

2022 분당차병원 협력 의료기관 의사 온라인 연수강좌

| 일 시 | 2022년 11월 5일 (토) 14:00 ~ 18:30
온라인(webinar) 연수강좌, 대한의사협회 4평점

| 주 최 | 차의과학대학교 분당차병원 진료협력센터



CHA 의과학대학교
분당차병원

2022 분당차병원 협력 의료기관 의사 온라인 연수강좌

모시는 글

안녕하십니까.

어느새 3년째 우리 모두가 코로나19를 견디며 살아가고 있습니다. 이러한 상황에서도 현장에서 변함없이 진료에 최선을 다하시는 선생님들께 존경을 표하며 건강과 무궁한 발전을 기원합니다.

또한 분당차병원에 보내주신 아낌없는 성원에 감사드립니다. 분당차병원 진료협력센터에서는 협력 병·의원 선생님들의 진료와 경험에 조금이라도 보탬이 되고자 다가오는 11월에 연수강좌를 준비했습니다. 폭넓고 알찬 프로그램으로 정성껏 준비한 이 행사에 여러 선생님들을 정중히 모시고자 합니다.

이번 연수강좌는 진료현장에서 자주 접하지만 진단적 접근이 까다로운 질환들에 대해 실질적인 도움이 되실 수 있는 다양한 내용으로 준비하였습니다.

토요일 오후, 협력 병·의원 선생님들의 귀한 시간을 허락하여 주신 것에 미리 감사드리며, 앞으로도 다양하고 유익한 주제의 연수강좌로 협력 병·의원 선생님들께 도움이 될 수 있도록 계속 노력하겠습니다.

2022년 11월

차의과학대학교 분당차병원
진료협력센터장 장수진 拜上



2022 분당차병원 협력의료기관 의사 온라인 연수강좌



PROGRAM

14:00-14:15	온라인 등록(입장)	
14:15-14:20	인사말	분당차병원 진료부원장
14:20-16:20	Session I	
14:20-14:50(30분)	우리 삶과 함께하는 우울과 불안 다루기	방민지 교수 (정신건강의학과)..... 4
14:50-15:20(30분)	고혈압, 당뇨, 투석, 부정맥 환자들이 알아야 하는 흔한 신경계 문제	신승훈 교수 (신경외과) 12
15:20-15:50(30분)	흔한 피부 습진, 어떻게 감별하고 치료할까?	신정우 교수 (피부과) 38
15:50-16:20(30분)	소아청소년기 사춘기 평가 및 성조숙증 환자 접근 관리 방법	최윤하 교수 (소아청소년과) 53
16:20-16:30(10분)	Break time	휴식시간
16:30-18:30	Session II	
16:30-17:00(30분)	개원가에서 흔히 접하는 갑상선 기능 이상 환자의 접근과 치료	송영신 교수 (내분비내과) 60
17:00-17:30(30분)	유방 병변의 초음파 진단과 치료 권고에 관한 A to Z	박아영 교수 (영상의학과) 73
17:30-18:00(30분)	개원가에서 시행할 수 있는 배란유도제 사용 및 배란 초음파 보기	신소연 교수 (난임센터)..... 83
18:00-18:30(30분)	성인 예방접종 : 폐렴사슬알균, 대상포진, 파상풍-디프테리아-백일해	이채령 교수 (감염내과)..... 91
18:30-18:40	폐회	장수진 교수 (진료협력센터소장)

2022 분당차병원

협력의료기관 의사 온라인 연수강좌



Session I

14:20-14:50

우리 삶과 함께하는 우울과 불안 다루기

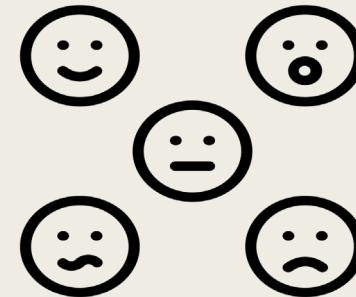
차의과학대학교 분당차병원 정신건강의학과

방민지 교수

우리 삶과 함께하는 우울과 불안 다루기

차의과학대학교 분당차병원
정신건강의학과
방민지

감정이란?



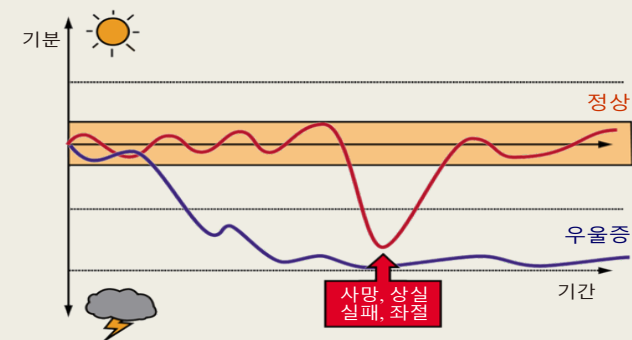
주관적 경험 + 생리적 반응 + 행동 표현으로 구성되는 복합적 현상

병적 우울과 병적 불안



어디까지가 정상이고 어디부터가 병적일까?

우울한 기분과 우울증?



정신의학에서 이야기하는 우울한 상태란?

- Mood – subjective, sustained, pervasive
- 일시적으로 기분만 저하된 상태를 뜻하는 것이 아니라 사고의 형태나 흐름, 사고의 내용, 동기, 의욕, 관심, 행동, 수면, 신체활동 등 전반적인 정신기능이 저하된 상태
- 병으로 진단하기 위해서는 증상이 사회적, 직업적 또는 다른 중요한 기능 영역에서 임상적으로 현저한 고통이나 손상을 초래해야 함.

우울증의 역학

- 주요우울장애
 - 한국 성인의 평생유병률은 3.3~5.6%, 시점유병률은 2% 안팎
 - 여자에서 2배 정도 많이 발생
 - 여성호르몬?
 - 더 많은 사회문화적 스트레스, 제한적인 대처전략 등
 - 남성의 경우 알코올 사용이 우울증을 가리기도 함.

우울증의 진단

■ 주요우울장애의 DSM-5 진단기준

A. 다음의 증상 가운데 5개(또는 그 이상)의 증상이 2주 연속으로 지속되며 이전의 기능 상태와 비교할 때 변화를 보이는 경우, 증상 가운데 적어도 하나는 (1) 우울 기분이거나 (2) 흥미나 즐거움의 상실이어야 한다.
주의점: 명백한 다른 의학적 상태로 인한 증상은 포함되지 않아야 한다.

1. 하루 중 대부분 그리고 거의 매일 지속되는 우울 기분(예: 슬픔, 공허감 또는 절망감)하거나 객관적으로 관찰됨(예: 눈물 흘림) (주의점: 아동, 청소년의 경우는 과민한 기분이 나타날 수도 있음)
2. 거의 매일, 하루 중 대부분, 거의 또는 모든 일상 활동에 대해 흥미나 즐거움이 뚜렷하게 저하됨
3. 체중 조절을 하고 있지 않은 상태에서 의미 있는 체중의 감소(예: 1개월 동안 5% 이상의 체중 변화)나 체중의 증가, 거의 매일 나타나는 식욕의 감소나 증가가 있음(주의점: 아동에서는 체중 증가가 기대치에 미달되는 경우)
4. 거의 매일 나타나는 불면이나 과다수면
5. 거의 매일 나타나는 정신운동 속도나 지연(객관적으로 관찰 가능함, 단지 주관적인 좌불안석 또는 처지는 느낌뿐만이 아님)
6. 거의 매일 나타나는 피로나 활력의 상실
7. 거의 매일 무기력함 또는 과도하거나 부적절한 죄책감(망상적일 수도 있음)을 느낌(단순히 병이 있다는 데 대한 자책이나 죄책감이 아님)
8. 거의 매일 나타나는 사고력이나 집중력의 감소 또는 유유부단함(주관적인 호소나 객관적인 관찰 가능함)
9. 반복적인 죽음에 대한 생각(단지 죽음에 대한 두려움이 아닌), 구체적인 계획 없이 반복되는 자살 사고, 또는 자살 시도나 자살 수행에 대한 구체적인 계획

우울증의 진단



우울증의 진단



우울증의 진단

■ 주요우울장애의 DSM-5 진단기준

B. 증상이 사회적, 직업적 또는 다른 중요한 기능 영역에서 임상적으로 현저한 고통이나 손상을 초래한다.

C. 삽화가 물질의 생리적 효과나 다른 의학적 상태로 인한 것이 아니다.

주의점: 진단기준 A부터 C까지는 주요우울 삽화를 구성하고 있다.

주의점: 중요한 삽화에: 사별, 재정적 파탄, 자연재해로 인한 상실, 심각한 질병이나 장애에 대한 반응으로 진단기준 A에 기술된 극도의 슬픔, 상실에 대한 반추, 불면, 식욕 저하, 그리고 체중의 감소가 나타날 수 있고 이는 우울 삽화와 유사하다. 비록 그러한 증상이 이해될 만하고 상실에 대해 적절하다고 판단된다 할지라도 정상적인 상실 반응 동안에 주요우울 삽화가 존재한다면 이는 주의 깊게 다루어져야 한다. 이러한 결정을 하기 위해서는 개인의 과거력과 상실의 고통을 표현하는 각 문화적 특징을 근거로 한 임상적인 판단이 필요하다.

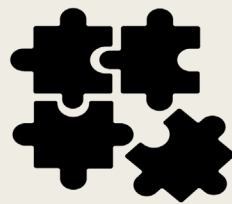
D. 주요우울 삽화가 조현정동장애, 조현병, 조현양상장애, 망상장애, 달리 명시된, 또는 명시되지 않는 조현병 스펙트럼 및 기타 정신병적 장애로 더 잘 설명되지 않는다.

E. 조증 삽화 혹은 경조증 삽화가 존재한 적이 없다.

우울증의 진단

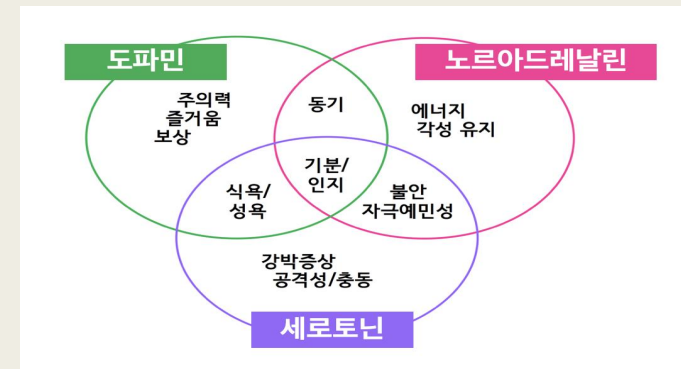


늘 해오던 일이
벅차게 느껴진다.

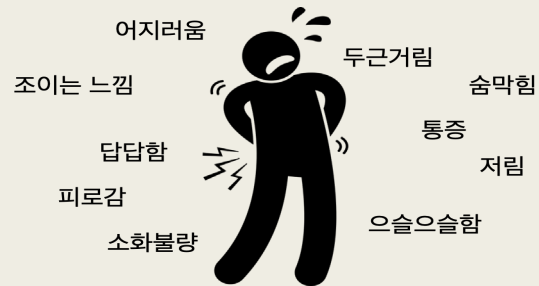


대인관계나 직업적 기능에
자꾸 문제가 발생한다.

우울증은 뇌의 변화



뇌와 몸의 연결고리



우울증은 마음만 힘들게 하는 것이 아니라,
우리의 몸에도 변화를 가져온다.

우울증의 치료



항우울제를 통한
약물치료



면담을 통한
정신치료



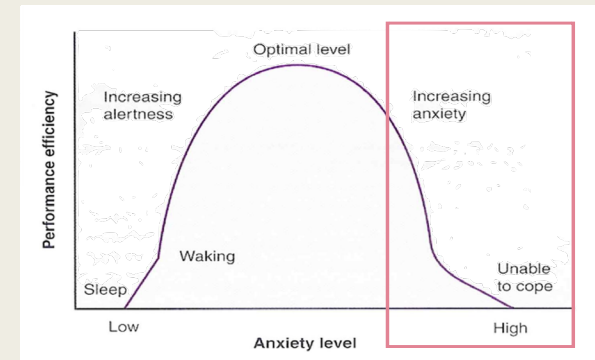
인지행동치료, TMS 등
기타 비약물적 치료

정상 불안?



위험에 대한 경고 신호로서 일어나는 정상적인 감정으로,
불쾌하고 모호한 두려움과 각종 자율신경계통의 과민 증상을 동반함.

병적불안



불안의 신체반응



공황장애와 공황발작

- 공황장애 ≠ 공황발작
- 공황발작: 갑작스럽게 심한 공포나 불편함이 수분 내 최고조에 이르고, 그 시간 동안 일련의 신체적 및 정신적 증상이 나타나는 것
- 공황장애: 반복적으로 나타나는 예상치 못한 공황발작 + 예기불안 + 회피 행동

공황장애와 공황발작

- 공황발작의 평생유병률: 약 23.5%
- 공황장애의 평생유병률: 약 4.8%
- 여자가 남자보다 2~3배 많으며 평균 발병 연령은 25세

공황장애의 진단

■ 공황장애의 DSM-5 진단기준

- A. 반복적으로 예상하지 못한 공황발작이 있다. 공황발작은 극심한 공포와 고통이 갑작스럽게 발생하여 수분 이내에 최고조에 이르러야 하며, 그 시간 동안 다음 중 4가지 이상의 증상이 나타난다.
- 주의점: 갑작스러운 증상의 발생은 차분한 상태나 불안한 상태에서 모두 나타날 수 있다.
1. 심계항진, 가슴 두근거림 또는 심장 박동수의 증가
 2. 발한
 3. 몸이 떨리거나 후들거림
 4. 숨이 가쁘거나 답답한 느낌
 5. 실신할 것 같은 느낌
 6. 흉통 또는 가슴 불편감
 7. 메스꺼움 또는 복부 불편감
 8. 어지럽거나 불안정하거나 명한 느낌이 들거나 쓰러질 것 같은
 9. 출거나 화끈거리는 느낌
 10. 감각이상(감각이 둔해지거나 따끔거리는 느낌)
 11. 비현실감(현실이 아닌 것 같은 느낌) 혹은 이인증(나에게서 분리된 느낌)
 12. 스스로 통제할 수 없거나 미칠 것 같은 두려움
 13. 죽을 것 같은 공포

공황장애의 진단

■ 공황장애의 DSM-5 진단기준

- B. 적어도 1회 이상의 발작 이후에 1개월 이상 다음 중 한 가지 이상의 조건을 만족해야 한다.
1. 추가적인 공황발작이나 그에 대한 결과(예: 통제를 잃음, 심장발작을 일으킴, 미치는 것에 대한 지속적인 걱정)
 2. 발작과 관련된 행동으로 현저하게 부적응적인 변화가 일어난다(예: 공황발작을 회피하기 위한 행동으로 운동이나 익숙하지 않은 환경을 피하는 것 등).
- C. 장애는 물질(예: 남용약물, 치료약물)의 생리적 효과나 다른 의학적 상태(예: 갑상선기능항진증, 심폐 질환)로 인한 것이 아니다.
- D. 장애가 다른 정신질환으로 더 잘 설명되지 않는다(예: 사회불안장애에서처럼 공포스러운 사회적 상황에서만 발작이 일어나서는 안 된다. 특정공포증에서처럼 공포 대상이나 상황에서만 나타나는는 안 된다. 강박장애에서처럼 강박 사고에 의해 나타나서는 안 된다. 외상후 스트레스 장애에서처럼 외상 사건에 대한 기억에만 관련되어서는 안 된다. 분리불안장애에서처럼 애착 대상과의 분리에 의한 것이어서는 안 된다).

공황장애의 진단

- 증상만으로는 신체질환과 공황장애를 구분하기 어렵고 동반된 경우도 다반사
 - 심장질환자의 약 1/3 -> 공황장애
 - 공황장애 환자의 약 21% -> 심장질환

표 12-2. 공황장애의 내외과적 감별질환

공황발작을 유발할 수 있는 약물	공황발작과 감별해야 할 내과적 질환
카페인(cafeine)	내분비질환
코카인(cocaine)	갑상선 기능항진증/기능저하증
메트암페타민(methamphetamine)	부갑상선기능항진증
테오필린(theophylline)	크롬친화세포종
기관지확장제(bronchodilator)	호흡기질환
콜레스티라지(cholestyramine)	천식
티록신(thyroxine)	만성폐쇄성호흡기질환
L-도파(L-dopa)	전정기능 이상
플루마제닐(flumazenil)	현기증
요항빈(yohimbine)	메니에르병
이소프로테레놀(isoproterenol)	심혈관계 질환
	특발성 심근병증
	심부전
	심신신경계 질환
	알코올 금단
	괴혈증
	두통
	위장관계 질환
	소화성궤양
	과민성대장증후군
	글루탐산노도나트륨 과민성

범불안장애의 진단

■ 범불안장애의 DSM-5 진단기준

- A. 직장이나 학업과 같은 수많은 일상 활동에 대한 과도한 불안과 걱정(염려)이 최소한 6개월 이상의 기간 중 안 그런 날보다 더 많은 날 동안 지속된다.
- B. 개인은 이런 걱정을 조절하기가 어렵다.
- C. 불안과 걱정은 다음의 6가지 증상 중 적어도 3가지 이상의 증상과 관련이 있다(지난 6개월 동안 적어도 몇 가지 증상이 있는 날이 없는 날보다 더 많다).
1. 안전부적 못하거나 긴장, 초조하고 신경이 곤두선 느낌
 2. 쉽게 피로해짐
 3. 집중하기가 어렵고 멍한 느낌
 4. 짜증이 잘 남
 5. 근육의 긴장
 6. 수면장애(잠이 들기 어렵거나 또는 유자가 어렵고 밤새 뒤척이면서 만족스럽지 못한 수면상태)
- D. 불안, 걱정 또는 신체적 증상들이 사회적, 직업적, 또는 다른 중요한 기능에 있어 임상적으로 유의한 고통 또는 장애를 일으킨다.
- E. 본 장애가 물질(예: 남용약물, 처방약물)이나 일반적인 질병(예: 갑상선 기능항진증)의 직접적인 생리적 영향 때문에 발생한 것이 아니다.
- F. 본 장애는 다른 정신 장애(예: 공황장애에서의 공황발작, 사회불안장애(사회공포증)에서의 부정적 평가, 강박장애에서의 오염이나 다른 강박사고, 분리불안장애에서의 애착된 사람과의 이별, 외상후스트레스장애에서의 외상 사건의 기억, 신경성 식욕부진증에서의 체중 증가, 신체증상장애에서의 신체적 증상, 신체이형장애에서 지각하는 외모의 결점, 질병불안장애에서 심각한 질병을 갖고 있다는 것, 조현병이나 망상장애에서의 망상적 믿음의 내용 등)과 관계된 불안이나 걱정)로 더 잘 설명되지 않는다.

신체증상 관련 질환들

■ 신체증상장애의 DSM-5 진단기준

- A. 고통스럽거나 일상에 중대한 지장을 일으키는 하나 이상의 신체 증상이다.
- B. 신체 증상 혹은 건강염려와 관련된 과도한 생각, 느낌 또는 행동이 다음 중 하나 이상으로 표현되어 나타난다.
1. 증상의 심각성에 대해 변증되고 지속적인 생각
 2. 건강이나 증상에 대한 지속적으로 높은 단계의 불안
 3. 이러한 증상을 또는 건강염려에 대해서 과도한 시간과 에너지 소비
- C. 어떠한 하나의 신체 증상이 지속적으로 나타나지 않더라도 증상이 있는 상태가 지속된다(전형적으로 6개월 이상).
- 다음의 경우 명시할 것:
- 통증이 우세한 경우(과거, 동통장애): 이 명시자는 신체 증상이 통증으로 우세하게 나타난다.
- 다음의 경우 명시할 것:
- 지속성: 지속적인 경과가 극심한 증상, 현저한 손상, 그리고 긴 기간(6개월 이상)으로 특징지어진다.
- 현재의 심각도를 명시할 것:
- 경도: 진단기준 B의 구체적인 증상들이 단 한 가지만 만족한다.
- 중등도: 진단기준 B의 구체적인 증상들이 2가지 이상 만족한다.
- 고도: 진단기준 B의 구체적인 증상들이 2가지 이상 만족하고, 여러 가지 신체적 증상(또는 하나의 매우 심한 신체 증상)이 있다.

신체증상 관련 질환들

■ 질병불안장애의 DSM-5 진단기준

- A. 심각한 질병에 걸려 있거나 걸리는 것에 대해 몰두한다.
 B. 신체 증상들이 나타나지 않거나, 신체 증상이 있더라도 단지 경도 정도다. 다른 의학적 상태가 나타나거나 의학적 상태가 악화될 고위험(예: 강한 가족력 이 있음)이 있을 경우, 병에 대한 몰두가 분명히 지나치거나 부적절하다.
 C. 건강에 대한 높은 수준의 불안이 있으며, 건강 상태에 대해 쉽게 걱정을 가진다.
 D. 지나친 건강 관련 행동(예: 반복적으로 질병의 신체 징후를 확인함)을 보이거나 순응도가 떨어지는 회피 행동(예: 의사 예약과 병원을 회피함)을 보인다.
 E. 질병에 대한 몰두는 적어도 6개월 이상 지속되지만, 그 기간 동안 두려움을 느끼는 구체적인 질병은 변화할 수 있다.
 F. 질병에 대해 몰두하는 것이 다른 정신질환, 즉 신체증상장애, 공황장애, 범불안장애, 신체이형장애, 강박장애 또는 신체형 망상장애 등으로 더 잘 설명되지 않는다.
 다음 중 하나를 명시할 것:
 진료추구형: 양진 또는 검사와 시술을 진행하는 것을 포함하여 의학적 치료를 자주 이용한다.
 진료회피형: 의학적 치료를 거의 이용하지 않는다.

불안장애는 생각의 병



불안은 없애는 것이 아니라 조절하는 것!
 불안을 어떻게 이해하고 받아들이는 것이 중요합니다.

불안장애의 치료



항우울제, 항불안제를 통한
약물치료



인지행동치료

불안장애의 치료



2022 분당차병원

협력의료기관 의사 온라인 연수강좌



Session I

14:50-15:20

고혈압, 당뇨, 투석, 부정맥 환자들이 알아야 하는 흔한 신경계 문제

차의과학대학교 분당차병원 신경외과

신승훈 교수

2022 11 05

2022년 차의과학대학교 분당차병원 협력 병의원 의사 온라인(webinar) 연수강좌

고혈압, 당뇨, 투석, 부정맥 환자들이 알아야하는 흔한 신경계 문제

신승훈,

차의과학대학교 분당차병원 뇌혈관센터
신경외과

Contents

- 뇌혈관질환의 분류
- Relationship:
 - HTN, DM, Arrhythmia, CKD, metabolic syndrome & Stroke
- 각론
 - ICH, Cerebral infarction
 - 1차 & 2차 예방: Control of HTN, DM, Arrhythmia ..
 - 급성기 치료
- Messages

뇌혈관질환 (Cerebrovascular disease)

증상이 발생한 뇌혈관질환 = 뇌졸중 (Stroke)

=> 응급 뇌혈관질환

무증상 뇌혈관질환

허혈성

급성 뇌경색
- LVO
- Non-LVO

Arrhythmia
Large artery
atherosclerosis
Small vessel
disease
Others

혈관박리
(Intra &
Extracranial)
모야모야병
뇌정맥혈전증
(CSVT)

출혈성

뇌내 출혈
지주막하 출혈
출혈된 해면상혈관종
뇌동정맥루 파열
혈관박리
경막하 혈종

허혈성

뇌혈관협착증
경동맥협착증
주골동맥협착증
혈관박리

허혈 + 출혈

모야모야병

출혈성

미파열 뇌동맥류
미파열 해면상혈관종
미파열 뇌동정맥기형

뇌혈관질환 (Cerebrovascular disease)

증상이 발생한 뇌혈관질환 = 뇌졸중 (Stroke)

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무증상 뇌혈관질환

허혈성

급성 뇌경색
- LVO
- Non-LVO

HTN

DM

Arrhythmia

CKD

뇌정맥혈전증
(CSVT)

출혈성

지주막하 출혈
출혈된 해면상혈관종
뇌동정맥루 파열
혈관박리
경막하 혈종

허혈성

뇌혈관협착증
경동맥협착증
주골동맥협착증
혈관박리

허혈 + 출혈

모야모야병

출혈성

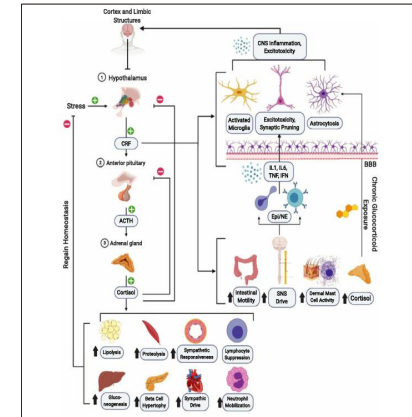
미파열 뇌동맥류
미파열 해면상혈관종
미파열 뇌동정맥기형

Risk factors of Neurovascular Disease & Stroke

- Cardiac
 - Hypertension
 - Arrhythmia
- Endocrinology
 - DM
 - Metabolic syndrome (obesity, hypercholesterolemia)
- Chronic kidney disease
- Age
- Medication

Corticotropin-Releasing factor (CRF) and Stress metabolism – Hypothalamic-Pituitary-Adrenal (HPA) Axis

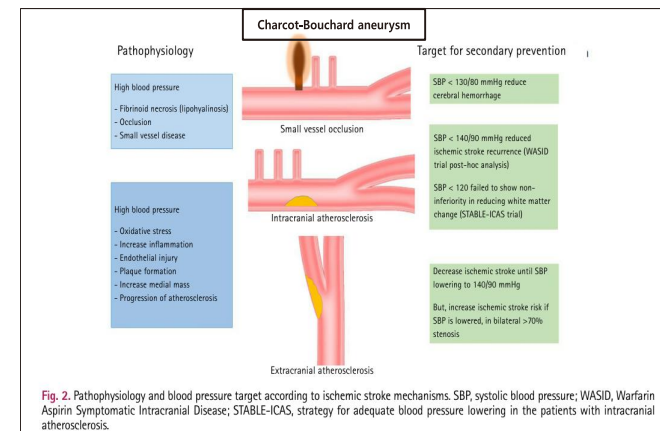
- Common phenomenon presented in the early acute stroke phase
- Stroke
 - Trigger generalized stress reaction involving the activation of the **hypothalamic-pituitary-adrenal axis**
 - Subsequently leads to
 - Increased levels of serum glucocorticoids
 - Activation of the sympathetic autonomic nervous system
 - Increased **cortisol, growth hormones, glucagon, and catecholamine** release
 - Increased levels of stress hormones
 - raise rates of aerobic glycolysis,
 - promote glucose release from gluconeogenesis and glycogenolysis,
 - inhibit insulin-mediated glycogenesis
 - Increase lactic acid, Neuronal damage



Hypertension

- Commonest contributing factor to primary ICH, cerebral infarction
- 3-4 fold
- Alcohol, diabetes, male sex, low cholesterol

BP & Stroke



Intracerebral hemorrhage - Hypertensive

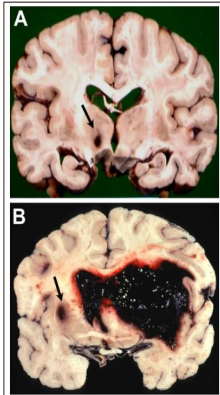


Fig. 1. (A) Asymptomatic intracerebral hemorrhage (arrow) localized to the left thalamus, not involving the internal capsule. (B) Massive, fatal putamenal hemorrhage with intraventricular extension, delineating the opposite end of the clinical spectrum. The satellite hemorrhage (arrow) in the basal ganglia resembles the asymptomatic hemorrhage (A).

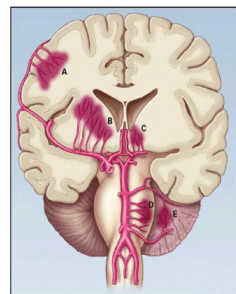
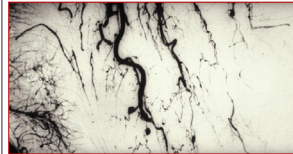


Fig. 6. Drawing showing the reason for the standard locations (A-E) of intracerebral hemorrhages, proximity to high pressure arteries in the face of arteriosclerotic disease. A, lobar; B, basal ganglia; C, thalamic; D, pontine; E, cerebellar hemorrhage. Reproduced with permission from Qureshi, Ali, Tahir, S, Broderick, J.P., Berger, H.H., Hondo, H., Hanley, D.F. Spontaneous intracerebral hemorrhage. N Engl J Med 2001;344:1450-60.

Charcot-Bouchard aneurysm



- Collagenized sacs of arterioles due to hypertensive vascular pathology
- Perforating A.: near High-pressure parent a.

Second brain injury – Hypertensive ICH

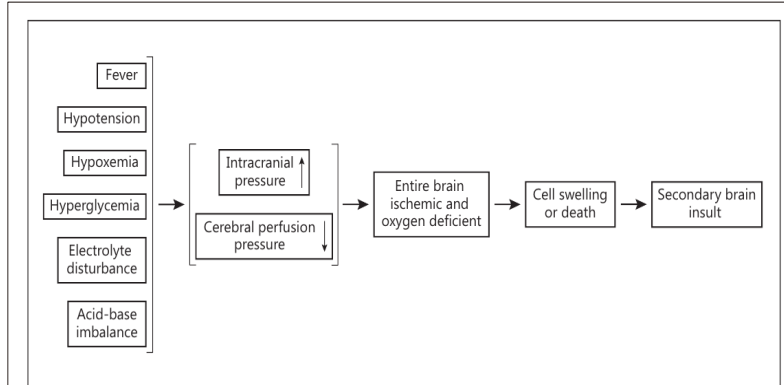


Fig. 1. Pathogenesis of secondary brain insult of hypertensive intracerebral hemorrhage.

Amyloid angiopathy

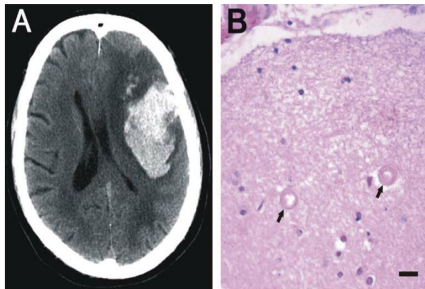


Fig. 2. CT scan showing hemorrhage in the left insula (A), associated with considerable left to right brain shift, secondary to amyloid angiopathy. Microscopy (B) reveals two cortical arterioles (arrows) that are acellular due to amyloid deposition. Bar (B) = 50 μ m.

Diabetes Mellitus

- Causes various microvascular and macrovascular changes, resulting in complications
- Susceptible to the consequences of cerebral small vessel diseases
- Hyperglycemia
 - Stroke occurrence
 - Poor clinical outcomes (higher mortality)

DM & Stroke

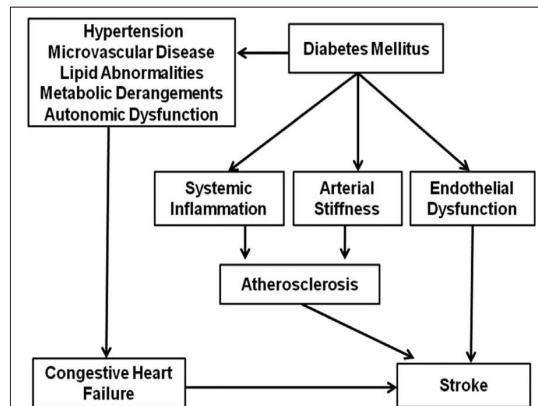


FIGURE 1.
Possible mechanisms of stroke in individuals with diabetes.

DM role in ischemic stroke

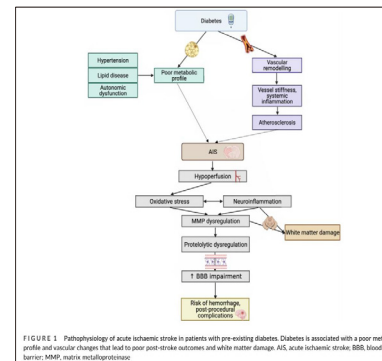


FIGURE 1 Pathophysiology of acute ischemic stroke in patients with pre-existing diabetes. Diabetes is associated with a poor metabolic profile and vascular changes that lead to poor post-stroke outcomes and white matter damage. AIS, acute ischemic stroke; BBB, blood-brain barrier; MMP, matrix metalloproteinase.

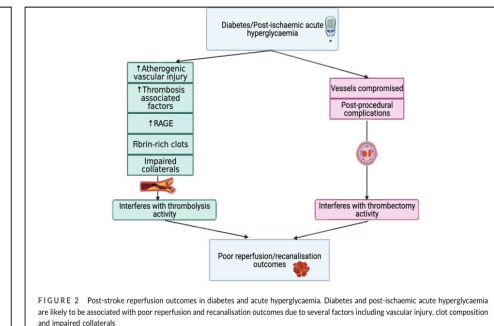


FIGURE 2 Post-stroke reperfusion outcomes in diabetes and acute hyperglycaemia. Diabetes and post-ischaemic acute hyperglycaemia are likely to be associated with poor reperfusion and recanalisation outcomes due to several factors including vascular injury, clot composition and impaired collaterals.

