal gestation, prior D&C, uterine anomaly, prior conization, prior PTB etc.

5. 조산 예방

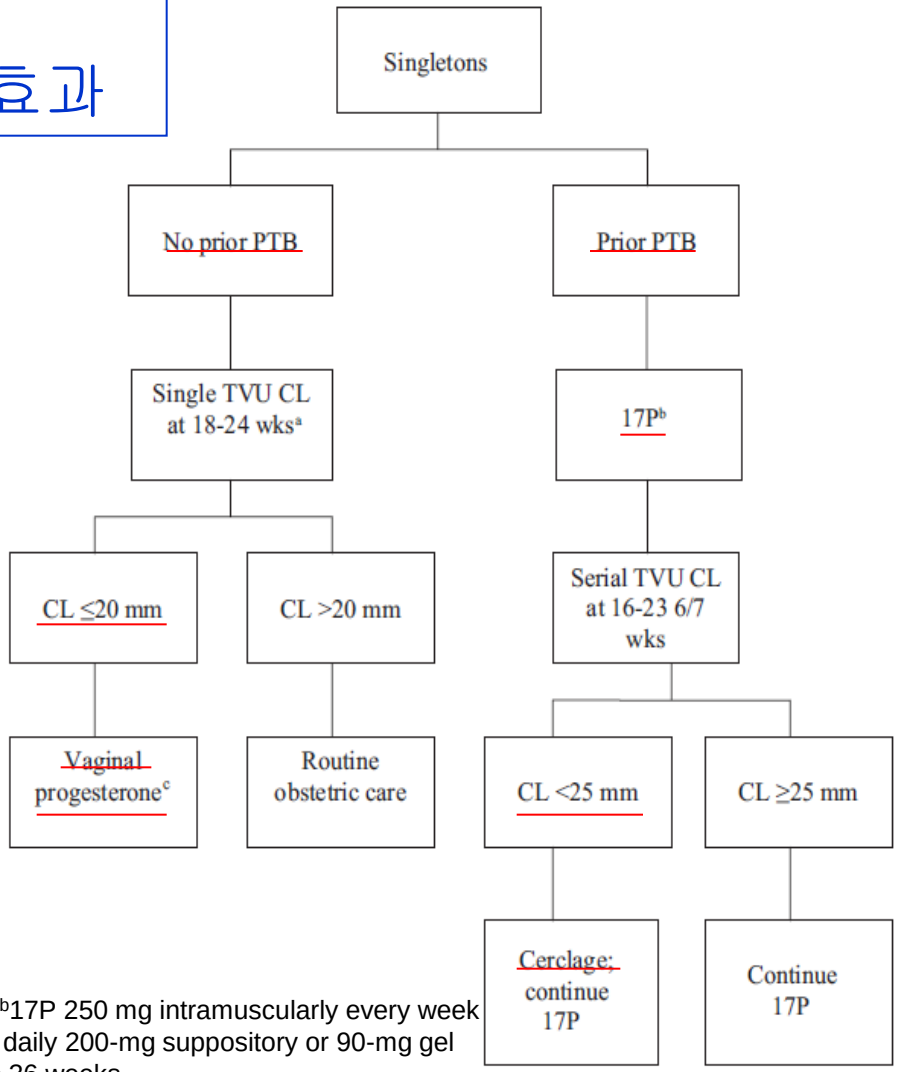
조산의 예측


SAGITTAL VIEW
Bladder
Amniotic Cavity
Bladder Reflection
B
A
Transducer
Cervix
External Os
Functional Internal Os
C. Lynn



5. 조산 예방

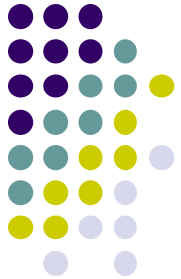
프로게스테론:
조산 예방 효과



[a] If TVU CL screening is performed; [b]17P 250 mg intramuscularly every week from 16-20 weeks to 36 weeks; [c]eg, daily 200-mg suppository or 90-mg gel from time of diagnosis of short CL to 36 weeks.

SMFM committee, Am J Obstet Gynecol 2012;206:373-86.

5. 조산 예방



- Measurement of cervical length
- Progesterone
- Tocolytics : Magnesium, beta-agonist, CCB, atosiban, etc…
- Cervical pessary
- Cervical cerclage
- Antibiotics

조산 임산부의 뇌성마비 예방

-Magnesium sulfate(MgSO4)

TABLE 42-10. Magnesium Sulfate for the Prevention of Cerebral Palsy[a]

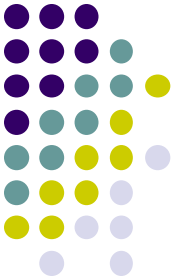
Perinatal Outcome[a]	Treatment: Magnesium Sulfate No. (%)	Treatment: Placebo No. (%)	Relative Risk (95% CI)
Infants with 2-year follow-up	1041 (100)	1095 (100)	—
Fetal or infant death	99 (9.5)	93 (8.5)	1.12 (0.85–1.47)
Moderate or severe cerebral palsy:			
Overall	20/1041 (1.9)	3/1095 (3.4)	0.55 (0.32–0.95)
< 28–31 weeks[b]	12/442 (2.7)	30/496 (6)	0.45 (0.23–0.87)
≥ 24–27 weeks[b]	8/599 (1.3)	8/599 (1.3)	1.00 (0.38–2.65)

[a]Selected results from the Beneficial Effects of Antenatal Magnesium Sulfate (BEAM) Study.
[b]Weeks' gestation at randomization.
Data from Rouse, 2008.

태아 신경 발달을 위해 무엇을 할 것인가?

6. 약물 조절

6. 감기가 걸렸을 때, 약을 먹지 않고 참는 것이 좋은가?

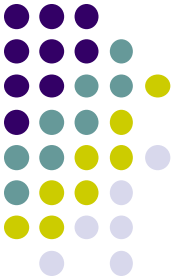


- 38.9 도 이상의 고열, 반복적인 기침은 태아기형, 유산, 조산의 위험성을 증가 시킴
- 타이레놀 등 약제는 임신 중에도 안전하게 사용 가능
- Ampicillin, cephalosporin 등의 항생제도 안전하게 사용 가능.

6. 약물 조절

- 감기, 고열, 기침 ⟷ 감기약
- 독감, 고열, 기침 ⟷ 독감 약제 (타미플루 등)

6. 약물 조절

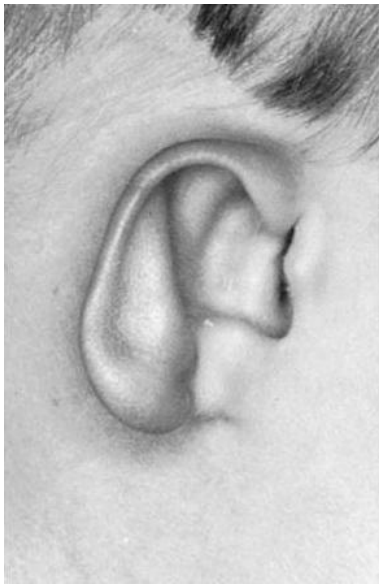


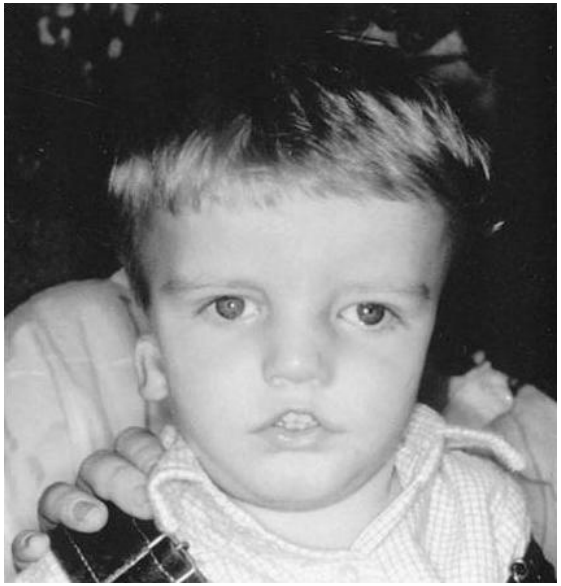
- 임신 중 신경발달을 저하시킬 수 있는 약제
  - ✓ 아큐탄: 여드름 치료제
  - ✓ 간질(뇌전증) 치료약물
  - ✓ 와파린 등

6. 약물 조절

1. 아큐탄: 여드름 치료제

- Fetal adverse effects:
  - ✓ Spontaneous abortion; deformities of cranium, ears (microtia, low-set ears, anotia), face, heart (TGA, TOF, VSD etc), limbs, liver; hydrocephalus, microcephalus.
  - ✓ Cognitive defects

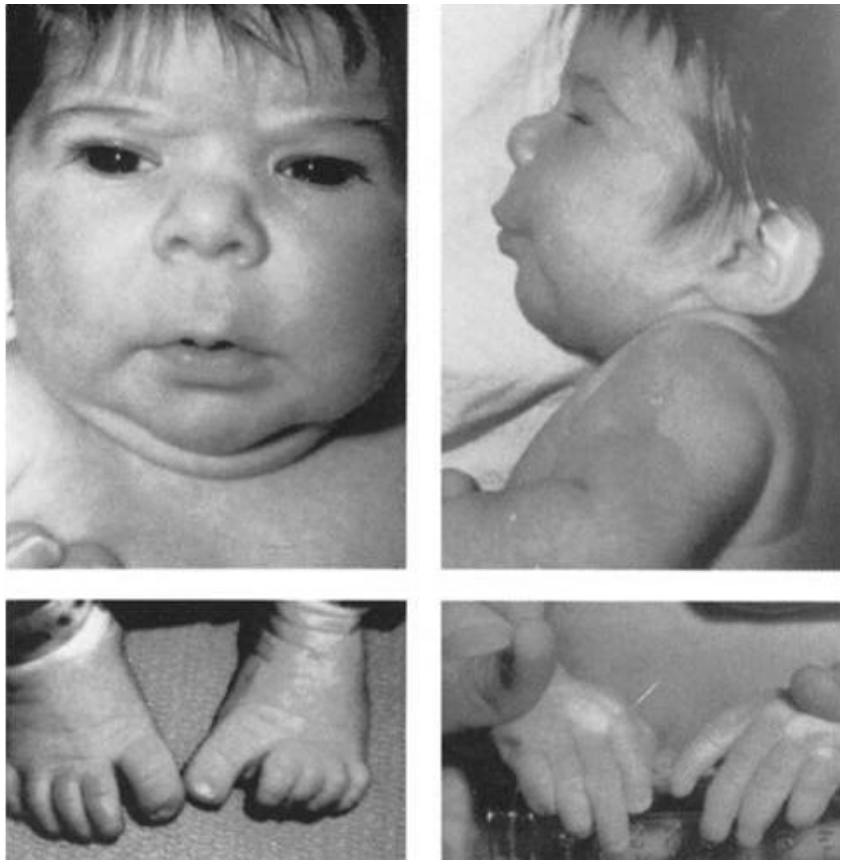




Left–bilateral microtia or anotia, Right–flat, depressed nasal bridge and ocular hypertelorism

6. 약물 조절

2. 간질(뇌전증) 치료제



Fetal hydantoin syndrome:
Upper facial features including upturned nose, mild midfacial hypoplasia, long upper lip with thin vermilion border.

