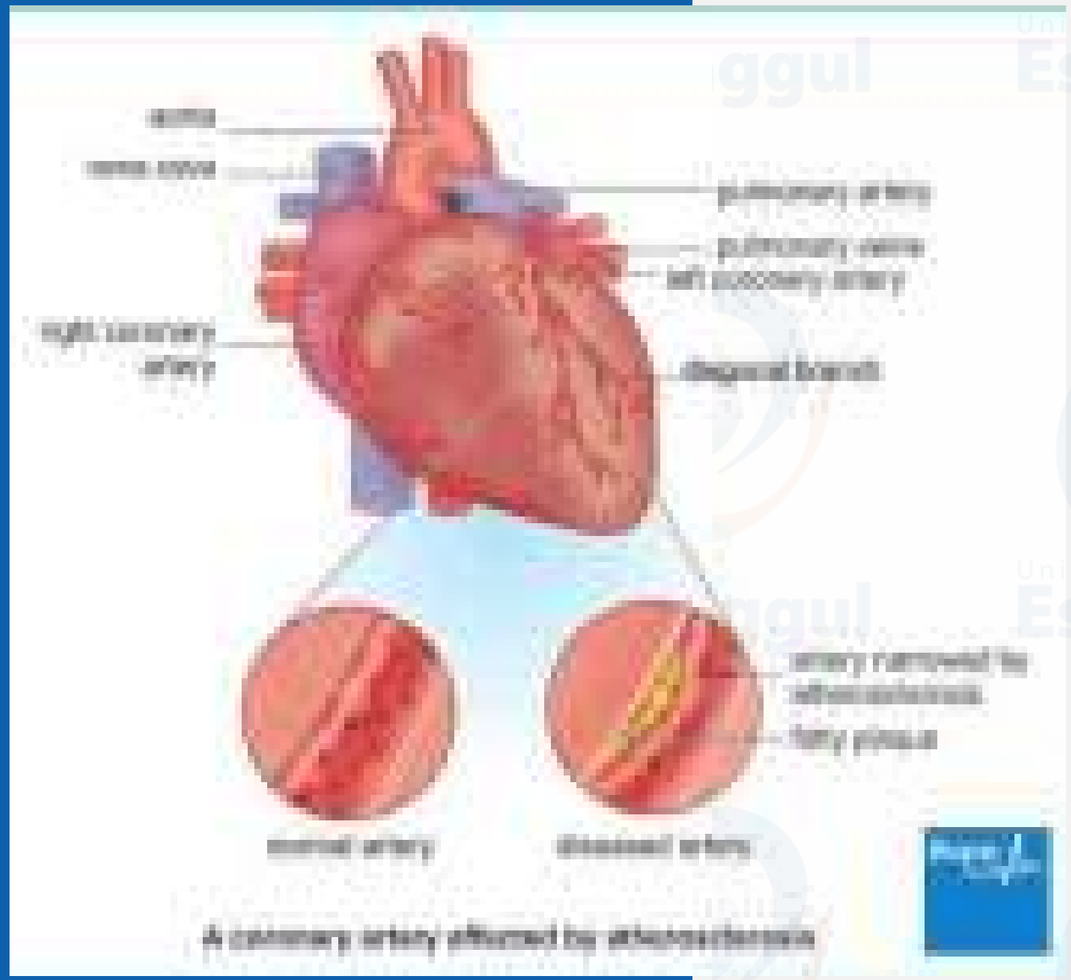

PSF316

Farmakoterapi kardiovaskular, endokrin dan kondisi khusus

Sesi Ke 1

Topik Sesuai RPS:

Mahasiswa mampu menjelaskan patofisiologi gangguan kardiovaskuler dan penanda laboratorium penyakit kardiovaskular

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Topik Sebelum UTS

Sesi 1

Pendahuluan: jenis penyakit kardiovaskular dan pemeriksaan labolatorium

Sesi 2

Patofisiologi dan farmakoterapi **stroke**

Sesi 3

patofisiologi dan farmakoterapi gagal jantung

Sesi 4

patofisiologi dan farmakoterapi sindrom koroner akut

Sesi 5

patofisiologi dan farmakoterapi Aritmia

Sesi 6

patofisiologi dan farmakoterapi gagal ginjal akut

Sesi 7

patofisiologi dan farmakoterapi gagal ginjal kronis

Ujian Tengah Semester

Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

patofisiologi dan farmakoterapi epilepsi

Sesi 12

patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

patofisiologi dan farmakoterapi rheumatoid arthritis

Sesi 14

patofisiologi dan farmakoterapi SLE

Ujian Akhir Semester

Our Rules

- UAS DAN UTS ada kisi- kisi- terms and condition applied
- Poin keaktifan dalam setiap pertemuan bisa dongkrak nilai
- Kuis dan tugas di e-learning akan dikombinasikan dengan nilai tugas lainnya
- Tugas selalu kelompok, dan selalu kita diskusikan di pertemuan selanjutnya
- Izin/ konfirmasi sakit (absensi) sebelum pertemuan dimulai oleh Kordinator Mata Kuliah

Komponen Penilaian

- UTS 25%
- UAS 25%
- Kuis dan Tugas 15%
- Keaktifan (20%)

References

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Goodman and Gildman Manual of Pharmacology and Therapeutics, edisi 3, 2008

Bagian farmakologi FK UI, Farmakologi & Terapi, edisi 5, Jakarta, 2003

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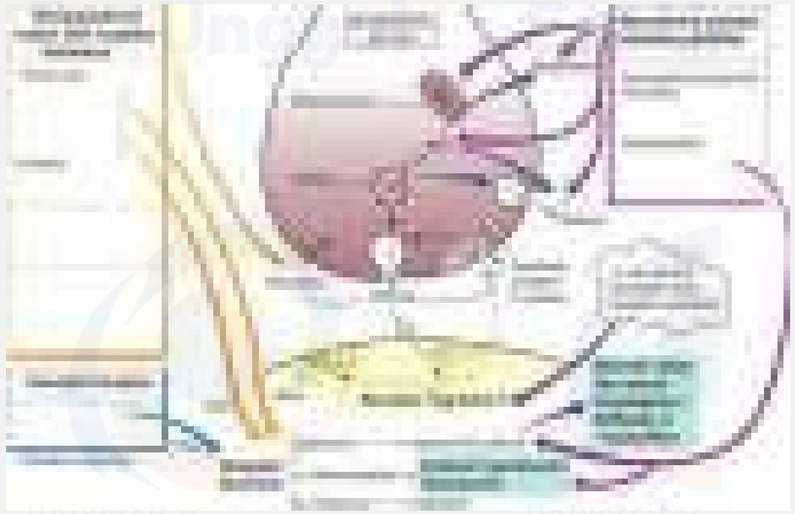
DiPiro, Y.T., et al. (Eds), 2008, Pharmacotherapy: a pathophysiological approach, 6 rth ed,