Antithrombotic Tx for secondary prevention of cardiovascular disease in diabetes

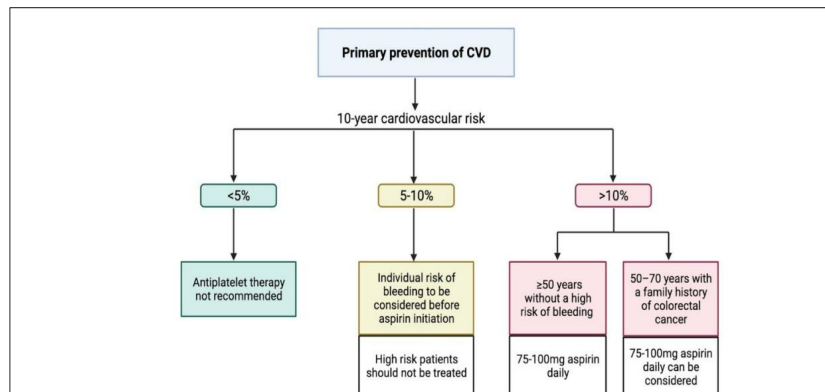


FIGURE 3 Antithrombotic therapies for primary prevention of cardiovascular disease in diabetes. Adapted from Patti et al.¹⁰⁶ CVD, cardiovascular disease.

Antithrombotic Tx for secondary prevention of cardiovascular disease in diabetes

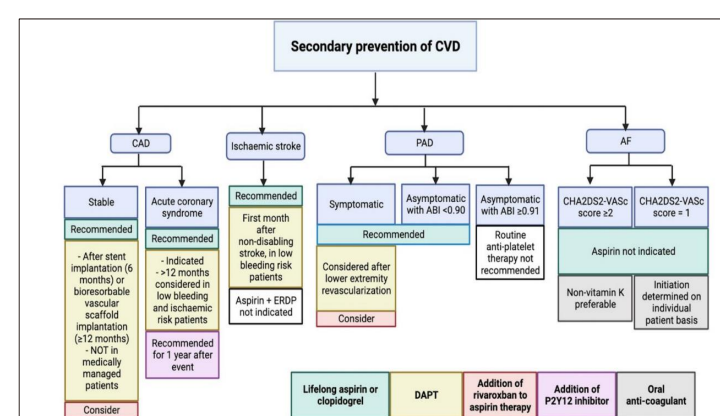


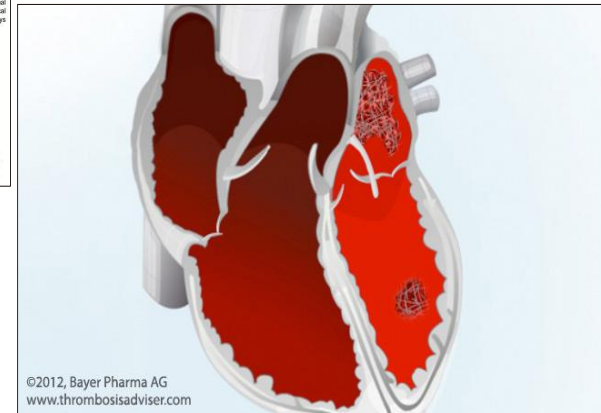
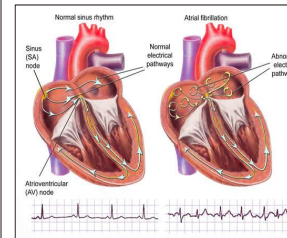
FIGURE 4 Antithrombotic therapies for secondary prevention of cardiovascular disease in diabetes. Adapted from Patti et al.¹⁰⁶ CVD, cardiovascular disease; DAPT, dual antiplatelet therapy; PAD, peripheral artery disease.

Arrhythmia

• Atrial fibrillation

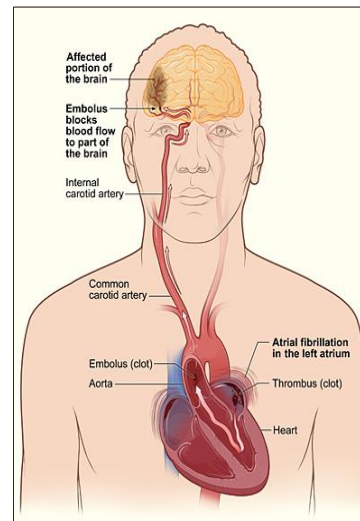
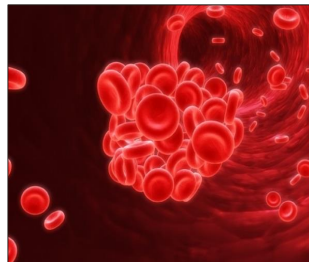
- mc cardiac arrhythmia
- Major cause of stroke, heart failure, sudden death, and cardiovascular morbidity
- mc preventable cause of cardioembolic stroke, accounting for 23.7% of all strokes

Atrial fibrillation

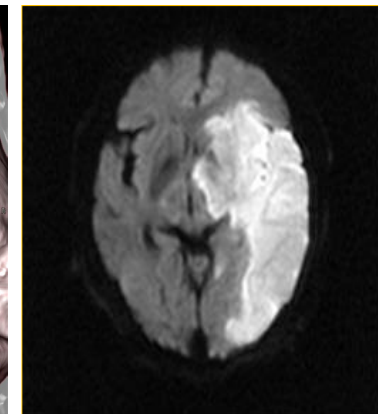
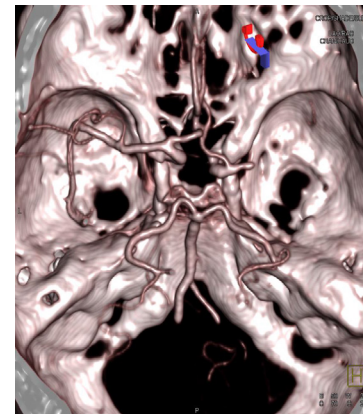


Mechanism of Stroke – nvAF

• Fibrin-rich clot



Emergent Large Vessel Occlusion(eLVO) - nvAF



Metabolic syndrome

- Hyperlipidemia
- Obesity

CKD

Table 1. Stroke subtypes and cerebral pathology in patients with kidney disease

	Effect of CKD	Effect of AKI	References
Ischemic stroke	↑	↑	[1, 5, 6, 24-36, 108, 109]
Hemorrhagic stroke	↑	↑	[18-22, 110]
Cerebral microbleeds	↑	Unknown	[20, 22, 111, 112]
SVD	↑	Unknown	[39-42, 113]

CKD, chronic kidney disease; AKI, acute kidney injury; SVD, small vessel disease.

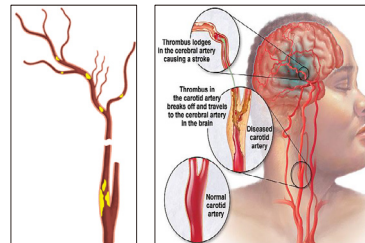
Table 2. Mechanisms whereby kidney disease can increase risk of stroke

Mechanism	Effect of CKD	Effect of AKI	References
Cerebral autoregulation	↓	Unknown	[57, 59]
Impaired CBF	↓	Unknown	[50, 55, 60, 65]
Rate of carotid atherosclerosis	↑	Unknown	[72-75]
Risk of AF	↑	↑	[108, 114]
Chronic platelet dysfunction	↑	↑	[1-3, 6, 115]
Cerebral oxygenation	↓	↓	[67-70, 116]

CKD, chronic kidney disease; AKI, acute kidney injury; CBF, cerebral blood flow; AF, atrial fibrillation.

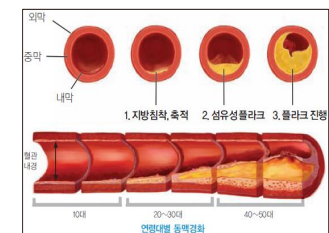
Phenotypes

- S-ICH
- Cerebral infarction
 - Occlusive
 - Large vessel occlusion
 - Non-large vessel occlusion
 - Small vessel disease
 - Large A atherosclerosis
 - Carotid A stenosis
 - Intracranial a stenosis
 - VA OS stenosis



I. Primary prevention – disease control

- HTN, DM, CKD, Metabolic syndrome – Atherosclerosis
 - Aggressive glucose control through lifestyle change or medications and modification of other associated risk factors (such as BP and dyslipidemia)
- Arrhythmia
- Asymptomatic
 - Intracranial stenosis
 - Carotid A stenosis
 - VA, Arch, Subclavian A stenosis



Primary & Secondary prevention –nv Atrial fibrillation

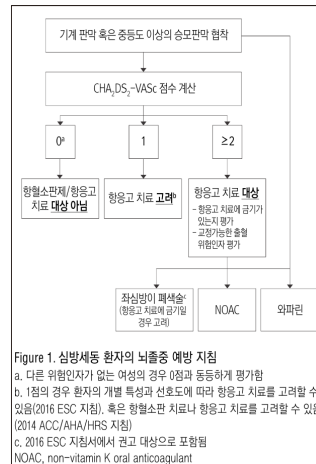
- Risk stratification
- Use of Oral anticoagulants

CHA₂DS₂-VASc score

위험인자	점수
심부전: 심부전에 의한 증상/징후가 있거나 또는 좌심실 구출률이 저하된 객관적인 증가가 있는 경우	+1
고혈압: 안정 시 적어도 2회 이상 측정된 혈압이 140/90 mmHg를 초과하거나 또는 현재 항고혈압 약제를 복용 중인 경우	+1
연령 75세 이상	+2
당뇨병: 공복혈당이 125 mg/dL (7 mmol/L)를 초과하거나 또는 경구 혈당강화제나 인슐린 제제로 치료 받고 있는 경우	+1
뇌졸중, 일과성 뇌허혈 발작(TIA), 혹은 전신 혈전색전증의 과거력	+2
혈관질환: 심근경색, 말초동맥질환 또는 대동맥 죽상판(plaque)의 과거력	+1
연령 65세 이상 74세 이하	+1
여성	+1
총점	9점

Stroke risk calculation & OACs

총점	%/y
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2



NOACs

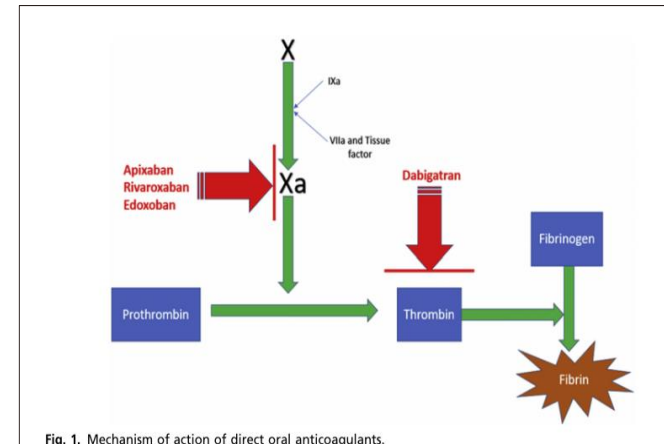


Table 2
Evidence table for the direct oral anticoagulants

	Dabigatran			Rivaroxaban		Apixaban		Edoxaban	
Trial, Year	RE-LY, ¹⁰ 2009			ROCKET AF, ¹¹ 2011		ARISTOTLE, ¹² 2011		ENGAGE AF-TIMI 48, ¹³ 2014	
Trial arms	Dabigatran 110 mg BD	Dabigatran 150 mg BD	Warfarin as per INR	Rivaroxaban 20 mg OD	Warfarin as per INR	Apixaban 5 mg BD	Warfarin as per INR	Edoxaban 30 mg OD	Warfarin as per INR
Number of patients	6015	6076	6022	7131	7133	9088	9052	7035	7036
Follow-up period (years)	2			1.9		1.8		2.8	
Age, years	71.5 ± 8.7 (Mean ± SD)			73 (65–78) [median (interquartile range)]		70 (65–76) [median (interquartile range)]		72 (64–78) [median (interquartile range)]	
Mean CHA ₂ DS ₂ -VASC	2.1			3.5		2.1		2.8	
	(Relative Risk, 95% CI)		% per Year	(Hazard Ratio, 95% CI)		% per Year	(Hazard Ratio, 95% CI)		% per Year
Stroke/systemic embolism	1.53% (0.91, 0.74–1.11)	1.11% (0.66, 0.53–0.82)	1.69%	2.1 (0.88, 0.75–1.03)	2.4%	1.27* (0.79, 0.66–0.95)	1.6%	1.57% (0.87, 0.73–1.04)	2.04% (1.13, 0.96–1.34)
Major bleeding	2.71%* (0.80, 0.69–0.93)	3.11% (0.93, 0.81–1.07)	3.36%	3.60% (1.04, 0.90–2.30; P = .58)	3.45%	2.13%* (0.69, 0.60–0.80)	3.09%	2.75%* (0.80, 0.71–0.91)	1.61%* (0.47, 0.41–0.55)
Intracerebral bleeding	0.23%* (0.31, 0.12–0.47)	0.30%* (0.42, 0.29–0.61)	0.74%	0.49%* (0.67, 0.47–0.93)	0.74%	0.33%* (0.42, 0.30–0.58)	0.8%	0.39%* (0.47, 0.34–0.63)	0.26%* (0.30, 0.21–0.43)
Death	3.75% (0.91, 0.80–1.03)	3.64% (0.88, 0.77–1.00)	4.13%	1.87% (0.85, 0.70–1.02)	2.21%	3.52%* (0.89, 0.80–0.99)	3.94%	3.99% (0.92, 0.83–1.01)	3.80% (0.87, 0.79–0.96)

Abbreviations: ARISTOTLE, Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation trial¹²; ENGAGE AF-TIMI 48, Effective Anticoagulation With Factor Xa Inhibitor in Atrial Fibrillation–Thrombolysis in Myocardial Infarction Study 48¹³; RE-LY, Randomized Evaluation of Long-Term Anticoagulation Therapy¹⁰; ROCKET AF, Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke And Embolism Trial in Atrial Fibrillation¹¹; SD, standard deviation; OD, once daily; BD, twice daily; INR, international normalized ratio.
* P value less than 0.05

Primary prevention - Atherosclerosis

- Use of Antiplatelets & Statin
- Surgical or Endovascular treatment

Carotid A stenosis

- Carotid A stenting
 - 무증상의 80% 이상 협착
 - 기타(증상 또는 협착의 정도와 상관없이 시행가능
 - Contralateral occlusion 을 동반한 50% stenosis
- Carotid endarterectomy 경동맥 내막절제술
 - 무증상의 70% 이상 협착
 - USA: 100,000/yr
 - South korea: 2,000/yr

Intracranial & Extracranial Vertebral A stenosis

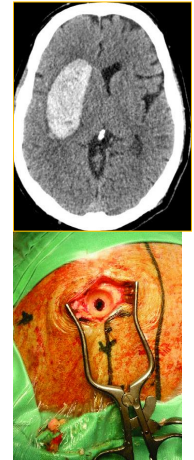
- 1차 예방에 관한 치료적응증 없음

II. 급성기 치료

- S-ICH
- Acute cerebral infarction
 - Large vessel occlusion
 - Non-large vessel occlusion

Spontaneous ICH

- Medical management
 - BP target: 130~ 150mmHg within 6h of symptom onset
 - To reduce hematoma expansion & mortality
 - ICP control with Mannitol
 - Reduce secondary brain injury
- Surgical treatment
 - Burr hole trephination & catheter insertion + Fibrinolytic irrigation
 - Navigation or Stereotactic-guide
 - Craniotomy & hematoma removal



고혈압성 뇌출혈

치료원칙 : 환자의 상태 및 출혈양에 따라 치료방법 결정

약물치료

정위적 혈종제거술
(Stereotactic, Navigation)

개두술 및 혈종제거술

Acute Cerebral infarction - presentation

- Large vessel **Acute** occlusion: 20-30%
 - ICA, MCA, VA, BA, PCA
- Small vessel occlusion (Lacune): 50-60%
- Cortical artery occlusion: < 20%
 - d/t carotid A, VA OS, Intracranial a stenosis
- Hypoperfusion infarction: <5%
 - severe carotid A stenosis

Acute Cerebral infarction – Treatment

- **IV rtPA (Actylase): ~ 10%**
 - Symptom onset <4.5hr
- **Mechanical thrombectomy (Endovascular): ~ 10%**
 - Symptom onset 4.5hr ~ 24hr
 - Symptom onset <4.5hr: Contraindication of IV rtPA
- **Conservative care**

Cerebral infarction (Ischemic Stroke)

- **TOAST classification**

TABLE 1. TOAST Classification of Subtypes of Acute Ischemic Stroke

Large-artery atherosclerosis (embolus/thrombosis)*

Cardioembolism (high-risk/medium-risk)*

Small-vessel occlusion (lacune)*

Stroke of other determined etiology*

Stroke of undetermined etiology

- a. Two or more causes identified
- b. Negative evaluation
- c. Incomplete evaluation

TOAST, Trial of Org 10172 in Acute Stroke Treatment.

*Possible or probable depending on results of ancillary studies.

TABLE 3. TOAST Classification of High- and Medium-Risk Sources of Cardioembolism

High-risk sources

- Mechanical prosthetic valve
- Mitral stenosis with atrial fibrillation
- Atrial fibrillation (other than lone atrial fibrillation)
- Left atrial/atrial appendage thrombus
- Sick sinus syndrome
- Recent myocardial infarction (<4 weeks)
- Left ventricular thrombus
- Dilated cardiomyopathy
- Akinetic left ventricular segment
- Atrial myxoma
- Infective endocarditis

Medium-risk sources

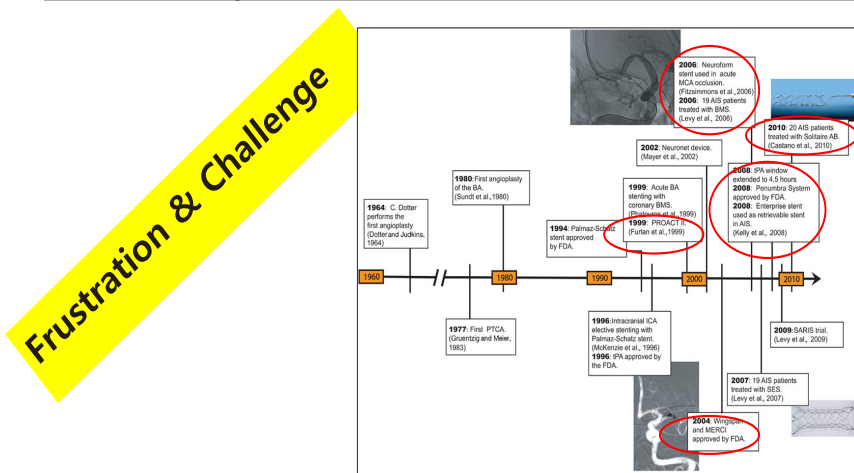
- Mitral valve prolapse
- Mitral annulus calcification
- Mitral stenosis without atrial fibrillation
- Left atrial turbulence (smoke)
- Atrial septal aneurysm
- Patent foramen ovale
- Atrial flutter
- Lone atrial fibrillation
- Bioprosthetic cardiac valve
- Nonbacterial thrombotic endocarditis
- Congestive heart failure
- Hypokinetic left ventricular segment
- Myocardial infarction (>4 weeks, <6 months)

TOAST, Trial of Org 10172 in Acute Stroke Treatment.

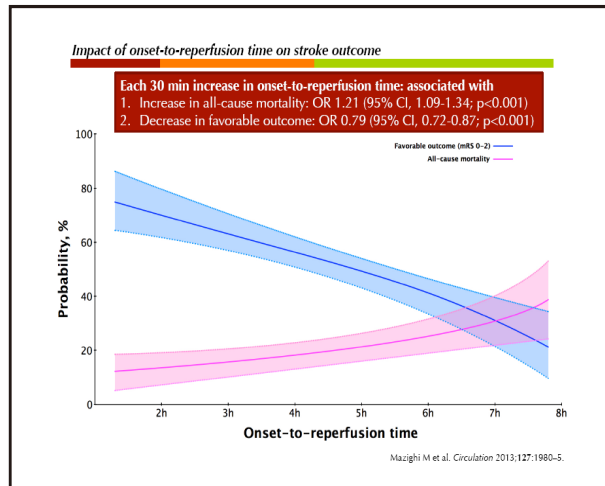
Cerebral infarction

- **Current Trends & Future Perspectives of Endovascular Treatment of Large Vessel Occlusion-Acute Ischemic Stroke (LVO-AIS)**

History of Endovascular Treatment for AIS



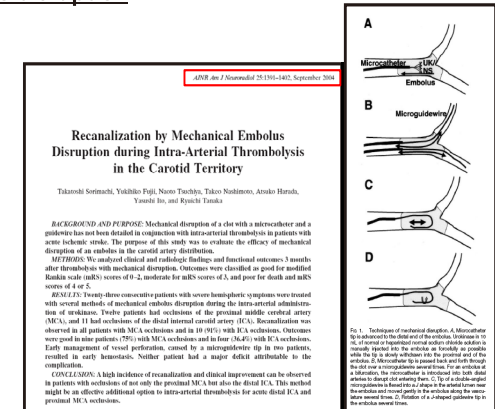
Reperfusion Time ~ Outcome



Failure of previous IA treatment in spite of angiographic recanalization

- IA UK thrombolysis with wire disruption

- 100% MCAO, 91% ICAO
- Good outcome
 - 75% MCAO
 - 36.4 ICAO



Distal embolization

Evidence for mechanical thrombectomy in 2013

- 3 randomized trials comparing IV t-PA to intra-arterial therapy published in NEJM 2013 **found no difference** in clinical outcomes:



The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL



Endovascular Treatment for Acute Ischemic Stroke — Still Unproven

Marc I. Chimowitz, M.B., Ch.B.

THE NEW ENGLAND JOURNAL of MEDICINE

Randomized Trial of Intravenous Tenecteplase for Acute Ischemic Stroke

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

Steno-Reverser Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

2015, SR Mechanical thrombectomy

5 Total Major Thrombectomy Trials Published in NEJM in 2015

	TICI 2b/3 rate	mRS 0-2 at 90 days	Death rate
MR CLEAN	59%	32.6% v. 19.1%	21% v 22%
ESCAPE	72%	53% v. 29%	10% v. 19%
EXTEND-IA	86%	71% v. 40%	9% v. 20%
SWIFT PRIME	88%	60% v. 36%	9% v. 12%
REVASCAT	66%	44% v 28%	18% v 16%

Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

Mayank Goyal, Bijoy K Menon, Wim H van Zwam, Diederik W J Dippel, Pieter J Mitchell, Andrew M Demchuk, Antoni Dávalos, Charles B L M Majole, Aad van der Lugt, Maria A de Miquel, Geoffrey A Dornan, Yvo BW EM Roos, Alain Bonafé, Reza Johari, Hans-Christoph Diener, Lucie A van den Berg, Eliad L Levy, Overt A Berkemer, Vitor M Pereira, Jeremy Rempel, Mónica Millán, Stephen M Davis, Daniel Roy, John Thornton, Luis San Roman, Marc Ribo, Debbie Beumer, Bruce Stouch, Scott Brown, Bruce CV Campbell, Robert J van Oostbrugge, Jeffrey L Saver, Michael D Hill, Tudor G Jovin, for the HERMES collaborators

HERMES collaborators

Mechanical thrombectomy(MT) plus IV t-PA versus IV t-PA alone for LVO

Result in a **50% relative risk reduction** of significant neurological disability, **with an outstanding number of 4 needed to treat to avoid 1 severe neurological deficit**

Copyrights apply

급성뇌경색(ELVO) – 동맥내 혈전제거기술

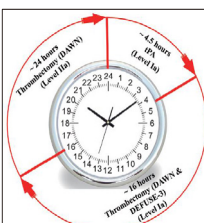
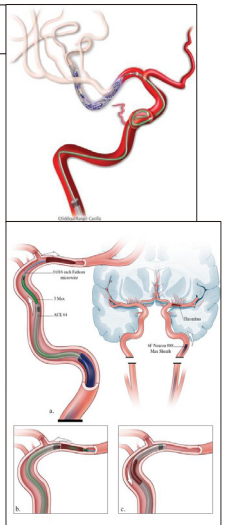
2015

Large Vessel Occlusion Stroke(LVOS)

New Golden Standard Treatment for Acute Ischemic Stroke

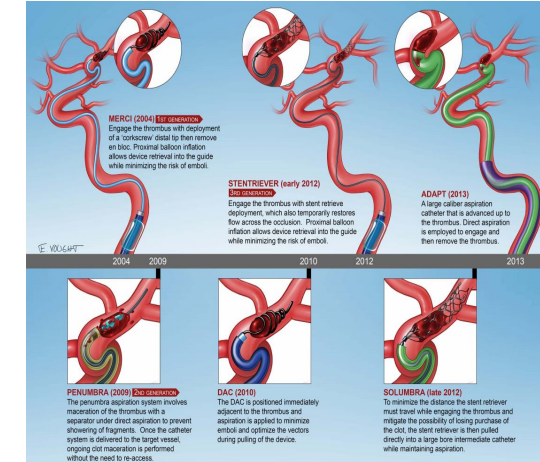
Paradigm Shift in Intra-Arterial Mechanical Thrombectomy for Acute Ischemic Stroke : A Review of Randomized Controlled Trials after 2015

Jae Jin Shon, Young Wook Kim
Department of Neurology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Gangnam, Korea

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Mechanical thrombectomy = Thrombus removal



MERCI (2004) [tissue retriever]
Engage the thrombus with deployment of a 'corkscrew' distal to then remove on bloc. Proximal balloon inflation allows device retrieval into the guide while minimizing the risk of embol.

STENTRIEVER (early 2012) [stent retriever]
Engage the thrombus with stent retriever deployment, which also temporarily restores flow across the occlusion. Proximal balloon inflation allows device retrieval into the guide while minimizing the risk of embol.

ADAPT (2013)
A large caliber aspiration catheter that is advanced up to the thrombus. Direct aspiration is employed to engage and then remove the thrombus.

PENUMBRA (2009) [aspiration]
The penumbra aspiration system involves maximization of the thrombus with a separator under direct aspiration to prevent showering of fragments. Once the catheter system is delivered to the target vessel, ongoing distal aspiration is performed without the need to re-access.

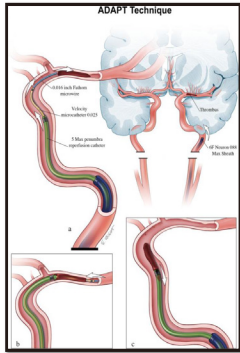
DAC (2010)
The DAC is positioned immediately adjacent to the thrombus and aspiration is applied to minimize embol and optimize the vectors during pulling of the device.

SOLIUMBRA (late 2012)
To minimize the distance the stent retriever must travel while engaging the thrombus and mitigate the possibility of using purchase of the clot, the stent retriever is then pulled directly into a large bore intermediate catheter while maintaining aspiration.

ADAPT(BGC) – Aspiration thrombectomy

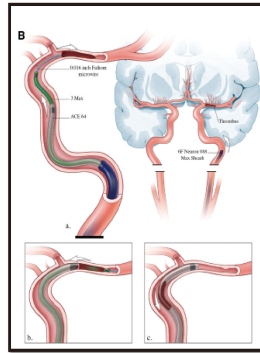
Clot retrieval

- Distal embolization



Clot ingestion

- Large bore aspiration catheter



Head to head study: SR vs CA

- **ASTER**(Contact Aspiration versus Stent retriever for Successful Revascularization), 2017, French
- **COMPASS**(Aspiration Thrombectomy Versus Stent Retriever Thrombectomy as First – Line Approach for Large Vessel Occlusion), 2019, North American



AHA/ASA, ESO guidelines update

Mechanical thrombectomy is

New Golden Standard Treatment
for Acute Ischemic Stroke

Mechanical Thrombectomy - 0 to 6 hours from onset

1. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) **prestroke mRS score of 0 to 1**; (2) **causative occlusion of the internal carotid artery or MCA segment 1 (M1)**; (3) **age ≥ 18 years**; (4) **NIHSS score of ≥ 6** ; (5) **ASPECTS of ≥ 6** ; and (6) **treatment can be initiated (groin puncture) within 6 hours of symptom onset**.

I

A

- The HERMES pooled patient-level data also showed that mechanical thrombectomy had a favorable effect over standard care in patients **≥ 80 years of age** (COR, 3.68 [95% CI, 1.95–6.92]).
- Patients **> 90 years of age**; very small number $\rightarrow$ the benefit of MT is unclear.

Mechanical Thrombectomy - 0 to 6 hours from onset

2. **Direct aspiration thrombectomy** as first-pass mechanical thrombectomy is recommended as **noninferior to stent retriever** for patients who meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or M1; (3) age ≥ 18 years; (4) NIHSS score of ≥ 6 ; (5) ASPECTS ≥ 6 ; and (6) treatment initiation (groin puncture) within 6 hours of symptom onset.

COMPASS trial & ASTER trial

3. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the MCA segment 2 (M2) or MCA segment 3 (M3) portion of the MCAs.

HERMES & SEER for M2 occlusion: not significant
Analysis of pooled data from SWIFT, STAR, DEFUSE 2, and IMS III for M2 occlusion
→ Reperfusion was associated with excellent functional outcomes (mRS score 0-1; OR, 2.2 [95% CI, 1.0-4.7])

FPE: Independent predictor of good clinical outcome

First Pass Effect

A New Measure for Stroke Thrombectomy Devices

Osama O. Zaidat, MD, Alicia C. Castonguay, PhD, Iulo Lofante, MD, Rishi Gupta, MD, Coleman O. Martin, MD, William E. Holloway, MD, Nils Mueller-Krone, MD, Joey D. English, MD, PhD, Guilherme Dabus, MD, Tim W. Malisch, MD, Franklin A. Marden, MD, Hormozd Borzoughami, MD, Andrew Xavier, MD, Ansar T. Rai, MD, Michael T. Froehner, MD, PhD, Amir Badraddin, MD, Thanh N. Nguyen, MD, M. Asif Taqi, MD, Michael G. Abraham, MD, Albert J. Yoo, MD, PhD, Valsabh Jureidhi, MD, Hesham Shaltoni, MD, Roberto Novakovic, MD, Alex Abou-Chebl, MD, Peng R. Chen, MD, Gavin W. Britz, MD, Chung-Huan J. Sun, MD, Vibhav Bansal, MD, Ritesh Kaulhal, MD, Ashish Nanda, MD, **Raul G. Nogueira, MD**

Background and Purpose—In acute ischemic stroke, fast and complete recanalization of the occluded vessel is associated with improved outcomes. We describe a novel measure for newer generation devices: the **first pass effect (FPE)**. FPE is defined as achieving a complete recanalization with a single thrombectomy device pass.

Methods—The North American Solitaire Acute Stroke Registry database was used to identify a FPE subgroup. Their baseline features and clinical outcomes were compared with non-FPE patients. Clinical outcome measures included 90-day modified Rankin Scale score, National Institutes of Health Stroke Scale score, mortality, and symptomatic intracranial hemorrhage. Multivariate analyses were performed to determine whether FPE independently resulted in improved outcomes and to identify predictors of FPE.

Results—A total of 354 acute ischemic stroke patients underwent thrombectomy in the North American Solitaire Acute Stroke registry. FPE was achieved in 89 out of 354 (25.1%). Mean middle cerebral artery occlusion (46% versus 52.5%) and fewer internal carotid artery occlusions (10.1% versus 22.7%) were present in the FPE group. Balloon guide catheters were used more frequently with FPE (64.0% versus 34.7%). Median time to recanalization was significantly faster in the FPE group (median 34 versus 67 minutes; $P=0.0003$). FPE was an independent predictor of good clinical outcome (modified Rankin Scale score 0-1 was more in 64.7% in FPE versus 35.3% in non-FPE cohort; $P=0.013$; odds ratio, 1.7; 95% confidence interval, 1.1-2.7). The independent predictors of achieving FPE were use of balloon guide catheters and non-internal carotid artery terminus occlusion.

Conclusions—The achievement of complete recanalization from a **single Solitaire thrombectomy device pass (FPE)** is associated with significantly higher rates of good clinical outcomes. The FPE is more frequently associated with the use of balloon guide catheters and less likely to be achieved with internal carotid artery terminus occlusion. (Stroke. 2019;49:660-666. DOI: 10.1161/STROKEAHA.117.050015.)

Key Words: first pass ■ recanalization ■ Solitaire ■ stent retriever ■ stroke ■ thrombectomy

One shot, one kill !!



First pass effect

- Achieving a complete recanalization with a single thrombectomy device pass

NO distal embolization

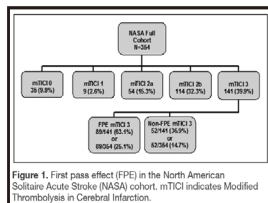
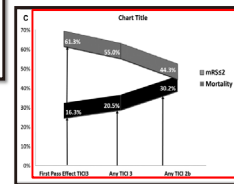
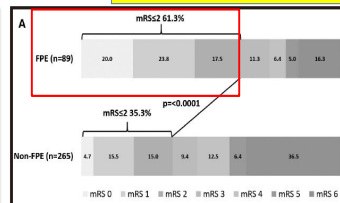


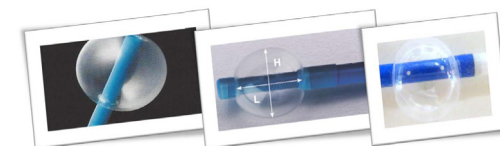
Figure 1. First pass effect (FPE) in the North American Solitaire Acute Stroke (NASAS) cohort. mTICI indicates Modified Thrombolysis in Cerebral Infarction.