Lower distal digital hypoplasia.

6. 약물 조절

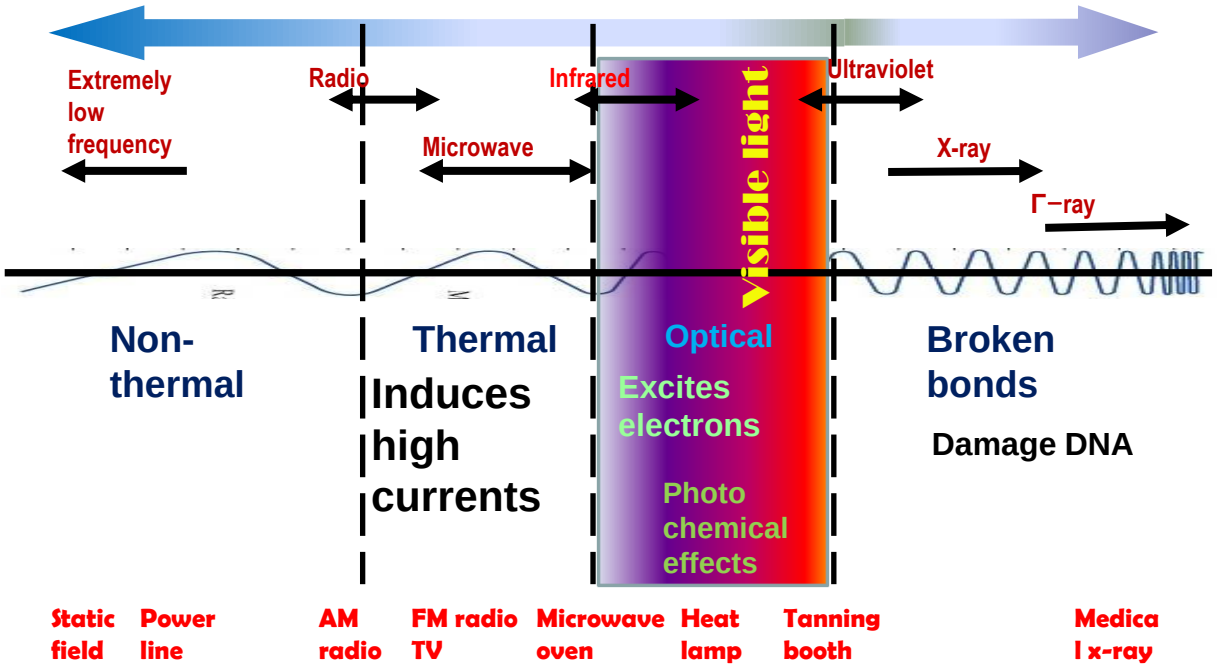
3. 와파린

Fetal warfarin syndrome

Chondrodysplasia punctata

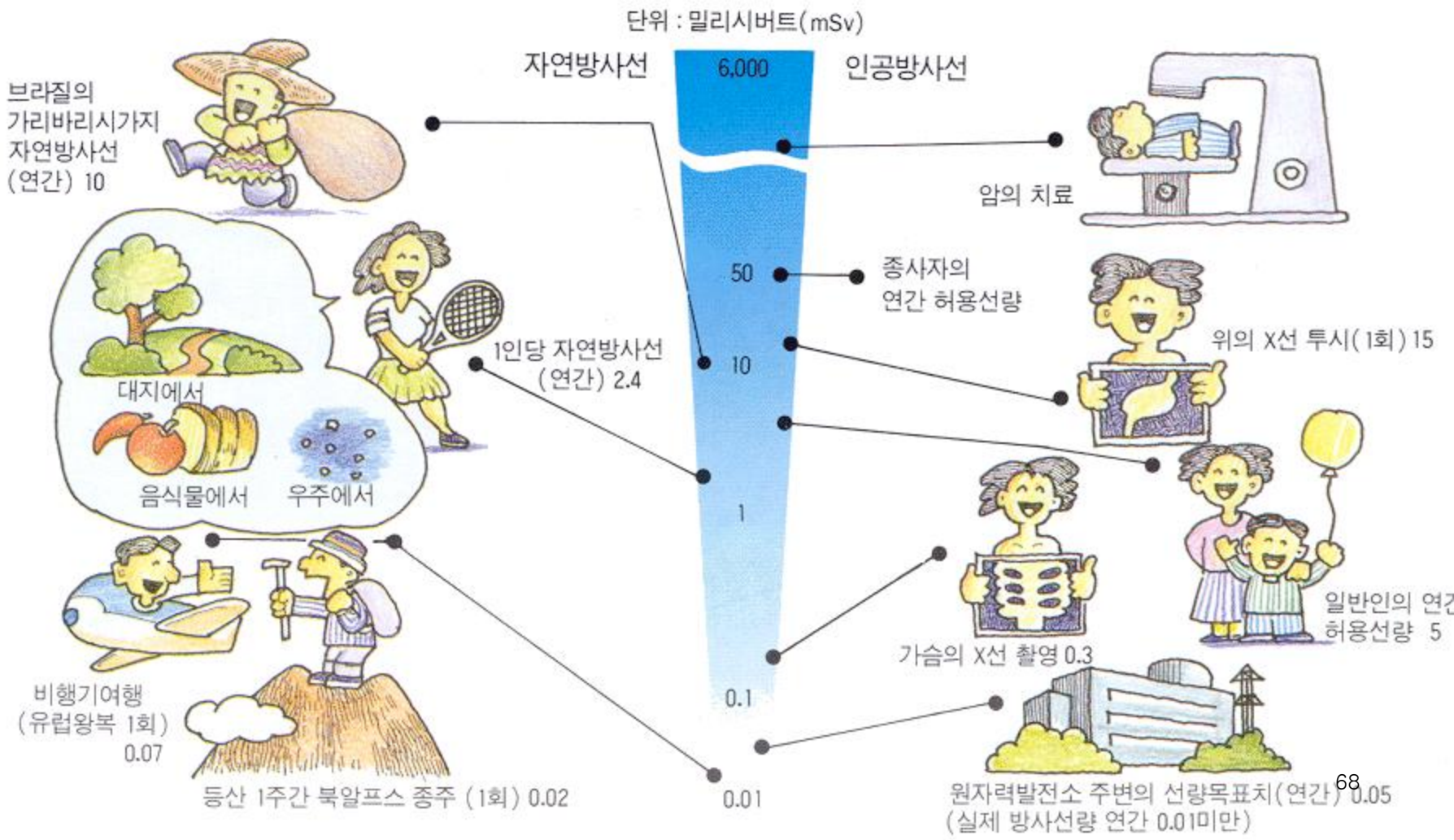
태아 신경 발달을 위해 무엇을 할 것인가?