Frank C. Lu, Toksikologi Dasar, Jakarta UI Press, 2010

Medical pharmacology at a glance



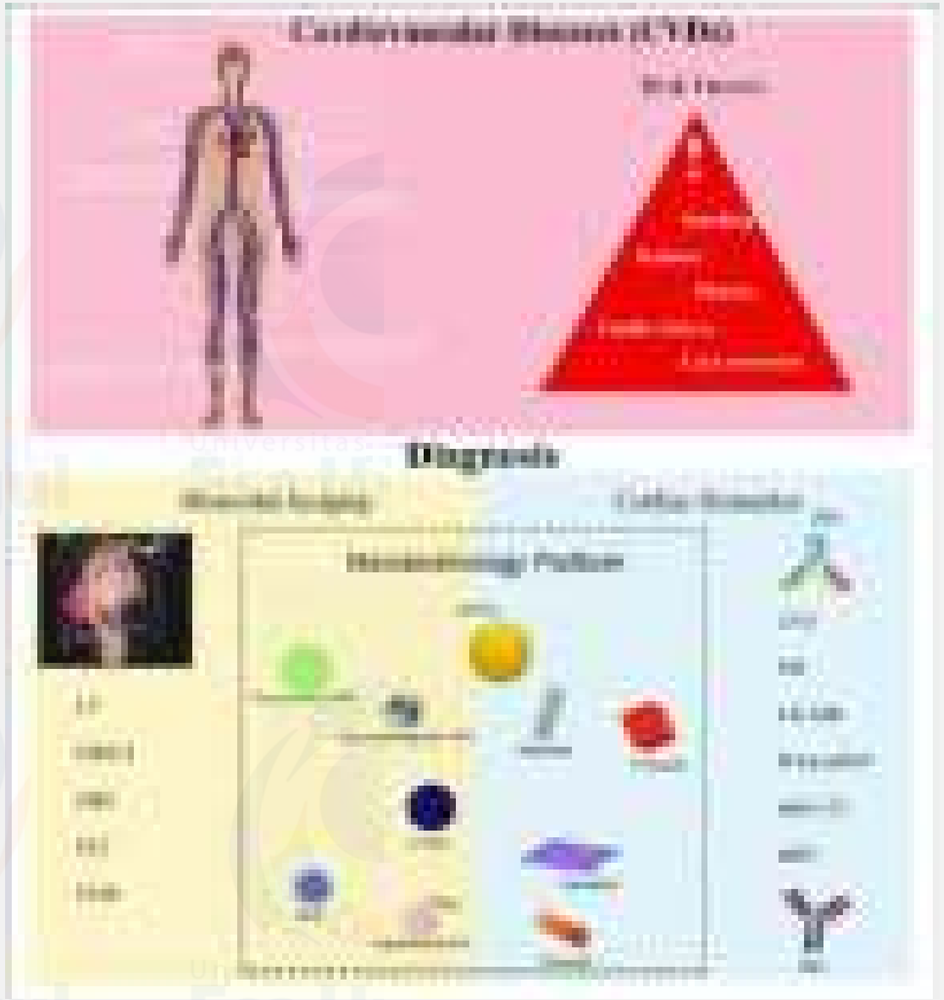
Apa itu penyakit pada Kardiovaskuler?

"Kardio dan Vaskuler: Jantung dań Pembuluh darah;"

Mencakup:

1. Kelainan pada jantung seperti: kardiomiopati, gagal jantung, aritmia, jantung iskemik, angina pektoris
2. Kelainan pada sistem pembuluh darah: aterosklerosis, hipertensi, **stroke,** skema regulasi ginjal

Penyebab kematian terbesar dan **silent disease**



Marker CVD

- Creatinin Kinase (CK)
- Creatinin Kinase Myocard Band (CKMB)
- Lactat Dehydrogenase (LDH)
- Cardiac Troponin T (cTnT)
- Cardiac Troponin I (cTnI)
- Myoglobin
- CRP dan hsCRP)
- D-dimer

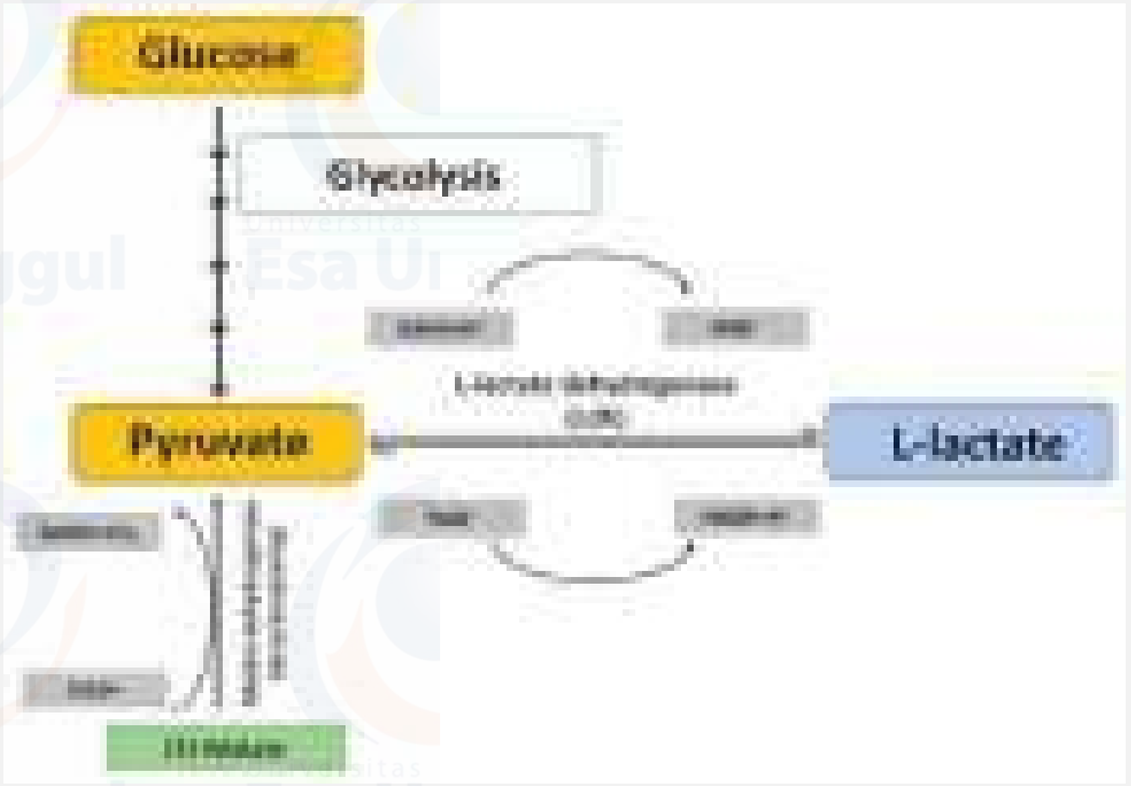
Creatinine Kinase

- Enzim yg mengkatalisis kreatin → kreatinin dalam sel otot,
- 2 sub unit: B & M
- isoform/ isoenzim : CKMB (myocardial) , CKBB (brain), CKMM (muscoscelet)
- CKMB: otot jantung & otot skelet
- Di otot jantung: mayoritas adalah CKMB, sisanya CKMM (otot rangka)
- Normal Wanita **<110 U/L, pria <130U/L**

Meningkat : - Angina pectoris berat
- Iskhemik reversibel
Kadar ↑ : 4 – 8 jam setelah IMA
Puncak : 12 – 24 jam
Menurun : hari ke 3
Normal : < 16 IU
Meningkat pd: AMI, kerusakan otot (skelet, jantung), gagal ginjal,

LDH (lactate-dyhidrogenase)

- Mengkatalisis laktat ↔ piruvat
- 5 jenis isoenzim
- Otot jantung: **LDH1, LDH2**
- Kadar ↑ : 8 – 12 jam setelah IMA
- Puncak : 24 – 48 jam
- Menurun : Hari ke 14
- Normal : LDH 1/LDH 2 : < 0,85
- Meningkat pd kerusakan otot jantung, gagal ginjal.