Balloon guiding catheter (BGC)

- Complete block of antegrade blood flow
 - Flow Prevention of distal thrombus migration
 - Flow reversal
- Improvement of Suction thrombectomy
- Aspiration or Suction thrombectomy via BGC
- Optimo, Cello, Flowgate²

Decrease distal embolization



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 4, 2018 VOL. 378 NO. 1

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Hagerup, A.P. Jadhav, D.C. Houston, A. Bonafé, R.J. Budd, P. Bhutta, D.S. Yang, M. Rhee, C. Cognard, R.A. Nand, C.A. Shi, A.E. Hassan, M. Miller, E. Levy, P. Mitchell, M. Chen, D. English, Q.A. Shah, T. Shan, Y.M. Pereira, E.P. Menta, E.W. Baster, M.G. Alarum, P. Cardona, E. Vazirani, F.A. Helling, L. Fong, J.F. Korman, D.A. Lopez, B.T. Jankovic, M.B. Turkel, V. Givoni, R.A. Vora, A.J. You, A.M. Malik, A.J. Furlan, M. Rubera, A. Aghaie, J. Al. Othman, W.G. Taha, R. Shalaby, T. Graves, R.J. Lewis, W.S. Smith, D.S. Lieberkind, J.L. Starr, and T.G. Jones, for the DAWN Trial Investigators

ORIGINAL ARTICLE

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

G.W. Albers, M.P. Marks, S. Kemp, S. Christensen, J.P. Tsai, S. Ortega-Gutierrez, R.A. McTaggart, M.T. Torbey, M. Kim-Tenser, T. Leslie-Mazwi, A. Sarraj, S.E. Kanner, S.A. Ansari, S.D. Yeatts, S. Hamilton, M. Miyash, J.J. Heel, G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators

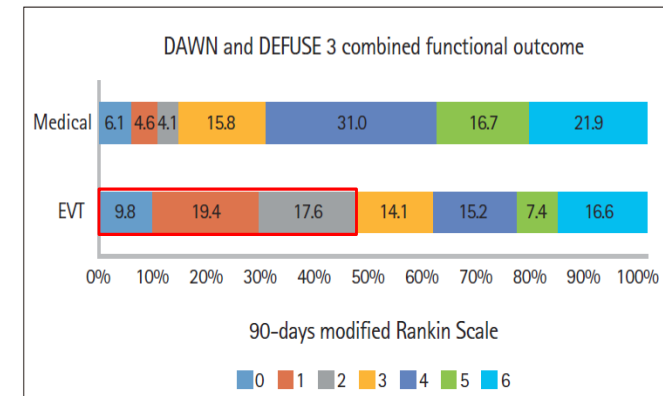
DAWN and DEFUSE 3 trial

2018

Inclusion criteria	DEFUSE-3 ¹⁰	DAWN ⁸
Time window	6–16 hours since time last known well	6–24 hours since time last known well
Age	18–90 years	≥18 years
mRS score before qualifying stroke	≤2; life expectancy ≥6 months	≤1; life expectancy ≥6 months
NIHSS score	≥6	≥10 (see below)
Arterial occlusion	ICA and/or M1 *	ICA and/or M1
Mismatch definition	Target mismatch profile on CT or MR perfusion imaging, as determined by an automated image postprocessing system: Infarct core volume <70 mL AND mismatch volume >15 mL (Tmax>6s) AND mismatch ratio (penumbra/core) ≥1.8	Clinical-imaging mismatch Age <80 years and NIHSS score ≥10 and infarct core 0–30 mL OR age <80 years and NIHSS score ≥20 and infarct core 31–51 mL OR age ≥80 years and NIHSS score ≥10 and infarct core 0–20 mL

defuse-3

6~24 hours after stroke onset



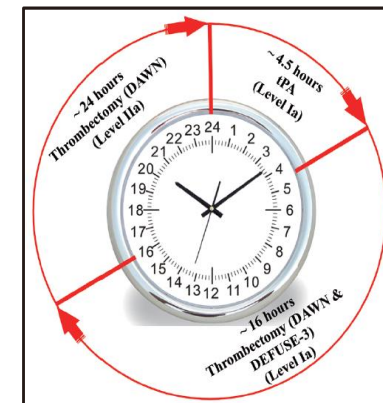
Journal of Stroke 2020;22(3):377-386

Mechanical Thrombectomy - 6 to 24 hours from onset

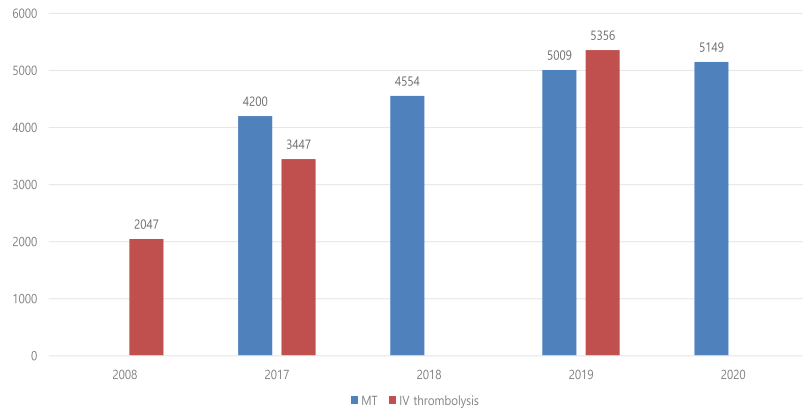
1. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A
2. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	Ila	B-R

New Era of Endovascular Treatment for Acute Ischemic Stroke(LVO)

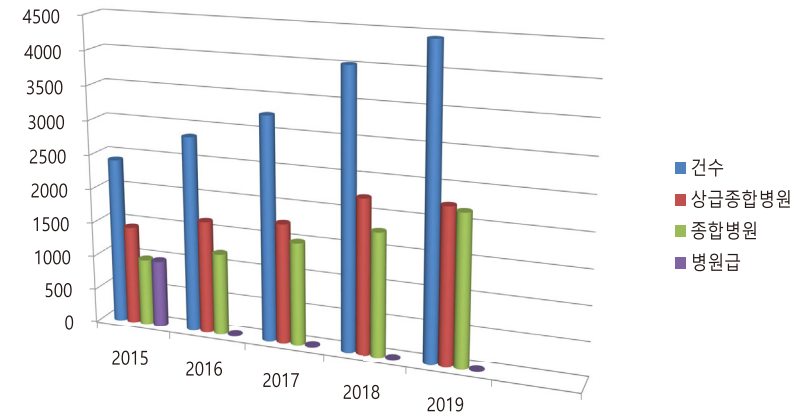
- Portfolio
- 2018



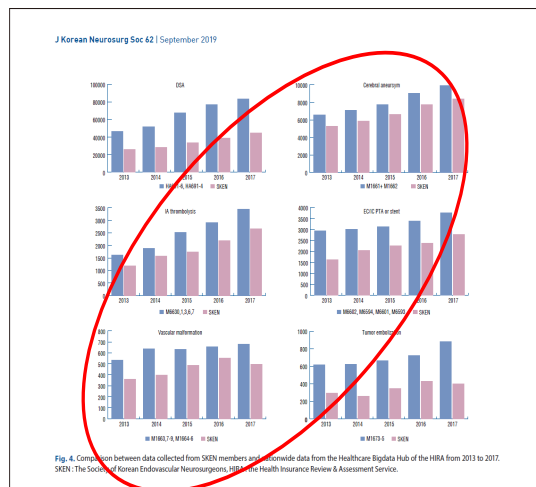
IV thrombolysis vs Mechanical thrombectomy



혈전제거술 (mechanical thrombectomy)



신경외과 – 뇌혈관 전문의(SKEN)



Korean Endovascular interventionist

	신경외과		영상의학과		신경과
인증의	251	ENS	134	ENS 46 INR 55 IVN 33	33 KSIN member
인증기관	90		45		72 (Primary Stroke center)

ENS: 신경외과 출신 전문의
INR: 영상의학과 출신 전문의
IVN: 신경과 출신 전문의

Endovascular only vs EVT + IV thrombolysis

- 현재까지는 정맥 내 혈전용해제 투여 후 혈전제거술의 치료 결과가 좋다.

SHRINE collaboration

- SKIP
- DEVT

SHRINE: Systemic Thrombolysis Randomization IN Endovascular Stroke Therapy Collaboration

Purpose: To evaluate the non-inferiority of endovascular treatment (EVT) alone (primary thrombectomy) versus intravenous alteplase followed by EVT (combined therapy) in large vessel occlusion stroke patients eligible for intravenous thrombolysis (IVT).

Trial Design: Pooled analysis of individual patient-level data from the SKIP (Japan) and DEVT (China) clinical trials. Primary Endpoint: Functional independence

Secondary Endpoint: Reduced disability on the mRS at 90 days in the pooled cohort

Results	N=221 Combined therapy "Bridging"	N=217 Primary Thrombectomy EVT alone	OR	Adjusted OR
90-day mRS 0-2	51.6% (114/221)	56.7% (123/217)	1.23 (0.84-1.79); p= .29	1.27 (0.84-1.92); p= .26
90-day mRS shift	-	-	1.07 (0.72-1.40); p= .68	1.01 (0.72-1.40); p= .99
90-day mRS 0-1	37.6% (83/221)	39.2% (85/217)	1.07 (0.73-1.57); p= .73	1.03 (0.67-1.58); p= 0.89
90-day mRS 0-3	67.0% (148/221)	70.0% (152/217)	1.15 (0.77-1.73); p= .49	1.11 (0.70-1.77); p= .66



Presented by: Raul Nogueira, International Stroke Conference 2021.
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Results reflect the data available at the time of presentation.

Results:

- The SHRINE collaboration provides additional data on the non-inferiority of primary thrombectomy versus combined therapy in patients presenting directly to thrombectomy-capable centers.
- The adjusted OR for 90-day Functional Independence was 1.27 (0.84 - 1.92), there is still the possibility that primary EVT is not non-inferior to bridging IVT/EVT. However, most point estimates favor primary EVT.

MR CLEAN-No IV

TRIAL: MR CLEAN-NO IV (Direct endovascular treatment (dEVT) versus intravenous alteplase followed by endovascular treatment in patients with acute stroke due to a large vessel occlusion - LVO)

Hypothesis: Direct EVT for patients with acute ischemic stroke caused by an intracranial proximal large vessel occlusion in the anterior circulation is superior to IV alteplase followed by EVT in terms of functional outcome.

Purpose: To assess the efficacy and safety of omitting IV thrombolysis before EVT in patients with AIS (anterior circulation LVO).

Methods: Multicenter randomized (1:1) clinical trial, IV alteplase (0.9 mg/kg) + EVT versus direct EVT at 20 sites; Netherlands, Belgium and France. PRIOBE design, IV-539

Primary Outcome: ordinal mRS

- Primary analysis: superiority dEVT
- Secondary analysis: non-inferiority dEVT

Safety Outcomes: Mortality and Symptomatic ICH, mRS dichotomizations, reperfusion (pTICI)



Presented by: Prof. Dr. Yoo Riou MD for the MR CLEAN-NO IV Trial Investigators © 2021 American Heart Association. All rights reserved.

	Allocated to direct EVT N=273 Ordinal mRS	Allocated to alteplase 0.9mg/kg + EVT N=266 Ordinal mRS	P value
Primary analysis: ordinal mRS	Overall acOR > Does not show dichotomizations		acOR 0.88 (95% CI 0.65-1.19)
Secondary Outcomes	16 (5.9%)	14 (5.3%)	1.30 (0.61-2.84)
Symptomatic ICH (safety)			
Mortality (Safety)	56 (20.5%)	42 (15.8%)	1.39 (0.84-2.30)

Results/Interpretation: Did not show non-inferiority or superiority of dEVT over alteplase +EVT in patients with ischemic stroke due to proximal anterior circulation occlusions. No difference in symptomatic hemorrhage rates. Preliminary pooled data from the DEVT, DIRECT-MT, MR CLEAN NO-IV AND SKIP trials suggests the true difference between dEVT and alteplase +EVT approaches one.

Results reflect the data available at the time of presentation.

ISC, 2021

NEWS • Conference News | ISC 2021

MR CLEAN-NO IV: No Advantage to Skipping tPA Before Stroke Thrombectomy

There may be scenarios where foregoing IV thrombolytics make sense, but most centers can stick with the guidelines, experts say.

by Todd Neale | MARCH 22, 2021



SWIFT DIRECT, and DIRECT-SAFE.

- Direct mechanical thrombectomy vs Bridging treatment

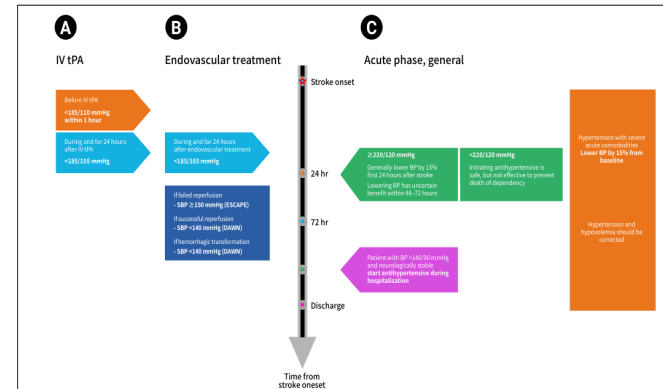
BP management – Ischemic stroke

Fig. 1. Blood pressure (BP) management according to treatment of ischemic stroke; (A) intravenous thrombolysis (IV tPA), (B) endovascular treatment, and (C) not indicated for reperfusion therapy and secondary stroke prevention. SBP, systolic blood pressure; ESCAPE, endovascular treatment for small core and anterior circulation proximal occlusion with emphasis on minimizing computed tomography (CT) to recanalization times; DAWN, diffusion-weighted imaging or computerized tomography perfusion assessment with clinical mismatch in the triage of wake up and late presenting strokes undergoing neurointervention.

Direct Transfer to Angiography Suite(DTAS)

- Suspect LVO

Evaluation of Direct Transfer to Angiography Suite (DTAS) vs. Computed Tomography Suite (DTCT) in Endovascular Treatment of Stroke: ANGIO-CAT A Randomized Clinical Trial

Purpose: This study was designed to study the impact of Direct to Angiography Suite (DTAS) on clinical outcomes as compared to conventional imaging (DTCT) workflow.

Trial Design: Prospective, randomized-controlled (1:1), open, treatment allocated trial of acute stroke patients with suspected large vessel occlusion (LVO) within 6 hours from symptom onset in which two strategies will be compared: DTAS vs. DTCT with prehospital suspected LVO. RACE score > 4 and NIHSS > 5. Follow-up for 90 days. Blinded Endpoint evaluation via telephone. Modified TTT analysis (whether received EVT or not).

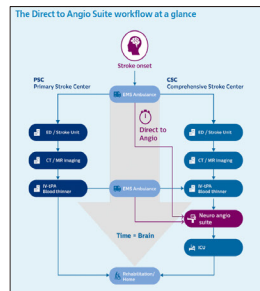
Primary Endpoints: Shift Analysis of Modified Rankin Score at 90 days (mRS).

Other Endpoints: Safety, and Secondary Efficacy Outcomes.

Results	Direct Transfer Angiography Suite DTAS	Direct to CT Suite DTCT	P-value
Door to puncture time (minutes median (IQR))	18 (15-24)	42 (35-51)	< 0.001
Onset to reperfusion times (minutes mean, SD)	290.5 (141.7)	308.9 (122.2)	0.32
Door to reperfusion time (minutes median (IQR))	57 (43-77)	84 (63-117)	< 0.001
mRS			
DTAS reduced the severity of disability (functional outcome) aOR for improvement of 1 point on the mRS score of 2.2, 95% CI			
Symptomatic ICH	1 (1.4%)	3 (4.1%)	0.28
90 Day Mortality	18 (20.2%)	28 (32.9%)	0.07

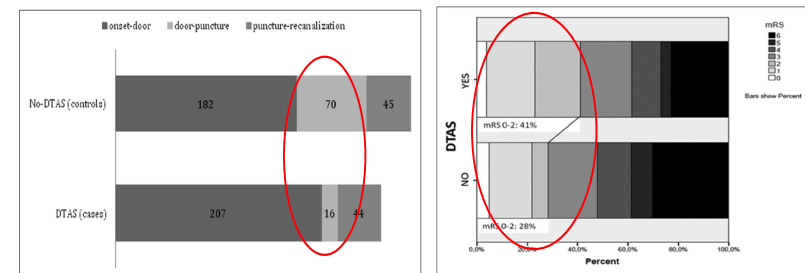
Conclusion: Among patients with LVO admitted within 6 hours after symptom onset, direct transfer to angiography suite(DTAS) reduced both in-hospital onset to reperfusion time, increased odds of undergoing EVT, and improved the post-stroke disability at 90 days.

Results reflect the data available at the time of presentation.

**Direct Transfer to Angio-Suite to Reduce Workflow Times and Increase Favorable Clinical Outcome
A Case-Control Study**

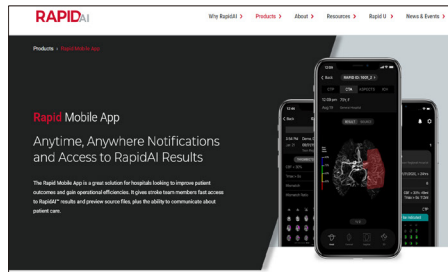
Beatriz Mendez, MD; Manuel Requena, MD; Ana Aires, MD; Nuno Martins, MD; Sandra Boned, MD; Marta Rubiera, MD, PhD; Alejandro Tomasello, MD; Pilar Coscojuela, MD; Marián Muchada, MD, PhD; David Rodríguez-Luna, MD, PhD; Noelia Rodríguez-Villatoro, MD; Jesús Juega, MD; Jorge Pagola, MD, PhD; Carlos A. Molina, MD, PhD; Marc Ribó, MD, PhD

Stroke 2018;49 Marc Ribó, Spain



Automated Image Interpretation & Triage

- RAPID_{AI}
- Viz.ai



Mobile Stroke Unit(MSU)

BEST-MSU Study- Benefits of Stroke Treatment Delivered by a Mobile Stroke Unit Compared to Standard Management by Emergency Medical Services

Purpose: To compare the 90-day stroke outcomes of tPA-eligible patients managed by a mobile stroke unit (MSU) to standard management (SM) by Emergency Medical Services (EMS).

Trial Design: Phase III alternating week (MSU or SM), multicenter, cluster-controlled, blinded assessment at entry and outcome, comparing the 90-day utility-weighted modified Rankin Scale (uw-mRS) of tPA-eligible patients managed by MSU vs SM.

1047 patients from 7 U.S. sites, 617 MSU group and 430 SM group

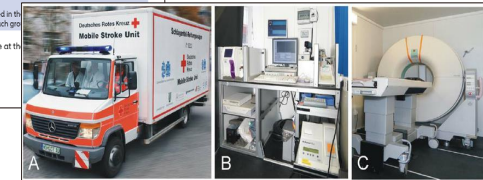
Primary Endpoint: 90-day uw-mRS

	Total n=1047	Mobile Stroke Unit n=617	Standard Management n=430
% of tPA eligible who were treated with tPA		97.1%	79.1%
% of patients treated within 60 minutes of last known well		33%	3%
Time from last known well until tPA treatment		72 minutes P<0.001	108 minutes P<0.001
90-day • mean uw-mRS score • mRS 0-1		0.726, P=0.002 53%, P<0.001	0.657, P=0.002 43%, P<0.001

Results: MSU management results in substantially less disability for stroke patients who qualify for tPA treatment compared to standard management by EMS, and this is likely due to faster stroke treatment, particularly within the first hour. For every 100 patients treated with an MSU rather than SM:

- 27 will have less disability.
- 11 more will be disability free (mRS 0-1)
- No increase in endovascular treatment or speed in the No safety issues, 3% mRS 0-1 and 2% ICH in each group

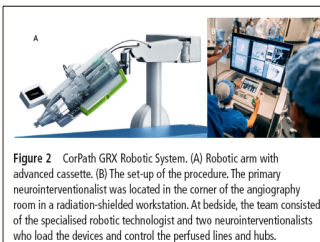
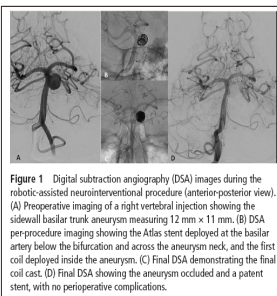
Results reflect the data available at the



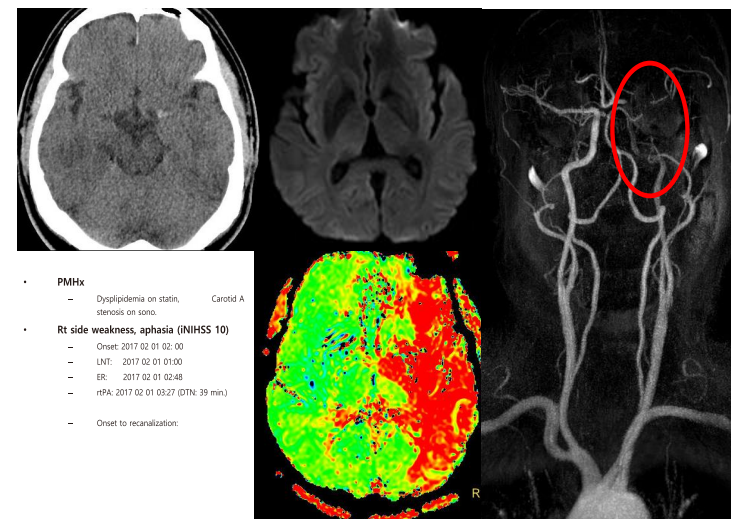
CorPath GRX Robotic System

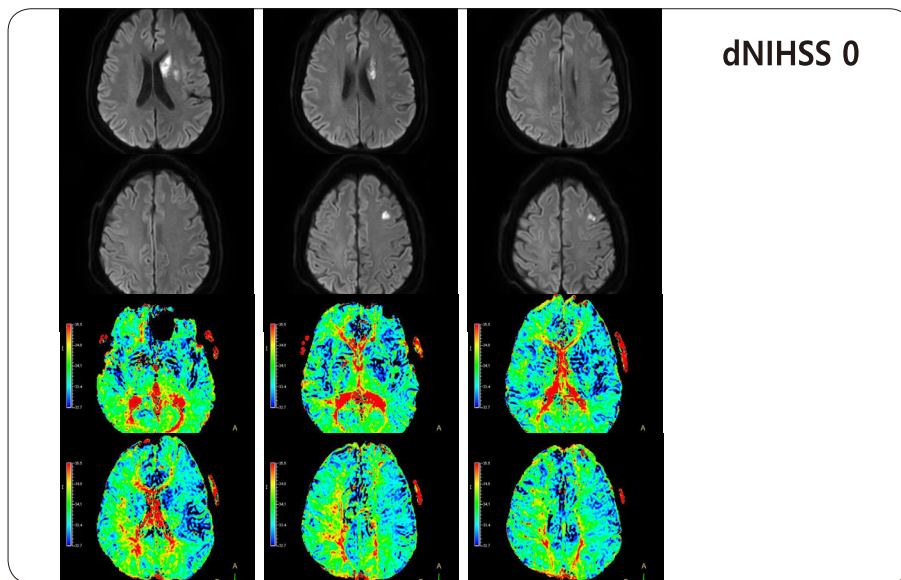


JNIS, 2019



M/57, Aphasia, Rt weakness, iNIHSS 10, iv rtPA nonresponder





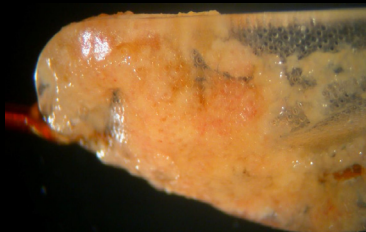
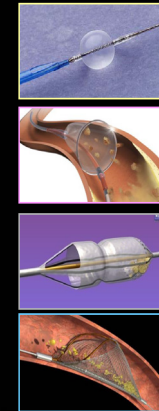
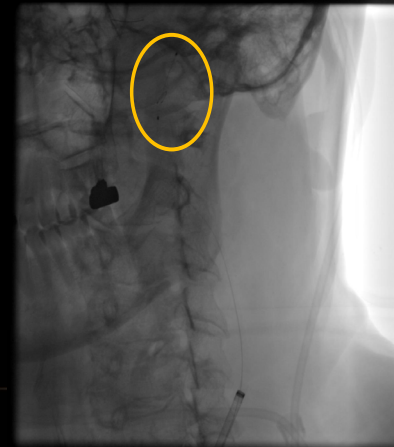
III. Secondary prevention

- Symptomatic
 - Intracranial stenosis
 - Carotid A stenosis
 - VA, Arch, Subclavian A stenosis

경동맥 협착증



원위부 색전방지 그물망 삽입

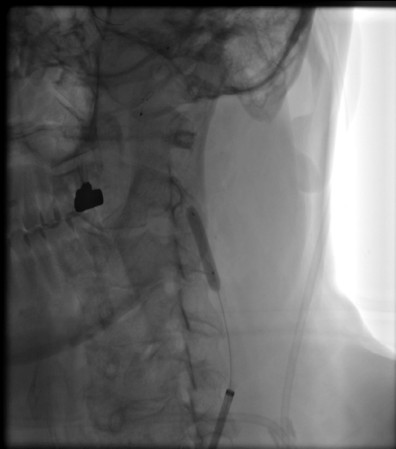


경동맥 스텐트 삽입술

Stent-assited Angioplasty
of Cervical Carotid Stenosis



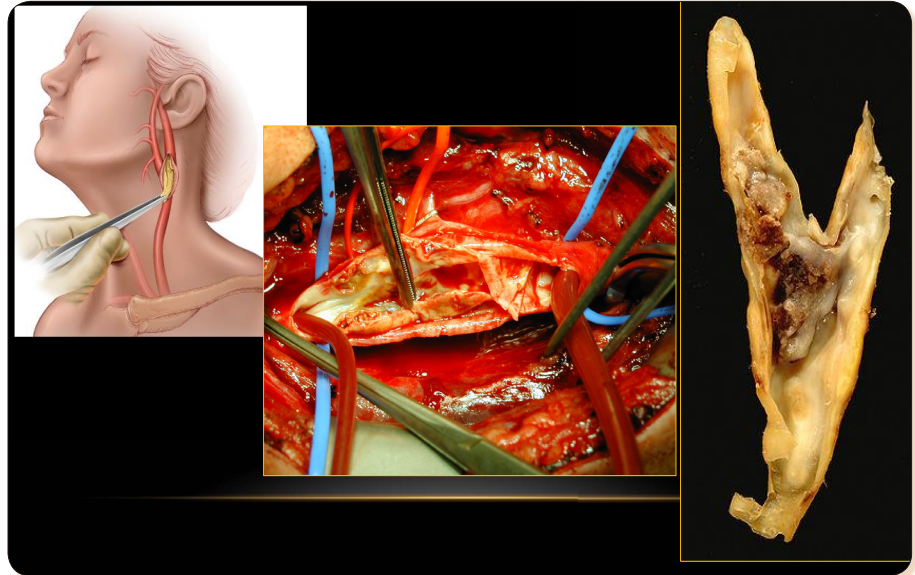
풍선성형술



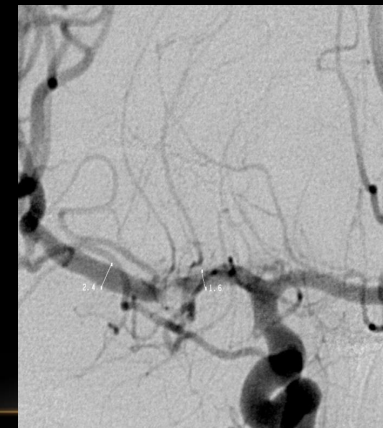
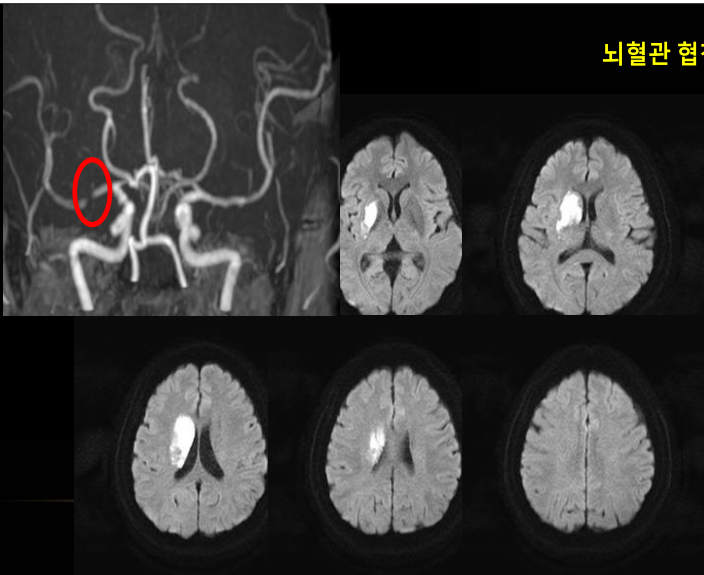
스텐트 삽입 - 뇌졸중 재발 방지



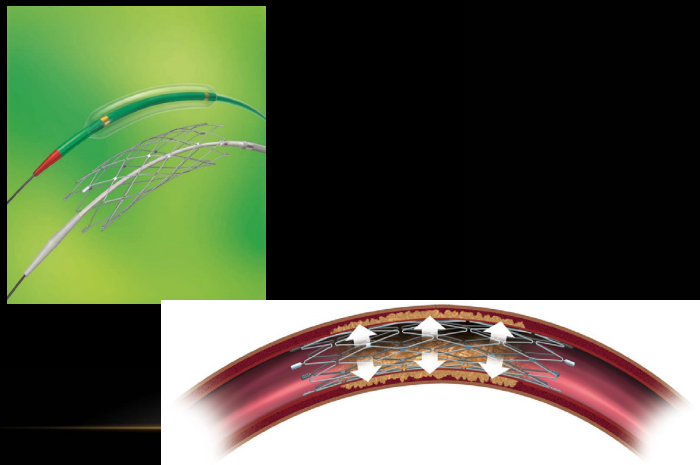
경동맥 내막 절제술



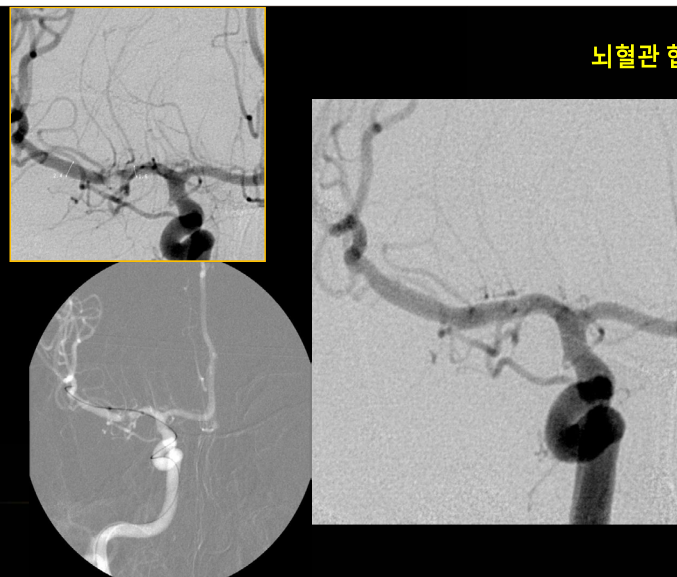
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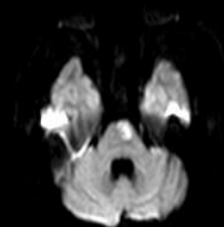
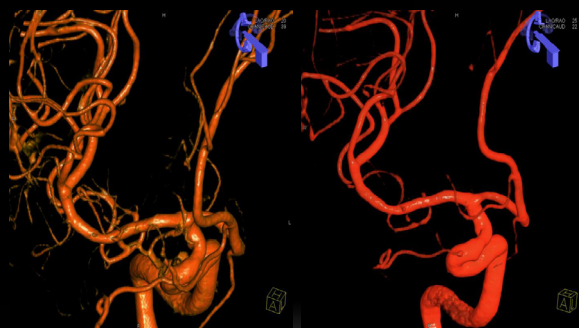
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뇌혈관 협착증



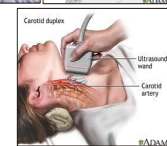
4 년뒤





Messages

- Stroke Awareness
- Strict BP & DM control
- Carotid Duplex
- Arrhythmia detection & NOAC
- TCD during Renal replacement therapy
- 진료협력센터



2022 분당차병원

협력의료기관 의사 온라인 연수강좌



Session I

15:20-15:50

흔한 피부 습진, 어떻게 감별하고 치료할까?

차의과학대학교 분당차병원 피부과

신정우 교수

분당차병원 피부과
신정우

흔한 피부 습진, 어떻게 감별하고 치료할까?