7. 방사선 피하기



7. 방사선

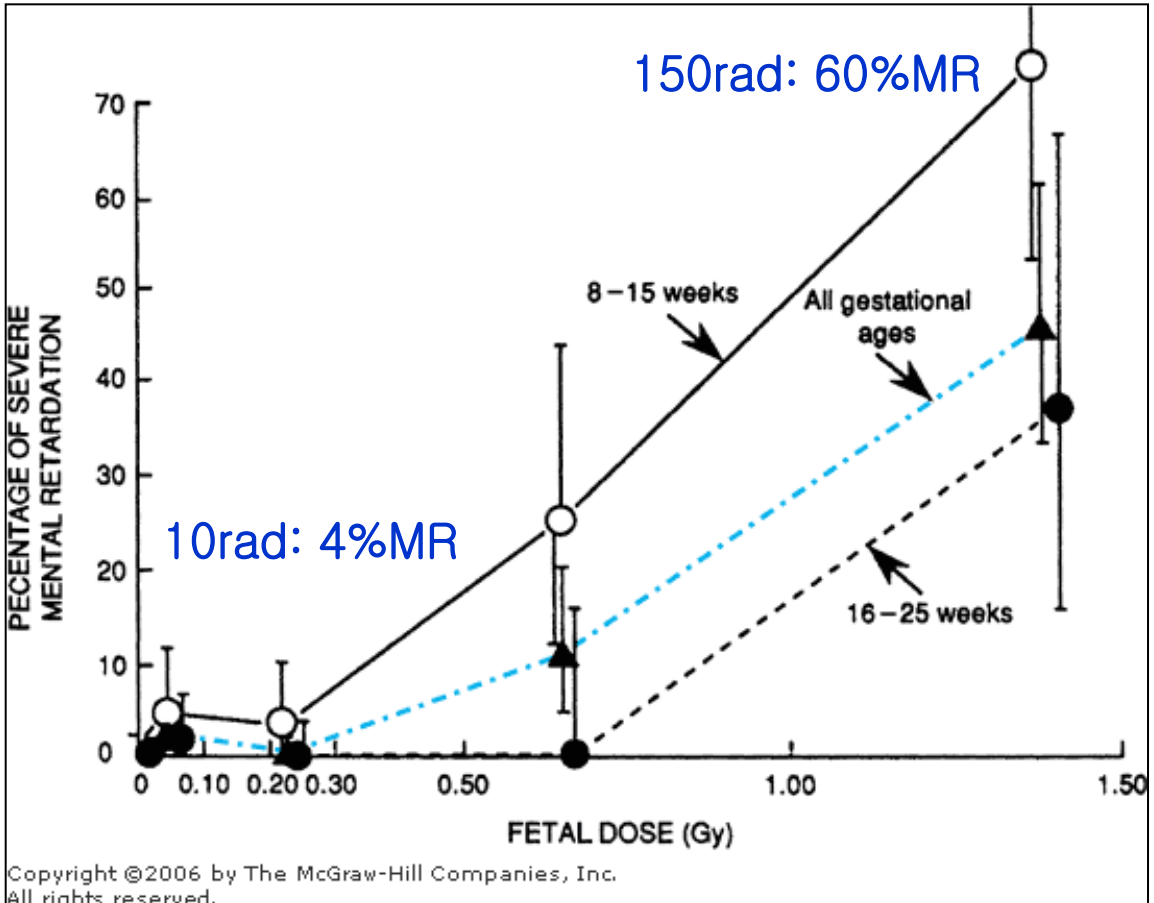
Ionizing radiation from Natural source



7. 방사선

Ionizing radiation

◆Anatomic bomb survivors from Hisroshima and Nagasaki (Greskovich & Macklis, 2000)



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7. 방사선

- 중추 신경계에 미치는 영향
- ✓ **임신 8-15주** 사이 가장 예민
- ✓ 25주 이후에는 태아 이상이 발생하는 경우는 드물다
- ✓ 10 rad 이하: 별다른 이상 없음
- ✓ 50 rad 이상 급성 방사선 노출시

: 소두증, 정신 지체, 성장 지연

태아 신경 발달을 위해 무엇을 할 것인가?

8. 중금속 피하기: 수은

8. 임신 중에 회는 먹으면 안 되는 건가요?

- 일반적으로 먹는 광어, 우럭, 연어 등의 일반적인 바다 회는 섭취 가능
- 물고기중 먹이 사슬의 가장 위에 존재하는 왕고등어, 황새치, 상어, 옥돔 등은 수은 함량이 높아 임신 중 섭취가 권장되지 않음.

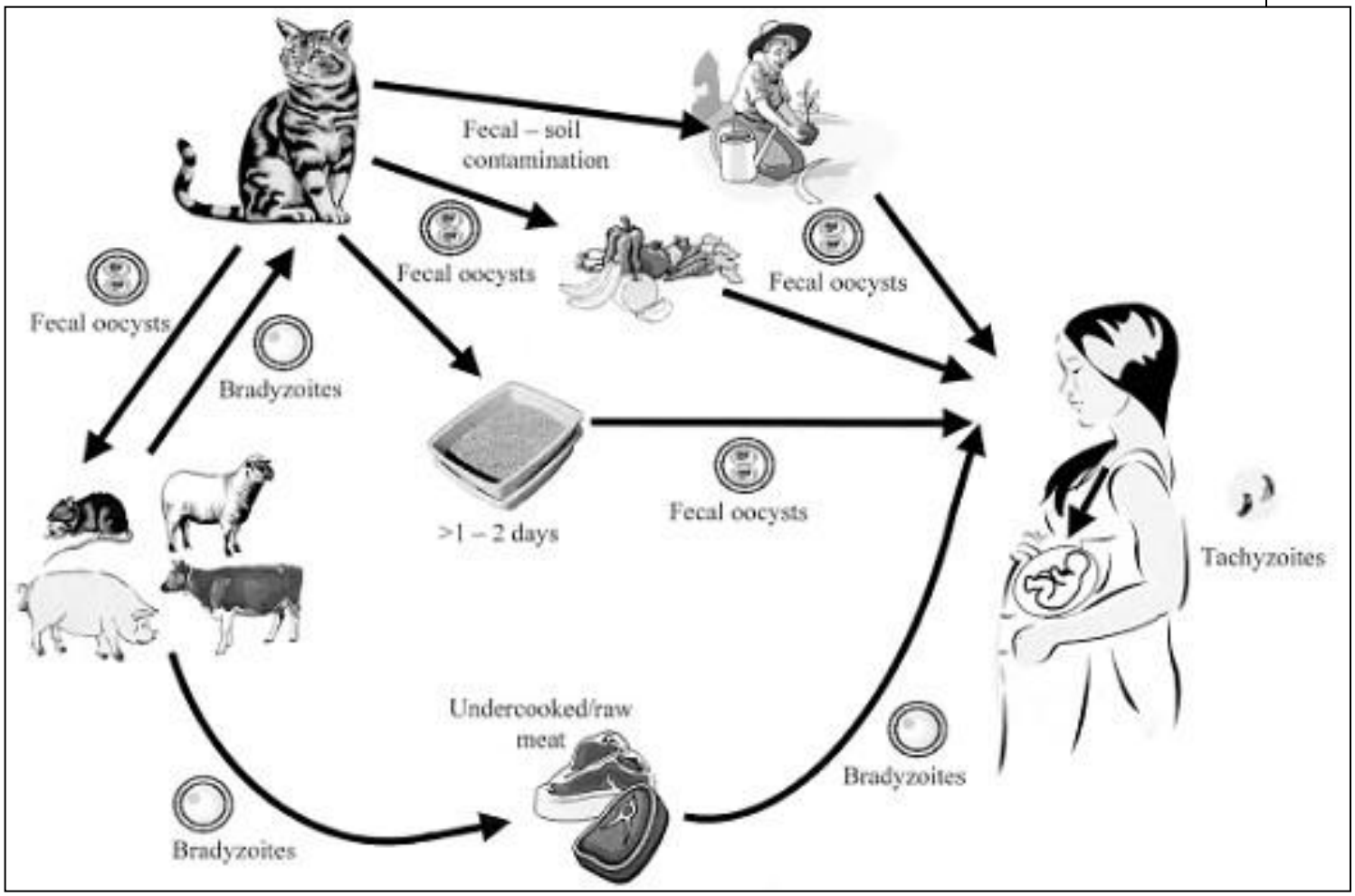
8. 수은

수은 함량이 높아 권장되는 않는 회 종류

태아 신경 발달을 위해 무엇을 할 것인가?

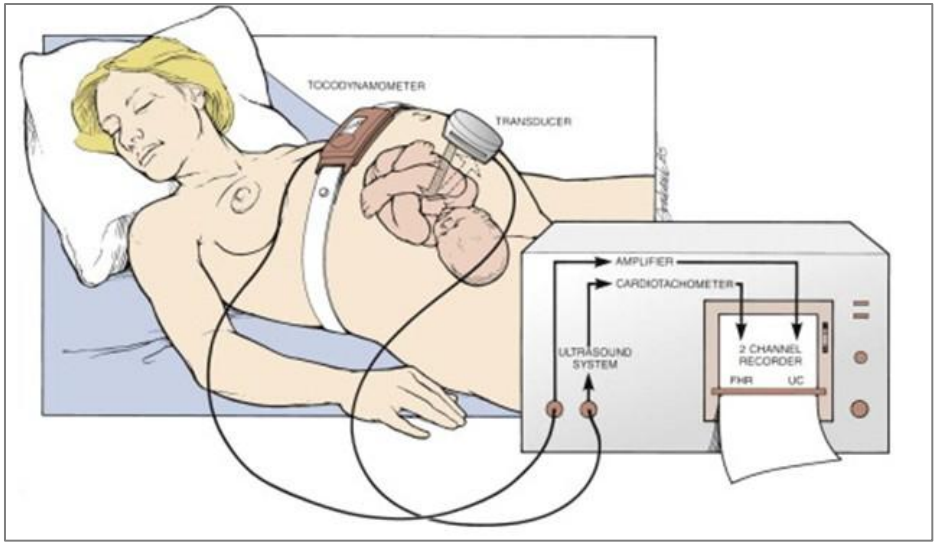
9. 톡소플라즈마 예방

9. 톡소플라즈마

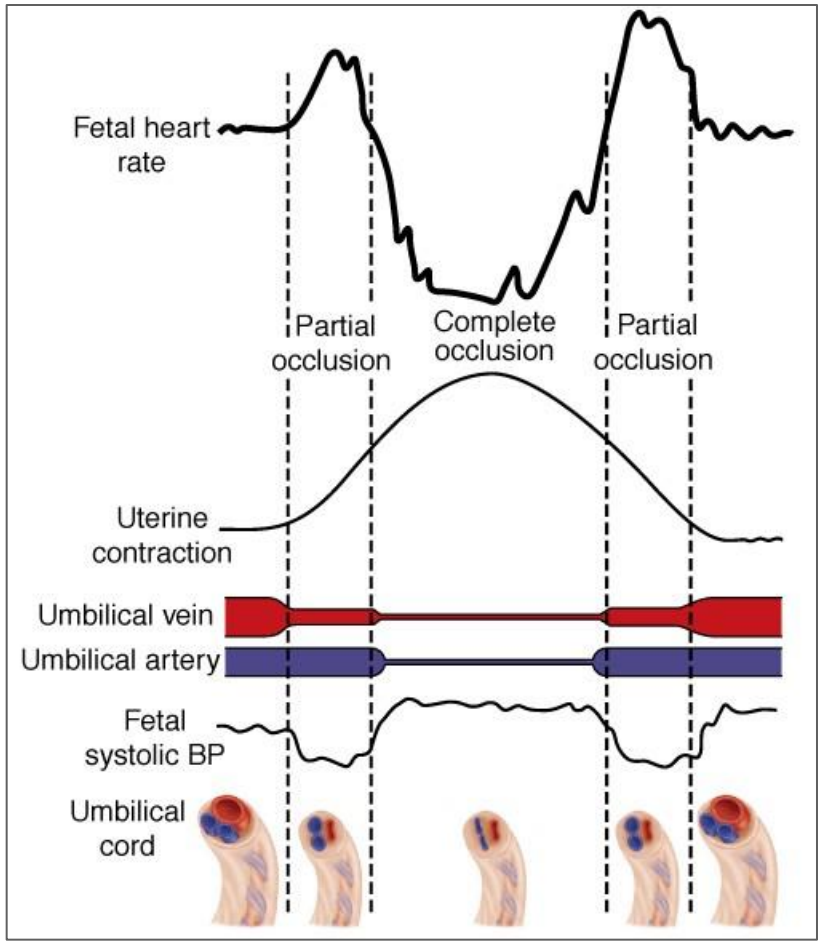

Fecal – soil contamination
Fecal oocysts
Fecal oocysts
Fecal oocysts
Bradyzoites
>1 – 2 days
Fecal oocysts
Tachyzoites
Undercooked/raw meat
Bradyzoites
Bradyzoites