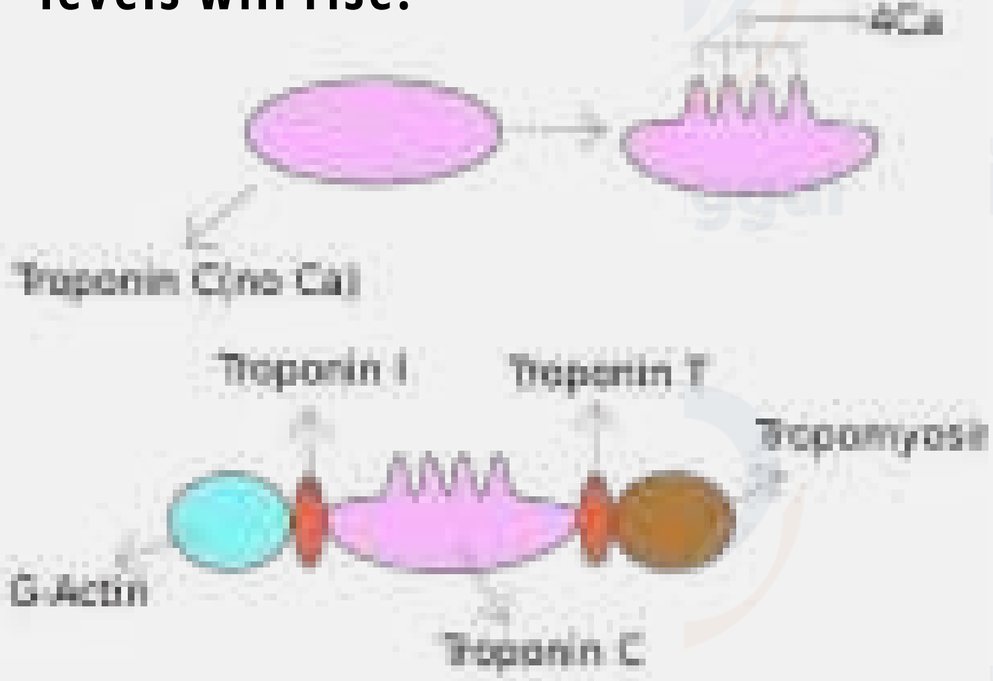


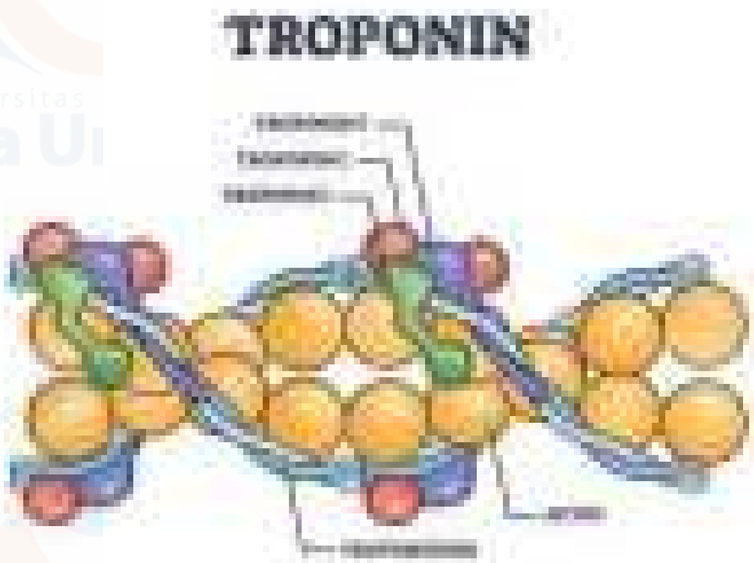
proses glikolisis - generate ATP (energi) untuk bergerak (otot)

Troponin

a protein that's found in the cells of your heart muscle.

But if your heart muscle is damaged, troponin leaks into your bloodstream, and your troponin blood levels will rise.



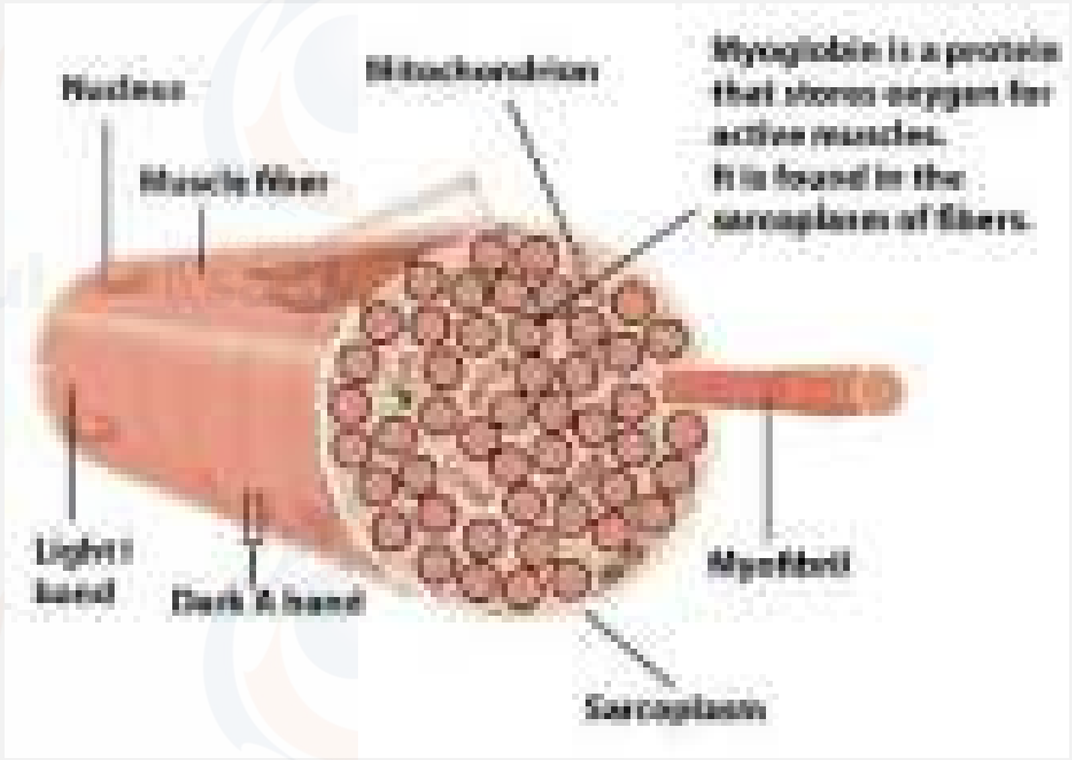


Kompleks Troponin terdapat pada filamen tipis & mengontrol proses kontraksi

Tn C:komponen yg ikat Ca & menginisiasi kontraksi
Tn I: komponen penghambat kontraksi pada keadaan istirahat
Tn T: Komponen pengikat kompleks troponin pd tropomiosin
Sebag besar Tn I di otot jantung membentuk kompleks dg Tn C & Tn T
3-6% Tn I bebas di sitoplasma otot jantung