1. Contact dermatitis

2. Atopic dermatitis

3. Seborrheic dermatitis

Contact dermatitis

Contact Dermatitis

- among the most common inflammatory dermatological conditions
- exposure to exogenous substances → immune response → inflammation in the skin and/or mucous membranes

Type of contact dermatitis	Primary immunological mechanisms	Examples of culprits	Evaluation technique examples
Allergic ⁶	Type IV hypersensitivity reaction	Metals, fragrances, preservatives, dyes, adhesives, topical medications (for example, antibiotics), rubber accelerators and antioxidants	Patch testing, repeat open application test/use test
Photoallergic	Type IV hypersensitivity reaction; requires light exposure (primarily on the ultraviolet A spectrum)	Chemical sunscreens, NSAIDs, fragrances	Photopatch testing
Irritant	Direct cellular damage	Soaps and detergents, water, acids, alkalis, adhesives, solvents, oils	No routine testing available; it is a diagnosis of exclusion
Photoirritant (also called phototoxic)	Direct cellular damage; requires light exposure (primarily on the ultraviolet A spectrum)	Plants and fruits, medications	No routine testing available
Protein	Type I and type IV hypersensitivity reactions	High-molecular-weight proteins, especially food proteins such as in vegetables ¹⁷¹ , spices ¹⁷² , animal protein ^{173,174} , wheat ¹⁷⁷ and milk ^{178,179} ; other substances include enzymes ¹⁸⁰ and latex ¹⁸¹ and cross-reactivity has been described between several protein sources ¹⁸²	Short-term occluded patch testing (may be done on finger or palm), prick-prick testing, skin-prick testing

+) Occupational CD encompasses all types of CD

Nature Reviews Disease Primers volume 7, Article number: 38 (2021)

Contact dermatitis

➤ Irritant contact dermatitis

- ✓ 직접 세포 독성
- ✓ 선천면역

➤ Allergic contact dermatitis

- ✓ 제 4형 과민반응
- ✓ 선천면역 반응 + 적응면역

➤ Photoirritant CD and photoallergic CD

- ✓ UVA 등 광노출이 필요함.
- ✓ ICD, ACD 기전과 동일

➤ Protein contact dermatitis

- ✓ 제1형 + 제4형 과민반응
- ✓ 밀, 우유, 라텍스 등 단백질에 대한 과민반응

Type of contact dermatitis	Primary immunological mechanisms	Examples of culprits	Evaluation technique examples
Allergic ¹	Type IV hypersensitivity reaction	Metals, fragrances, preservatives, dyes, adhesives, topical medications (for example, antibiotics), rubber accelerators and antioxidants	Patch testing, repeat open application test/use test
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Protein	Type I and type IV hypersensitivity reactions	High-molecular-weight proteins, especially food proteins such as in vegetables ²¹ , spices ²² , animal protein ^{23,24} , wheat ²⁵ and milk ^{26,27} ; other substances include enzymes ²⁸ and latex ²⁹ and cross-reactivity has been described between several protein sources ³⁰	Short-term occluded patch testing (may be done on finger or palm), prick-prick testing, skin-prick testing

Nature Reviews Disease Primers volume 7, Article number: 38 (2021)

Allergic contact dermatitis

이전에 감작된 물질에 노출되었을 때 유발되는 제4형 지연과민반응

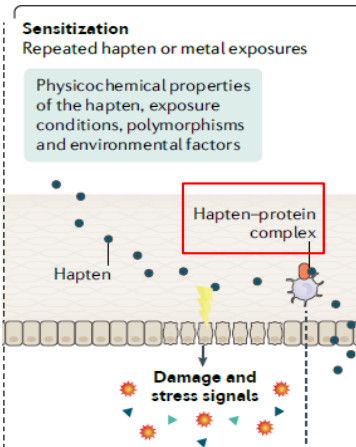
➤ Sensitization

- ✓ permeation of the allergen into the skin
- ✓ formation of **hapten-self- protein complexes**
- ✓ local inflammatory milieu
- ✓ **efficient T cell priming by migratory skin dendritic cells (DCs)**

➤ Elicitation

- ✓ Subsequent exposure to the chemical
- ✓ **localization to the skin and reactivation of hapten- specific effector and memory T cells**
- ✓ **kill haptenized keratinocytes**
- ✓ local erythema and epidermal spongiosis

Nature Reviews Disease Primers volume 7, Article number: 38 (2021)

Allergic contact dermatitis1> Initial sensitization: the formation of **hapten-self- protein complexes**

Nature Reviews Disease Primers volume 7, Article number: 38 (2021)

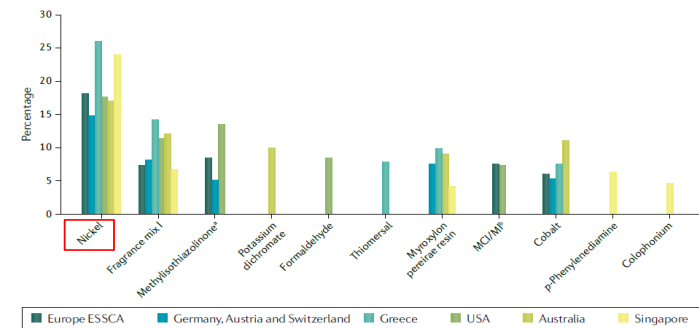
Trends in allergens

Fig. 1 | **Top sensitizers in various regions worldwide.** Prevalence of the most common allergens among various locations. Nickel is the most commonly identified contact allergen worldwide, followed by methylisothiazolinone or fragrance mix, depending on the region. The presented data is based on studies from Europe (12 countries, time period 2013–2014)⁴¹, Germany, Austria and Switzerland (2007–2018)⁴², Greece (2010–2016)⁴³, North America (2015–2016)⁴⁴, Australia (2001–2010)⁴⁵ and Singapore (2009–2013)⁴⁶. ^aCombined average of percentage of patients sensitized to methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) 0.01% or 0.02%. ESSCA, European Surveillance System on Contact Allergies.

Nature Reviews Disease Primers volume 7, Article number: 38 (2021)

Allergen	KCDRG (1983~1985) N=937	KCDRG (1986~1993) N=2326	KCDRG (2009~2010) N=795	KCDRG (2015~2016) N=214
Nickel sulfate	12.9	17.9	34.1	28.5
Thimerosal	6.7	5.7	12.6	6.1
Cobalt chloride	NA	13.8	11.1	17.3
p-Phenylenediamine	7.3	3.4	8.4	7.5
p-tert-butylphenol/formaldehyde resin	1.0	2.4	6.2	5.1
Potassium dichromate	11.8	11.3	5.6	8.9
Carba mix	NA	1.4	5.6	NA
Fragrance mix	NA	12.9	5.2	9.3
Colophony	NA	3.3	4.3	1.9
Taruum mix	3.2	2.6	3.7	0.9
Black rubber mix	2.7	1.0	3.5	NA
Epoxy resin	1.2	2.5	3.3	NA
Wood alcohol	3.0	3.3	2.9	0.9
Kitchen CG	NA	NA	2.9	1.4
Neomycin sulphate	7.6	7.2	2.6	2.3
Banum of Peru	7.0	4.7	2.6	4.2
Parabens mix	3.4	2.5	2.5	0.5
Formaldehyde	4.4	2.4	2.4	0.9
Quaternium 15	2.9	1.9	2.1	0.5
Cane mix	NA	NA	2.0	NA
Ethylene diamine dihydrochloride	1.4	1.3	1.7	NA
Moruga mix	2.3	2.2	1.7	0.5
Verapamil/styrene/styrene	NA	NA	1.5	0
Quinine mix	NA	1.8	1.3	NA

Korean Contact Dermatitis Research Group (KCDRG), not available (NA)

nickel sulfate 금속
Thimerosal 방부제
cobalt chloride 금속
Phenylenediamine 염색약
p-tert-butylphenol/formaldehyde resin 접착제
potassium dichromate 시멘트, 유리, 가죽
fragrance mix 향료

Nickel Allergy

- Choose jewelry carefully.** It's common for a nickel allergy to develop from wearing jewelry containing nickel. Earrings, earring backs and watches are some of the biggest culprits; however necklaces, rings and bracelets containing nickel can also trigger symptoms. To avoid exposure, only wear jewelry that is nickel-free, hypoallergenic, or made from metals such as surgical-grade stainless steel, 18-, 22-, or 24-karat yellow gold, pure sterling silver, or platinum. In addition, wear watchbands made of leather, cloth or plastic.
- Check your clothing.** It's also common for belt buckles, bra hooks, and metal buttons, zippers and snaps to contain nickel. If your clothing has these, replace them with ones that are plastic or plastic-coated. You can also create a barrier between these items and your skin by coating the items with clear nail polish. However, the nail polish will need to be re-applied often.
- Cover electronics.** Recent reports suggest that some electronic devices, including cell phones, laptops, and tablets, may contain nickel. To avoid exposure, always use a protective cover on your electronic devices.
- Substitute household objects containing nickel with objects made of other materials.** Examples include brass keys, titanium-coated or stainless-steel razors, pots and pans with silicone handles, and titanium or plastic eyeglass frames.
- Avoid foods containing nickel if you are extremely sensitive to nickel.** Some foods that contain high amounts of nickel include soy products—such as soybeans, soy sauce, and tofu—licorice, buckwheat, cocoa powder, clams, cashews, and figs.

Allergen of the Year by American Contact Dermatitis Society

Awards [edit]

- 2023 - Lanolin
- 2022 - Aluminum
- 2021 - Acetophenone azine
- 2020 - Isobornyl acrylate [2][3]
- 2019 - Parabens (Non) Allergen [4]
- 2018 - Propylene Glycol [5]
- 2017 - Alkyl Glucoside [6]
- 2016 - Cobalt [7]
- 2015 - Formaldehyde [8]
- 2014 - Benzophenones [9][10]
- 2013 - Methylisothiazolinone [11] - This chemical is used as a preservative in many cosmetics, lotions, and makeup removers; some of its side effects include flaky or scaly skin, breakouts, redness or itchiness, and moderate to severe swelling in the eye area.
- 2012 - Acrylate [12][13]
- 2011 - Dimethyl fumarate [14][15] - Dimethyl fumarate is the chemical associated with 'poisoned chairs' and 'toxic sandals'.
- 2010 - Neomycin (antibiotic) [16][17]

CONTACT ALLERGEN OF THE YEAR

Aluminum—Allergen of the Year 2022

Bruze, Magnus MD, PhD; Netterlid, Eva PhD; Siemund, Ingrid MD, PhD

Author Information

Dermatitis: 1/2 2022 - Volume 33 - Issue 1 - p 10-15

doi: 10.1097/DER.0000000000000836

Aluminum

- **allergen-specific immunotherapy (ASIT)⁹⁻¹⁷ and aluminum-containing vaccines^{7,11,18-34}** Other aluminum sources such as **antiperspirants/deodorants^{7,35-37}** astringent solutions,^{38,39} and elemental aluminum⁴⁰

Table 1

Vaccines licensed in the US containing aluminum in adjuvants [4]

Vaccines with aluminum adjuvant	Vaccines without aluminum adjuvant
DTP (diphtheria-tetanus-pertussis vaccine)	Inactivated Polio Virus
DTaP (diphtheria-tetanus-acellular pertussis vaccine)	Measles vaccine
Hib (Haemophilus influenzae type b) conjugate vaccines (not all)	Mumps vaccine
Pneumococcal conjugate vaccine	Rubella vaccine (MMR).
Hepatitis B vaccines	Varicella vaccine
All combination DTaP, Tdap, Hib	Influenza vaccines
Hepatitis B vaccines	
Hepatitis A vaccines	
Human Papillomavirus vaccine	
Anthrax vaccine	
Rabies vaccine	

[Open in a separate window](#)

Dermatitis: 1/2 2022 - Volume 33 - Issue 1 - p 10-15 doi: 10.1097/DER.0000000000000836

Injection site pruritic nodule

또는

데오도란트 바른 자리의 습진

Management of Allergic contact dermatitis (ACD)

• First-line treatments of ACD

- **avoidance of allergens**, skin care education, personal protective equipment, emollients and soap substitutes, protective cream, **topical corticosteroids**, topical tacrolimus/pimecrolimus, local and systematic application of antibiotics, oral prednisone, and alitretinoin.

• Second-line treatments

- ultraviolet therapy (PUVA, UVB), azathioprine, methotrexate, acitretin, and low-nickel diet

Corticosteroid Classification & Cross-reactivity

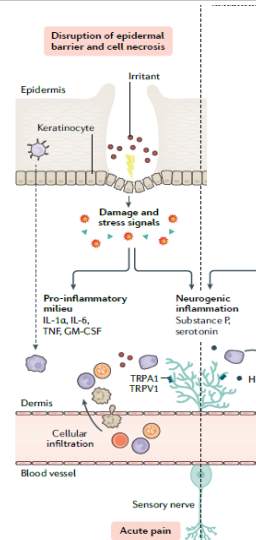
GROUP	1	2	3
Typical members	Budesonide Clotprednol Cortisone acetate Dichlorisone acetate Difluprednate Fludrocortisone acetate Fluorometholone Fluprednisolone acetate Hydrocortisone Hydrocortisone aceponate Hydrocortisone acetate Hydrocortisone-17-butyrate Hydrocortisone-21-butyrate Hydrocortisone hemisuccinate Isofluprednol acetate Maziapredone Medrysone Methylprednisolone aceponate Methylprednisolone acetate Methylprednisolone hemisuccinate Prednicarbate Prednisolone Prednisolone caproate Prednisolone pivalate Prednisolone sodium metasulphobenzate Prednisolone succinate Prednisone Tixocortol pivalate Triamcinolone	Amcinonide Budesonide (R-isomer)^Δ Desonide^Δ Fluchlorisone Flumoxonide Flunisolide Flucinolone acetonide Flucisnolide Halcinonide ^Δ Triamcinolone acetonide Triamcinolone benetonide Triamcinolone diacetate Triamcinolone hexacetonide	Alclomethasone dipropionate Beclomethasone dipropionate Betamethasone Betamethasone 17-valerate Betamethasone dipropionate Betamethasone sodium phosphate Clobetasol propionate Clobetasone butyrate Cortivazol ^Δ Desoxymethasone Dexamethasone Dexamethasone acetate Dexamethasone sodium phosphate Diflucortolone valerate Diflorasone diacetate Flumethasone pivalate Flucortin butyl Flucortolone Flucortolone caprylate Flucortolone pivalate Fluprednidene acetate Halomethasone Meprednisone ^Δ Fluticasone propionate Mometasone furoate

Allergy. 2011 Oct;66(10):1367-74.
Contact Dermatitis. 2012 Jan;66(1):38-45.

Irritant Contact Dermatitis

외부 자극 물질에 의해 **피부 장벽기능이 손상**되며 유발되는 피부염

- release of **stress-associated molecular patterns and DAMPs** by injured cells
- sensed by receptors of the **innate immune system**
- release of a **myriad of chemokines, proteases, and derivatives of arachidonic acid metabolism**
- Irritants may also excite **nociceptors**
- release of **vasoactive peptides**
- producing **acute pain and neurogenic inflammation**
- **vasodilation and the infiltration of diverse leukocytes** from the blood into the skin, which further amplify the reaction



Nature Reviews Disease Primers volume 7, Article number: 38 (2021)

Irritant Contact Dermatitis

➢ How chemicals cause skin irritation are poorly understood

- ✓ vary from the disorganization of the lipid bilayers of cell membranes to the damage of epidermal barrier proteins

➢ Corrosives (부식성 물질)

- ✓ acids, bases or detergents
- ✓ trigger an **intense cell necrosis**
- ✓ causing major disruption of the skin barrier
- ✓ **irreversibly damage** of the skin beyond repair

➢ Irritant substances (자극물질)

- ✓ **reversible local inflammatory reaction** caused by the innate immune system
- ✓ Water or solvent
- ✓ minimal and reversible effects on epidermal cells
- ✓ require repetitive applications before an ICD reaction occurs

Irritant Contact Dermatitis

- Damage to the epidermis -> **Barrier disfunction**
- **Clinical manifestations**
 - ✓ erythema, induration and oedema, painful and burning areas of skin
- **Resolution of inflammatory reaction**
 - ✓ removal of the offending agent
 - ✓ elimination and replacement of injured or dead cells by skin repair processes

Nature Reviews Disease Primers volume 7, Article number: 38 (2021)

Hand eczema Covid: School hand-washing 'damaging children's skin'

© 16 March 2021



<https://www.bbc.com/news/uk-england-lincolnshire-56415838>



JORDAN FERRIS

Jordan Ferris' daughter, Grace, has been left with bleeding hands because of the eczema.

Management of Irritant contact dermatitis (ICD)



- **First-line treatments**
 - **physical protection of skin**, protective cream/emollient, **topical corticosteroids**, and topical tacrolimus/pimecrolimus.
- **Second-line treatments**
 - ultraviolet therapy (PUVA (psoralen + UVA), UVB), and bexarotene gel
- **Third-line treatments**
 - Superficial radiation therapy and oral alitretinoin

Atopic dermatitis

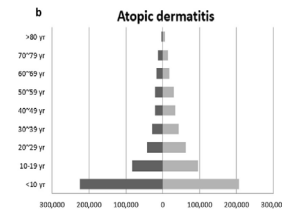
아토피피부염이란?

- 주로 유아기 혹은 소아기에 시작되는 만성 재발성의 염증성 피부질환으로
소양증(가려움증)과 피부건조증, 특징적인 습진을 동반

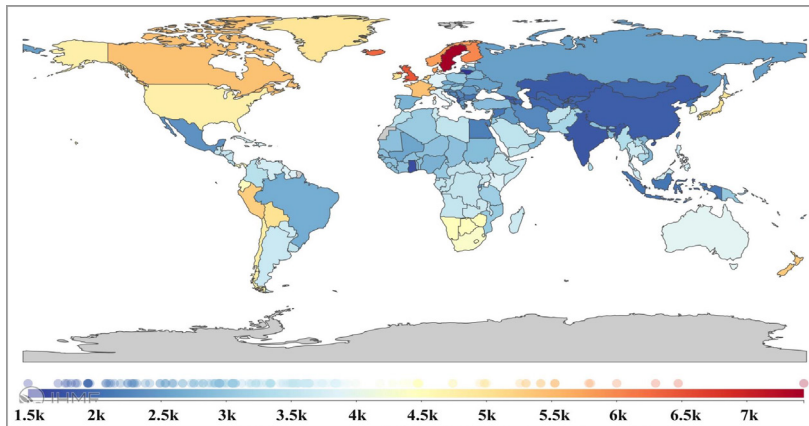
Prevalance of AD

- Prevalence ranging from 7.2 to 22.6%,
 - In adults : 1%-3%
 - In children : 10%-20%
- Primarily a disease of **early childhood**
- Since 1960s, the prevalence of AE has increased more than **3-fold**

ISSAC (The International Study of Asthma and Allergies in Childhood) - KOREA	6-12 years	12-15 years
1995	7.3%	3.9%
2000	10.7%	6.1%



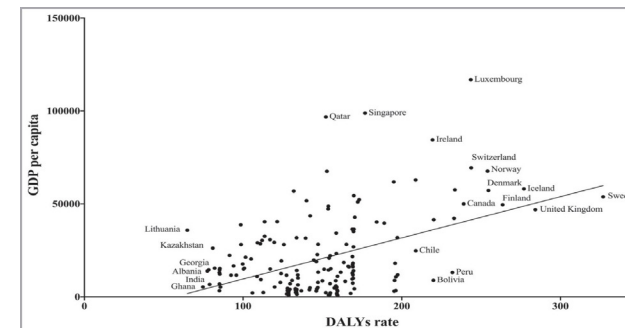
Allergy Asthma Immunol Res. 2016;8(3):181-190
Allergy Asthma Immunol Res. 2015 Mar;7(2):101-5
Acta Derm Venereol. 2013;93:438-41
Eur Clin Respir J. 2015; 2: 10.3402/ecrj.v2.24642



Global Burden of Disease project 2017 data

Br J Dermatol. 2021 Feb;184(2):304-309

DALY of AD correlates with GDP



The disability-adjusted life year (DALY): a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death.

The global burden of atopic dermatitis: lessons from the Global Burden of Disease Study 1990–2017* Br J Dermatol. 2021 Feb;184(2):304-309

Hanifin and Rajka's diagnostic criteria, 1980

Major 3개, Minor 3개

Limitation

- 일부 항목은 매우 드물거나 특이적이지 않음
- 백인에서만 나타나기도
- 측정자 간 차이가 큼

	Patients	Controls
Major features		
(1) Pruritus	100	-
(2) Chronic or chronically relapsing dermatitis	100	-
(3) Typical distribution of skin lesion	91.7	-
(4) Personal and/or family history of atopy	80.1	18.7*
Minor features		
(1) Xerosis	85.2	11.3*
(2) White dermographism	84.2	0.7*
(3) Hand and/or foot dermatitis	81.9	-
(4) Dennie-Morgan infraorbital fold	78.1	49.3*
(5) Itch when sweating	77.6	12.0*
(6) Anterior neck folds	75.2	54.7*
(7) Food intolerance	74.4	6.7*
(8) Intolerance to wool	71.3	29.3*
(9) Course influenced by emotional factors	68.4	-
(10) Immediate skin test reactivity	66.8	NE
(11) Elevated serum IgE	65.7	NE
(12) Tendency toward cutaneous infection	65.3	9.4*
(13) Cheilitis	56.9	12.7*
(14) Orbital darkening	53.4	7.3*
(15) Ichthyosis and/or keratosis pilaris	52.8	8.7*
(16) Early age of onset	48.1	-
up to 6 months	75.9	-
up to 3 years	82.9	-
up to 5 years	24.5	11.3*
(17) Recurrent conjunctivitis	23.1	2.0*
(18) Nipple eczema	20.8	4.0*
(19) Pityriasis alba	14.3	NE
(20) Anterior subcapsular cataracts	0.0	NE
(21) Keratoconus	0.0	NE

NE = No examination. *p < 0.001. For patient results, 100% = 481 patients, unless indicated otherwise.
 † 100% = 404 patients.
 ‡ 100% = 286 patients.
 § 100% = 323 patients.

보다 간단한 진단기준!

United kingdom working party, 1994

Table 1. UKWP criteria for AD in children

UKWP criteria for AD in children	
sensitive	Must have:
	• An itchy skin condition in the last 12 months
specific	Plus three or more of:
	• Onset below age 2* • History of flexural involvement • History of a generally dry skin • Personal history of other atopic disease† • Visible flexural dermatitis as per photographic protocol

Br J Dermatol. 1994 Sep;131(3):383-96

감별진단

- 움: 겨드랑이, 사타구니, 손목, burrow, 밤에 특히 심한 가려움증
- 지루피부염: 두피, 귀 뒤, 노란 지루성 인설, 생후 6개월 이내
- 접촉피부염: 특정 접촉부위 반복
- 어린선: 어릴 때부터, 주로 팔뚝, 전완, 염증성 병변은 드묾.
- 건선: 비교적 뚜렷한 경계, 하얀 인설, 발병 연령
- 광과민성 피부염: 햇빛 노출 부위



〈그림. 연령별 아토피피부염 증상〉

보건복지부 대한의학회

소아기

- 얼굴은 오히려 덜 침범
- 팔오금, 오금, 목 같이 접히는 부위에 뚜렷한 병변
- 건조한 형태

유아기:

- 뺨이나 이마, 머리
- 몸통이 거칠고 건조
- 팔다리는 접히는 부위보다는 팔다리의 바깥쪽
- 진물이나 가피(딱지) 형태의 급성 병변의 양상

성인기

- 오랫동안 굳어 피부가 두껍게 보이는 현상(태선화)
- 접히는 부위뿐 아니라 얼굴이나 손도 흔히 침범

① 유아기 ② 소아기 ③ 청소년/성인기

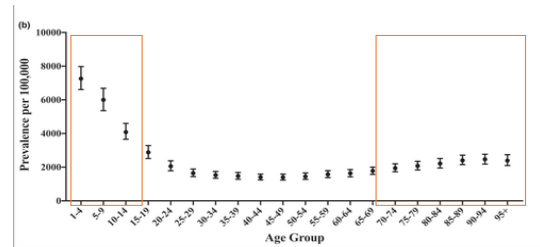
Global burden of Disease

: Comprehensive global study—analysing 286 causes of death, 369 diseases and injuries, and 87 risk factors in 204 countries and territories

The Global Burden of Disease (GBD) Study

Atopic Dermatitis

: **highest disease burden among skin diseases** as measured by disability-adjusted life-years (DALYs)



2012~2017년 아토피 진료실인원 현황

구분	아토피 진료실인원(명)						12년 대비 17년 증가율
	2012년	2013년	2014년	2015년	2016년	2017년	
계	995,558	1,008,823	977,761	950,518	954,252	932,483	-6.3%
19세 이하	659,151	655,077	609,918	576,272	556,818	526,538	-20.1%
20세 이상	336,407	353,746	367,843	374,246	397,434	405,945	20.7%

[표-2] 2012~2017년 아토피 인구10만명 당 진료실인원 현황

구분	아토피 인구10만명 당 진료실인원 (명)						12년 대비 17년 증가율
	2012년	2013년	2014년	2015년	2016년	2017년	
계	2,005	2,018	1,943	1,883	1,880	1,831	-8.7%
19세 이하	6,121	6,215	5,921	5,743	5,683	5,529	-9.7%
20세 이상	865	897	919	925	970	980	13.3%

※ 국민건강보험공단 제출자료, 청춘속의원실 재구성

Clinical phenotypes of AD

sana

Morphologic AD phenotypes

- Nummular or discoid dermatitis
- Prurigo nodularis
- Erythroderma
- Lichenified dermatitis
- Follicular/papular dermatitis
- Dyshidrosis or Pompholyx



G Girolomoni. Ther Adv Chronic Dis 2021, 12: 1-20

JOURNAL OF DERMATOLOGICAL TREATMENT
2022, VOL. 33, NO. 4, 2397-2399
<https://doi.org/10.1080/10944665.2021.1966356>Taylor & Francis
Taylor & Francis Group

LETTER TO THE EDITOR

The atopic dermatitis spectrum disorder. Recognizing the clinical heterogeneity in patients with atopic related skin conditions in order to improve therapeutic decision-making and outcomes: an expert panel consensus statement

Table 1. Example of conditions included in the atopic dermatitis spectrum.

Chronic hand eczema (excluding contact dermatitis)

Nummular eczema

Follicular eczema

Lichenoid eczema

Dyshidrosis

Prurigo nodularis

Lichen simplex chronicus

Nipple eczema

Asteatotic eczema

Gestational eczema

Eczema of older adults or atopic dermatitis of the elderly (excluding mycosis fungoides)

Eyelid dermatitis (excluding contact dermatitis)

The list is not comprehensive and may include other conditions.

Table 2. Atopic dermatitis consensus statements.

- Atopic dermatitis (AD) is a condition with varied clinical presentations and heterogeneous phenotypes. There is currently no gold standard test or biologic marker that can be used for diagnosis. In reality, AD exists as a spectrum in which seemingly distinct dermatologic disorders can present as a manifestation of atopic dermatitis.
- While disorders such as prurigo nodularis, hand dermatitis, and others may be distinct entities, the underlying etiology for many of these is atopic dermatitis.
- AIM statement: This consensus group aims to recognize the diversity of AD presentations across seemingly separate phenotypes and propose to re-categorize them as belonging to the AD spectrum disorder.
- Diseases often exist in a spectrum, some of which are already officially recognized as such in ICD-10 (e.g. autism spectrum disorder).
- AD spectrum manifests in many different ways. Within this AD spectrum disorder, many entities are related on several different domains – such as histology, associated disorders, response to therapy, and others.
- Some examples of entities that can be considered within the AD-spectrum include: prurigo nodularis, chronic hand eczema (excluding contact dermatitis), lichen simplex chronicus, nummular eczema, follicular eczema, lichenoid eczema, dyshidrosis, nipple eczema, asteatotic eczema, gestational eczema, eczema of older adults (excluding mycosis fungoides), eyelid dermatitis (excluding contact dermatitis).
- The extent of overlap among these conditions includes, but is not limited to, clinical overlap, epidemiologic overlap, histologic overlap, comorbidity overlap, treatment response overlap, and pathophysiologic/immunologic overlap. Conditions need not overlap in every respect to be considered part of the AD spectrum.
- Recognition of AD-spectrum disorder as a valid categorization will lead to timely access to AD- specific treatment, support and improved patient outcomes.

Atopic dermatitis spectrum disorder

: 아토피피부염이 기저질환일 수 있으며, 아토피 피부염 치료제가 효과적일 수 있는 질환들

Treatment of AD

sana

(a) Treatment of atopic dermatitis: adult

- For every grade, *additional* therapeutic options are given
- Add antiseptics / antibiotics in cases of superinfection
- Consider compliance and diagnosis, if therapy has no effect
- Refer to full text for restrictions, especially for treatment marked with ¹
- Licensed indication are marked with ², off-label treatment options are marked with ³

SEVERE:
SCORAD >50 / or
persistent eczema

Hospitalization;
short course of cyclosporin A^{1,2}, dupilumab²,
short course of oral glucocorticosteroids^{1,2},
longer course of systemic immunosuppression: methotrexate³,
azathioprin³, mycophenolate mofetil³, PUVA¹; alitretinoin^{1,3}

MODERATE:
SCORAD 25-50 / or
recurrent eczema

Proactive therapy with topical tacrolimus² or class II or class III
topical glucocorticosteroids³, wet wrap therapy, UV therapy (UVB
311 nm, medium dose UVA1),
psychosomatic counseling,
climate therapy

MILD:
SCORAD <25 / or
transient eczema

Reactive therapy with topical glucocorticosteroids class II² or
depending on local cofactors:
topical calcineurin inhibitors², antiseptics incl. silver²,
silver coated textiles¹
topical crisaborole³

BASELINE
Basic therapy

Educational programmes,
emollients, bath oils,
avoidance of clinically relevant allergens
(encasings, if diagnosed by allergy tests)

A Wollenberg, *J Eur Acad Dermatol Venereol* 2020, 34(12): 2717-2744

Treatment of AD

sana

(b) Treatment of atopic dermatitis: children

- For every grade, *additional* therapeutic options are given
- Add antiseptics / antibiotics in cases of superinfection
- Consider compliance and diagnosis, if therapy has no effect
- Refer to full text for restrictions, especially for treatment marked with ¹
- Licensed indication are marked with ², off-label treatment options are marked with ³

SEVERE:
SCORAD >50 / or
persistent eczema

Hospitalization;
dupilumab^{1,2};
course of systemic immunosuppression: cyclosporin A³,
methotrexate³, azathioprin³,
mycophenolate mofetil^{1,3}

MODERATE:
SCORAD 25-50 / or
recurrent eczema

Proactive therapy with topical tacrolimus² or class II or class III
topical glucocorticosteroids³, wet wrap therapy,
UV therapy¹ (UVB 311 nm),
psychosomatic counseling,
climate therapy

MILD:
SCORAD <25 / or
transient eczema

Reactive therapy with topical glucocorticosteroids class II² or
depending on local cofactors:
topical calcineurin inhibitors², antiseptics incl. silver²,
silver coated textiles¹
topical crisaborole³

BASELINE
Basic therapy

Educational programmes,
emollients, bath oils,
avoidance of clinically relevant allergens
(encasings, if diagnosed by allergy tests)

A Wollenberg, *J Eur Acad Dermatol Venereol* 2020, 34(12): 2717-2744

Cyclosporin

- Calcineurin inhibitor
- **First choice of systemic anti-inflammatory drugs**
- **Side effects**
 - Acute and chronic nephrotoxicity, hypertension, infections, gingival hyperplasia, elevated blood lipids, liver enzymes and bilirubin
 - Dose dependent and observed more frequently in adults than in children
 - Close monitoring of serum creatinine, blood pressure and protein in the urine is obligatory
- Start with 3 mg/kg/day and raised up to 5 mg/kg/day
- Concomitant topical treatment with TCI or TCS is recommended

Other systemic anti-inflammatory drugs

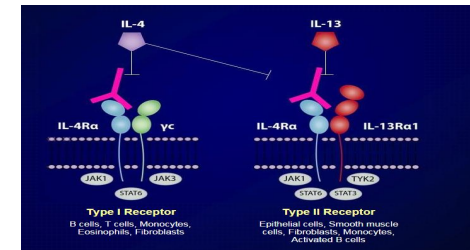
- Systemic corticosteroids
- Methotrexate
- Azathioprine
- MMF

Phototherapy

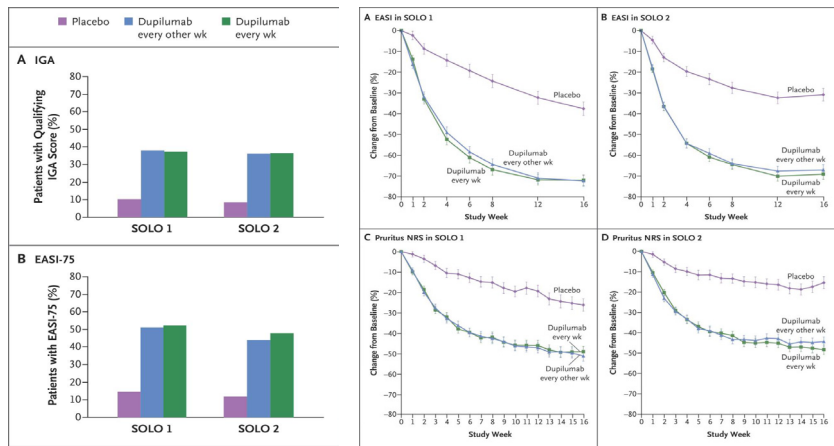
- Narrow band UVB
 - Suppress immune response in the skin
 - Reduce microbial colonization
 - Combination of UV light with TCI or cyclosporin is not recommended

Dupilumab

- Fully-human, high affinity (KD=30 pM) monoclonal antibody against the alpha subunit of the interleukin 4 receptor (IL-4R)
- IgG4 isotype
- Blocks action of IL-4 and IL-13 at Type I and II receptors
- No evidence of antibody-dependent, complement- or cell-mediated cytotoxicity
- Route of administration: subcutaneous

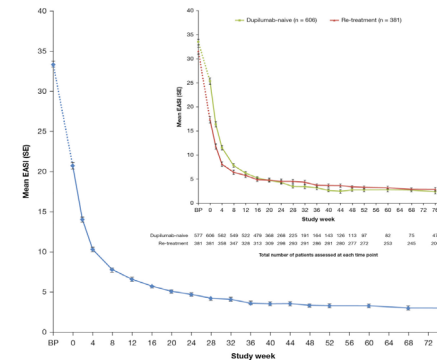


N Engl J Med. 2016 Dec 15;375(24):2335-2348
N Engl J Med. 2014 Jul 10;371(2):130-9



Phase 3 trials, *N Engl J Med.* 2016 Dec 15;375(24):2335-2348

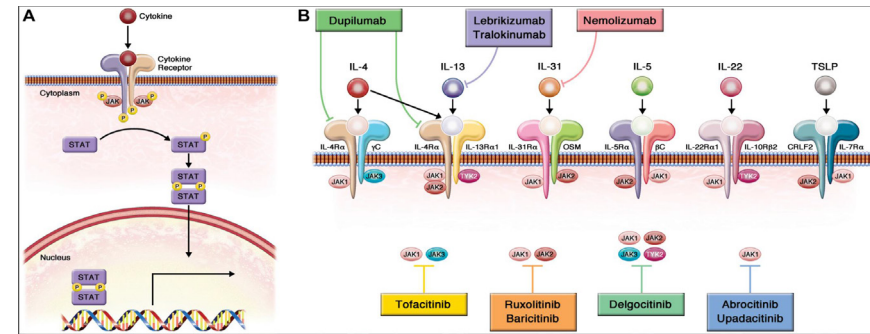
Dupilumab shows long-term safety and efficacy in patients with moderate to severe atopic dermatitis



J Am Acad Dermatol. 2020 Feb;82(2):377-388

JAK inhibitor

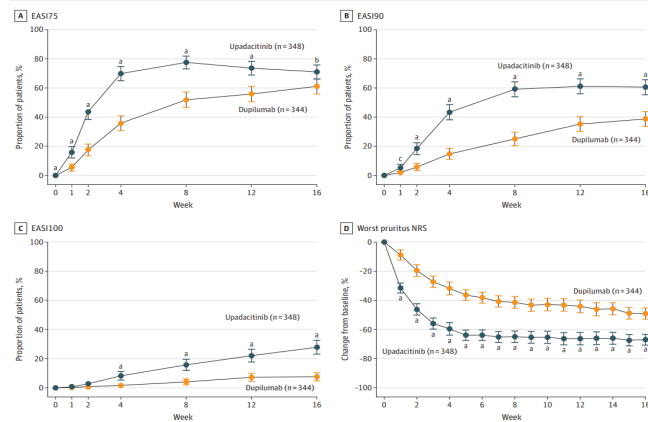
- Baricitinib: 올루미언트 (Olmiant®, Lilly)
- Upadacitinib: 린보크 (Rinvoq®, AbbVie)
- Abrocitinib: 시빈코 (CIBINQO®, Pfizer)



J Allergy Clin Immunol. 2021 Oct;148(4):927-940

692 patients

Figure 2. Efficacy Over Time



Dupilumab/JAK inhibitor 보험기준

- 3년 이상 증상이 지속되는 성인(만 18세 이상)
- 국소치료제 4주 이상 /전신 면역억제제 (Cyclosporine 또는 Methotrexate)를 3개월 이상 치료하였음에도 반응 50%이상 감소)이 없거나 부작용 등으로 사용할 수 없는 경우
- dupilumab 약제 투여시작 전 EASI 23 이상

6세 이상 18세 미만 중등~중증 소아 청소년 아토피피부염 - 비보험

Topical corticosteroids (TCS)

- Topical corticosteroids
 - Still the **first-line anti-inflammatory treatment option in AD.**
 - The choice of the TCS depends on the patient's age, disease severity and location of AD lesions.
 - For routine treatment of flares, once-daily application of a potent TCS is sufficient, usually for 3–5 days.
 - **The most constructive way to use TCS and avoid steroid-related side-effects is not to spare them during acute flares, but through early TCS intervention combined with consequent baseline emollient skincare to stabilize the disease.**
 - Side effects
 - Atrophy, striae, purpura, telangiectasia, hypertrichosis, acne-like rashes

A Wollenberg. *J Eur Acad Dermatol Venereol* 2020, 34(12): 2717-2744!!퍼센트!!
!!제형!!