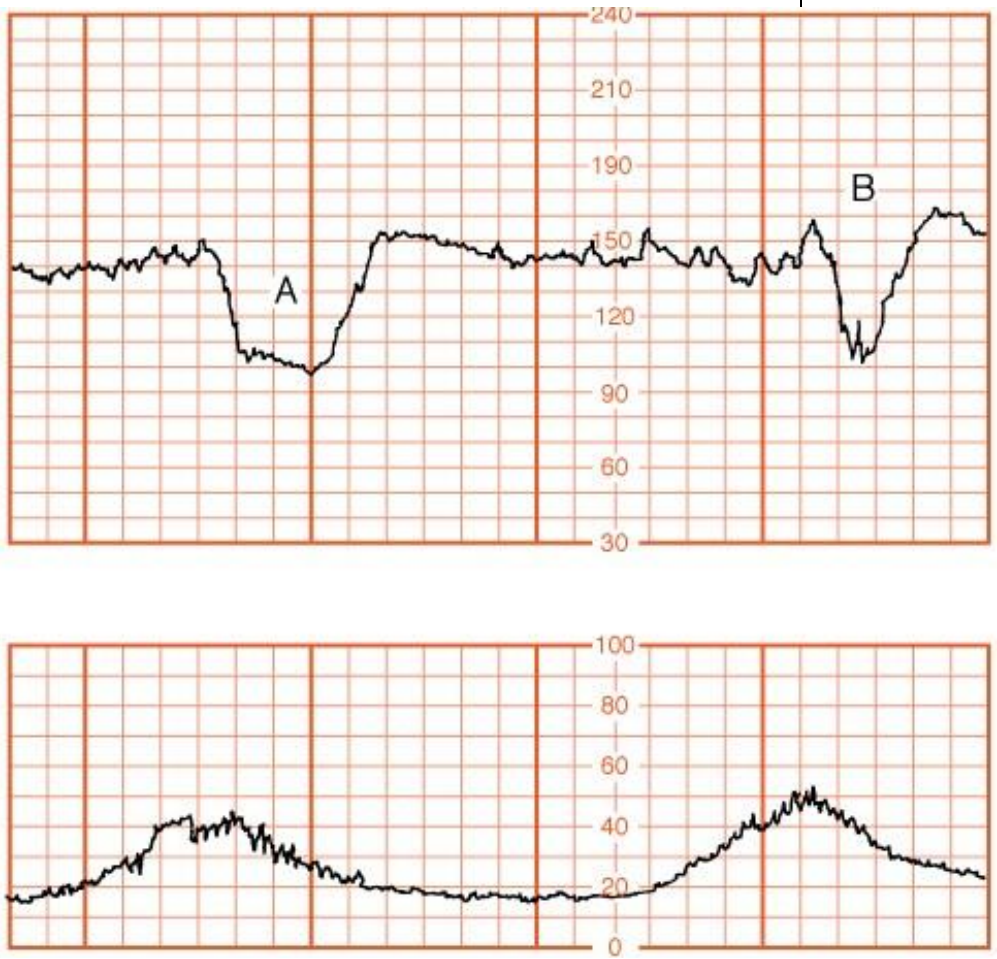
태아 신경 발달을 위해 무엇을 할 것인가?

10. 태아저산소증 피하기
-태아발육장애, 양수과소증



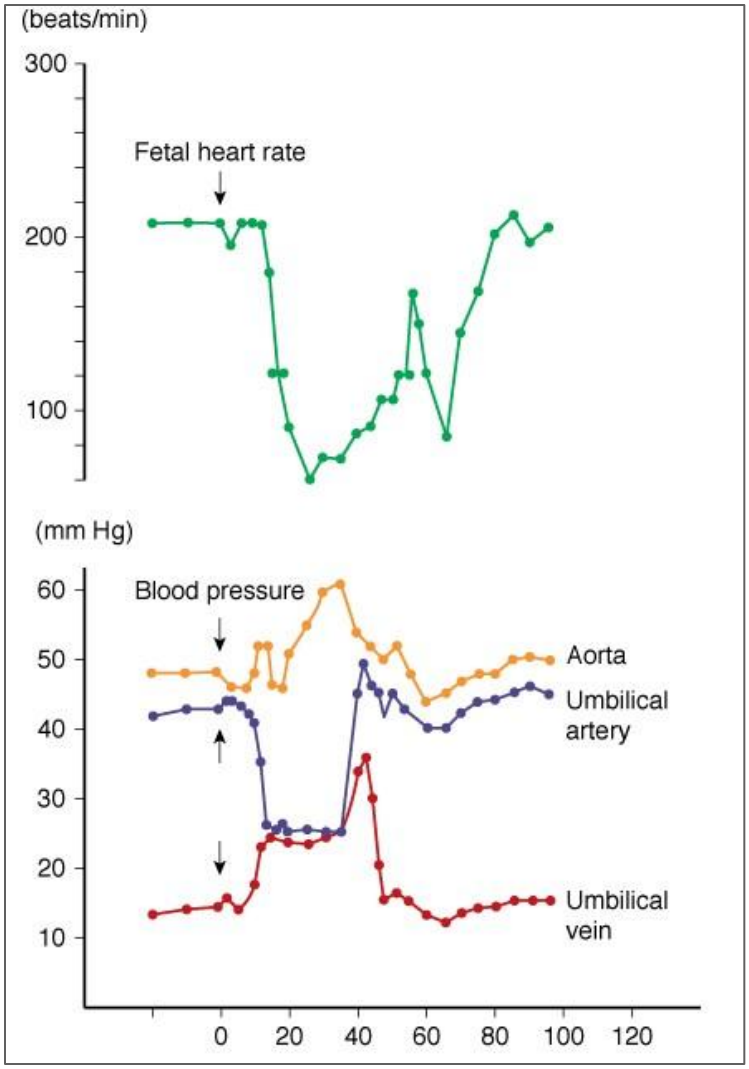
탯줄 눌림-Variable deceleration





Lee et al. Obstet Gynecol. 1975

탯줄 눌림-Variable deceleration



- Experimental evidence: fetal sheep

✓ Partial occlusion of umbilical cord, 1 min every 3 min:

-Brain damage only after 2 hours

✓ Total occlusion of umbilical cord, 1min every 5 min:

-No significant acidemia after 4hours.