Mioglobin

Mio: otot**, globin:** protein dalam darah

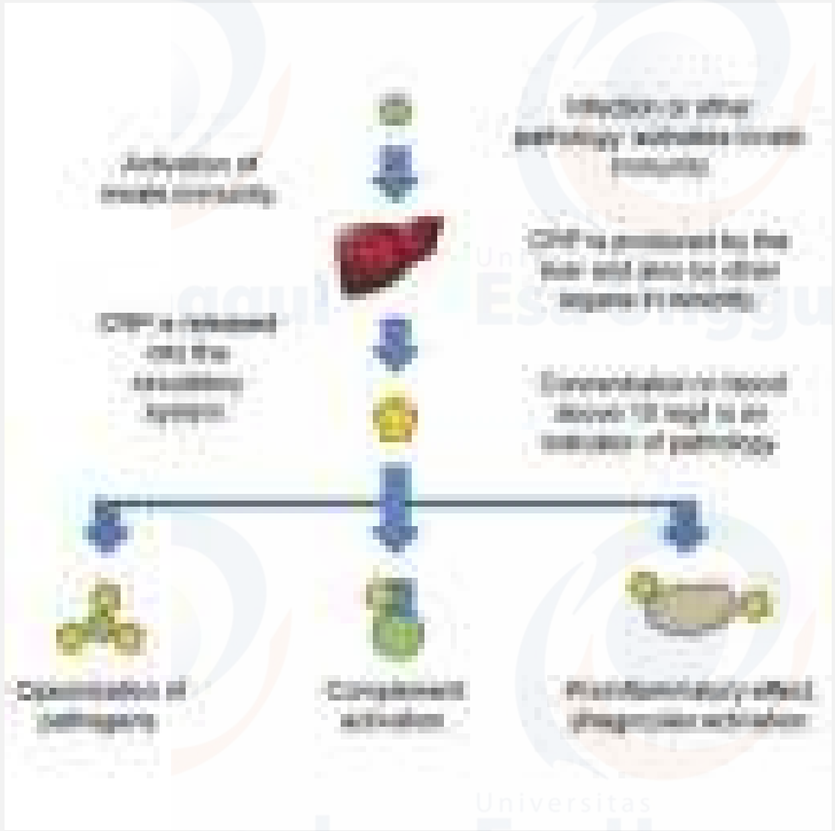


Pria: 16-76 ng/ml
Wanita: 7-64 ng/ml
Cut off point : 70 ng/ml

- a protein located primarily in the striated muscles of vertebrates (sitoplasma sel otot skelet dan jantung
- It encodes a single polypeptide chain with one oxygen binding site. Myoglobin contains a **heme prosthetic group that can reversibly bind to oxygen.**
- Kerusakan jantung menstimulus peningkatan myoglobin
- Ekskresi oleh ginjal -- gangguan filtrasi ginjal -- eliminasi menurun --kadar dalam darah meningkat
- Dideteksi: 2 jam setelah IMA & Puncak: 8-12 jam & Hilang: < 24 jam post infark

CRP

a pentameric protein synthesized by the liver, **whose level rises in response to inflammation**



- **Protein fase akut**
- **Penanda inflamasi**
- **Sintesis: Hati, induksi: IL-6 sebagai proinflammatory**
- **Kecepatan normal sintesis 1-10 mg/hr, inflamasi akut: > 1 gr/hr**
- **waktu paruh biologis 19 jam**

hs CRP

spesific on arterial inflammation

a marker of inflammation that predicts incident myocardial infarction, stroke, peripheral arterial disease, and sudden cardiac death

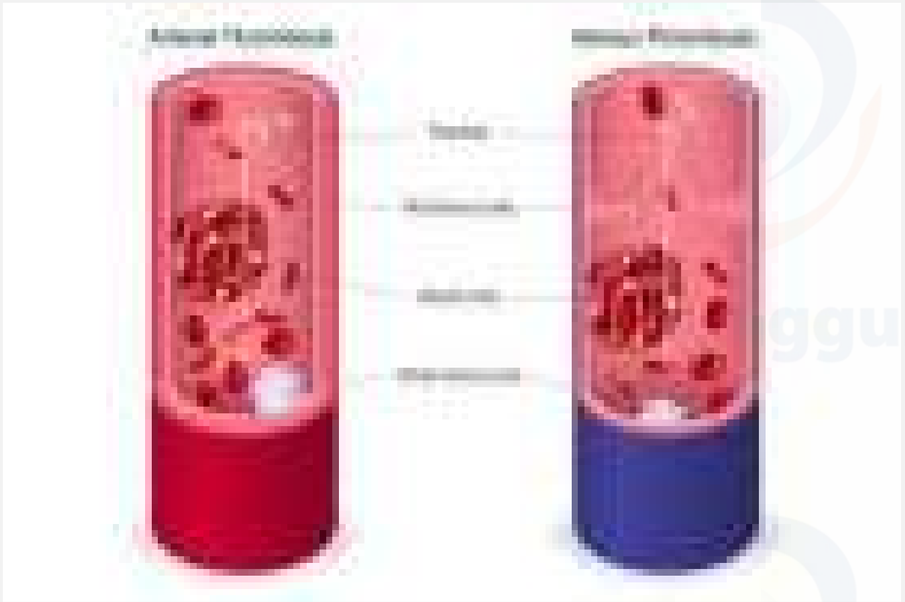
hs-CRP Value	Cardiovascular Disease Risk Level*
< 1 mg/L	low risk
1-3 mg/L	average risk
> 3 mg/L	high risk

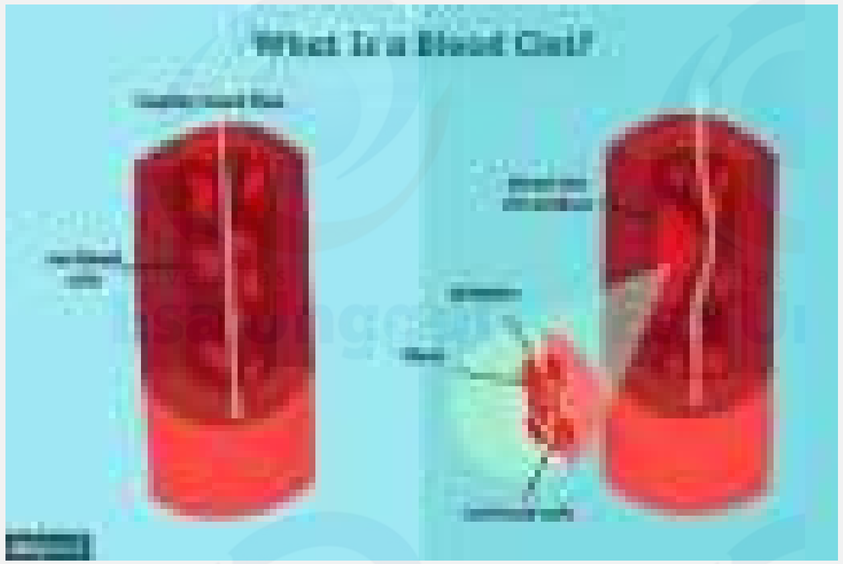
* Risk levels published in 2003 American Heart Association / Centers for Disease Control and Prevention Scientific Statement

D-Dimer

Marker pemecahan pembekuan darah (fibrinolitik/ trombolitik)

Fragmen protein yang dibuat tubuh ketika gumpalan darah larut dalam tubuh. D-dimer biasanya tidak terdeteksi atau hanya terdeteksi pada tingkat yang sangat rendah, kecuali jika tubuh membentuk dan memecah gumpalan darah yang signifikan