표 27-1 국소스테로이드의 강도

강도(Potency)	화학명(Generic name)	제형(Formulation)
Class 1 (매우 강한 제제)	Betamethasone dipropionate 0.05%	Ointment
	Clobetasol propionate 0.05%	Cream, lotion, ointment, solution
	Halobetasol propionate 0.05%	Cream, ointment
	Diflurasone diacetate 0.05%	Ointment
Class 2 (강한 제제)	Betamethasone dipropionate 0.05%	Ointment, cream
	Mometasone furoate 0.1%	Ointment
	Fluocinonide 0.05%	Cream, gel, solution
	Diflurasone diacetate 0.05%	Ointment
	Desoximetasone 0.25%	Cream, ointment
	Desoximetasone 0.05%	Gel
Class 3 (강한 제제)	Amcinonide 0.1%	Cream
	Betamethasone dipropionate 0.05%	Cream
	Betamethasone valerate 0.1%	Ointment, solution
	Fluocisone propionate 0.005%	Ointment
	Diflurasone diacetate 0.05%	Cream
Class 4 (중등도 제제)	Mometasone furoate 0.1%	Cream, lotion
	Methylprednisolone aceponate 0.1%	Cream, lotion, ointment
	Triamcinolone acetonide 0.1%	Ointment
	Betamethasone valerate 0.12%	Foam
	Fluocinolone acetonide 0.025%	Ointment
	Hydrocortisone valerate 0.2%	Ointment
	Prednicarbate 0.25%	Ointment
Class 5 (중등도 제제)	Fluocisone propionate 0.05%	Cream
	Betamethasone dipropionate 0.05%	Lotion
	Triamcinolone acetonide 0.1%	Cream
	Hydrocortisone butyrate 0.1%	Cream, lotion
	Hydrocortisone valerate 0.2%	Cream
	Fluocinolone acetonide 0.025%	Cream
	Betamethasone valerate 0.05%	Cream, lotion, solution
	Prednicarbate 0.25%	
Class 6 (약한 제제)	Alclometasone dipropionate 0.05%	Cream, lotion
	Desonide 0.05%	Cream, lotion
	Triamcinolone acetonide 0.025%	Cream
Class 7 (약한 제제)	기타 hydrocortisone, dexamethasone, flunethasone, prednisolone, methylprednisolone 제제	

피부과학 6판

표 27-1 국소스테로이드의 강도

강도(Potency)	화학명(Generic name)	제형(Formulation)	
Class 1 (매우 강한 제제)	Betamethasone dipropionate 0.05%	Ointment	도모호론, 베타베이트 디푸코
	Clobetasol propionate 0.05%	Cream, lotion, ointment, solution	
	Halobetasol propionate 0.05%	Cream, ointment	
	Diflurasone diacetate 0.05%	Ointment	
Class 2 (강한 제제)	Betamethasone dipropionate 0.05%	Ointment, cream	실크론지 에로폼 연고
	Mometasone furoate 0.1%	Ointment	
	Fluocinonide 0.1%	Cream, ointment	
	Fluocinonide 0.05%	Cream, gel, solution	
	Diflurasone diacetate 0.05%	Ointment	
	Desoximetasone 0.25%	Cream, ointment	
Class 3 (강한 제제)	Amcinonide 0.1%	Cream	에스파손 로션, 에스파손겔, 데속시원겔, 데타손 로션, 연고
	Betamethasone dipropionate 0.05%	Cream	
	Betamethasone valerate 0.1%	Ointment, solution	
	Fluocisone propionate 0.005%	Ointment	
	Diflurasone diacetate 0.05%	Cream	
Class 4 (중등도 제제)	Mometasone furoate 0.1%	Cream, lotion	라벤다 크림, 네오덤 크림
	Methylprednisolone aceponate 0.1%	Cream, lotion, ointment	
	Triamcinolone acetonide 0.1%	Ointment	
	Betamethasone valerate 0.12%	Foam	
	Fluocinolone acetonide 0.025%	Ointment	
	Hydrocortisone valerate 0.2%	Ointment	
	Prednicarbate 0.25%	Ointment	
Class 5 (중등도 제제)	Fluocisone propionate 0.05%	Cream	에로폼, 모메타손, 더모타손 크림 아드반탄, 토피솔
	Betamethasone dipropionate 0.05%	Lotion	
	Triamcinolone acetonide 0.1%	Cream	
	Hydrocortisone butyrate 0.1%	Cream, lotion	
	Hydrocortisone valerate 0.2%	Cream	
	Fluocinolone acetonide 0.025%	Cream	
	Betamethasone valerate 0.05%	Cream, lotion, solution	
	Prednicarbate 0.25%		
Class 6 (약한 제제)	Alclometasone dipropionate 0.05%	Cream, lotion	리도맥스 크림 0.3%
	Desonide 0.05%	Cream, lotion	
	Triamcinolone acetonide 0.025%	Cream	
Class 7 (약한 제제)	기타 hydrocortisone, dexamethasone, flunethasone, prednisolone, methylprednisolone 제제		더마툼, 락티케어 제마지스 크림
Class 6 (약한 제제)			리도맥스 로션 0.3%
Class 7 (약한 제제)			데스오웬
Class 7 (약한 제제)			리도맥스 크림 0.15%

피부과학 6판

Proactive treatment - TCS

- Hanifin et al.
 - Fluticasone propionate 0.05%
 - 20 weeks
 - Flare 7.7배 감소
- Berth-Jones et al.
 - Fluticasone propionate 0.05% cream
 - 16 weeks
 - Recurrence-free period 2배
 - Recurrence 횟수 5.8배
- Peserico et al.
 - Methylprednisolone aceponate 0.1%
 - 16 weeks
 - No flare during the entire study period (66%)
- **No sign of skin atrophy during proactive treatment of TCS**

Br J Dermatol 2002;147:528-537
BMJ 2003;326:1367.
Br J Dermatol 2008;158:801-807
Ann Dermatol. 2012 Aug;24(3):253-60

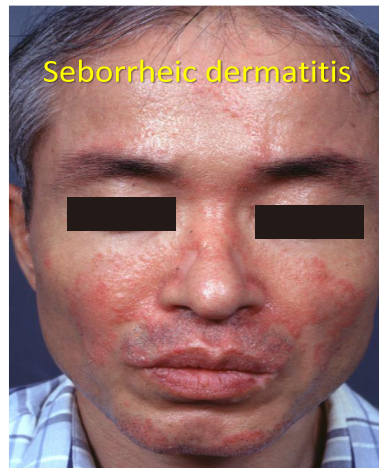
Topical calcineurin inhibitor

- Topical calcineurin inhibitor
 - Tacrolimus 0.03%, 0.1%, pimecrolimus 1.0%
 - Inhibiting synthesis of proinflammatory cytokines
 - Alternative therapy to corticosteroids, similar to a corticosteroid with moderate activity
 - Do not cause skin atrophy and protect barrier function
 - 화끈거림, 자극감 설명 필요
 - 냉찜질, 약 냉장보관 도움
 - 1~2주 내 호전
 - 특히 tacrolimus 는 oint 제형으로 사용감이 불편함을 미리 설명

Proactive treatment – TCI

- Wollenberg et al.
 - Tacrolimus ointment 0.1% twice weekly
 - 257 adults
 - Over 12 months
 - Induction phase twice daily for up to 6 weeks
 - Significantly fewer flares with tacrolimus 0.1% (56.9% vs. 29.6%), significantly reduced duration of flares (12.4% vs. 31.5%)
 - Median flare-free time was longer with proactive treatment with tacrolimus (142 days vs. 15 days)
- Thaçi et al.
 - European children study
 - Tacrolimus 0.03% twice weekly
 - Over 12 months
 - Proactive therapy reduced the number of flares, prolonged the flare-free time
- Paller et al.
 - Thrice weekly proactive use of tacrolimus 0.03%
 - 40 weeks
 - Median flare-free time 169 days vs. 43 days

Allergy 2008;63:742-750
Br J Dermatol 2008;159:1348-1356
Pediatrics 2008;122:e1210-1218



Seborrheic dermatitis

- Infantile and adult forms exist
- Characterized by erythema and greasy scaling
- Scalp, ears, face, chest, and intertriginous areas
- Etiology unknown but may be related to increased sebum secretion, abnormal sebum composition, certain drugs, or *Malassezia* yeasts
- Parkinson's disease, HIV, neuroleptic drugs



Image: Seborrheic Dermatitis (Infant) - MSD Manual Professional Edition (msdmanuals.com)

Xerotic eczema



Winter

Old aged: 장벽기능저하

Irritants (frequent bathing)

Atopy

Treatment of Eczema

- Identifying and removing the cause
- Elimination of triggering factors
 - heat, food, drug, psychogenic factors, etc
- Classic dermatological therapies
 - Moisturizing therapy
 - Topical corticosteroids, topical calcineurin inhibitor (Tacrolimus, pimecrolimus)
 - Antihistamines
 - Systemic corticosteroid, cyclosporine, methotrexate
 - Dupilumab, JAK inhibitors for atopic dermatitis

스테로이드제에 반응하지 않을 때

- 스테로이드에 대한 접촉피부염? – 점점 더 가려워지는지?
- 진균 감염? – 염증은 좋아지는데 점점 더 넓어지는지?
- 옴? – 밤에 특히 가렵지 않은지? 접하는 부위 위주로 popular lesion들이 있지는 않은지? Burrow 가 관찰되지 않는지? 함께 생활하는 가족들은 비슷한 증상이 없는지?

만성 습진에서 스테로이드제 장기간 치료가 부담될 때

- Topical calcineurin inhibitor – 피부암 발생과 연관성 떨어짐.
- Proactive treatment – 증상이 조절된 후에는 일주일에 2~3번으로 유지
- 나이와 피부 부위에 맞는 스테로이드제 고르기
- 습진의 초기에 적극적으로 사용하는 것이 오히려 스테로이드 총사용량을 줄일 수 있음.

2022 분당차병원

협력의료기관 의사 온라인 연수강좌



Session I

15:50-16:20

소아청소년기 사춘기 평가 및 성조숙증 환자 접근 관리 방법

차의과학대학교 분당차병원 소아청소년과

최윤하 교수

협력기관 의료진 대상
'온라인 연수강좌'

소아청소년기 사춘기 평가 및 성조숙증 접근 관리 방법

분당차여성병원
소아청소년과 소아내분비분과
최윤하



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CONTENTS

- ✓ 정상 사춘기 발달
- ✓ 성조숙증이란?
- ✓ 성조숙증의 원인
- ✓ 성조숙증의 진단
- ✓ 성조숙증의 치료
- ✓ 치료 경과

2



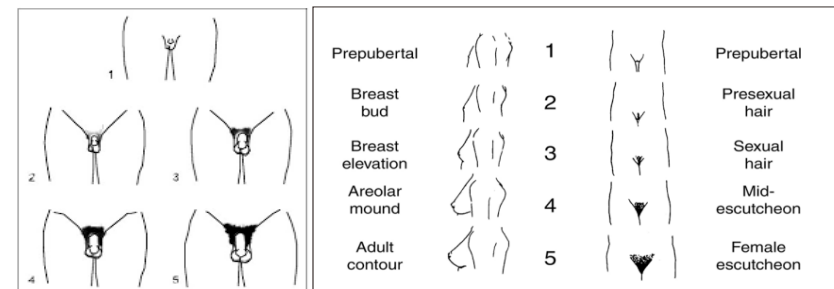
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▪ 사춘기 (Puberty)' 란?

→ 시상하부-뇌하수체 호르몬 변화에 의해
부신과 성선에서 성호르몬의 급격한 분비가 일어나,
신체 급성장이 생기고 생식능력이 완성되며
정신심리학적으로 소아에서 성인으로 이행하는
연속선상의 시기

3

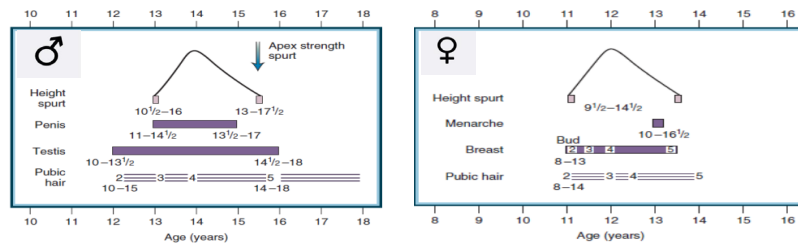
▪ 정상 사춘기 : Tanner / SMR (Sexual Maturity Rating)



Physiologic Growth and Development During Adolescence. *Pediatr Rev* (2004) 25 (6): 194-200.
Spring Pediatric Endocrinology 5th edition. Fig 16.30.

4

■ 정상 사춘기

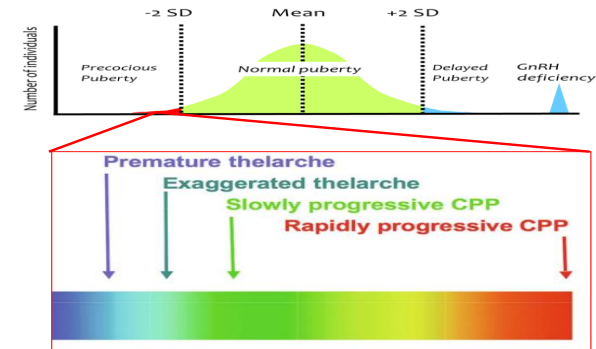


- ✓ 만 11-12세 전후(범위, 만 9-15세)
- ✓ 첫 증상 : 고환크기 증가(≥4ml), 음낭 피부 얇아짐
- ✓ 급성장 : 고환 증가 시작 약 2년 후 (SMR 4단계)

- ✓ 만 10-11세 전후(범위, 만 8-13세)
- ✓ 첫 증상 : 유방발달 시작 (비대칭 발달 가능)
- ✓ 급성장 : 유방발달 1년 후 (SMR 2-3단계)

5

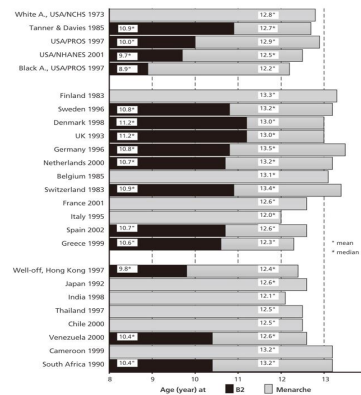
■ 성조숙증이란?



The spectrum of gonadotropin secretion in girls with normal and abnormal puberty. *Sperling Pediatric Endocrinology 5th Edition, Fig 16.31.*

6

■ 성조숙증이란?



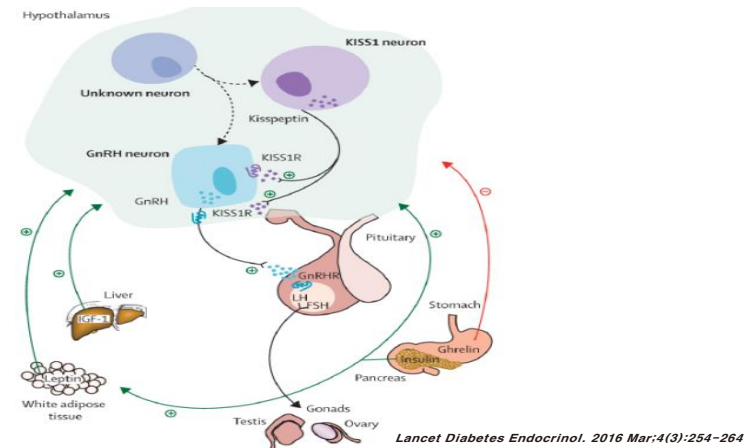
	Girls			Boys	References
	Thelarche	Pubarche	Menarche		
White, USANCHS 1973	12.8 ^a				
Tanner & Davies 1985	10.9 ^a				
USAPROS 1997	10.0 ^a				
USANHANES 2001	10.7 ^a				
Black A., USAPROS 1997	10.8 ^a				
Finland 1983	13.3 ^a				
Sweden 1996	13.2 ^a				
Denmark 1998	13.0 ^a				
UK 1993	13.2 ^a				
Germany 1996	13.0 ^a				
Netherlands, 2000	13.2 ^a				
Belgium 1985	13.1 ^a				
Switzerland 1983	13.4 ^a				
France 2001	12.6 ^a				
Italy 1995	12.0 ^a				
Spain 2002	12.8 ^a				
Greece 1999	12.9 ^a				
Well-off, Hong Kong 1997	12.4 ^a				
Japan 1992	12.6 ^a				
India 1998	12.1 ^a				
Thailand 1997	12.5 ^a				
Chile 2000	12.5 ^a				
Venezuela 2000	12.4 ^a				
Cameroon 1999	13.2 ^a				
South Africa 1990	13.2 ^a				

- ✓ 평균치의 2표준편차보다 빠른 나이에 이차성징이 발생하는 것
- ✓ 임상적으로 여아에서 만 8세 이전, 남아에서 만 9세 이전에 이차성징이 나타나는 것

Average (mean or median) ages at onset of breast development (B2) or menarche in different well-off populations around the world. *Endocr Rev 2003;24:666-693*

7

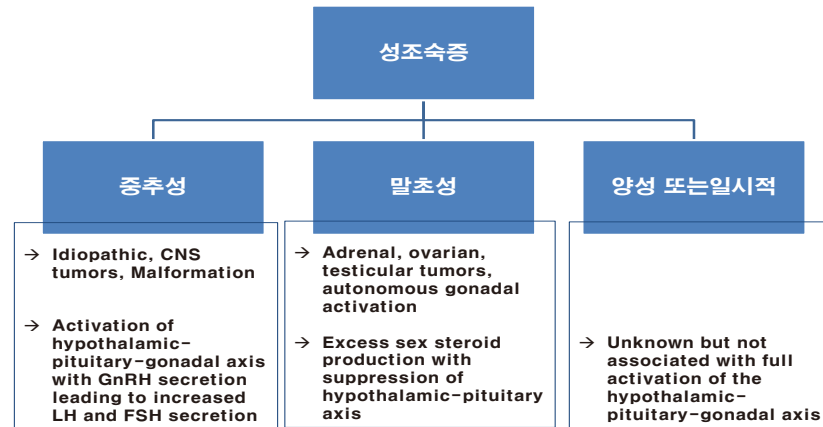
■ 시상하부-뇌하수체-생식샘 축



Lancet Diabetes Endocrinol. 2016 Mar;4(3):254-264

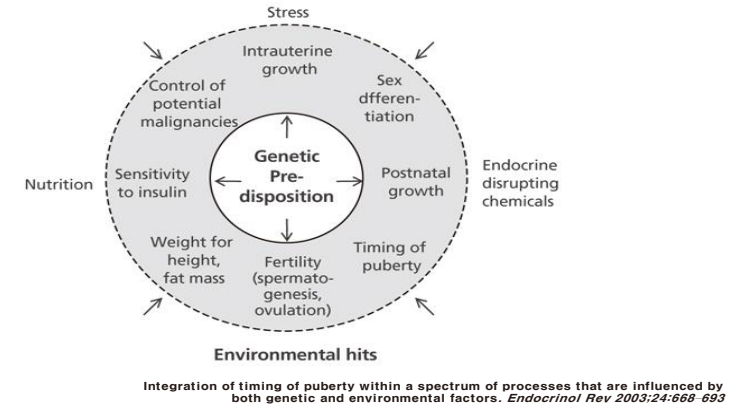
8

■ 성조숙증의 분류



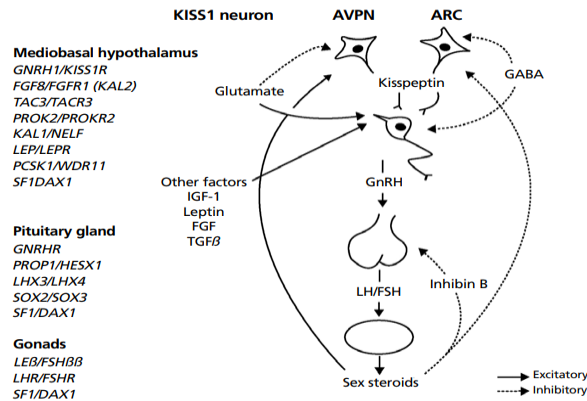
9

■ 성조숙증의 원인



10

■ 성조숙증의 원인 – 가계력, 유전자 이상



11

Mutations in several genes involved in each site have been shown to cause isolated GnRH deficiency in humans. *Curr Opin Endocrinol Diabetes Obes 2013;20:62-68*

■ 성조숙증의 원인

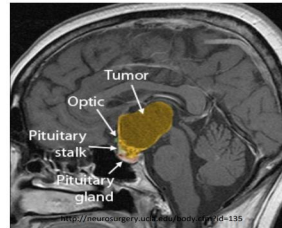
- 부당경량아 혹은 미숙아
 - 출생 전후의 좋지 않았던 건강상태에 따른 스트레스, 체지방의 급격한 증가, 영양과잉이나 영양결핍, 에너지 불균형 등
- 비만
 - 비만아에서 증가된 렙틴이 시상하부에 직접 작용하여 GnRH의 파동성 분비 자극 또는 뇌하수체 및 성선에서 성호르몬 분비를 촉진
- 스트레스와 가정환경
- 내분비 교란 물질
 - 살충제 dichlorodiphenyltrichloroethane, dichlorodiphenyldichloroethane, 코팅제로 흔히 사용되는 polybrominated biphenyls, 플라스틱의 성분인 bisphenol A와 phthalate 등
 - 여성호르몬(estrogen)이나 남성호르몬(androgen)의 수용체에 작용하거나 성호르몬 수용체와 경쟁적으로 결합하여 호르몬 작용을 방해
 - 호르몬의 운반, 대사, 조절을 교란

12

■ 성조숙증의 원인 - 구조적 원인

- 중추성 병변

- **Cranioopharyngioma**
 - Papilledema or optic atrophy
- **Hypothalamic Hamartoma**
 - m/c brain lesion
 - Ectopic neural tissue of GnRH secretory neurons



- 성선 종양

- m/c reproductive neoplasm in children
- < 5%, malignant
- Germ cell tumors, epithelial cell tumors, sex cord-stromal tumors
- Tumor markers : α -fetoprotein, hCG, CEA

- Ovarian cysts

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■ 성조숙증의 진단

• Signs

- Rapid advancement through Tanner Stages
- Spurt growth velocity
- Bone age advanced

• Hormonal criteria

- 기저 LH ≥ 0.6 mIU/mL, E2 ≥ 10 pg/mL, T ≥ 25 ng/dL
- 성호르몬 혈청 농도는 초기 중추성 성조숙증일 때 일중 변동이 심할 수 있음
- 확진 검사 : 성선자극호르몬방출호르몬 자극 검사
: peak LH ≥ 5.0 IU/L

• 성선 종양이 의심되는 경우,

human chorionic gonadotropin, α -fetoprotein 측정

• Sella MRI ix.

- 중추성 성조숙증으로 진단된 모든 남아
- 6세 미만 중추성 성조숙증 진단받은 여아
- 유방 발달이 빨리 진행되는 여아 중, 혈중 E2 ≥ 30 pg/mL

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■ 놓치면 안되는 가성 성조숙증 Signs



café-au-lait spots/ macules

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■ 놓치면 안되는 가성 성조숙증 Signs



Hyperpigmentation



Hirsutism & Acne

16

■ 놓치면 안되는 가성 성조숙증 Signs



Mucocutaneous pigmentation

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■ 치료

- 적응증

- 나이 기준 보다 어린 소아 +
- 사춘기 진행단계 Tanner stage 3-6개월마다 다음 단계로 **빠르게 진행**하는 경우
- GnRH 자극검사에서 확인
- 골연령이 실제 연령보다 2 표준편차 이상 성숙
- 예측 성인 신장 유전적 목표성인신장보다 작은 경우
- 여아에서 초경 시작 나이 9세 이전인 경우
- 정신심리적으로 미숙한 상태에서 초경을 시작하게 되는 경우

- 국내 보험기준

- 이차성징성숙도가 Tanner stage 2 이상 + 골연령이 해당 역연령보다 증가
- GnRH 자극검사에서 LH 혈중농도 기저치 2-3배 증가, 최고 농도 5 IU/L 이상
- 투여 시작 : 역연령 여아 만9세 미만/ 남아 만 10세 미만
- 투여 종료 : 역연령 여아 만 11세 364일/ 남아 12세 364일

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■ 치료 : GnRH agonist

	용량	간격	
Leprolide acetate			
Leuplin	3.75mg	4 weeks	Takeda
Leuplin	11.25mg	12 weeks	Takeda
Lorelin	3.75mg	4 weeks	Dongkuk
Luphere	3.75mg	4 weeks	Daewoong
Triptorelin acetate			
Decapeptyl	3.75mg	4 weeks	Ferring
Dipherelin	3.75mg	4 weeks	Ipsen
Dipherelin	11.25mg	12 weeks	Ipsen

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■ 치료 경과

• 임상조건

- 치료 시작 첫 한 해 동안, 3개월 간격으로 사춘기 진행 단계, 신장, 체중, 신체 비율 f/u
- 이차성징 징후 소실 여부 확인
- 성장 속도 감소 여부 확인 : 사춘기 전 성장 속도로 성장
병적 성장 감속 있을 경우, 추가 성장호르몬 병합 투여 고려

• 영상조건

- 최소 1년 간격으로 골연령 평가
- 키 표준편차점수(Height SDS) 통한 예측성인신장 변화 추정
- 골연령 증가 추이 감소 또는 정지 확인 (BA/CA < 1)

• 내분비

- Single LH determination 1-2hrs after GnRHa injection : LH < 2 IU/L

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■ 치료 종료 시점 및 종료 후 관리

- 여아에서 역연령 11.0세 전후, 골연령 12.0세 전후에 치료를 종료할 경우 가장 큰 최종키에 도달하는 것으로 보고됨
→ 일정 연령 이후에는 GnRHa 치료를 지속하더라도 의미 있는 최종키 증가가 관찰되지 않음
- 인구의 정상 연령에 가까운 시점에 초경이 시작하는 것을 목표로 하여 치료 종료를 결정하는 것이 타당
→ 치료 종료 후 수개월 내에 성호르몬이 다시 정상적으로 분비되어 사춘기 발달이 진행, 초경은 평균 16개월(12- 18개월) 이내에 나타남
- 치료 종료 후 초경까지의 성장속도는 치료종료 당시의 키, 골연령, 부모 키에 따라 다를 수 있음
→ 치료를 종료한 후에도 생식샘 기능, 체질량지수, 골밀도, 정신사회 발달, 최종키 등에 대한 지속적 인 평가가 필요
→ 통상적으로 최종키에 도달할 때까지, 그리고 완성된 생식 기능이 확인될 때까지(여아의 경우 생리가 시작하여 규칙적인 주기가 관찰될 때까지) 정기적인 추적 관찰을 시행

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- 사춘기 지연 치료로 키를 키울 수 있다?
- 사춘기 지연 치료는 키를 안 크게 한다?
- 치아 발달과 성조숙증이 연관이 있다?
- 두유가 성조숙증을 유발한다? / 우유차가 초경을 늦춘다?
- 비만한 아이들이 성조숙증이 잘 온다?
- 성장호르몬 치료를 하면 사춘기가 빨리 온다?

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■ Take Home Message

- ✓ 성조숙증 치료 목적을 신중히 고려하여 GnRHa 요법 적응증에 합당한 환자를 선택해야 하며, 최종 성인예측 키와 정신심리적 유익한 효과가 예상되는 경우에 한하여 치료를 진행
- ✓ 중추성 성조숙증의 진단 및 관리를 위한 국내 가이드라인이 확립되어 있으나 최근 급증하고 있는 성조숙증 유병률을 고려하여 진단, 치료 및 모니터링 지침과 관련하여 추가적인 업데이트 필요

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경청해 주셔서 감사합니다



2022 분당차병원

협력의료기관 의사 온라인 연수강좌



Session II

16:30-17:00

개원가에서 흔히 접하는 갑상선 기능 이상 환자의 접근과 치료

차의과학대학교 분당차병원 내분비내과

송영신 교수

개원가에서 흔히 접하는 갑상선기능이상 환자의 접근과 치료

차의과학대학교 분당차병원 내분비대사내과
송영신



Diagnosis of Hypothyroidism

Case 1

- 50/F, fatigue, weight gain (9kg/year), hoarseness, cold intolerance
- P/E of thyroid gland: slightly enlarged, firm, not tender

T3 (Total)	73	87-184 ng/dl
Free T4	0.63	0.70-1.80 ng/dl
TSH	45.4	0.4-4.1 uIU/ml

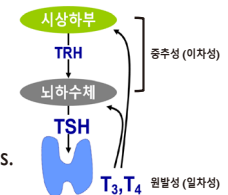
- Thyroid function status?
- Further tests?

Causes of hypothyroidism

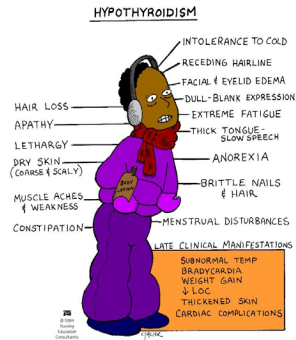
- **Primary:** **↓ Free T4 & ↑ TSH**
 - Autoimmune (Hashimoto's thyroiditis) – m/c
 - Iatrogenic, drugs, congenital, iodine deficiency, infiltrative ds.