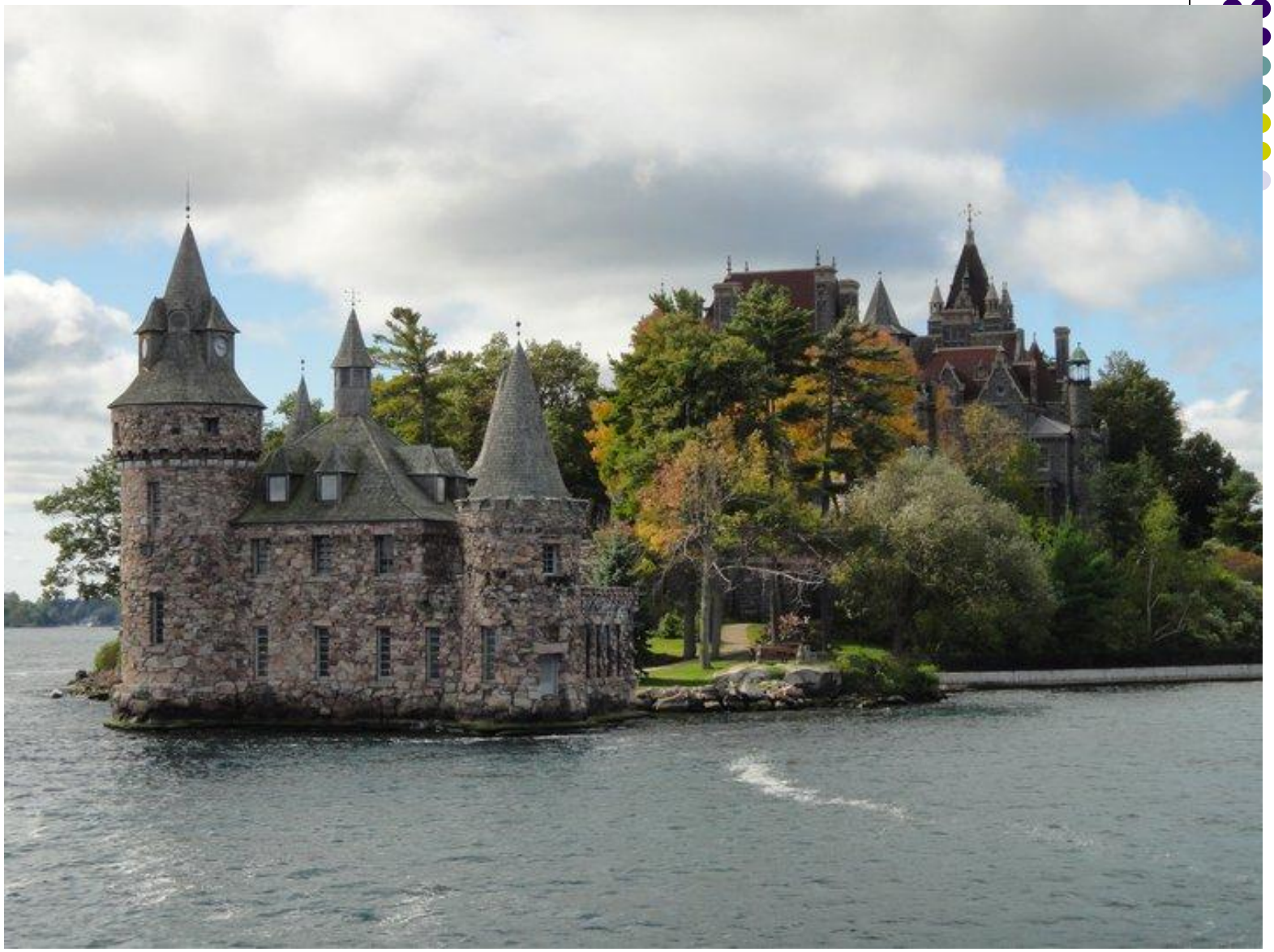
10. 태아저산소증 피하기

<태아 건강 평가법>

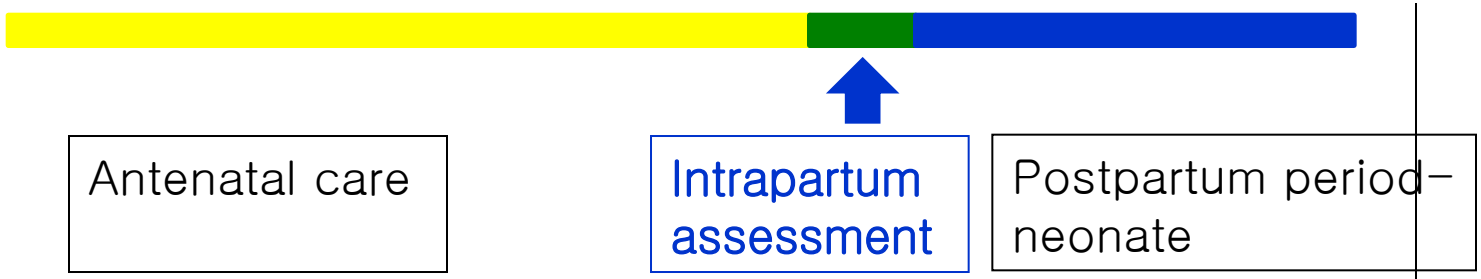
RISK FACTOR	TEST	FREQUENCY	START
All pregnancies	**FMC**	**Daily**	**24-28 wk**
Low-risk pregnancies	**FMC**	**Daily**	**24-28 wk**
IUGR(태아발육장애)	**mBPP/Doppler**	**Once or twice weekly**	**At diagnosis**
Oligohydramnios	**mBPP**	**Twice weekly**	**At diagnosis**
Decreased fetal movement	mBPP	PRN	At diagnosis
Previous fetal death	**mBPP**	**Once or twice weekly**	**32-34 wk, or 1 wk before previous fetal death**
	Alternative: BPP or CST	**Weekly**	
Postterm pregnancy	**mBPP**	**Once or twice weekly**	**≥41 wk**

FMC: fetal movements count
mBPP: modified biophysical profile
BPP: biophysical profile

1. 엽산, 복합비타민
2. 알코올: 절대 금주
3. 고열: 38.9 ℃ 이상 피하기
4. 갑상선 기능저하증 치료하기
5. 조산 예방 및 MgSO4
6. 약물 조절
7. 방사선 피하기
8. 중금속: 수은 피하기
9. 감염: 톡소플라즈마, CMV, 풍진, 수두, 성병 예방 및 치료
10. 태아 저산소증 피하기



Thousand Islands- Boldt Castle



Strategy to avoid intrapartum injury

- Unfortunately, because in most cases the genesis of cerebral palsy occurred long before labor, this did little to mitigate risks for CP

  -O'Callaghan 2013.

- Only 2-5% of CP cases could be attributed to intrapartum hypoxia

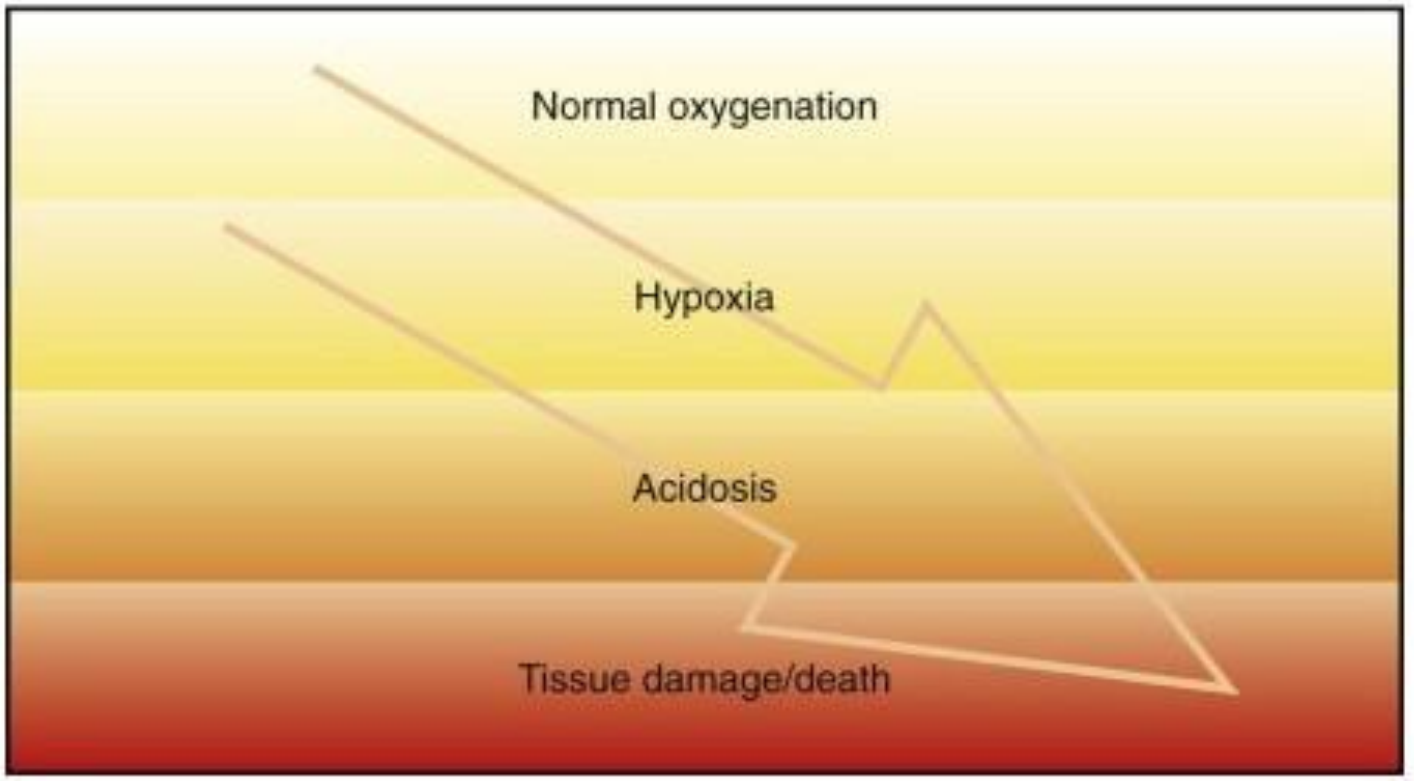
  -Strijbis 2006, Stanley 1991.

뇌성마비 **(Cerebral Palsy)**의 주산기 위험인자

TABLE 33-2. Perinatal Risk Factors Reported to Be Increased in Children with Cerebral Palsy

Risk Factors	Risk Ratio	95% CI
Hydramnios	6.9	1.0–49.3
Placental abruption	7.6	2.7–21.1
Interval between pregnancies < 3 months or > 3 years	3.7	1.0–4.4
Spontaneous preterm labor	3.4	1.7–6.7
Preterm delivery at 23–27 weeks	78.9	56.5–110
Breech or face presentation, transverse lie	3.8	1.6–9.1
Severe birth defect	5.6	8.1–30.0
Nonsevere birth defect	6.1	3.1–11.8
Time to cry > 5 minutes	9.0	4.3–18.8
Low placental weight	3.6	1.5–8.4
Placental infarction	2.5	1.2–5.3
Chorioamnionitis		
Clinical	2.4	1.5–3.8
Histological	1.8	1.2–2.9
Others[a]	—	—

Intrapartum fetal evaluation to identify abnormal FHB



The purpose of fetal heart rate monitoring is to detect fetal hypoxia and metabolic acidosis

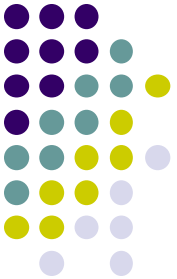
Acute peripartum or Intrapartum event leading to Hypoxic-Ischemic Encephalopathy(HIE)

TABLE 33-1. Findings Consistent with an Acute Peripartum or Intrapartum Event Leading to Hypoxic-Ischemic Encephalopathy

Neonatal Findings
Apgar score: < 5 at 5 and 10 minutes
Umbilical arterial acidemia: pH < 7.0 and/or base deficit ≥ 12 mmol/L
Neuroimaging evidence of acute brain injury: MRI or MRS consistent with HIE
Multisystem involvement consistent with HIE
Type and Timing of Contributing Factors
Sentinel hypoxic or ischemic event occurring immediately before or during delivery
Fetal heart rate monitor patterns consistent with an acute peripartum or intrapartum event

HIE = hypoxic ischemic encephalopathy; MRI = magnetic resonance imaging; MRS = magnetic resonance spectroscopy.
From the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics, 2014.

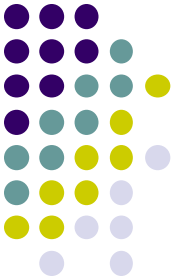
Acute peripartum or Intrapartum event leading to Hypoxic-Ischemic Encephalopathy(HIE)



- Apgar score <5 at 5 and 10 minutes
- Umbilical artery pH <7.0 and/or a base deficit of ≥12 mmol/L.
- Suggestive MR neuroimaging obtained within 24 to 96 hours of birth and read by a radiologist with expertise in pediatric neuroradiology, or suggestive MRI or MR spectroscopic findings. Repeat imaging at 10 days is more predictive of the full extent of the injury.
- Presence of multisystem organ failure.