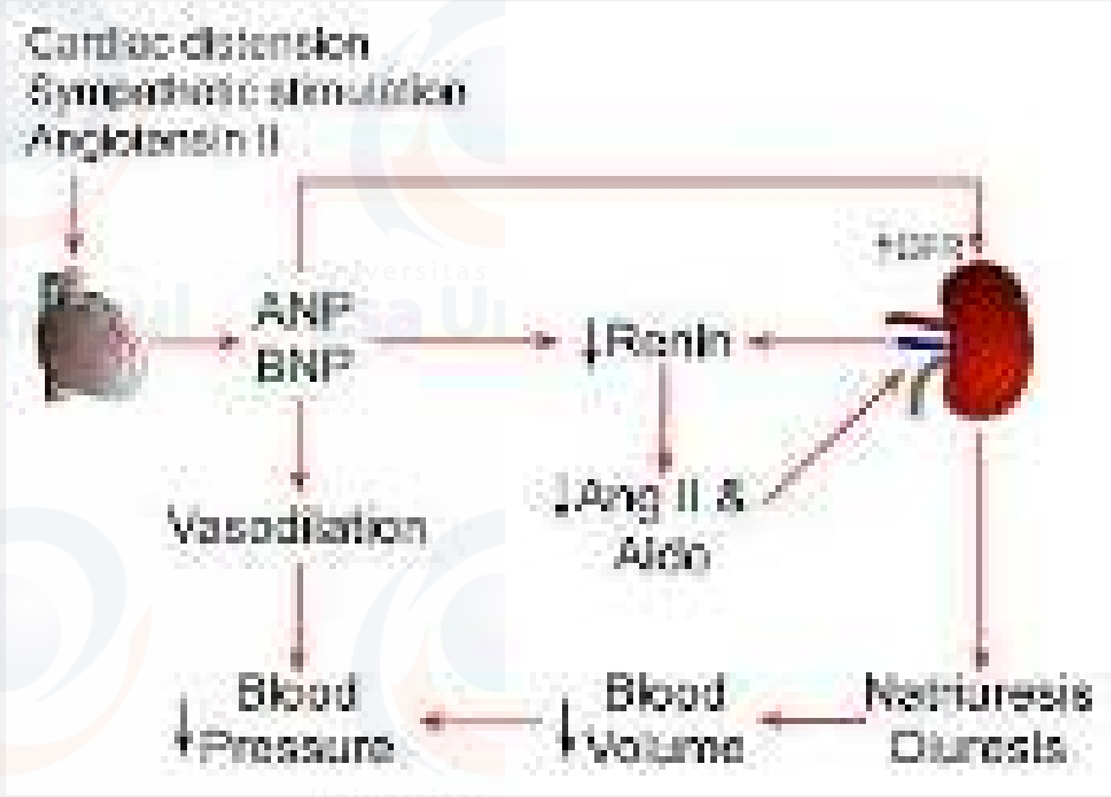


kondisi terkait:
Trombosis/ keadaan hiperkoagulabilitas & fibrinolisis (Kadar D-Dimer)
Trombus : bekuan/ massa gumpalan darah yg terbentuk krn aktivitas koagulasi, dpt menyumbat sirkulasi, melakat pd arteri, vena, kapiler, bilik jantung

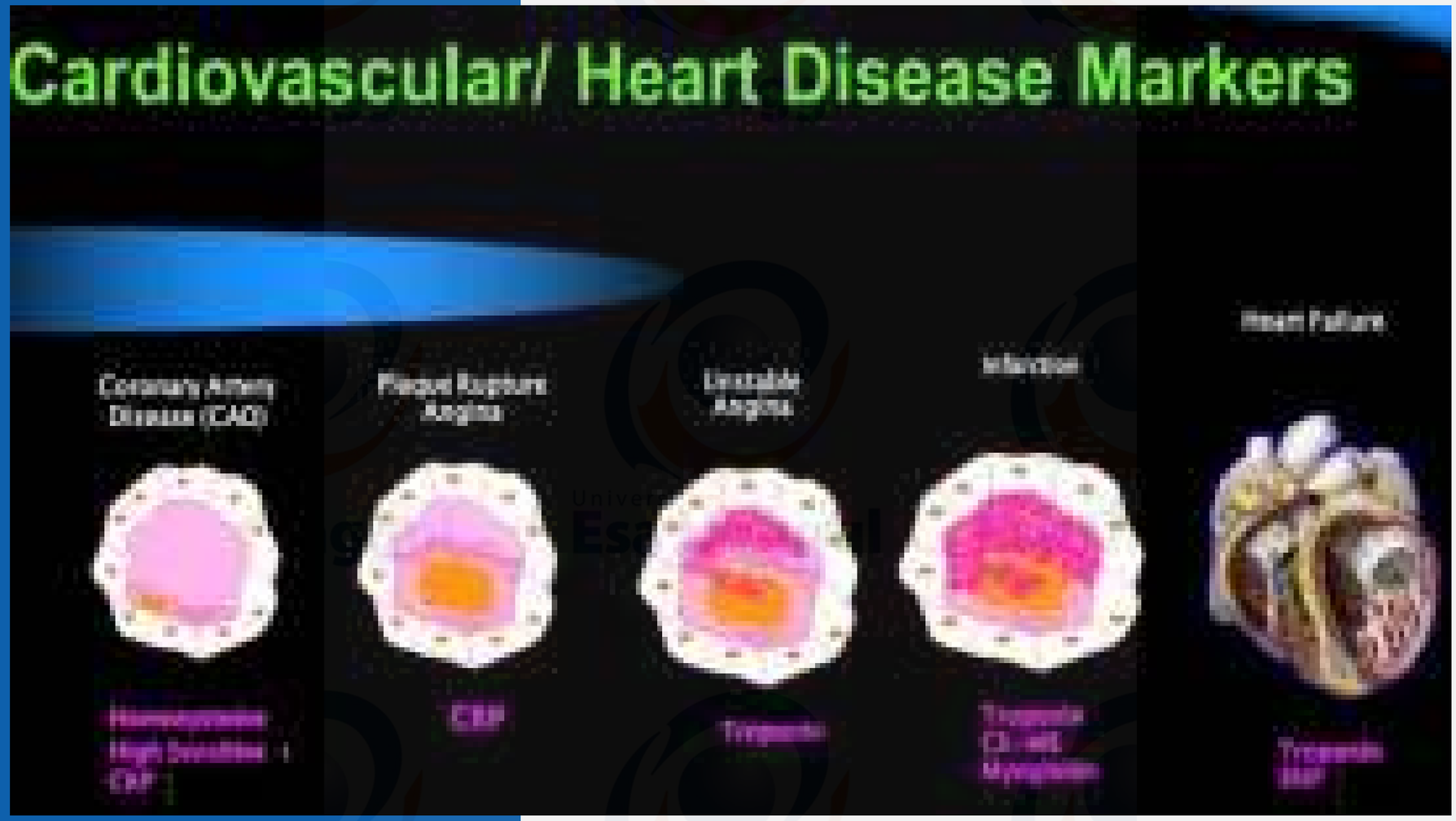
B-type Natriuretic Peptide (BNP)