- **Transient**
 - Painless/postpartum thyroiditis, subacute thyroiditis

- **Central (secondary, tertiary):** **↓ Free T4 & → or ↓ TSH**
 - Brain tumors, pituitary surgery or irradiation, hemorrhage, infection



Symptoms and signs of hypothyroidism



- **General:** Fatigue, Weight gain, Cold intolerance
- **Dermatological:** Dry skin and hair, Myxedema
- **Musculoskeletal:** Stiffness, Muscle aches, ↓ DTR
- **Cardiovascular:** Bradycardia, Pericardial effusion, CHF
- **Metabolic:** ↓ Basal metabolic rate, ↑ Cholesterol, ↑ TG
- **Gastrointestinal:** Constipation, Ileus
- **Neuropsychological:** Cognitive dysfunction, Depression
- **Hematopoietic:** ↓ Erythropoiesis, Anemia
- **Reproductive:** Hypermenorrhea, Infertility, ↑ Prolactin

Primary hypothyroidism: Hashimoto's thyroiditis

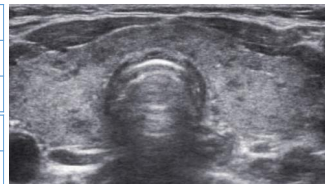
= Chronic lymphocytic thyroiditis, chronic autoimmune thyroiditis

- The most common cause of hypothyroidism in iodine-sufficient areas of the world
- Female > Male
- Thyroid goiter
- Thyroid cell destruction by both humoral and cellular immune responses
- **Autoantibodies:** thyroid peroxidase Ab (anti-TPO, >90%), anti-thyroglobulin Ab (Tg Ab, 50-60%), TSH receptor Ab (TSH-R-blocking, 10%)
- Hashitoxicosis: a transient hyperthyroidism caused by inflammation associated with HT

Case I

- 50/F, fatigue, weight gain (9kg/year), hoarseness, cold intolerance
- P/E of thyroid gland: slightly enlarged, firm, not tender

T3	73	87-184 ng/dl
Free T4	0.63	0.70-1.80 ng/dl
TSH	45.4	0.4-4.1 uIU/ml
Anti-TPO	179	0-34 IU/ml
Thyroglobulin Ab	349	0-151 IU/ml

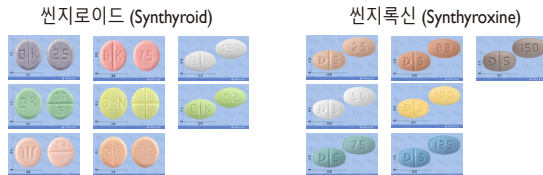


➤ Diagnosis?

Treatment of Hypothyroidism

Synthetic thyroid hormones

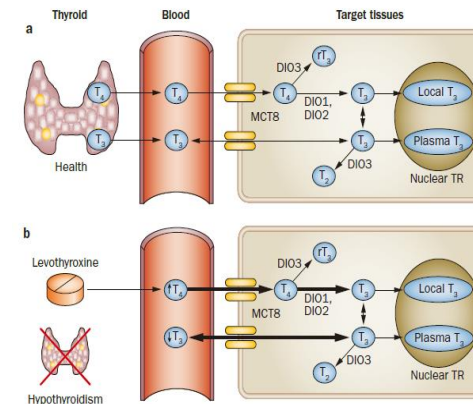
- **Levothyroxine (LT4)**: Golden standard



- **Liothyronine (T3)**: short half-life, before RAI or I-scan
- **Comthyroid (T3 12.5 ug + T4 50 ug)**:
 - Insufficient evidence to support the routine use of a combination of T4 and T3 therapy
 - Candidates: patients who not felt well on T4 monotherapy (thyroidectomy, RAI, low T3)



Thyroid hormone production and metabolism



- T4 80 ~ 100 µg/day
: All T4 is produced in the thyroid
- T3 30 ~ 40 µg/day
: Most T3 (80%) is produced by extrathyroidal deiodination of T4

Nat. Rev. Endocrinol. 2014;10:164-174

Levothyroxine (LT4)

- **Long half-life** of LT4 (around 7 days) → taking **once a day**
- LT4 should be **taken on an empty stomach** with water.
→ 30 to 60 minutes before breakfast or at bedtime 4 hours after dinner
- LT4 **should not be taken with other meds** (antacids, calcium, iron) or drinks (coffee, milk) that interfere with its absorption.
- Peak levels of fT4 is about 4 hours after taking LT4.
→ **On the day of the TFT test, take LT4 after the test.**

Treatment

- **Goals of therapy**
 - Amelioration of symptoms
 - Normalization of serum TSH (In case of central hypothyroidism, serum T4)
- **Dose and monitoring**
 - <65 years of age & cardiovascular disease (-): 1.6µg/kg/day (athyretic patients)
 - ≥65 years of age or cardiovascular disease (+): **Start with a dose of ≤25~50 µg/day and gradually increase the dose**
 - **TSH reaches a steady state about 6 weeks** after initiation of treatment or dose adjustment. → **TFT follow-up at 4 ~ 8 weeks**

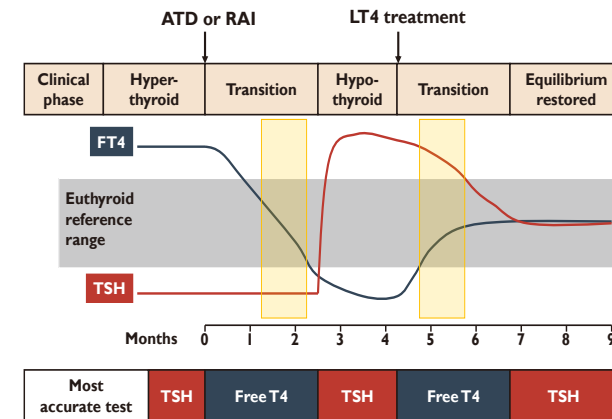
Case 2

- 56/F, Hypothyroidism treated with LT4 100 µg daily

T3 (Total)	93	87-184 ng/dl
Free T4	1.21	0.70-1.80 ng/dl
TSH	13.6	0.4-4.1 uIU/ml

- Possible causes?
- Management?

Lag in TSH reset during unstable thyroid status



Case 2

- 56/F, Hypothyroidism treated with LT4 100 µg daily

T3 (Total)	93	87-184 ng/dl
Free T4	1.21	0.70-1.80 ng/dl
TSH	13.6	0.4-4.1 uIU/ml

- Possible causes?
- Management?

LT4 therapy in specific conditions

- Subclinical hypothyroidism
- Pregnancy
- Thyroid cancer after thyroidectomy

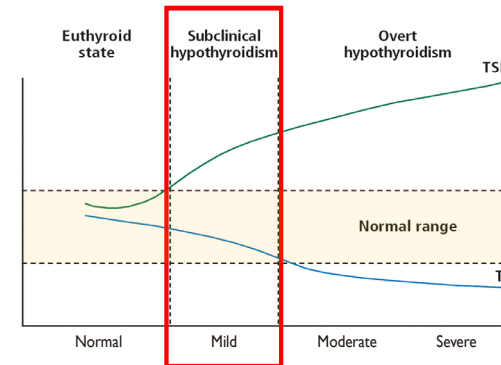
Case 3

• 56/F, Fatigue, Health checkup results

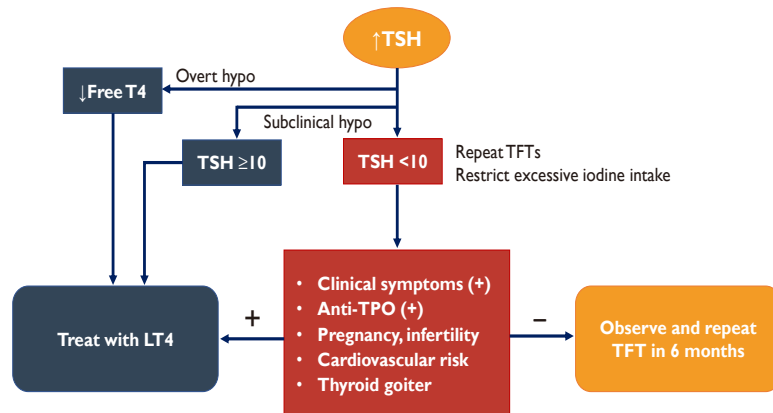
T3 (Total)	93	87-184 ng/dl
Free T4	1.21	0.70-1.80 ng/dl
TSH	13.6	0.4-4.1 uIU/ml

- Thyroid function status?
- Treatment?

Subclinical hypothyroidism



Treatment of subclinical hypothyroidism



Case 3

• 56/F, Fatigue, Health checkup results

T3 (Total)	93	87-184 ng/dl
Free T4	1.21	0.70-1.80 ng/dl
TSH	13.6	0.4-4.1 uIU/ml

- Thyroid function status?
- Treatment?

Case 4

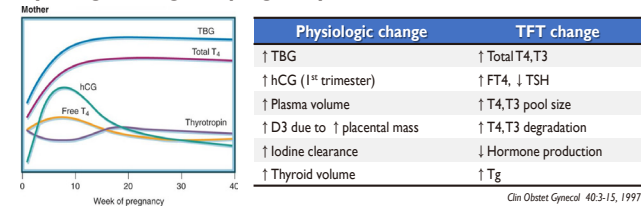
- 34/F, Pregnant, GA 6 wks

T3 (Total)	93	87-184 ng/dl
Free T4	1.21	0.70-1.80 ng/dl
TSH	13.6	0.4-4.1 uIU/ml

➤ Treatment?

Hypothyroidism in pregnancy

- Physiologic changes in pregnancy



- Reference range for TSH in pregnancy

	ATA guidelines (2011)	ETA guidelines (2014)	KTA guidelines (2014)	ATA guidelines (2017)
1 st trimester	0.1-2.5 mIU/L	≤ 2.5 mIU/L	0.1-2.5 mIU/L	Population-based or ≤ 4.0 mIU/L
2 nd trimester	0.2-3.0 mIU/L	≤ 3.0 mIU/L	0.2-3.0 mIU/L	
3 rd trimester	0.3-3.0 mIU/L	≤ 3.5 mIU/L	0.3-3.5 mIU/L	

Hypothyroidism in pregnancy

- Sources of thyroid hormone for the fetus
 - Thyroid hormone crosses the placenta, starting in 1st trimester.
 - Fetal thyroid is capable of trapping iodine by 12 weeks and can synthesize thyroxine by 14 weeks of gestation.
- Effects of overt hypothyroidism
 - Increased risk of adverse pregnancy complications & Detrimental effects on fetal neurocognitive development
 - Premature birth
 - Low birth weight
 - Pregnancy loss
 - Lower offspring IQ
 - Gestational hypertension

2017 ATA guidelines for thyroid disease during pregnancy

Recommendations for subclinical hypothyroidism in pregnancy

- Pregnant women with TSH >2.5 mU/L should be evaluated for TPO Ab status.

TPO Ab (+)	TPO Ab (-)	LT4 therapy
TSH > pregnancy-specific reference range or 4.0	TSH > 10	Recommend
TSH > 2.5	TSH > pregnancy-specific reference range or 4.0	Consider
	TSH within pregnancy-specific reference range or < 4.0	Not recommend

2017 ATA guidelines for thyroid disease during pregnancy

✓ 미국갑상선학회(ATA) 및 대한갑상선학회(KTA) 임신관련 갑상선질환 진료권고안 개정위원회 구성 및 update 예정

Case 4

- 34/F, Pregnant, GA 6 wks

T3 (Total)	93	87-184 ng/dl
Free T4	1.21	0.70-1.80 ng/dl
TSH	13.6	0.4-4.1 uIU/ml

- Thyroid function status?
- Treatment?

Case 5

- 68/F, on LT4 150 µg daily; PTC, gross ETE+, N1a (4/10) pT3bN1aM0
 - s/p Total thyroidectomy, s/p High-dose RAI (10YA)
- Underlying atrial fibrillation, osteopenia

T3 (Total)	160	87-184 ng/dl
Free T4	1.73	0.70-1.80 ng/dl
TSH	<0.05	0.4-4.1 uIU/ml
Thyroglobulin	<2	0-34 IU/ml
Thyroglobulin Ab	<20	0-151 IU/ml

- Neck USG: No evidence of recurrence

- Management?

LT4 therapy for TC patients after thyroidectomy

- Goal of LT4 therapy for differentiated thyroid cancer(DTC) patients
 - Replacement of deficient thyroid hormone
 - Reducing the risk of recurrence by TSH suppression
- Initial TSH suppression → Assess the risk stratification (KTA, ATA guideline)

Low risk

Papillary thyroid cancer (with all of the following):

- No local or distant metastases
- R0 resection; No ETE
- No aggressive histology
- No vascular invasion
- No RAI-avid metastatic foci outside the thyroid bed
- Clinical N0 or ≤5 pathologic N1 micrometastases
- Intrathyroidal, encapsulated follicular variant of PTC
- Intrathyroidal, minimally-invasive FTC
- Intrathyroidal, PTMC, unifocal or multifocal

Indeterminate risk

Microscopic ETE; RAI-avid metastatic foci in the neck; Aggressive histology; PTC with vascular invasion; Clinical N1 or >5 pathologic N1 (<3 cm); Multifocal PTMC with ETE and BRAF^{V600E} mutated (if known)

High risk

Gross ETE; Incomplete resection; Distant metastases; Postoperative serum thyroglobulin suggestive of distant metastases; Pathologic N1 with any metastatic LN >3 cm; Widely-invasive FTC

LT4 therapy in TC patients after thyroidectomy

- TSH suppression during long-term follow-up → Assess the dynamic risk stratification
- Dynamic risk stratification: Evaluation for the response to therapy (6-18 months after surgery)
 - Excellent response: no clinical, biochemical, or structural evidence of disease
 - Biochemical incomplete response: abnormal Tg or rising anti-Tg Ab in absence of localizable disease
 - Structural incomplete response: persistent or newly identified loco-regional or distant metastases
 - Indeterminate response: nonspecific biochemical or structural findings that cannot be confidently classified as either benign or malignant
- Optimal TSH goals for individual patients must balance the potential benefit of TSH suppression with the possible harm from subclinical thyrotoxicosis (↑ of angina in patients with ischemic heart disease, ↑ risk of atrial fibrillation in older patients, and ↑ risk of osteoporosis in postmenopausal women).

✓ 대한갑상선학회 갑상선결절/분화갑상선암 진료권고안 개정위원회 구성 및 진행 중

TSH suppression therapy after thyroidectomy

Risk	Initial TSH goal, mIU/L	TSH goal during follow-up, mIU/L	
Low risk	- Undetectable Tg or Lobectomy → 0.5 ~ 2.0 - Low-Tg level → 0.1 ~ 0.5	Excellent response	0.5 ~ 2.0
		Biochemical incomplete response	0.1 ~ 0.5
		Structural incomplete response	< 0.1 ^a
		Indeterminate response	0.5 ~ 2.0
Intermediate risk	0.1 ~ 0.5	Excellent response	0.5 ~ 2.0
		Biochemical incomplete response	0.1 ~ 0.5
		Structural incomplete response	< 0.1 ^a
		Indeterminate response	0.1 ~ 0.5 ^b
High risk	< 0.1	Excellent response	0.1 ~ 0.5 ^b
		Biochemical incomplete response	0.1 ~ 0.5
		Structural incomplete response	< 0.1 ^a
		Indeterminate response	0.1 ~ 0.5 ^b

^a If TSH suppression therapy is not contraindicated.

^b Maintain for 5 years after surgery, thereafter, alleviate suppression and monitor for recurrence.

Case 5

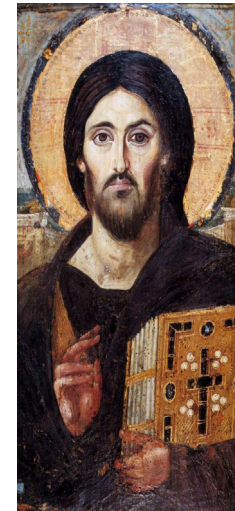
- 68/F, on LT4 150 µg daily; PTC, gross ETE+, N1a (4/10) pT3bN1aM0
 - s/p Total thyroidectomy, s/p High-dose RAI (10YA)
- Underlying atrial fibrillation, osteopenia

T3 (Total)	160	87-184 ng/dl
Free T4	1.73	0.70-1.80 ng/dl
TSH	<0.05	0.4-4.1 uIU/ml
Thyroglobulin	<2	0-34 IU/ml
Thyroglobulin Ab	<20	0-151 IU/ml

- Neck USG: No evidence of recurrence

➤ Management?

Diagnosis of Hyperthyroidism



Unknown Artist

Christ Icon

6th C

Saint Catherine's Monastery
Sinai



Bartolomeo Vivarini

15th C, Renaissance

National Gallery
Washington

Case 6

- 36/F, 3 months postpartum, fatigue, palpitation, hand tremor
- P/E of thyroid gland: slightly enlarged, firm, not tender

T3 (Total)	272	87–184 ng/dl
Free T4	3.46	0.70–1.80 ng/dl
TSH	<0.05	0.4–4.1 uIU/ml

- Thyroid function status?
- Further tests?

Classification of thyrotoxicosis

Mechanism	Diseases	Frequency
Thyrotoxicosis with Hyperthyroidism		
Abnormal stimulator	Graves' disease	82.7%
Thyroid autonomy	Toxic adenoma Toxic multinodular goiter	0.5%
Oversecretion of TSH	TSH-secreting pituitary adenoma	
Thyrotoxicosis without Hyperthyroidism		
Inflammatory disease	Painless thyroiditis Subacute thyroiditis	16.8%
Exogenous thyroid H.	Factitious (iatrogenic) Ectopic thyroid	

Cho BY. Clinical thyroidology, 4th ed. 2014

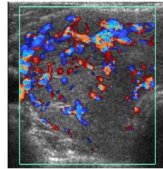
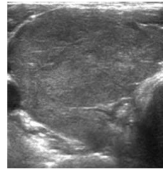
Differential diagnosis of thyrotoxicosis

	Graves' disease	Painless thyroiditis
Onset	Acute-insidious	Acute
Severity	Mild-severe	Mild
Duration	> 3 months	< 3 months
Goiter	Less firm, small-large	Firm, small
Bruit	+	-
Proptosis	+	-
T3/T4 ratio	> 20	< 20
RAI uptake	Increase	Decrease
TSH-R Ab	+	-
Vascularity	Increased	Not increased

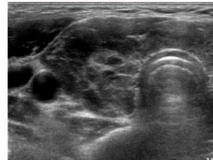
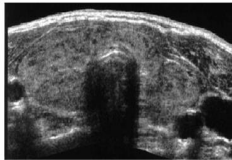
✓ 우리병원 오더명: TSH-receptor Ab, TS Ab (Thyroid Stimulating Ab)

Thyroid USG

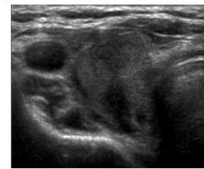
그레이브스병



무통성
산후 갑상선염



아급성 갑상선염



민현기 임상내분비학 (3판)

Diagnosis of thyrotoxicosis

- 갑상선기능 이상 확인 검사:

TSH, Free T4, (Total T3)

- 갑상선기능 이상의 원인 검색:

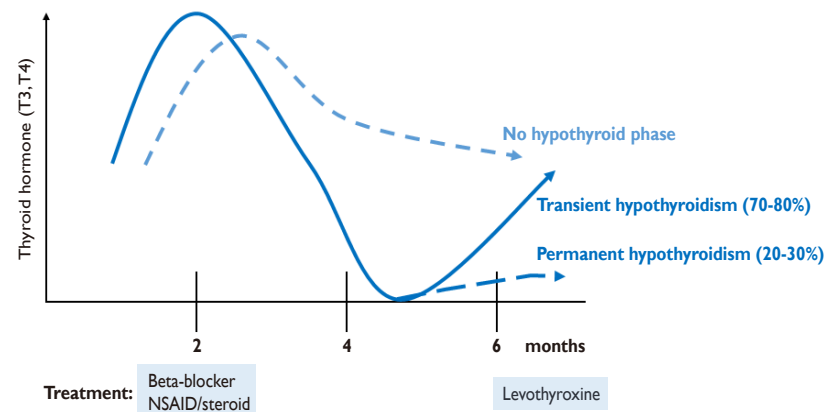
TSH-R-Ab (TSH receptor Ab, TBII, TSI), TS Ab

TPOAb (thyroperoxidase Ab, microsomal Ab)

TgAb (thyroglobulin Ab)

Scan, Doppler USG

Phases of painless/subacute thyroiditis



Case 6

- 36/F, 3 months postpartum, fatigue, palpitation, hand tremor
- P/E of thyroid gland: slightly enlarged, firm, not tender

T3 (Total)	272	87-184 ng/dl
Free T4	3.46	0.70-1.80 ng/dl
TSH	<0.05	0.4-4.1 uIU/ml
TSH-R Ab	0.23	0-1 IU/l
Anti-TPO	179	0-60 U/ml
Thyroid USG	Normal vascularity	

- Diagnosis?
- Management?

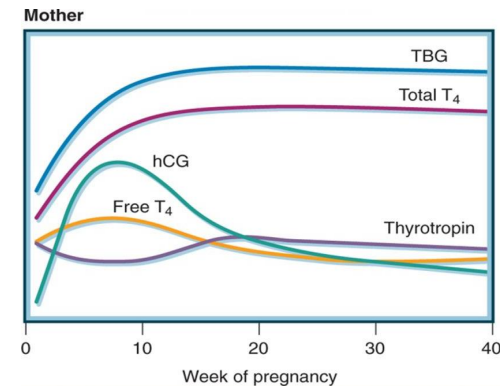
Case 7

- F/34, Pregnant (GA 8wk),
- CC) Palpitation and hyperemesis gravidum

T3 (Total)	150	87-184 ng/dl
Free T4	1.58	0.70-1.80 ng/dl
TSH	0.01	0.4-4.1 uIU/ml

- Thyroid function status?
- Further tests?

Pregnancy induced thyroid function changes



Case 7

- F/34, Pregnant (GA 8wk),
- CC) Palpitation and hyperemesis gravidum

T3 (Total)	150	87-184 ng/dl
Free T4	1.58	0.70-1.80 ng/dl
TSH	0.01	0.4-4.1 uIU/ml
TSH-RAb	0.23	0-1 IU/l
Anti-TPO	179	0-60 U/ml

- Diagnosis?
- Management?

Treatment of Hyperthyroidism

Case 8

- 36/F, 3 months postpartum, fatigue, palpitation, hand tremor
- P/E of thyroid gland: slightly enlarged, firm, not tender

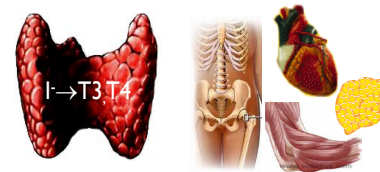
T3 (Total)	272	87-184 ng/dl
Free T4	3.46	0.70-1.80 ng/dl
TSH	<0.05	0.4-4.1 uIU/ml
TSH-R Ab	39.73	0~1 IU/l
Anti-TPO	129.8	0~60 U/ml
Thyroid USG	Increased vascularity	

- Diagnosis?
- Management?

Treatment of Graves' disease

Treatment goals for GD

- To inhibit the production of thyroid hormones
- To block the effect of the hormones on the body



Three treatment modalities of GD

1. Antithyroid drugs (ATDs)

- Blocking of hormone synthesis

2. Radioactive iodine (RAI)

- Destruction of the thyroid

3. Thyroidectomy

- Removal of the thyroid

Currently, there is no scientific evidence to support the recommendation of alternative therapies for the treatment of hyperthyroidism.

Strong recommendation, moderate-quality evidence
2016 ATA guideline for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis

Antithyroid drugs

• Methimazole (MMI) vs. Propylthiouracil (PTU)

- MMI should be used in virtually every patient who chooses ATD therapy for GD.

- Except for

- During the first trimester of pregnancy
- In the treatment of thyroid storm
- In patients with minor reactions to MMI who refuse radioactive iodine therapy or surgery.

PTU

Strong recommendation, moderate-quality evidence
2011 & 2016 ATA guideline for hyperthyroidism

- MMI has the benefit of once-a-day administration and a reduced of major side effects compared to PTU.

Antithyroid drugs

- 투약 : Methimazole 10~15 mg bid, 베타차단제 (propranolol 20~40mg 2~3회)
- 갑상선기능이 정상화되면 용량을 반으로 감량
- 1일 유지용량: PTU 25~50 mg/d, MMI 2.5~5mg/d
- 중단 기준: TFT 정상화 및 TSH-R 항체 소실



1. 항갑상선제 부작용 : 갑작스런 고열을 동반한 인후염 (무과립구증), 파로, 쇠약감, 호흡곤란, 복부 통증, 식욕상실, 가려움증, 쉽게 멎거나 멍들거나 황달 발생 등의 간기능 이상이 의심되면 즉시 투약을 중단하고 내원하도록 교육
2. 치료 경과 : 치료기간이 길고 (18개월 이상), 관해율이 35~71% 정도로 치료 종료후에도 정기적인 검사 필요함. 중증의 부작용 발생 혹은 재발시 다른 치료 (RAI, surgery) 할 수 있음을 설명
3. 금연 교육
4. 체중 증가 주의



2022 분당차병원

협력의료기관 의사 온라인 연수강좌



Session II

17:00-17:30

유방 병변의 초음파 진단과 치료 권고에 관한 A to Z

차의과학대학교 분당차병원 영상의학과

박아영 교수

유방 병변의 초음파 진단과 치료 권고에 관한 A to Z

분당차병원 영상의학과 박아영



목차

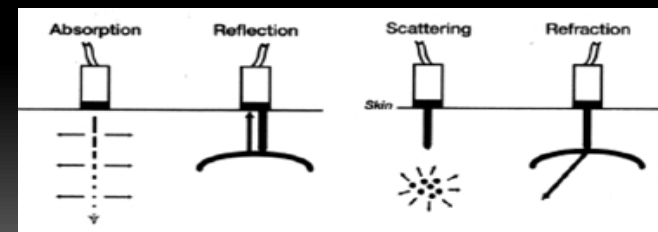
- 초음파의 basic physics
- 유방초음파의 optimal image acquisition
- BI-RADS에 기초한 유방 병변의 진단 및 치료 권고
- 초음파에서 발견되는 유방암의 다양한 얼굴
- False-negative, false-positive 줄이는 방법

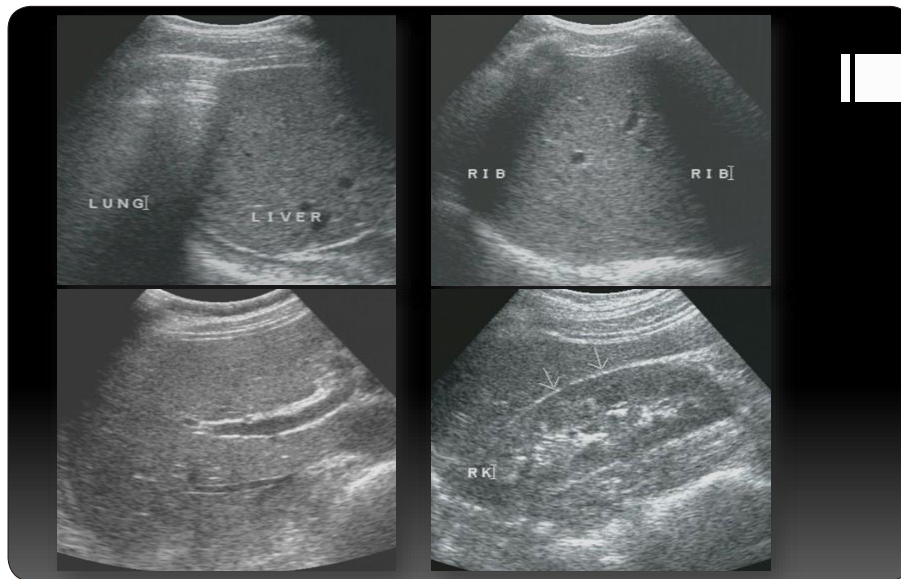
Basic physics

- 음파는 음원에서 발생한 파동에 의한 압력의 변화가 매질을 통해 전파되는 것. 매질을 이루고 있는 입자들이 압축과 팽창을 반복하면서 전파
- 초음파는 가청영역 (20-20,000 Hz) 범위를 넘어서는 주파수를 갖는 음파
- 의학용 주파수: 2-20 MHz

Basic physics

- 초음파가 체내의 연조직을 통과할 때 반사, 굴절, 흡수 및 산란이 일어나며, 이 중 반사가 진단 초음파의 기본이 되는 작용이다.

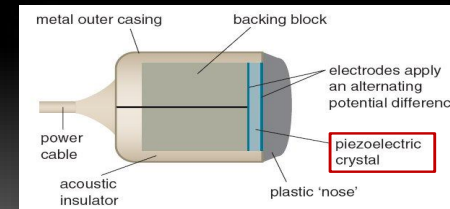




Basic physics

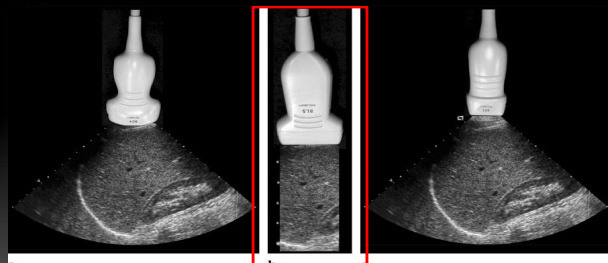
Transducer (탐촉자):

- 본체에서 발생한 전기에너지를 소리에너지로 변환하여 피사체 내로 통과시킨 후 반사되어 돌아오는 소리에너지를 다시 전기에너지로 변화하여 본체로 돌려보냄으로써 가장 핵심적인 역할



Basic physics

Transducer의 종류 - 모양



Abdominal, pelvic

Small parts

Cardiac, cranial etc.

Transducers with curvilinear (a), linear (b), vector (c) arrays along with sample image FOVs.

Basic physics

Transducer의 종류 - frequency

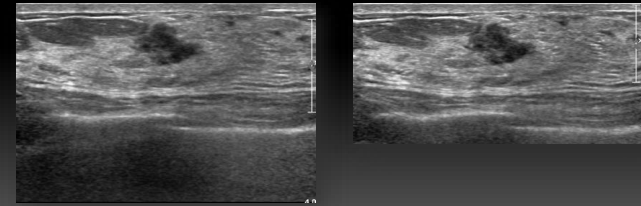
- High frequency scan (7-15 MHz)
 - High resolution, but the least amount of penetration
 - 유방, 갑상선 등의 표재성 장기
 - Linear probe
- Lower frequency scan (2-5 MHz)
 - More penetration, but poorer resolution
 - 복부나 골반 등 심부장기
 - Curved

유방초음파의 optimal image acquisition

- Depth
- Focal zone
- Gray-scale, time-gain-compensation
- Harmonic image
- Compounding image

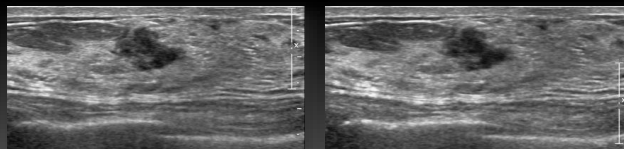
유방초음파의 optimal image acquisition

- Depth
 - 유방 두께를 고려한 적절한 depth 조정 필요.
 - 불필요하게 깊은 구조물을 포함한 영상은 resolution 저하



유방초음파의 optimal image acquisition

- Focal zone
 - 미세한 시간차를 두고 압전결정소자에 순차적으로 전압을 가함으로써 음속을 집속 (focusing)할 수 있음. 집속음속에서 단편두께가 가장 얇아지는 부분을 focus zone이라 하며, 이 부분에서 resolution이 가장 좋음. 목표물의 깊이에 맞게 focus의 위치와 수 조절 필요.



유방초음파의 optimal image acquisition

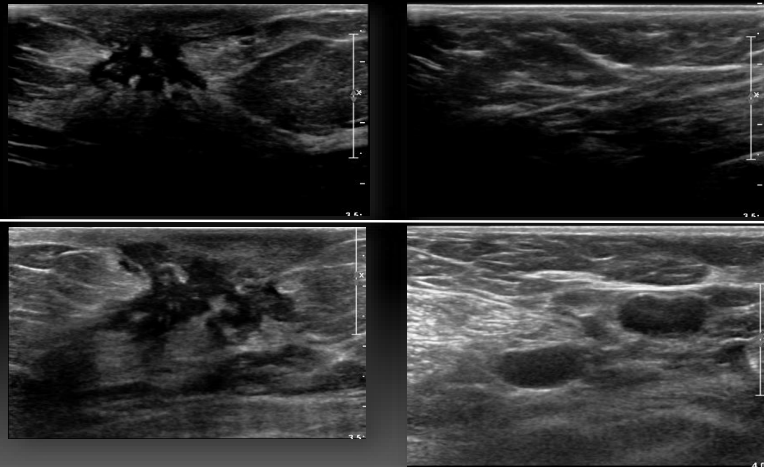
- Gray-scale
- Time-gain compensation
 - 초음파는 탐촉자에서 멀어질수록 감쇠에 의해 도달하는 초음파의 강도가 떨어지고, 돌아오는 에코의 강도도 깊은 부위일수록 약해짐. 이를 보정하기 위해 에코가 수신된 시간에 따라 신호의 증폭 정도를 설정하는 기능



Time-gain compensation off

Time-gain compensation on

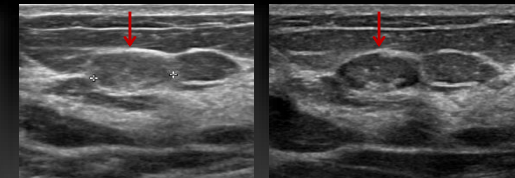
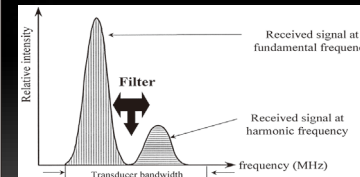
A 66-year-old female with Lt. breast IDC and suspicious ipsilateral axillary LNs



유방초음파의 optimal image acquisition

Harmonic imaging

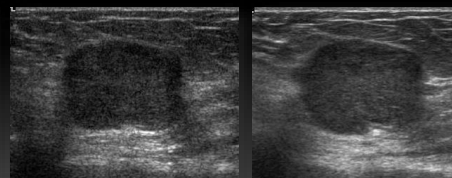
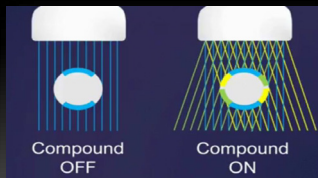
- 처음 송신된 주파수의 정수배의 주파수만 이용하여 영상을 구성
- Contrast 증가, noise 감소, 병변의 경계가 명확해짐



유방초음파의 optimal image acquisition

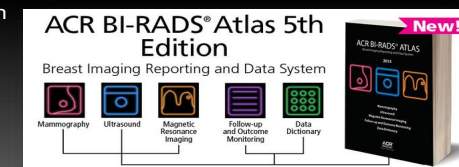
Compounding imaging

- 음속을 여러 방향으로 기울여 얻은 영상
- 병변의 경계가 명확해짐, Noise 감소



BI-RADS에 기초한 유방 병변의 진단 및 치료 권고

- BI-RADS (Breast Imaging Reporting and Data System)
- Designed to standardize reporting
- Used by medical professionals to communicate a patient's risk of developing breast cancer
- ACR BI-RADS Atlas 2013
 - Mammography, 5th Edition
 - Ultrasound, 2nd Edition
 - MRI, 2nd Edition



ULTRASOUND		
Tissue composition (screening only)	a. Homogeneous background echotexture – fat	
	b. Homogeneous background echotexture – fibroglandular	
	c. Heterogeneous background echotexture	
Masses	Shape	Oval
		Round
		Irregular
	Orientation	Parallel
		Not parallel
	Margin	Circumscribed
		Not circumscribed
		- Indistinct
		- Angular
		- Microlobulated
	Echo pattern	- Spiculated
		Anechoic
		Hyperechoic
		Complex cystic and solid
		Hypoechoic
	Posterior features	Isoechoic
		Heterogeneous
No posterior features		
Enhancement		
Shadowing		
Combined pattern		

Calcifications	Calcifications in a mass		
	Calcifications outside of a mass		
	Intraductal calcifications		
	Architectural distortion		
	Duct changes		
Associated features	Skin changes	Skin thickening	
		Skin retraction	
	Edema		
	Vascularity	Absent	
		Internal vascularity	
		Vessels in rim	
	Elasticity assessment	Soft	
		Intermediate	
		Hard	
	Special cases	Simple cyst	
Clustered microcysts			
Complicated cyst			
Mass in or on skin			
Foreign body including implants			
Lymph nodes – intramammary			
Lymph nodes – axillary			
Vascular abnormalities		AVMs (arteriovenous malformations/ pseudoaneurysms)	
		Mondor disease	
Postsurgical fluid collection			
Fat necrosis			

Table 5. Concordance Between BI-RADS® Assessment Categories and Management Recommendations.