2014 The American College of Obstetricians and Gynecologists and the American Academy of Pediatrics

Acute peripartum or Intrapartum event leading to Hypoxic-Ischemic Encephalopathy(HIE)



- Suggestive intrapartum findings:

a Sentinel hypoxic-ischemic event occurring immediately before or during labor and delivery, including uterine rupture, severe abruption, umbilical cord prolapse, amniotic fluid embolism or other causes of maternal hemodynamic collapse, and fetal exsanguination (eg, associated with vasa previa, fetal-to-maternal hemorrhage, twin demise with monochorionic placentation).

b Suggestive fetal heart rate pattern (eg, conversion of a Category 1 to Category III tracing). The observation of a Category III tracing upon admission is strong evidence of pre-existent insult and NNE with or without the subsequent diagnosis of CP may occur despite appropriate management and expeditious delivery within 30 minutes.

- Spastic quadriplegic or dyskinetic CP.

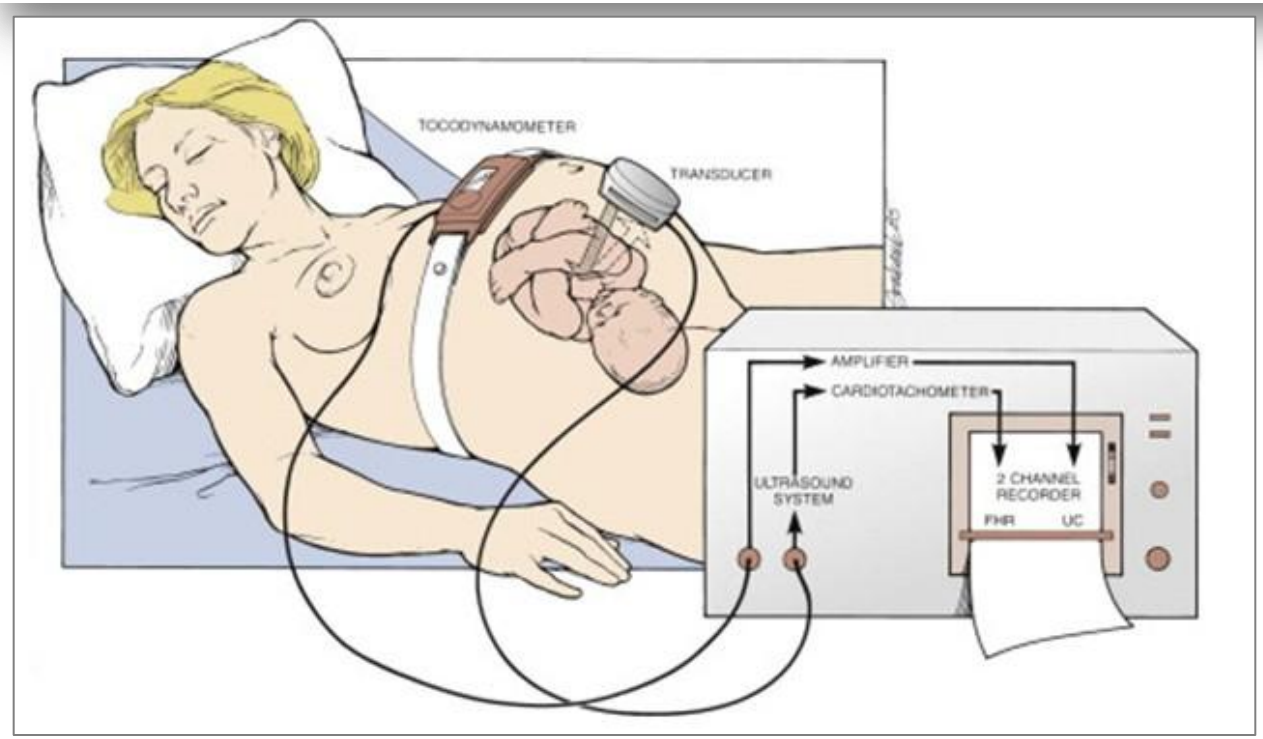
2014 The American College of Obstetricians and Gynecologists and the American Academy of Pediatrics

Current Commentary

The 2008 National Institute of Child Health and Human Development Workshop Report on Electronic Fetal Monitoring

Update on Definitions, Interpretation, and Research Guidelines

George A. Macones, MD, Gary D. V. Hankins, MD, Catherine Y. Spong, MD, John Hauth, MD, and Thomas Moore, MD



– Macones GA et al. Obstet Gynecol. 2008

Three-Tier Fetal Heart Rate Interpretation System

Category I Normal

Category I fetal heart rate (FHR) tracings include all of the following:

- Baseline rate: 110–160 beats per minute (bpm)
- Baseline FHR variability: moderate
- Late or variable decelerations: absent
- Early decelerations: present or absent
- Accelerations: present or absent

Category II Indeterminate

Category II FHR tracings include all FHR tracings not categorized as Category I or Category III. Category II tracings may represent an appreciable fraction of those encountered in clinical care. Examples of Category II FHR tracings include any of the following:

Baseline rate

- Bradycardia not accompanied by absent baseline variability
- Tachycardia

Baseline FHR variability

- Minimal baseline variability
- Absent baseline variability not accompanied by recurrent decelerations
- Marked baseline variability

Accelerations

- Absence of induced accelerations after fetal stimulation

Periodic or episodic decelerations

- Recurrent variable decelerations accompanied by minimal or moderate baseline variability
- Prolonged deceleration ≥2 minutes but <10 minutes
- Recurrent late decelerations with moderate baseline variability
- Variable decelerations with other characteristics, such as slow return to baseline, "overshoots," or "shoulders"

Category III Abnormal

Category III FHR tracings include either:

- Absent baseline FHR variability and any of the following:
  - Recurrent late decelerations
  - Recurrent variable decelerations
  - Bradycardia
- Sinusoidal pattern

Three-Tier Fetal Heart Rate Interpretation System

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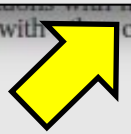


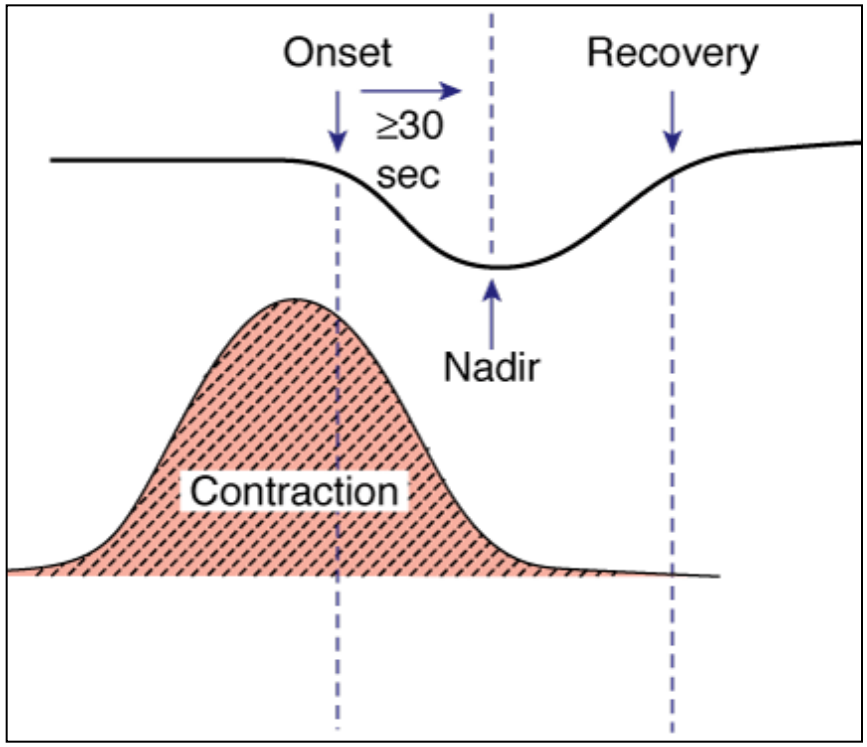
- Variable decelerations with [illegible] characteristics, such as slow return to baseline, "overshoots," or "shoulders"

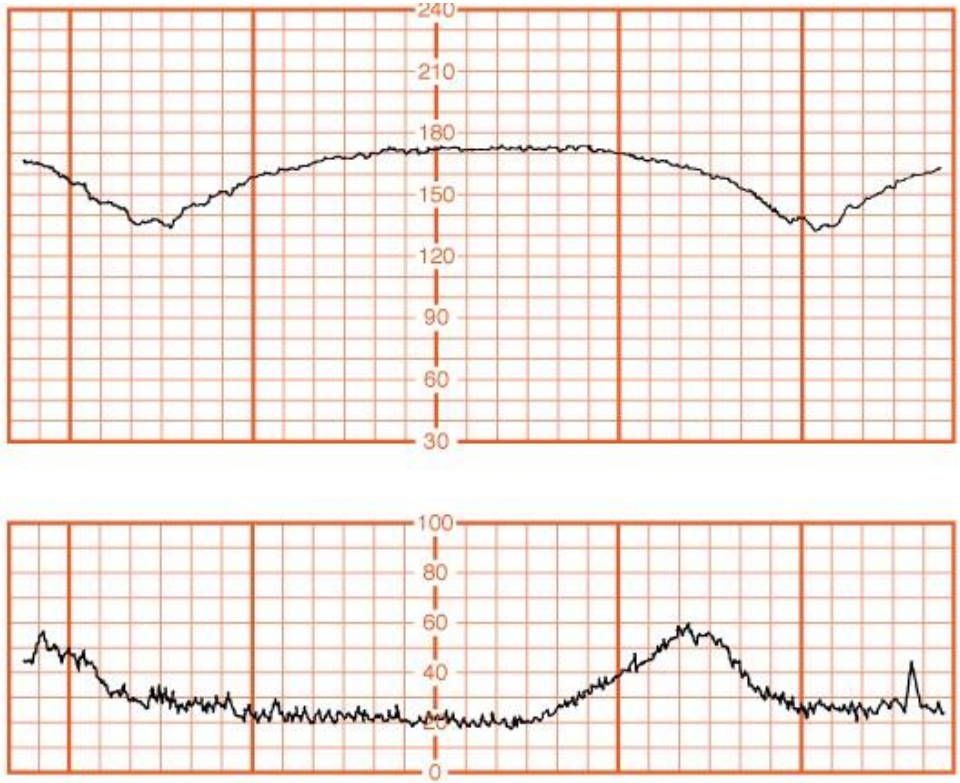
Category III

Category III FHR tracings include either:

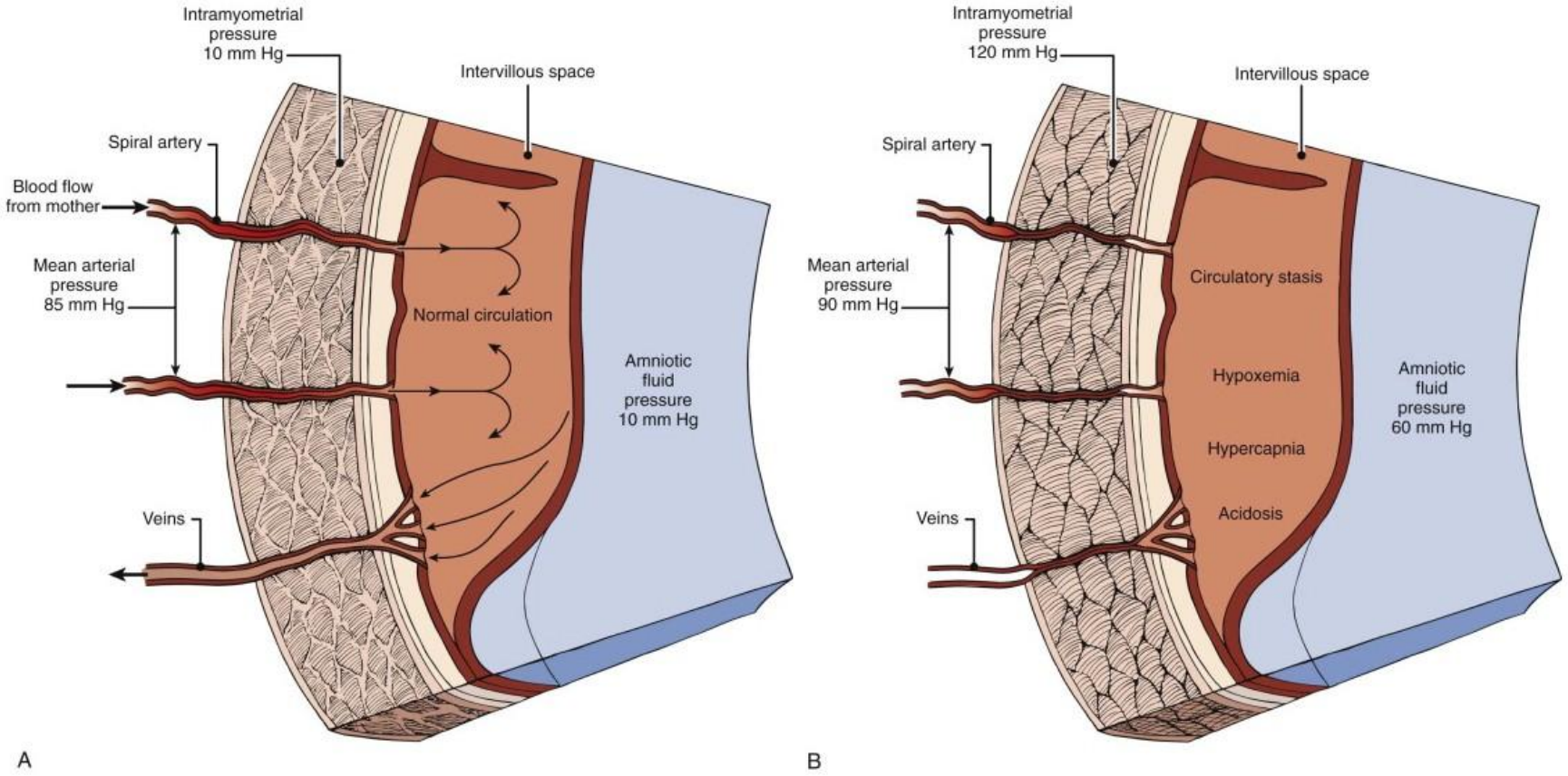
- Absent baseline FHR variability and any of the following:
  - Recurrent late decelerations
  - Recurrent variable decelerations
  - Bradycardia
- Sinusoidal pattern