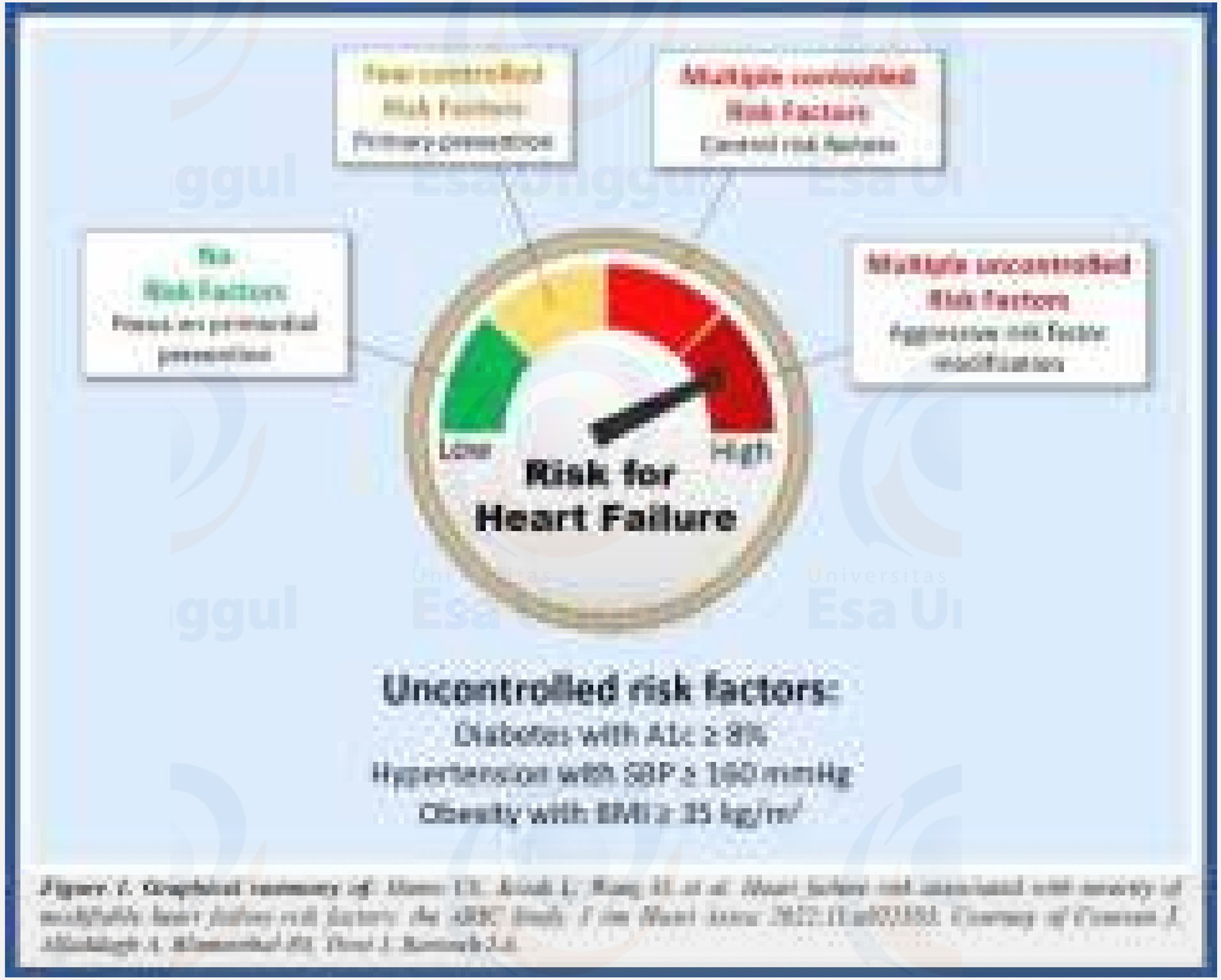
It's made inside the pumping chambers of your heart when pressure builds up from heart failure.

Heart failure happens when your heart is not pumping blood well. This causes cells inside your heart to release BNP. This opens up blood vessels in your body to take pressure off your heart. A BNP blood test correctly shows heart failure about 9 out of 10 times.



BNP: B-type natriuretic peptide -- jantung dan otak (brain NP)
ANP: Atrial natriuretic peptide -- kelainan atrium


Cardiovascular/ Heart Disease Markers
Coronary Artery Disease (CAD)
Plaque Rupture Angina
Unstable Angina
Infarction
Heart Failure
CRP
Troponin


Low
High
Risk for
Heart Failure
Uncontrolled risk factors:
Diabetes with A1c ≥ 8%
Hypertension with SBP ≥ 160 mmHg
Obesity with BMI ≥ 35 kg/m²

Rise your hand!

any question?

PSF316

Farmakoterapi Stroke

Sesi Ke 2

Topik Sesuai RPS:
Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi Penyakit Stroke

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Topik Sebelum UTS

Sesi 1

Pendahuluan: jenis penyakit kardiovaskular dan pemeriksaan labolatorium

Sesi 2

Patofisiologi dan farmakoterapi **stroke**

Sesi 3

patofisiologi dan farmakoterapi gagal jantung

Sesi 4

patofisiologi dan farmakoterapi sindrom koroner akut

Sesi 5

patofisiologi dan farmakoterapi Aritmia

Sesi 6

patofisiologi dan farmakoterapi gagal ginjal akut

Sesi 7

patofisiologi dan farmakoterapi gagal ginjal kronis

Ujian Tengah Semester

Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

patofisiologi dan farmakoterapi epilepsi

Sesi 12

patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

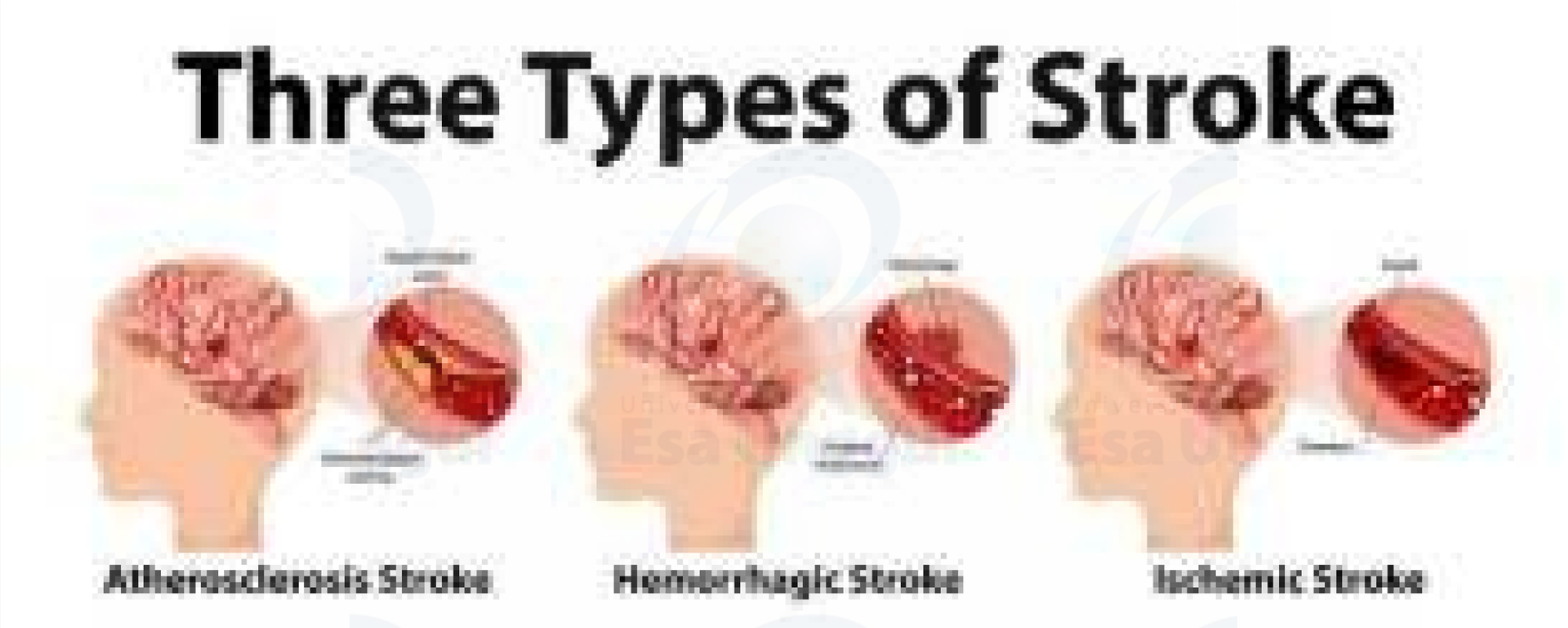
patofisiologi dan farmakoterapi rheumatoid arthritis

Sesi 14

patofisiologi dan farmakoterapi SLE

Ujian Akhir Semester

Apa itu Stroke?