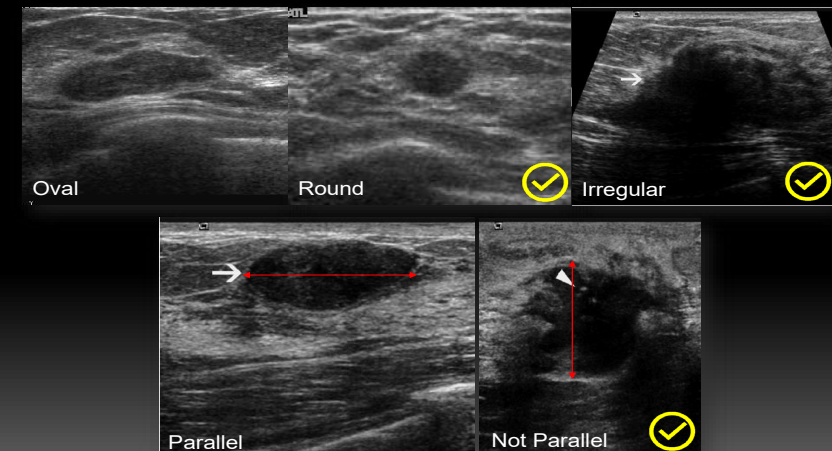
Assessment	Management	Likelihood of Cancer
Category 0: Incomplete — Need Additional Imaging Evaluation	Recall for additional imaging	N/A
Category 1: Negative	Routine screening	Essentially 0% likelihood of malignancy
Category 2: Benign	Routine screening	Essentially 0% likelihood of malignancy
Category 3: Probably Benign	Short-interval (6-month) follow-up or continued surveillance	> 0% but ≤ 2% likelihood of malignancy
Category 4: Suspicious	Tissue diagnosis	> 2% but < 95% likelihood of malignancy
Category 4A: Low suspicion for malignancy		> 2% to ≤ 10% likelihood of malignancy
Category 4B: Moderate suspicion for malignancy		> 10% to ≤ 50% likelihood of malignancy
Category 4C: High suspicion for malignancy		> 50% to < 95% likelihood of malignancy
Category 5: Highly Suggestive of Malignancy	Tissue diagnosis	≥ 95% likelihood of malignancy
Category 6: Known Biopsy-Proven Malignancy	Surgical excision when clinically appropriate	N/A

BI-RADS에 기초한 유방 병변의 진단 및 치료 권고

■ 초음파에서 양성 과 악성의 감별점

	Benign	Malignant
Shape	Oval	Round or Irregular
Orientation	Parallel	Not parallel
Margin	Circumscribed	Not circumscribed
Secondary findings	Compressible/mobile	Skin thickening, Nipple retraction, Axillary lymphadenopathy, Fixed/Hard

Masses- Shape and orientation

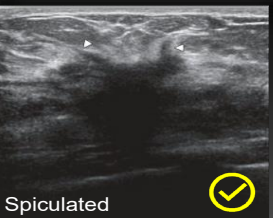
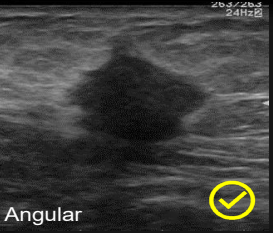
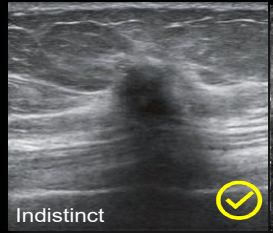


Masses- Margin

Circumscribed



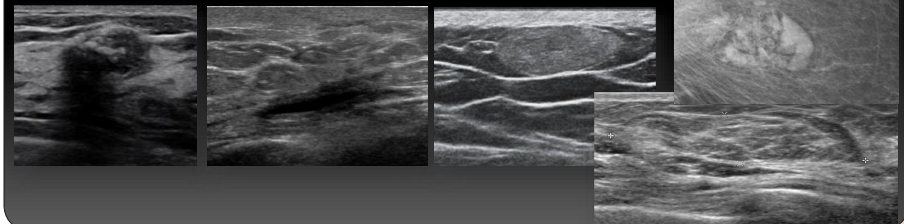
Not Circumscribed



BI-RADS에 기초한 유방 병변의 진단 및 치료 권고

BI-RADS 2

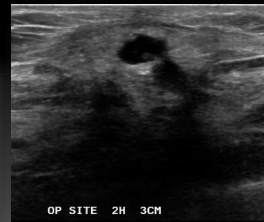
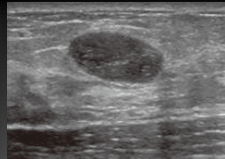
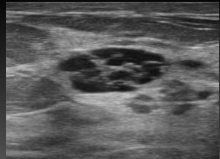
- Simple cysts, intramammary LN, postsurgical fluid collection, breast implants, complicated cysts or probable fibroadenomas without change for at least 2 or 3 years



BI-RADS에 기초한 유방 병변의 진단 및 치료 권고

BI-RADS 3

- Solid mass with a circumscribed margin, oval shape, parallel orientation
- Isolated complicated cyst
- Clustered microcysts
- Fat necrosis



BI-RADS Category 3
Probably benign

6 months follow up

Stable
6 months from initial

6 months follow up

Stable
12 months from initial

12 months follow up

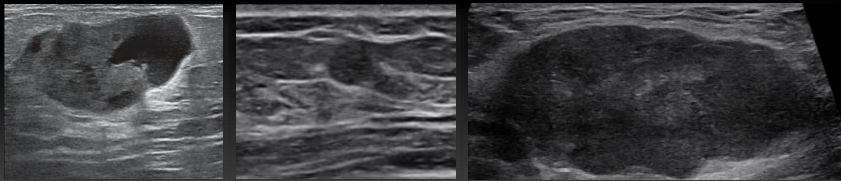
Stable
24 months from initial

Category 2 benign

BI-RADS에 기초한 유방 병변의 진단 및 치료 권고

■ BI-RADS 4

- The findings, not classic appearance of malignancy, but suspicious to justify a recommendation for biopsy



BI-RADS에 기초한 유방 병변의 진단 및 치료 권고

■ BI-RADS 4 biopsy 후

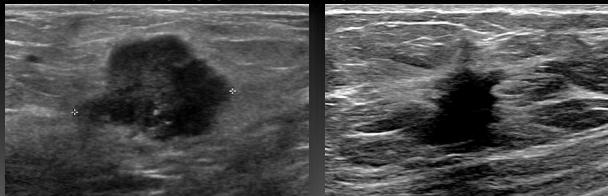
- 영상소견과 병리결과와의 일치 여부 판단 및 추후 방침 권고

	Concordant malignancy	Discordant malignancy	Concordant benign	Discordant benign	Borderline or high risk
Imaging	BI-RADS 4,5	BI-RADS 2,3	BI-RADS 2,3,4a	BI-RADS 4,5	any
Pathology	Malignant	Malignant	Benign	Benign	High-risk
Recommendation	Appropriate action	Appropriate action	F/U imaging	Repeat biopsy, surgical or vacuum-assisted	Case-by-case approach, surgical biopsy

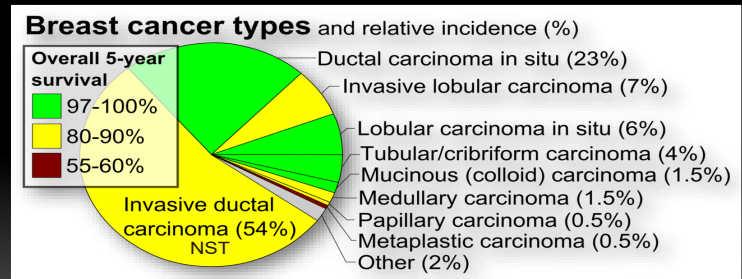
BI-RADS에 기초한 유방 병변의 진단 및 치료 권고

■ BI-RADS 5

- A high probability of malignancy (>95%)
- Previously, lesions for which 1-stage surgical treatment can be considered without biopsy
- Nowadays, imaging-guided biopsy first.



초음파에서 발견되는 유방암의 다양한 얼굴



Ultrasonography 2016;35:281-288

초음파에서 발견되는 유방암의 다양한 얼굴

- Molecular subtypes
 - Gene expression profiling
 - Immunohistochemical staining for ER, PR, HER2
 - 영상소견, 예후, 치료방법 다양

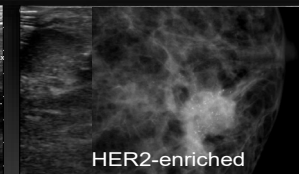
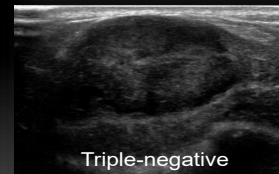
Table 1. Surrogate definitions of intrinsic subtypes of breast cancer classification from the St. Gallen Consensus 2013

Intrinsic subtype	Clinicopathologic surrogate definition						Type of therapy
	ER	PR	HER2	Ki-67	Recurrence risk ^{a)}		
Luminal A	Luminal A-like	+	+	Low <14%	Low (if available)		Endocrine therapy is often used alone. Cytotoxic therapy may be added.
Luminal B	Luminal B-like ²⁾ (HER2-negative)	+	- or low	-	High	High (if available)	Endocrine therapy for all patients, cytotoxic therapy for most.
ErbB-2 overexpression	Luminal B-like (HER2-positive)	+	Any	Over-expressed or amplified	Any	NA	Cytotoxics+anti-HER2+endocrine therapy
Basal-like	HER2-positive (non-luminal)	Absent	Absent	Over-expressed or amplified	NA	NA	Cytotoxics+anti-HER2
	Triple negative (ductal)	-	-	-	NA	NA	Cytotoxics

Ultrasonography 2016;35:281-288

Table 3. Imaging phenotypes according to the molecular subtypes

Clinical grouping	Mammography	Ultrasonography
Triple-negative	A mass with a relatively circumscribed margin without calcifications	A distinct mass with a circumscribed margin and posterior acoustic enhancement
HR (-) and HER2 (+)	Microcalcifications, branching or fine linear calcifications High suspicion for malignancy	Irregular mass with a not-circumscribed margin (circumscribed margin showing decreased possibility of HER2 type) High suspicion for malignancy
HR (+) and HER2 (-)	A mass with a poorly circumscribed margin	A mass with a poorly circumscribed margin and posterior acoustic shadowing

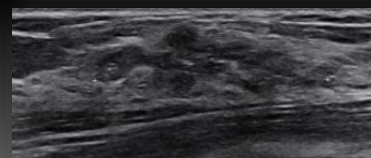
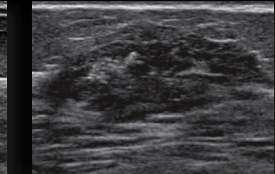
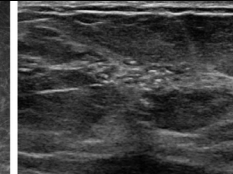
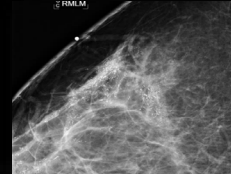


초음파에서 발견되는 유방암의 다양한 얼굴

- Ductal carcinoma in situ
 - Tumor cells within the terminal ductal lobular unit with preservation of the basement membrane
 - 62-98% calcifications on mammography
 - Calcifications more common in high-grade DCIS

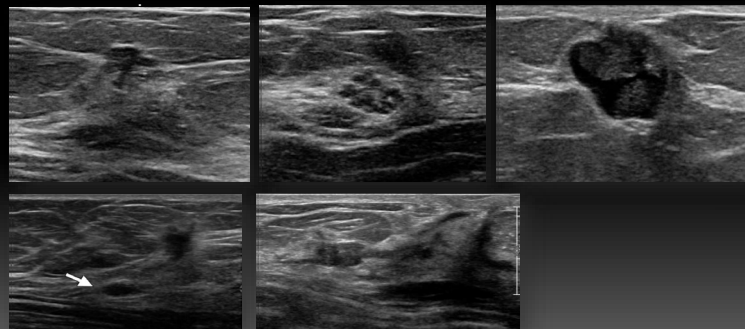
초음파에서 발견되는 유방암의 다양한 얼굴

- Calcified DCIS

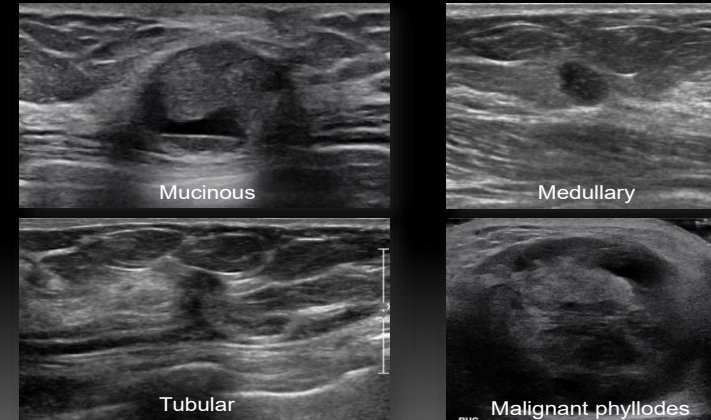


초음파에서 발견되는 유방암의 다양한 얼굴

▪ Non-calcified DCIS

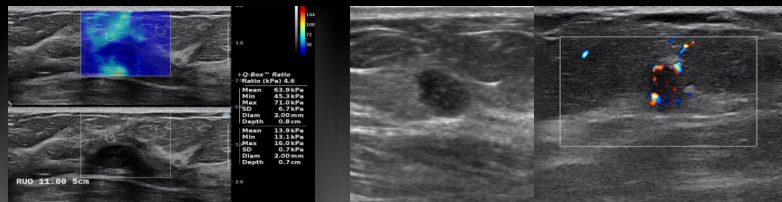


초음파에서 발견되는 유방암의 다양한 얼굴



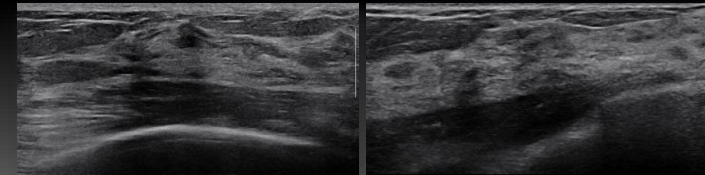
False-negative 줄이는 방법

- 환자의 증상 (palpable lump, nipple discharge)에 귀 기울이기
- Typical benign US feature 외의 소견을 놓치지 않기
- 과거 영상과 비교 (>20% size increase → Biopsy)
- Doppler US, US elastography 적극 활용



False-positive 줄이는 방법

- 적절한 setting (gain, focal zone 등 설정, harmonic or compounding image 활용)
- 다양한 plane으로 관찰
- Isoechoic mass vs fat lobule
- Cooper's ligament 직하방 혹은 subareolar area shadowing



2022 분당차병원

협력의료기관 의사 온라인 연수강좌



Session II

17:30-18:00

개원가에서 시행할 수 있는 배란유도제 사용 및 배란 초음파 보기

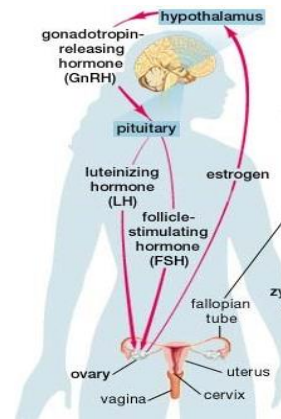
차의과학대학교 분당차병원 난임센터

신소연 교수

배란 유도제 사용 및 배란 초음파 보기

2022.11.
분당차병원 난임센터 신소연

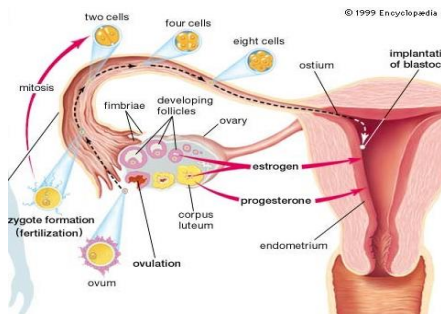
임신의 과정



▶ Reproductive Hormones ; H-P-O axis

- ▶ 임신 및 출산에 관련된 호르몬 분비
- ▶ 시상하부 (hypothalamus)
 - ▶ **GnRH** : 생식 호르몬의 총괄을 맡는 가장 상위 호르몬
pulsatile → FSH, LH 분비촉진
Continuous → FSH, LH 분비 억제
- ▶ 뇌하수체 (pituitary) - Gonadotropin
 - ▶ **FSH** : 난포자극호르몬 - 난소의 난포의 성장
 - ▶ **LH** : 황체형성호르몬 - **배란의 신호**, 난포의 황체화 유도
- ▶ 난소 (ovary)
 - ▶ **Estrogen** : 난포가 성장하면서 분비, 자궁내막을 두껍게 함
 - ▶ **Progesterone** : 배란 후 난포가 황체로 바뀐 뒤 분비되는 호르몬. 임신을 유지시킴

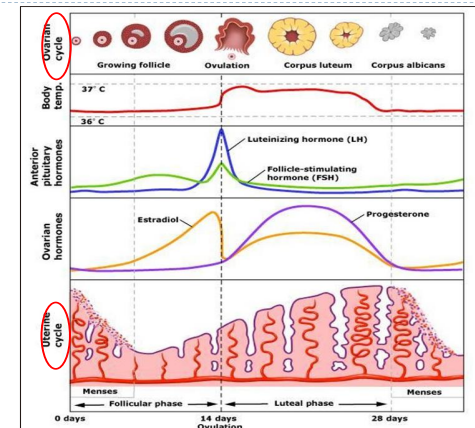
임신의 과정



▶ 배란 → 수정 → 착상

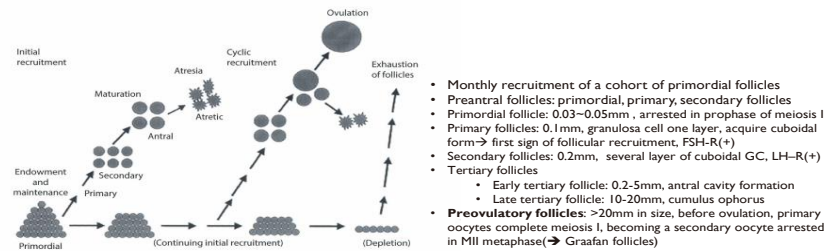
- ▶ 배란
 - ▶ 난포의 성장(FSH)→배란(LH)
- ▶ 수정
 - ▶ 난관에서 일어남
 - ▶ 배란된 난자는 10~12 시간이 지나면 수정능력이 상실됨
 - ▶ 배아 생성
- ▶ 착상
 - ▶ 배아 : 난관을 지나 자궁으로 들어가면서 세포분열을 함
 - ▶ 수정 후 7일 정도 지나 포배기 상태로 자궁내막에 착상

여성 생식 주기

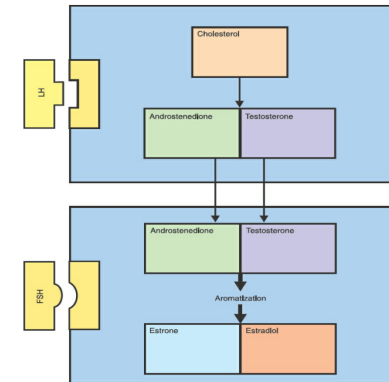


Ovarian follicular development

- ▶ Number of oocytes
 - ▶ 6~7million by 20wks of gestation
 - ▶ At birth, 1~2 million oocytes remain
 - ▶ At puberty, 300,000 available for ovulation
 - ▶ Of these, only 400~500 ultimately released during ovulation
 - ▶ Oocytes arrested in prophase, remain until the time of ovulation



Two-cell, Two gonadotropin theory



난임의 정의

- ▶ **Primary** : 1년 이상 피임 없이 규칙적으로 잠자리를 가졌으나 임신되지 않는 경우를 뜻함
- ▶ **Secondary** : 분만 유산 자궁 외 임신 이후 1년 이내 임신이 되지 않는 경우
- ▶ **RPL : Repeated Pregnancy Loss (ASRM)**
 - ▶ ≥2 clinical pregnancy 유산
 - cf) 화학유산, 착상실패
- ▶ **RIF : Repeated Implantation Failure**
 - ▶ 반복착상실패
- ▶ **POR : poor ovarian reserve**
 - ▶ 난소 저 반응군 : Gonadotropin 고용량 투여하여도 자라는 난포의 개수가 적은 여성
 - ▶ Bologna criteria
 - ▶ AMH <0.5~1.1 이하
 - ▶ Advanced maternal age(≥40 years) 이거나 다른 risk factor
 - ▶ Previous poor ovarian response(이전 주기 취소, conventional protocol상 3개 이하의 난자채취)

난임 시술의 종류

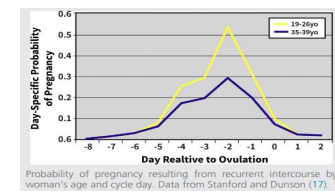
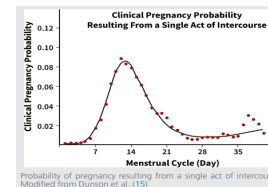
- ▶ **TI : Timed Intercourse**
 - ▶ 배란될 날짜 예측하여 잠자리 할 날을 지정해 줌
 - ▶ 초음파 통해 난포가 성장해 가는 것을 추적관찰 후 배란 예정일 지정 : 1 cycle 3-5회 시행
- ▶ **OI: Ovulation induction**
 - ▶ To induce mono-follicular growth and ovulation in anovulatory women.
- ▶ **SO: superovulation**
 - ▶ 다수의 난포를 배란 시켜 임신을 도모하려는 목적으로 흔히 이용됨
- ▶ **COH: controlled ovarian stimulation**
- ▶ **IUI : Intrauterine insemination**
- ▶ **IVF - ET: in vitro fertilization-Embryo transfer**
 - ▶ 신선배아이식(fresh ET)
 - ▶ 냉동배아이식(frozen-thawed ET, thawing ET)
- ▶ **ICSI: Intracytoplasmic sperm injection**
- ▶ **IMSI: Intracytoplasmic morphologically selected sperm injection**

Ovarian reserve

- ▶ Size of non-growing, resting, primordial follicle
- ▶ Not decline at the same pace at a given age for all women
- ▶ AMH
 - ▶ Granulosa cells of preantral and small antral follicle
 - ▶ Anytime in menstrual cycle
 - ▶ Interpreted as a age specific reference age.
 - ▶ Excessive(AMH>3.5ng/ml), poor(<1ng/mL)
- ▶ AFC(Antral follicle count)
 - ▶ TVS, 2~10mm ovarian follicle counted and total for both ovaries
- ▶ FSH
 - ▶ Gardner참고하기

Fertile window

- ▶ Sperm can survive for up to 6 days.
- ▶ Egg less than a day
- ▶ Day 10~17 is fertile, many women can conceive outside of this range.
- ▶ TI가 어려울 경우 주 2-3회 coitus



Ovulation induction

- ▶ Amenorrhea, oligomenorrhea and chronic anovulation patient to conceive
- ▶ 임신 확률을 높이기 위해 과배란(난포 개수 많게) 을 유도 할 수 있음
- ▶ Normal FSH, E2
- ▶ Ovulation factor: 30~40% of female infertility
- ▶ Clomiphen Citrate (first choice , relatively low cost)
 - ▶ Non-steroidal estrogen analogue, only effective when H-P-O axis intact; E2 level 정상, FSH, prolactin normal인 경우.
 - Hypogonadotropic patient에서는 효과 없음
 - ▶ CC-E2 receptor at hypothalamic level mimics hypo-estrogenic status → 혈중 FSH상승, 배란 촉진 효과
 - ▶ 생리 시작 후3~5일째 부터 5일간 복용 ; 50mg/d starting dose ~ 250mg/d까지 가능, 클로미펜 투여후 9~10일 후 방문하게 한다.
 - ▶ Combined with metformin may increase the likelihood of ovulation
 - ▶ 구역, 구토, 시야혼탁, 암점 등의 부작용 가능성
 - ▶ Estrogen antagonist로 자궁내막 발달이 잘 안될 수 있음.

병명	1. [의약품] Clomiphen Citrate 50mg 골고루분산제 1000mg정
연도	2022년
의사	김민준 (내과)
처방기간	2022.09.20 ~ 2022.10.20

★ 약물 공급 중단

1. 약물종류 : Clomiphen 50mg
2. 공급종단 사유 : 제약사 생산 중단
3. 공급종단일 : 2022년 9월 30일
4. 대체약 : 없음

- 원내외 제고가 소진되어 처방이 불가능합니다

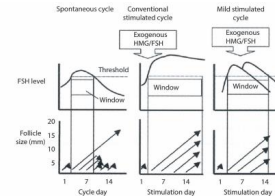
Ovulation induction

- ▶ Letrozole: Femara, Bretra
 - ▶ PCOS에서 effective
 - ▶ Higher pregnancy rate in meta analysis, Low multiple pregnancy rate
 - ▶ 2.5mg tablet; 1T /day usually 2T for 5 days
 - ▶ Letrozole은 혈중 estradiol상승, negative feedback이 걸려 다수의 난포가 자라지 않음.
 - ▶ 2T(5mg)까지 급여.
 - ▶ 자궁내막에 부정적 영향 적음
- ▶ Metformin
 - ▶ PCOS환자에서 병용시 배란율 임신율에 유리
 - ▶ Clomiphene resistant인 경우 배란율 증진 가능
 - ▶ 일차 경우 배란 유도제로 사용 X
- ▶ CC, LE : Pregnancy category X → 임신 이 아님을 확인하고 시작
- ▶ Baseline testing에서 large cyst가 없음을 확인하고 시작한다.
- ▶ 이시 follicle은 preovulatory diameter 로 19~25mm까지 자라게 되며, ~30mm까지 클 수 있다.
- ▶ LH testing , US 같이 이용되며, LH kit는 follicle이 14mm에 도달하게 되면 시작한다.
- ▶ ~80%에서는 CC/LE로 ovulation induction이 된다.
- ▶ Contraindication: liver disease, pre-existing large ovarian cyst

Ovulation induction

▶ FSH 제제

- ▶ Not respond to CC or LE
- ▶ Clomiphene에 생리 5~7일 정도에 투여 하기도 함
- ▶ Gonadotropin : 37~150 IU/d SC for 3~5days #7-#12
- ▶ Ovulation trigger: 5000~10000 IU hCG(IVF-C 5000IU), rhC occur
- ▶ hMG: Hypogonadotropic hypogonadal anovulation



▶ hCG 제제

- ▶ final follicular maturation; LH action
- ▶ Urinary hCG(IVF-C 5000~10000IU) or rhCG(ovidrel, 250ug = 5000~6000IU urinary
- ▶ 투여후 대략 40hr때에 ovulation
- ▶ Ovulatory dysfunction이 있거나, IU하는 환자에게는 이득이 있다.

Superovulation

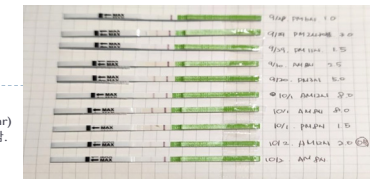
- ▶ In unexplained infertility, more than one egg to be ovulated, increasing the probability of conception.
- ▶ With superovulation: 15-20% will pregnant per cycle, and 50% will be pregnant by 6 months of treatment

Ovulation induction

- ▶ Cx: multiple pregnancy(10~30%), OHSS→Careful monitoring!
- ▶ Ovarian or pituitary function must be present.
- ▶ Normal length of the menstrual cycle in reproductive-age women varies 21~35 days
- ▶ Cycle length variability during the follicular phase
- ▶ Luteal phase usually fixed at 14 days, can range from 7~19 days
- ▶ Minimal symptoms: premenstrual breast swelling, bloating, mood changes
- ▶ Anovulatory women: FSH, prolactin, TSH testing!!!