자궁태반 부전-Late deceleration

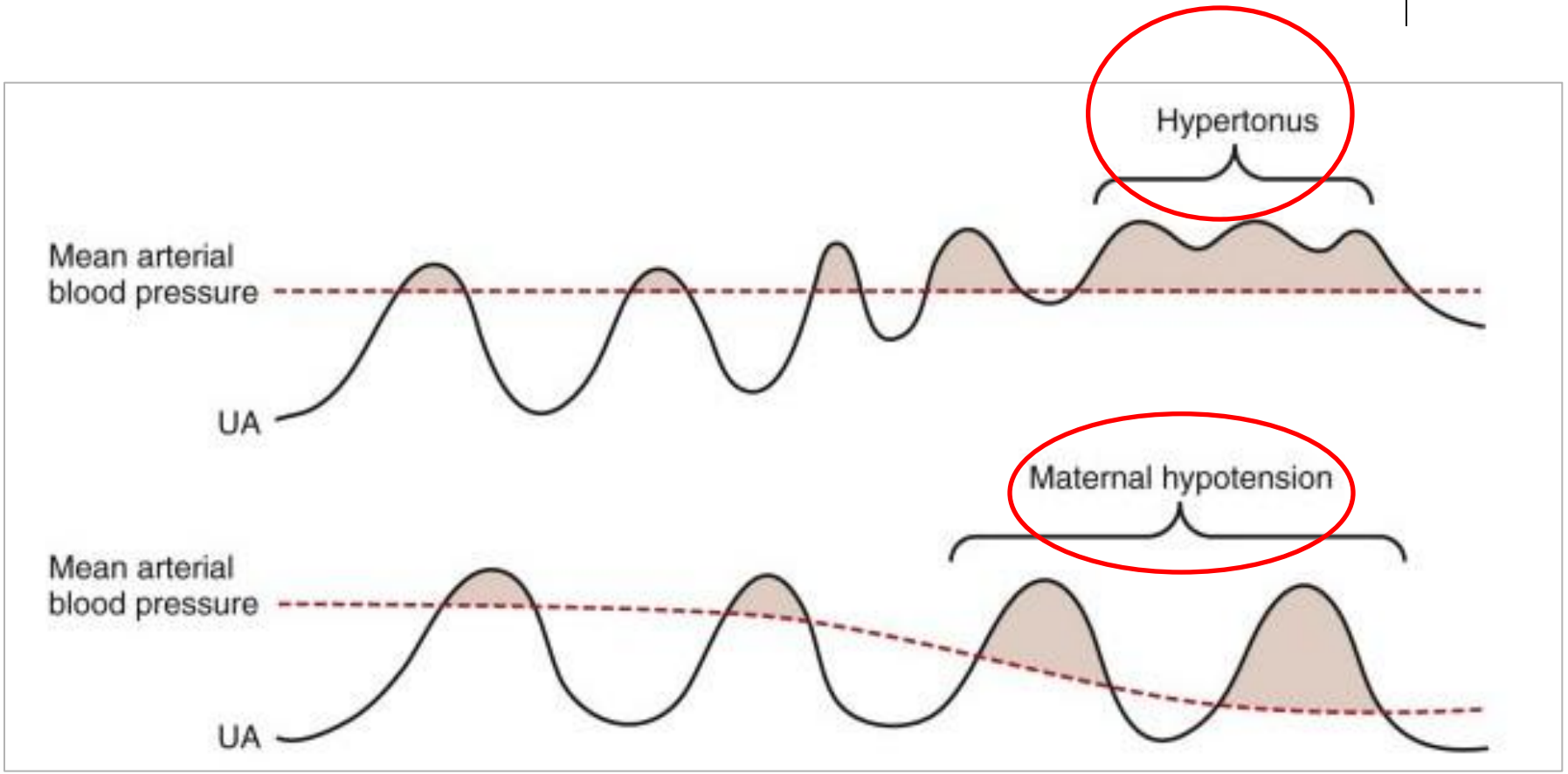




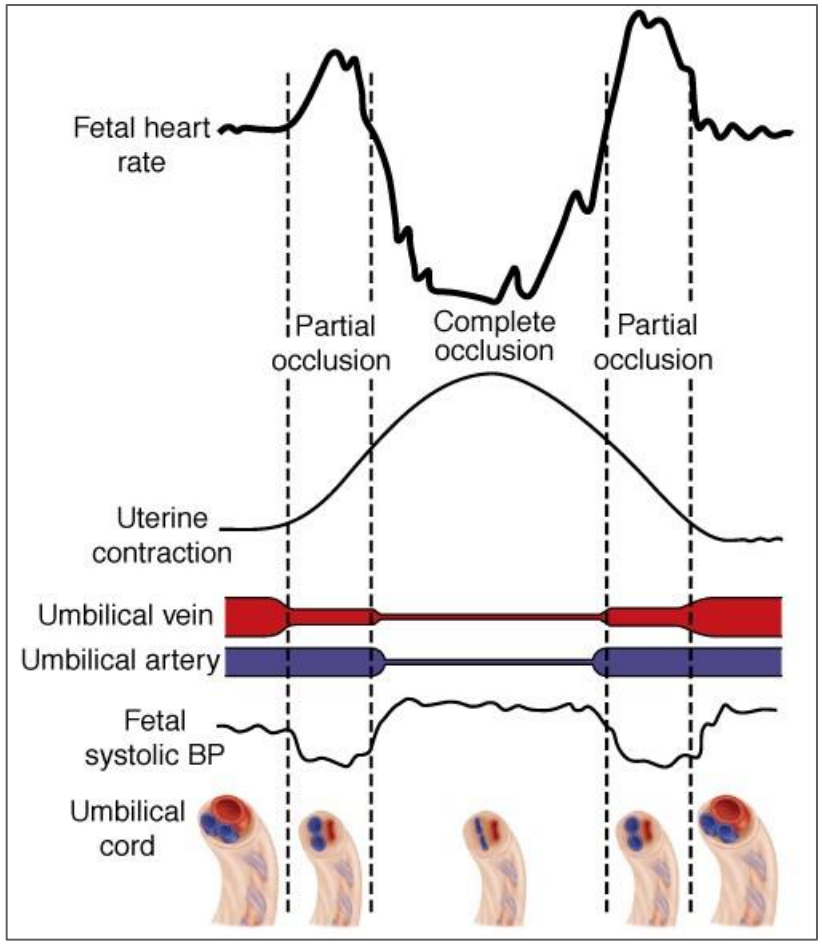
자궁태반 부전-Late deceleration

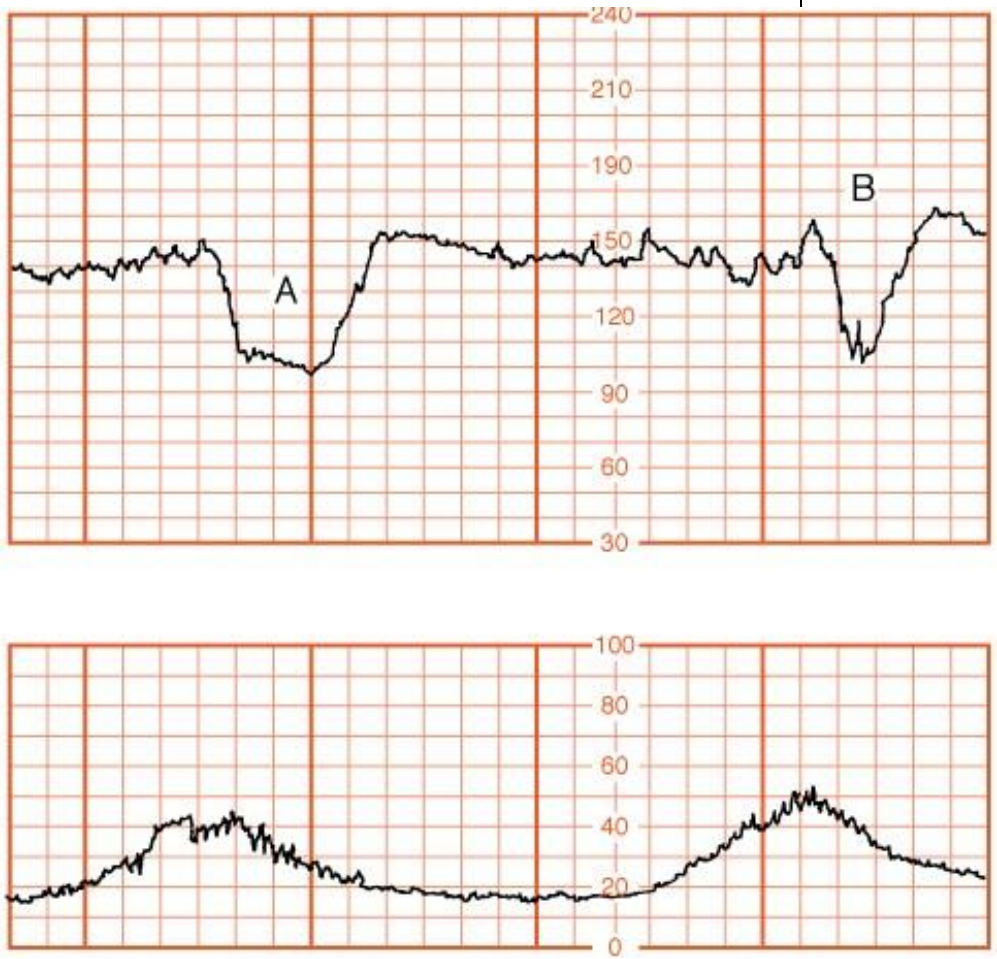


자궁태반 부전-Late deceleration



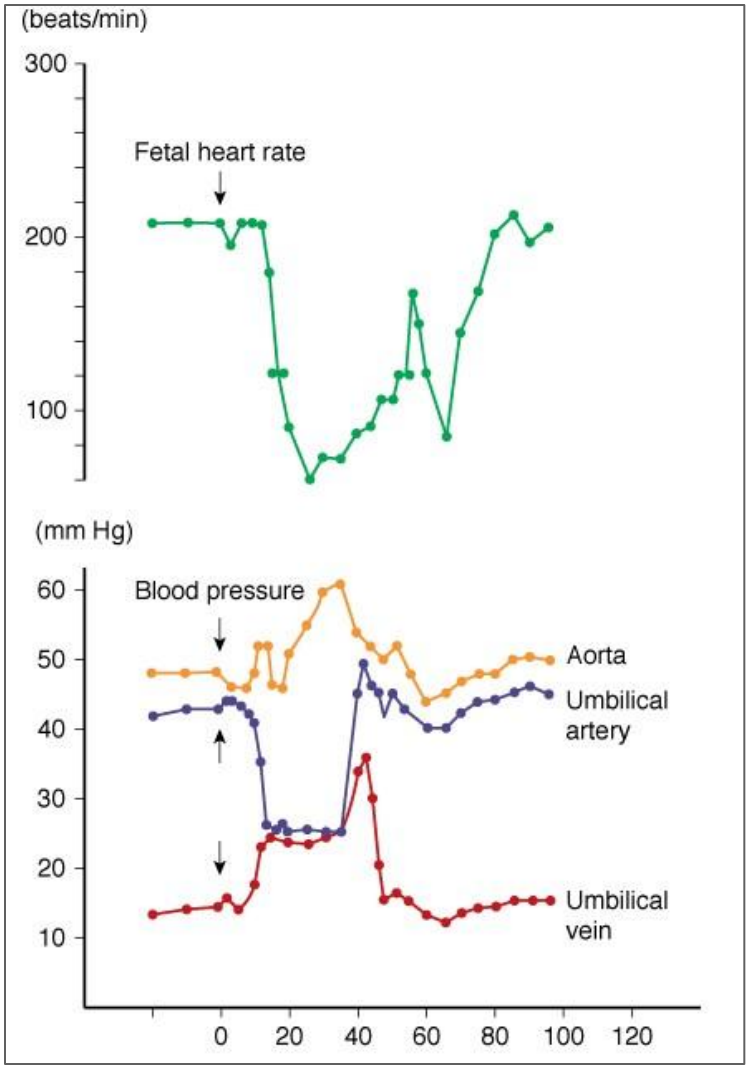
탯줄 눌림-Variable deceleration





Lee et al. Obstet Gynecol. 1975

탯줄 눌림-Variable deceleration



- Experimental evidence: fetal sheep

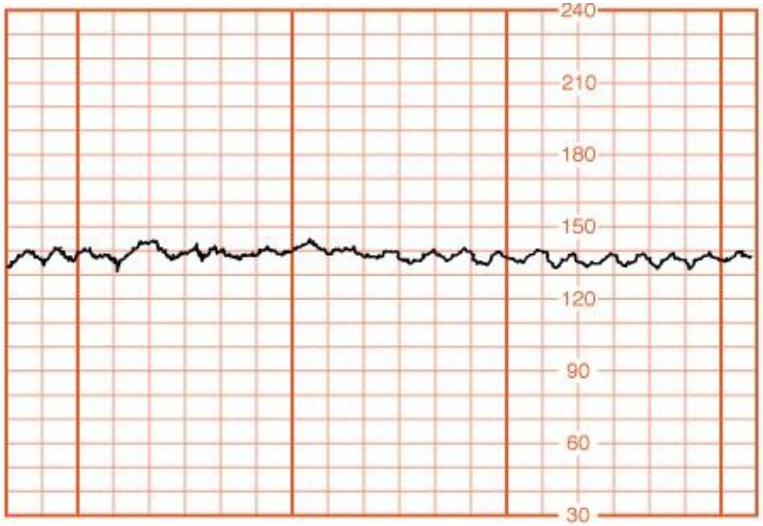
✓ Partial occlusion of umbilical cord, 1 min every 3 min:

-Brain damage only after 2 hours

✓ Total occlusion of umbilical cord, 1min every 5 min:

-No significant acidemia after 4hours.

태아빈혈-Sinusoidal fetal heart rates



- Severe fetal anemia
  - Rh-D isoimmunization
  - Feto-maternal hemorrhage
  - TTTS
  - Vasa previa with bleeding

- Definition(NICHD)

-Having a visually apparent, smooth, sine wave-like undulating pattern in FHR baseline with a cycle frequency of 3-5/min that persists for ≥ 20 minutes.

Summary

<1> Antenatal strategy to avoid neurodevelopmental disorder

1. 엽산, 복합비타민
2. 알코올: 절대 금주
3. 고열: 38.9 ℃ 이상 피하기
4. 갑상선 기능저하증 치료하기
5. 조산 예방 및 MgSO4
6. 약물 조절
7. 방사선 피하기
8. 중금속: 수은 피하기
9. 감염: 톡소플라즈마, CMV, 풍진, 수두, 성병 예방 및 치료
10. 태아 저산소증 피하기

Summary

<2> Strategy to avoid intrapartum injury

1. 전체 뇌성마비의 2-5%만이 진통 중 저산소증과 연관 있고, 대부분의 뇌성마비를 예방할 수 있는 single intervention은 알려져 있지 않다.
2. 태아 저산소증 피하기: 주의 깊은 태아 심박동 관찰-자궁태반 부전, 탯줄 눌림, 태아 빈혈 소견 등.

Thank you for your attention !