Kematian jaringan otak yang terjadi karena berkurangnya aliran darah oksigen dan nutrisi ke otak

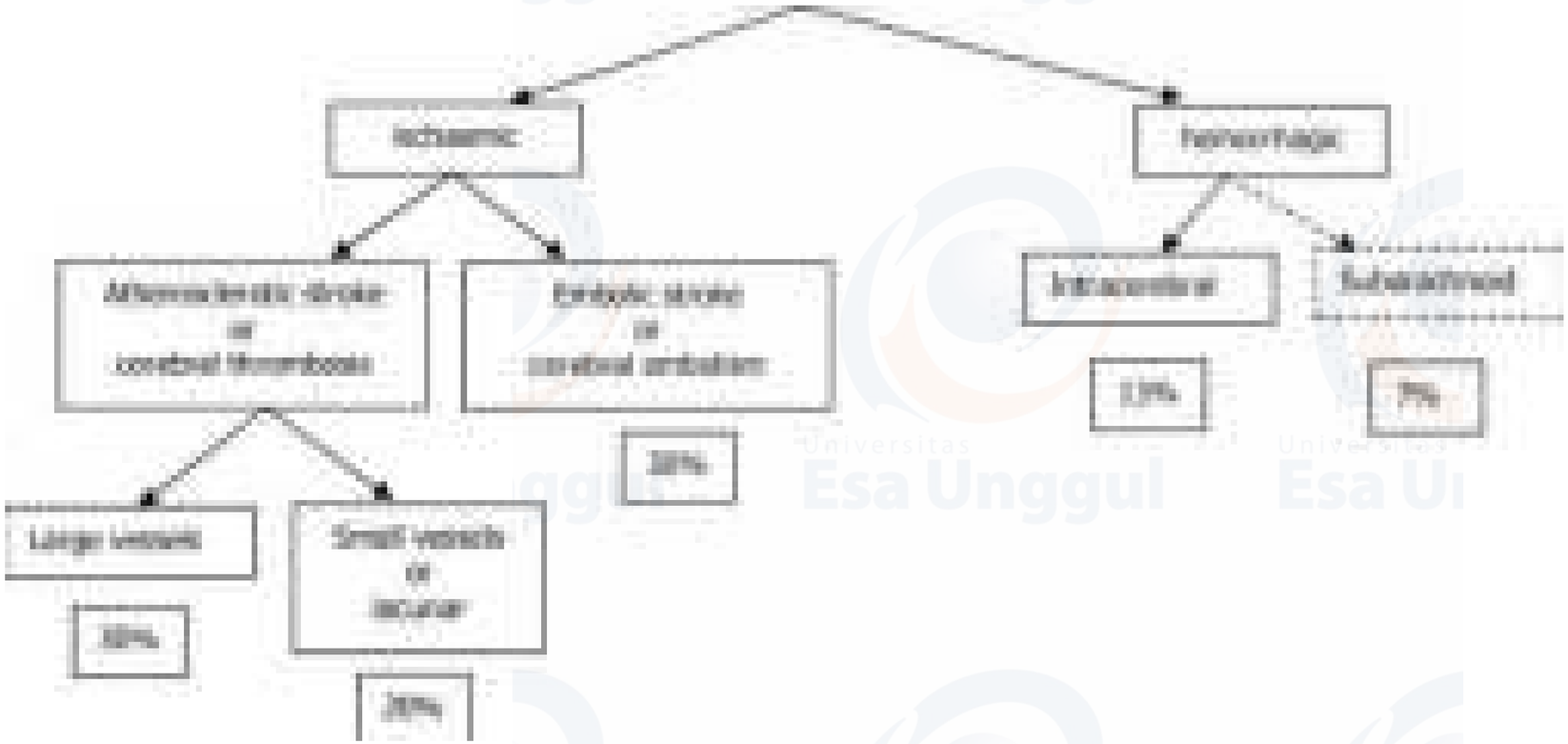
Penyebab kematian no 3 di Indonesia maupun dunia

Faktor Resiko

Faktor resiko

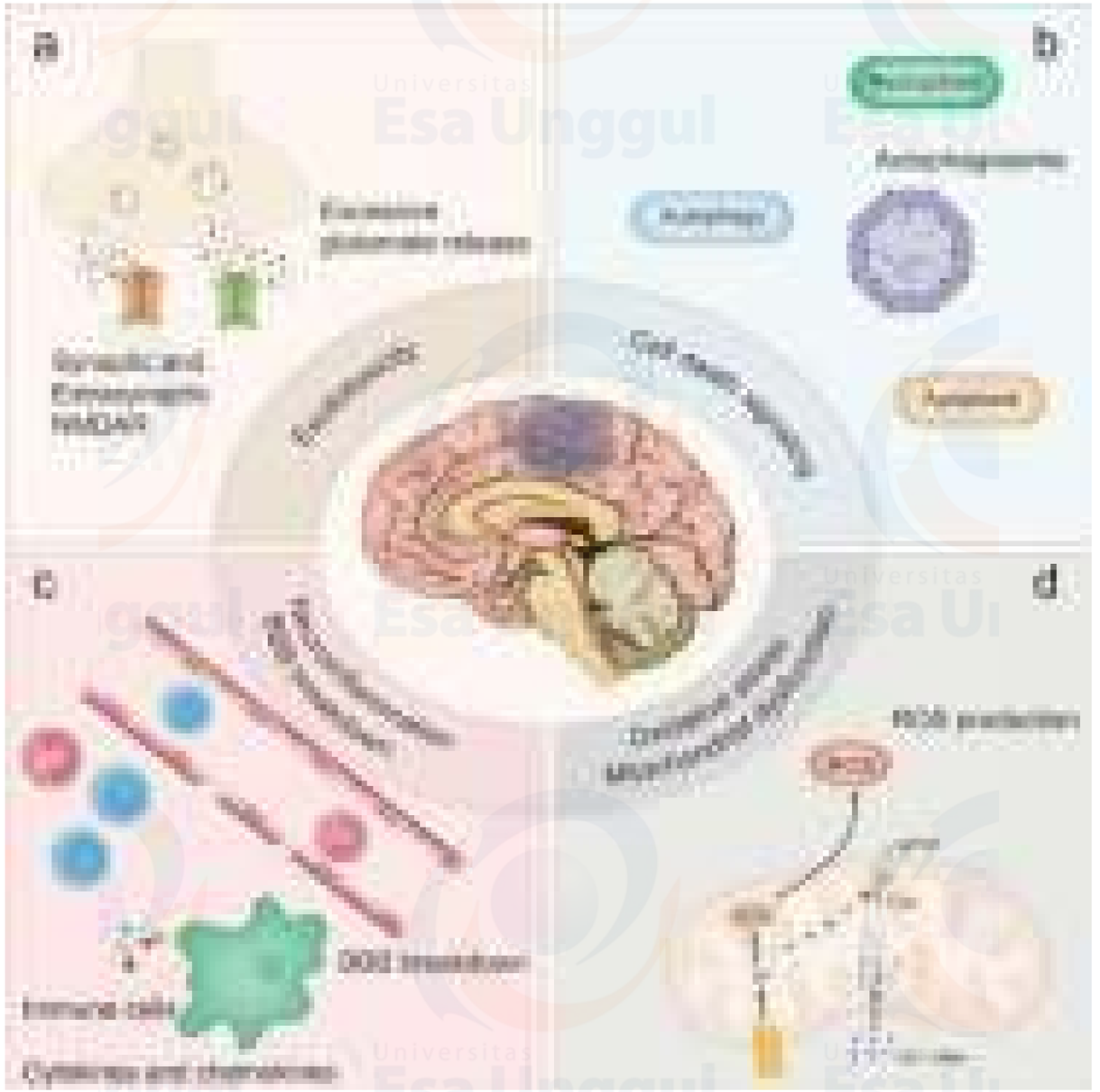
Bisa dikendalikan	Potensial bisa dikendalikan	Tidak bisa dikendalikan
■ Hipertensi ■ Penyakit jantung ■ Fibrilasi atrium ■ Endokarditis ■ Stenosis mitralis ■ Infark jantung ■ Merokok ■ Anemia sel sabit ■ *Transient Ischemic Attack (TIA)* ■ Stenosis karotis asimtomatik	■ Diabetes Melitus ■ Hipertonosistolemia ■ Hipertrofi ventrikel kiri	■ Umur ■ Jenis kelamin ■ Heredite ■ Ras dan etnis ■ Geografi

Klasifikasi Stroke



- **Embolism**: an embolus originating somewhere else in the body (e.g. the heart) causes obstruction of a cerebral vessel, resulting in hypoperfusion to the area of the brain the vessel supplies.
- **Thrombosis**: a blood clot forms locally within a cerebral vessel (e.g. due to atherosclerotic plaque rupture).
- **Systemic hypoperfusion**: blood supply to the entire brain is reduced secondary to systemic hypotension (e.g. cardiac arrest).
- **Cerebral venous sinus thrombosis**: blood clots form in the veins that drain the brain, resulting in venous congestion and tissue hypoxia.