▶ LH monitoring(배란테스트기)

- ▶ 하루 2회 사용시 detection 가능성 증가, (duration of the surge <12hr)
- ▶ Serum peak이 관찰되고 나면 2시간 후 urine LH detection이 가능함.
- ▶ 35~50mIU/mL정도 threshold를 detection함.
- ▶ 예상 배란일 3일 전 or 초음파 상 follicle이 14mm 부터 사용 가능
- ▶ 양성 나오면 그날 or 다음날 부부관계를 권한다.
- ▶ Irregular cycle인 경우 사용 불가능
- Dominant follicle: 20~25mm에 도달 하면 urine LH test를 해보고 양성이면 다음날 부부관계, 음성 → hCG투여하고 2일 후 부부관계를 권한다.
- TI시점을 엄격하게 잡아주는 것이 심리적 스트레스로 작용할 수 있음.
- 난자의 수정가능 시기는 배란 후 12~24hr, sperm 2~3일간 수정 가능함. 엄격하게 시간 따질 필요는 없음
- 혈중 AMH높은 경우, clomiphene 사용시 이 실패 가능성 높음.
- 고용량 clomiphene
- Metformin 병합
- FSH or FSH/LH 제제
- Step up: FSH 75IU로 1주 투여 → 반응 없을 경우 1주 마다 75IU씩 증가
- Low dose step-up: FSH 75IU로 투여 → 반응 없을 경우 1주마다 37.5IU씩 증량
- Step-down: FSH 150IU투여 → 난포자라면 37.5IU씩 감량



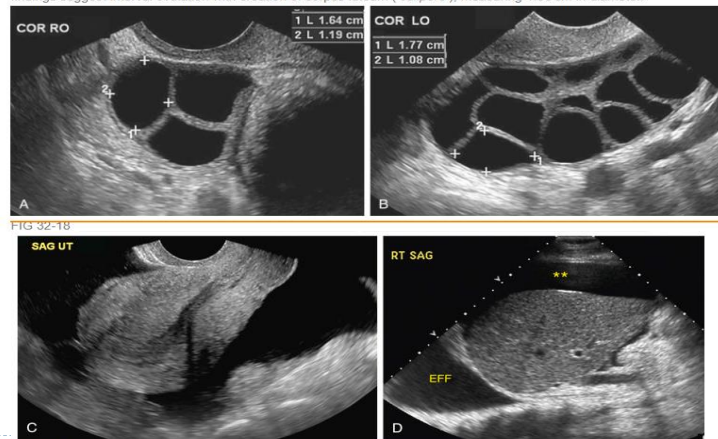


FIG 32-21

PCOS

- ▶ Most common cause of oligo- or anovulation in the general population
- ▶ Diagnosis of PCOS
 - ▶ Oligo-ovulation or anovulation (manifested as oligomenorrhea or amenorrhea)
 - ▶ Hyperandrogenemia (elevated androgen level) or hypandrogenism (clinical manifestation of androgen excess)
 - ▶ Polycystic ovaries detected by US
 - ▶ Serum LH:FSH 증가,
- ▶ 5% of weight loss improve pregnancy rate
- ▶ Ovulation induction: first line treatment for anovulatory infertility
- ▶ Clomiphene citrate : vasomotor flushes, mood swings, breast tenderness, pelvic discomfort, nausea,
- ▶ CC first choice , relatively low cost
 - ▶ E2 level 정상, FSH, prolactin normal인 경우.
 - ▶ Hypogonadotropic patient에서는 효과 없음
 - ▶ CC 50mg #3-5, for 5 days
 - ▶ Combined with meformin may increase the likelihood of ovulation
 - ▶ 50mg/d starting dose ~ 250mg/d까지 가능

- ▶ Letrozole
 - ▶ PCOS에서 effective
 - ▶ Higher pregnancy rate in meta analysis
 - ▶ Low multiple pregnancy rate
 - ▶ 2.5mg tablet; 1T /day
 - ▶ Pregnancy category X → 임신 이 아님을 확인하고 시작
 - ▶ Baseline testing에서 large cyst가 없음을 확인하고 시작한다.
 - ▶ O시 follicle은 preovulatory diameter 로 19~25mm까지 자라게 되며, ~30mm까지 클 수 있다.
 - ▶ LH testing , US 같이 이용되며, LH kit는 follicle이 14mm에 도달하게 되면 시작한다.
- ▶ Metformin
 - ▶ Oral biguanide approved for the treatment of T2DM
 - ▶ Increase frequency of spontaneous ovulation
 - ▶ Cx: GI upset, lactic acidosis, avoided before surgery of contrast radiologic dye use
 - ▶ 5000mg tid, 850mg bid, 1000mg bid, lowest dose → increased gradually.
- ▶ Dexamethasone
 - ▶ Oral dexamethasone improve ovulation rates, resistant to clomiphene alone.
 - ▶ Mechanism of action is unclear.
 - ▶ 0.5mg*5d starting on the day of clomiphene, 0.5mg*6weeks prior to starting clomiphene
 - ▶ 2mg*10d. Starting on the day of clomiphene

- ▶ Gonadotropin
 - ▶ Fail to ovulate with oral agents
 - ▶ Serum E2 and TVS
 - ▶ Baseline, 4~5 days after treatment initiation, 1-3 days until follicular maturation
 - ▶ 37.5~75IU/d generally recommended,
 - ▶ increase dose by 50% of the previous dose after 7 days if no follicle > 10mm observed.
 - ▶ Treatment duration 7~12days, Usually less than 225IU
 - ▶ hCG recommended, 1~2 follicle 16~18mm, E2 /follicle 150~300pg/mL
 - ▶ Ovulation expected 24~48hr after the hCG trigger.
 - ▶ Leuprolide (GnRH a, 500ug SC) to minimize OHSS but supplement progesterone
 - ▶ Intercourse는 24-48hr; UII는 24-36시간 이내,
 - ▶ CC or LE사용 후 gonadotropin을 sequential하게 사용하면 gonadotropin 사용량도 줄이고 cancellation rate도 감소한다.
 - ▶ Cancellation considered!!
 - ▶ E2 1000~2500pg/mL
 - ▶ 3개 이상 follicle ≥ 16mm
 - ▶ 2개 이상 ≥ 16mm + 2개 이상 ≥ 14mm

Hyperprolactinemia

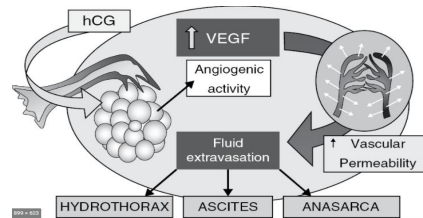
- ▶ Pituitary MRI for r/o macroadenoma or intracranial pathology
- ▶ Dopamine agonist: Bromocriptine, cabergoline
 - ▶ In symptomatic hyperprolactinemia
 - ▶ Bromocriptine
 - ▶ normalize prolactin level and induce ovulation in 80~90% of patients
 - ▶ 1.25mg → 2주후 재평가 → 2.5mg bid or tid에 대부분 반응
 - ▶ Cx: nausea, vomiting, postural hypotension, headache
 - ▶ 1.25mg qid : (PRL<50ng/mL)
 - ▶ 2.5mg qd : PRL<100ng/mL
 - ▶ 5mg vaginal daily
 - ▶ Cabergoline
 - ▶ 0.25mg twice-weekly

Hypogonadotropic hypogonadism

- ▶ Low LH, FSH, E2
- ▶ **Causes:** craniopharyngioma, pituitary adenomas, AV malformation, central space-occupying lesion, stress, extreme weight loss, anorexia, excessive exercise, low BMI
→ functional hypothalamic suppression
- ▶ **Treatment**
 - ▶ Exogenous leptin
 - ▶ GnRH pulsatile therapy (esp Kallmann syndrome)

OHSS (난소 과 자극 증후군) -급여

- ▶ 치료
 - ▶ Severe 할 경우 입원이 필수
 - ▶ Dopamine agonist(caverlactin) 혈관 투과성 증가 예방, OHSS 예방
 - ▶ 초음파 유도 하 복막천자
 - ▶ Clexane 투약
 - ▶ Hepatotonic (adelavine)
 - ▶ Calcium gluconate
 - ▶ 산소 치료
 - ▶ 수액치료
 - ▶ Albumin



난임 시술시 야기 될 수 있는 질환

- ▶ **Multiple pregnancy**
 - ▶ 여러 개의 배아를 이식함으로 발생
 - ▶ 조산 / 유산
 - ▶ 산모의 건강 위협
- ▶ **Heterotopic pregnancy**
- ▶ 진단
 - ▶ 초음파상 여러 개의 G/sac
- ▶ 치료 : Selective abortion

2022 분당차병원

협력의료기관 의사 온라인 연수강좌



Session II

18:00-18:30

**성인 예방접종 : 폐렴사슬알균, 대상포진, 파상풍-
디프테리아-백일해**

차의과학대학교 분당차병원 감염내과

이채령 교수

성인예방접종

분당차병원 이채령

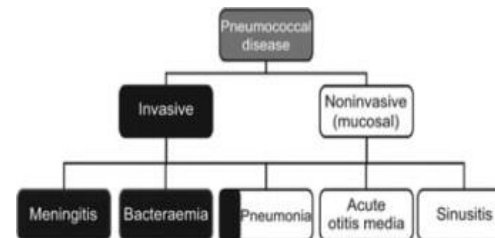
순서

1. 폐렴사슬알균/폐렴구균
2. 대상포진
3. 파상풍-디프테리아-백일해

폐렴사슬알균/폐렴구균 예방접종

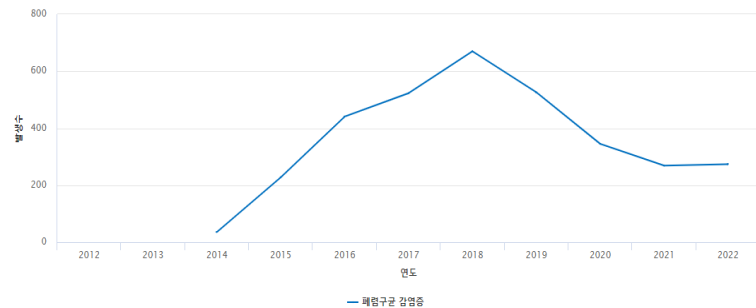
Streptococcus pneumoniae

- Gram positive diplococci or short chain
- encapsulated ; complex polysaccharides
- 100 serotypes
- Pneumococcal disease
 - Invasive disease : bacteremia, osteomyelitis, meningitis
 - non-invasive : pneumonia, otitis media, sinusitis



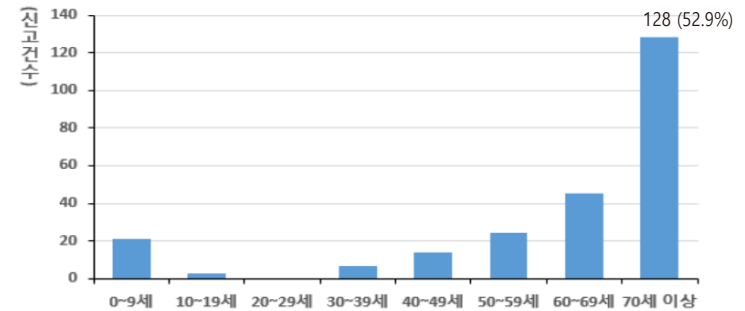
Drijckoningen et al. Clin Microbiol Infect. 2014 May;20 Suppl 5:45-51

Invasive Pneumococcal Disease



구분	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
폐렴구균 감염증	-	-	36	228	441	523	670	526	345	269	274

감염병포털 www.kdca.go.kr/npt



[그림 15] 연령별 환자 및 사망자 누적 신고 현황(2021)

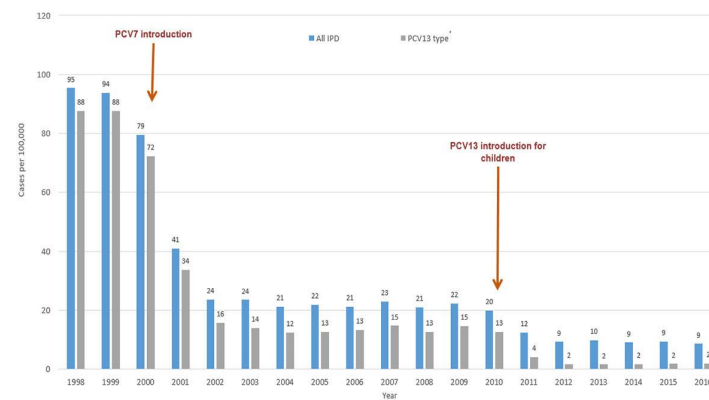
2022년도 예방접종 대상 감염병 관리 지침

Immunogenicity of pneumococcal vaccines

	Polysaccharide Vaccines	Conjugate Vaccines
T-dependent	No	Yes
Effective in < 2 years-old	No	Yes
Immune response	IgM	IgM + IgG
Induction immunological memory	No	Yes
Reduction mucosal carriage	No	Yes

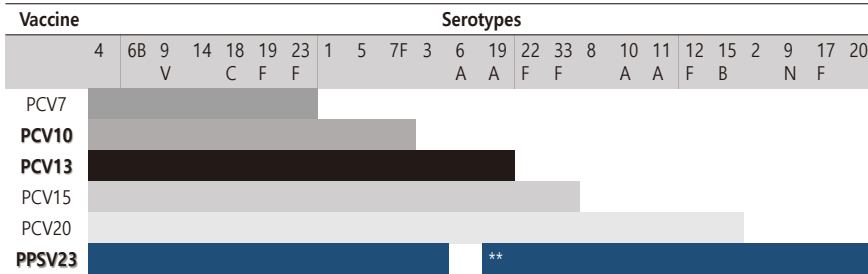
Eskola. Pediatr Infect Dis J. 2000 Apr;19(4):388-93

Trends in invasive pneumococcal disease among children aged <5 years old, 1998-2016



CDC. Epidemiology and prevention of vaccine-preventable disease, chapter 17 Pneumococcal Disease. P279-295

Pneumococcal Vaccine



** PPSV23 vaccine does not contain serotype 19A, but contains 19 other serotypes present in PCV20

Song et al. J Korean Med Sci. 2013 Jan;28(1):4-15

Pneumococcal vaccination

국가 예방접종사업

소아 : 2개월① → 4개월② → 6개월③ → 12-15개월④ (PCV10 또는 PCV13)

** 24개월 이후 고위험군에 한하여 PPSV23 접종

65세 이상 : PPSV23 1회

2019 대한감염학회 권장 성인예방접종

- 65세 이상 건강한 성인 PPSV23 1회 접종

PCV13 → PPSV23 최소 1년 간격 순차적으로 접종

Pneumococcal vaccination

2019 대한감염학회 권장 성인예방접종

- 65세 이상 고위험군 PCV13 → PPSV23 로 최소 8주 간격 순차적으로 접종

고위험군

면역기능저하 HIV 감염증, 만성신부전과 신증후군, 면역억제제나 방사선 치료를 하는 질환(악성종양, 백혈병, 림프종, 호치킨병) 또는 고형장기이식, 조혈모세포이식

기능적 또는 해부학적 무비증

만성질환 당뇨병, 만성심혈관질환, 만성폐질환, 만성간질환
뇌척수액 누출, 인공 와우 이식 상태

Pneumococcal vaccination

2019 대한감염학회 권장 성인예방접종

- 16~49세 고위험군

- PCV13과 PPSV23은 같은 날 동시 접종 하지 않음.
- PCV13 1회 접종
- 65세 이후 1회 PPSV23 접종
- PPSV23 간 재접종 간격은 최소 5년
- PPSV23 최대 3회까지 접종

1) 만성질환자, 뇌척수액 누출, 인공 와우 이식 환자가 65세 이전 PPSV23 1회 접종

→ 65세 이후 이전 접종과 5년 이상 간격두고 PPSV23 재접종 (총 2회)

2) 면역저하자, 무비증 환자가 65세 이전 PPSV23 1회 접종

→ 5년 간격 두고 재접종

→ 재접종 시기가 65세 이전인 경우, 65세 이후 2차 접종과 5년 간격 두고 PPSV23 3차 접종 (총 3회)

Pneumococcal vaccination

Q. 고위험군에서, PCV13 접종 전에 이미 PPSV23 1회 접종. 그 이후 스케줄은?

→ 최소 8주 간격 두고 PCV 13 접종

기저 질환 및 연령에 따라 추가 접종 스케줄 확인

Q. 고위험군 임신부의 접종

→ 예방접종 받은 임신부에게서 태어난 신생아에게서 부작용 보고는 없으나, 관련 연구가 없어 우리나라는 물론 미국 지침에도 아무런 권고 사항이 없음

Q. Influenza 예방접종과 동시 접종

→ 일부 소아에서 febrile seizure 보고. 그러나 위험성 매우 낮으며 소아에서도 동시 접종 가능.
60세 이상 성인 1149 환자 대상, 우리나라 연구 - 면역 간섭 없고, 안전성도 우수

Song et al. Vaccine. 2017 Jan 5;35(2):313-320

대상포진 예방접종

Herpes zoster, shingles



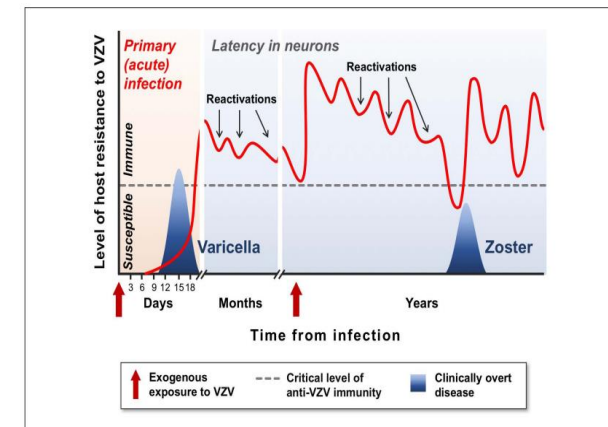
- Pain, itching, tingling
- Rash along dermatomes clusters of vesicle

Complication

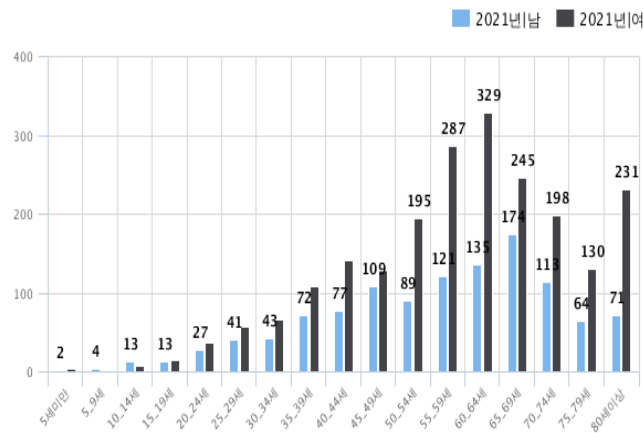
- Post-herpetic neuralgia
- Herpes zoster ophthalmicus
- Bacterial superinfection
- Cranial nerve and peripheral nerve palsies
- Visceral involvement
meningoencephalitis, pneumonitis, hepatitis, acute retinal necrosis

John Pozniak, with zoster blisters on his neck and shoulder. Taken May 5, 2006, in San Jose, California, United States. Copyright © 2006, John Pozniak, and released under the terms of the GNU Free Documentation License ver. 1.2 or any later version. wikipedia

Herpes zoster, shingles

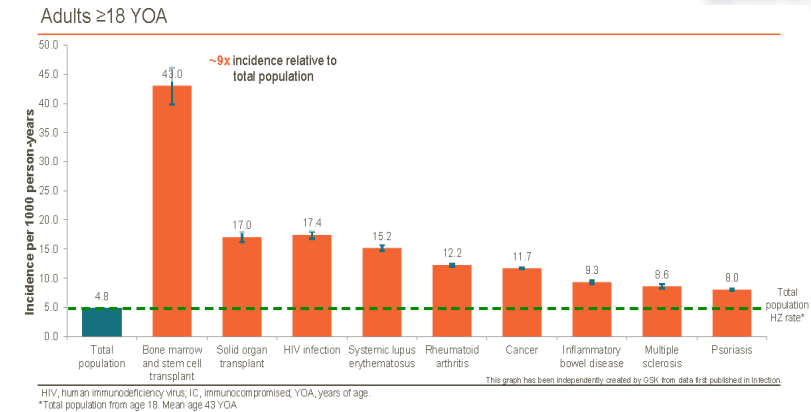


Freer et al. New Microbiol. 2018 Apr;41(2):95-105



Kwon et al. Ann Dermatol. 2019 Aug;31(4):486-488
보건의료빅데이터개방시스템 <http://opendata.hira.or.kr/op/opc/olap4thDsinfo.do>

Zoster in Immunocompromised patients



Chen et al. Infection 2014;42:325-34

Age (years)	Vaccine	HZ cases VE _{HZ} (95% CI)
	Placebo	
50-59 (ZEST) ¹	11,211	70% (54, 81)
	11,218	

Age (years)	Vaccine	HZ cases VE _{HZ} (95% CI)	Vaccine	PHN cases VE _{PHN} (95% CI)
	Placebo		Placebo	
Overall (≥60) (SPS) ²⁻⁴	19,254	51% (44, 58)	19,254	67% (48, 79)
	19,247		19,247	
60-69 (SPS) ²⁻⁴	10,370	64% (56, 71)	10,370	66% (20, 87)
	10,356		10,356	
70-79 (SPS) ^{3,4}	7,621	41% (28, 52)	8,884	74% (49, 87)
	7,559		8,884	
≥80 (SPS) ³	1,263	18% (-29, 48)	8,891	
	1,332		8,891	

Schmader et al. Clin Infect Dis. 2012 Apr;54(7):922-8
Oxman et al. N Engl J Med. 2005 Jun 23;352(22):2271-2284

Varicella-zoster vaccination

국가 예방접종사업

소아 : 12-15개월 VAR 1회

2019 대한감염학회 권장 성인예방접종

- 60세 이상 성인 Zoster vaccine live (ZVL) 1회 접종
- 50-59세 성인은 개별 피접종자의 상태에 따라 접종 여부 결정

금기

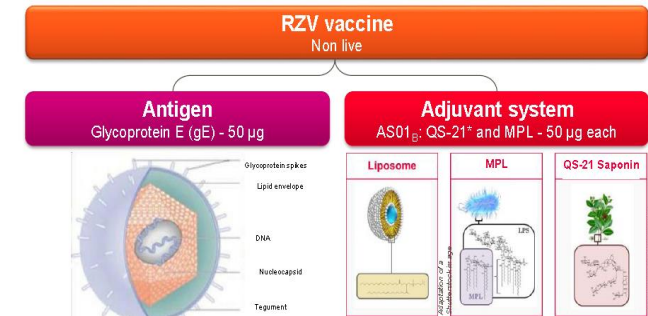
면역기능저하 항암치료 중인 고형암, 2주이상 고용량 스테로이드 (20mg/day), 면역억제제 사용, 장기이식, 조혈모세포이식, CD4 <200/mm³ HIV 감염인,

임신부
백신 성분에 대하여 중증 과민반응을 보였던 경우

Limitation of Zoster Vaccine Live

- Limited efficacy across older age groups
- Decline in efficacy over time
- Contraindicated in immunocompromised populations

Recombinant Zoster Vaccine, RZV



Lal et al. N Eng J Med 2015; 372:2087-96
Cunningham et al. N Eng J Med 2016 75:1-19-32

VE_{HZ} for RZV in ZOE-50 and ZOE-70

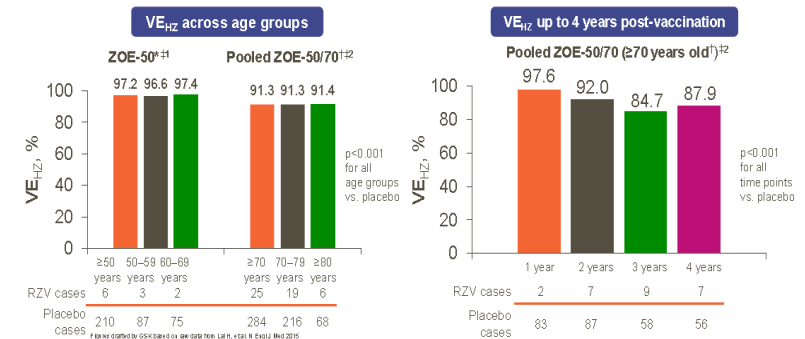
Age (years)	RZV*		Placebo*		VE _{HZ} (95% CI) [†]
	HZ cases (N)	Rate of HZ (per 1,000 person-years)	HZ cases (N)	Rate of HZ (per 1,000 person-years)	
ZOE-50 [‡]					
Overall (≥50)	6 (7,344)	0.3	210 (7,415)	9.1	97.2 (93.7, 99.0)
50–59	3 (3,492)	0.3	87 (3,525)	7.8	96.6 (89.6, 99.3)
60–69	2 (2,141)	0.3	75 (2,166)	10.8	97.4 (90.1, 99.7)
Pooled analysis of ZOE-50 and ZOE-70 [‡]					
Overall (≥70)	25 (8,250)	0.8	284 (8,346)	9.3	91.3 (86.8, 94.5)
70–79	19 (6,468)	0.8	216 (6,554)	8.9	91.3 (86.0, 94.9)
≥80	6 (1,782)	1.0	68 (1,792)	11.1	91.4 (80.2, 97.0)

*Modified vaccinated cohort (excludes subjects not receiving dose 2 or who developed HZ within 1 month after dose 2); [†]p<0.001 for all comparisons vs placebo.
[‡]Mean follow-up 3.2 years; CI, confidence interval; N, number of subjects; HZ, herpes zoster; RZV, recombinant zoster vaccine; VE_{HZ}, vaccine efficacy for HZ

Lal et al. N Eng J Med 2015; 372:2087-96
Cunningham et al. N Eng J Med 2016 75:1-19-32

RZV VE_{HZ} by subject age and time post-vaccination

VE similar in all age groups and was 87.9% 4 years post-vaccination in patients ≥70 years old^{†1,2}

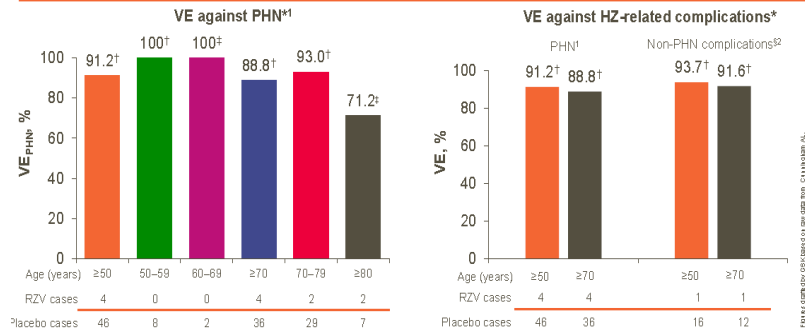


^{†1}Mean follow-up 3.2 years (ZOE-50); ^{†2}Mean follow-up 3.7 years (pooled ZOE-50/70 data for subjects ≥70 years old); [‡]Modified vaccinated cohort (excludes subjects not receiving dose 2 or who developed HZ within 1 month after dose 2); HZ, herpes zoster; RZV, recombinant zoster vaccine; VE_{HZ}, vaccine efficacy against HZ

Lal et al. N Eng J Med 2015; 372:2087-96
Cunningham et al. N Eng J Med 2016 75:1-19-32

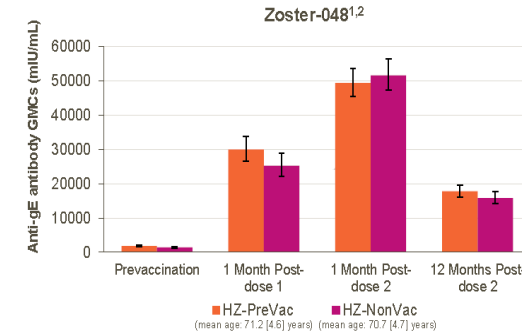
PHN and non-PHN complications across age groups

Among patient groups ≥50 years of age in pooled analysis (ZOE-50 and ZOE-70)

Cunningham et al. N Engl J Med 2016; 375:19-32
Kovacs IM et al. Vaccine 2018; 36:1537-41

Previous ZVL prior to ≥ 5 years

Geometric mean concentrations of anti-gE antibody



gE = glycoprotein E; GMC, geometric mean concentrations; RZV, recombinant zoster vaccine;

Dagnew et al. J Infect Dis 2020;1-8 2.

RZV IC clinical programme overview

	 HUMAN IMMUNODEFICIENCY VIRUS (HIV) People living with HIV ¹	 AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANT (aHSCT) Post-autologous ²	 HAEMATOLOGICAL MALIGNANCIES While on immunosuppressive chemotherapy ³	 RENAL TRANSPLANTS Post-renal transplant ⁴	 SOLID TUMOUR Solid tumour malignancies while on immunosuppressive chemotherapy ⁵
Trial	Zoster-015 ¹	Zoster-002	Zoster-039	Zoster-041	Zoster-028
Phases	Phase 1/2a (N=123)	Phase 3 (N=1,846)	Phase 3 (N=562)	Phase 3 (N=264)	Phase 2/3 (N=232)
Trial type	Placebo controlled, ≥18 years of age				
Primary endpoints	Immunogenicity/ Safety	Efficacy	Immunogenicity/ safety [†]	Immunogenicity/safety	
Dose timeline	Month 0, 2, 6 (3 doses)	Month 0, 1–2			

[†]Prior to the phase 3 programme, SHINGRIX was studied in a phase 1/2a trial in HIV patients; [†]Efficacy was evaluated in a post-hoc analysis³

aHSCT, autologous hematopoietic stem cell transplant; HIV, human immunodeficiency virus; IC, immunocompromised

1. Berkowitz EM, et al. J Infect Dis 2015;211:1279-87; 2. Bastidas A, et al. JAMA 2019;322:123-33; 3. Dagnew AF, et al. Lancet Infect Dis 2019;19:986-1000; 4. Vink P, et al. Clin Infect Dis 2020;70:181-90; 5. Vink P, et al. Cancer 2019;125:1301-12

56

RZV approval in Korea

대상포진의 예방

- 만 50세 이상의 성인 2개월 간격 2회 접종
- 만 18세 이상에서 질병 혹은 치료로 인한 면역저하 또는 면역억제로 인하여 대상포진의 위험이 높거나 높을 것으로 예상되는 사람.
(예, 자가조혈모세포이식 환자, 고형암, 혈액암, 고형장기 이식 환자)

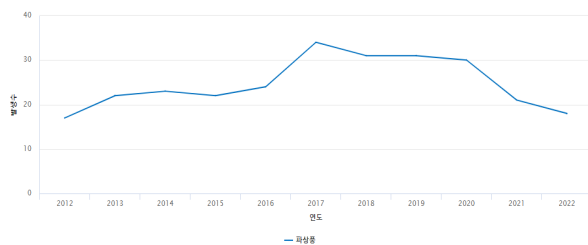
ACIP recommendation

- 만 50세 이상의 성인 (0, 2~6개월 간격 2회)
- 이전의 수두 병력, 수두 예방접종 이력 확인 불필요**
- 이전 대상포진 앓았던 사람도 접종 가능
- 현재 대상포진 앓고 있는 사람에게는 접종하지 않음
- 이전 ZVL 접종 받은 사람도 5년 경과 후 RZV 접종 가능
- 다른 사백신과 동시 접종 가능 (서로 다른 부위에)
** 면역증강제가 포함된 백신과의 동시 접종은 연구 중

ACIP

파상풍-디프테리아-백일해 예방접종

Tetanus

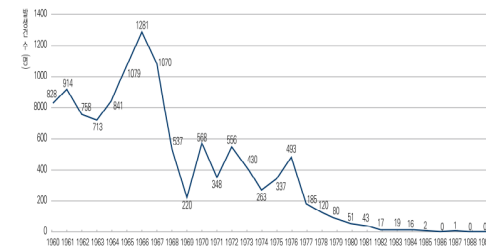
*Clostridium tetani*

- tetanus toxins via wound
- painful spasm of muscle masseter and neck muscle (lockjaw)
- abdominal rigidity
- seizure like activity
- Incubation period 3-21 days

구분	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
파상풍	17	22	23	22	24	34	31	31	30	21	18

감염정보포털 www.kdca.go.kr/npt

Diphtheria



[그림 4] 우리나라의 연도별 디프테리아 발생 현황

구분	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
디프테리아	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Corynebacterium diphtheria

- respiratory droplets
- Toxin
- Fever
- sore throat,
- swollen glands in the neck
- with pseudomembrane
- Skin ulcer

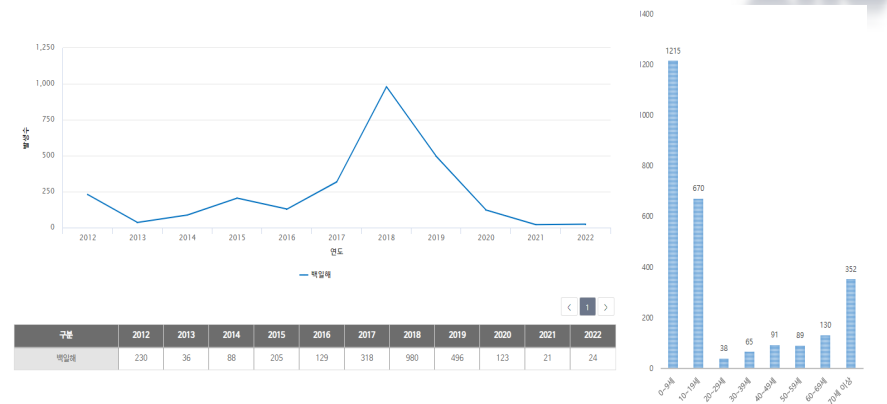
2022년도 예방접종 대상 감염병 관리 지침
감염정보포털 www.kdca.go.kr/npt

Pertussis

Bordetella pertussis

- Transmission by respiratory droplets
- Catarrhal stage similar to viral upper respiratory infection, mild cough, coryza
1-2 weeks
- Paroxysmal stage paroxysm of coughing, whooping cough
dyspnea, cyanosis in child
posttussive vomiting
2-8 weeks
- Convalescent stage cough subside
- Complication young infants
apnea, seizures, respiratory distress, pneumonia, hypotension/shock

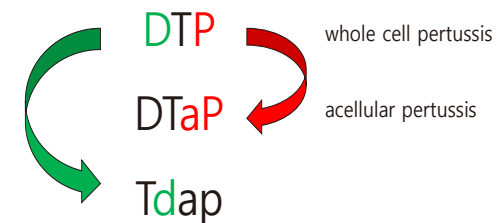
감염병포털 www.kdca.go.kr/npt



감염병포털 www.kdca.go.kr/npt

R_0	12 to 18	12 to 17	6 to 7	5 to 7	5 to 7	4 to 7	2 to 4	1 to 4 people	R_0
DISEASE	Measles	Pertussis (Whooping cough)	Rubella	Polio	Smallpox	Mumps	SARS	Ebola	DISEASE
HOW IT SPREADS	Airborne	Airborne droplets	Airborne droplets	Fecal-oral route	Airborne droplets	Airborne droplets	Airborne droplets	Bodily fluids	HOW IT SPREADS

<https://graphics.thomsonreuters.com/15/measles/index.html>



vaccination

국가 예방접종사업

- 소아 2개월 DTaP ① → 4개월 DTaP ② → 6개월 DTaP ③
 → 15-18개월 DTaP ④ → 4-6세 DTaP ⑤
 → 11-12세 Tdap/Td ⑥

2019 대한감염학회 권장 성인예방접종

- 소아 접종을 완료한 18세 이상 - 매10년마다 Td 접종
 Tdap 접종력이 없다면 10년마다 접종 시 1회는 Tdap으로 접종
- 소아 접종을 받지 않았거나 불분명 - 3회 기초접종 : Tdap → 4-8주 후 Td → 6-12개월 후 Td
 매 10년마다 Td 추가 접종

vaccination

2019 대한감염학회 권장 성인예방접종

- 조혈모세포이식 환자 - 소아용 DTaP로 3회 기초접종
- 임신부 - **매 임신 27-36주에 Tdap 접종**
 임신 중 Tdap 접종하지 않은 경우 출산 직 후 접종
- 생후 12개월 미만의 영아와 밀접 접촉하는 의료기관, 보육시설 종사자, 신생아의 가족 중에
 접종력이 없다면 밀접 접촉 2주 전까지 Tdap 접종

성인예방접종 3판, 대한감염학회

TABLE 1

Newborn antibody levels stratified whether mothers Tdap

Outcome Antibodies	Mother did not receive Tdap, mean (SEM) n = 52	Mother received Tdap, mean (SEM) n = 52	P value ^a
Diphtheria	0.571 (0.157)	1.970 (0.291)	< .001
Tetanus	4.237 (1.381)	9.015 (0.981)	.004
PT	11.010 (1.796)	28.220 (2.768)	< .001
FHA	26.830 (4.022)	104.15 (21.664)	.002
PRN	24.700 (5.765)	333.01 (56.435)	< .001
FIM 2/3	82.83 (14.585)	1198.99 (189.937)	< .001

FHA, filamentous hemagglutinin; FIM, fimbriae; PRN, pertactin; PT, pertussis toxin; Tdap, tetanus, reduced diphtheria, and acellular pertussis antigens vaccine.

^a Significant at .05 level.

Gall. Effect of maternal immunization with Tdap. Am J Obstet Gynecol 2011.

Gall et al. Am J Obstet Gynecol. 2011 Apr;204(4):334.e1-5.