Manifestasi Klinis Stroke



Algoritma Terapi Stroke

Terapi yang diberikan tergantung jenis stroke.
Situs Target: aliran pembuluh darah otak

Berdasarkan waktu pemberian terapi:

1. Terapi fase Akut
2. Terapi pencegahan/ sekunder/ rehabilitasi

Pendekatan Terapi:

1. restorasi aliran darah otak dengan menghilangkan hambatan clots
2. menghentikan kerusakan seluler karena hipoksia/ iskemik

THEURAPETIC WINDOW: 12 -24 jam
GOLDEN PERIOD: 3-6 jam

Algoritma Terapi Stroke

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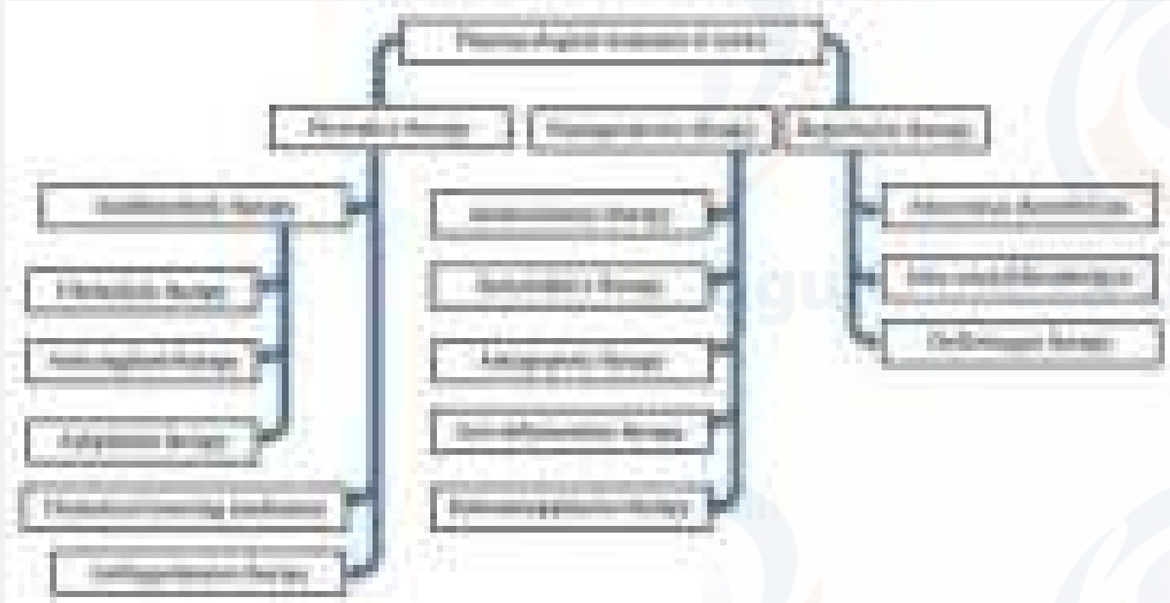
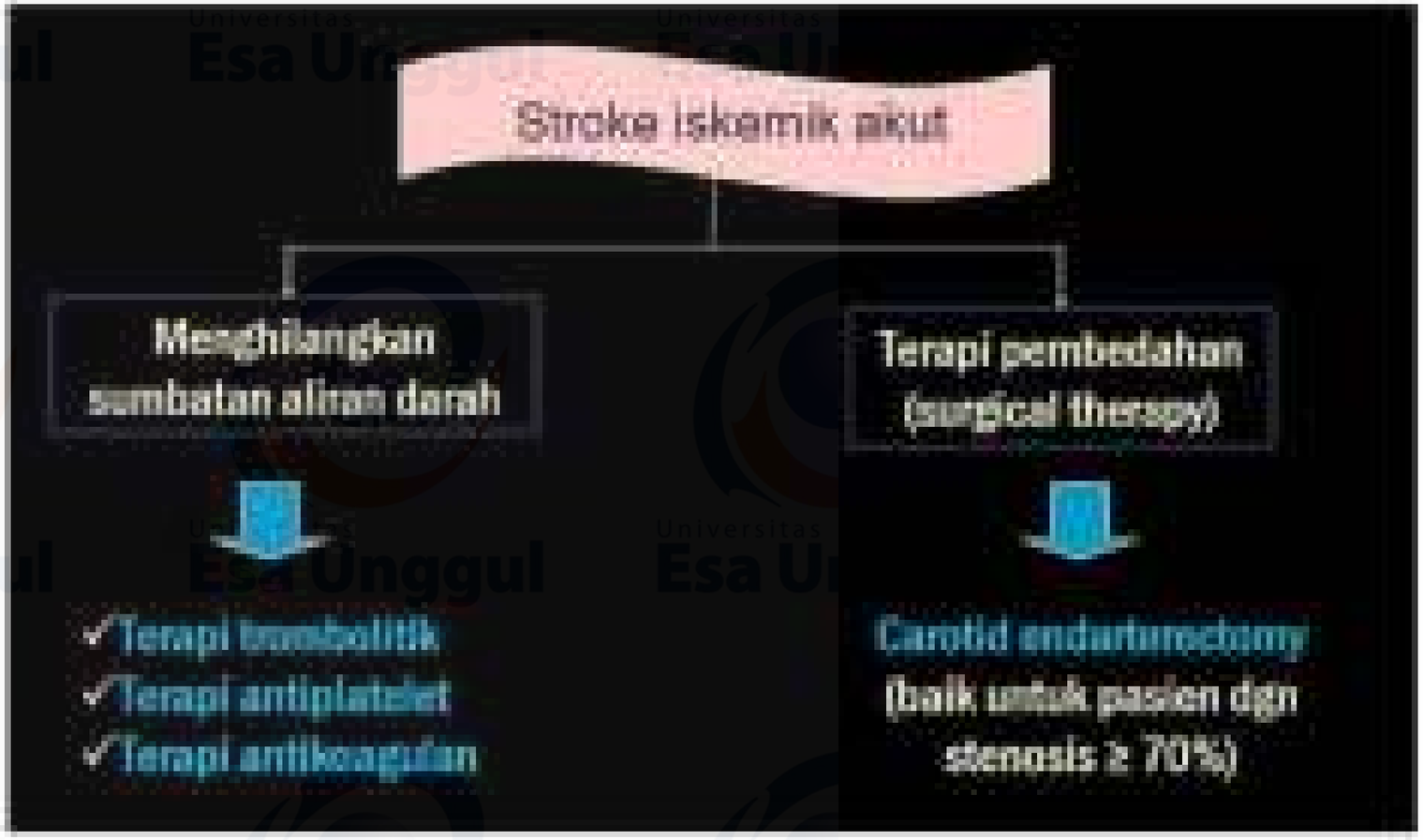
THEURAPETIC WINDOW: 12 -24 jam
GOLDEN PERIOD: 3-6 jam

Tatalaksana Emergency Stroke



Stroke Iskemik



Stroke Hemoregik

- **Blood pressure (BP) Management:**

beta-blockers (labetalol, esmolol), ACE inhibitor (enalapril), calcium channel blocker (nicardipine), or hydralazine

- **Management of Raised Intracranial Pressure (ICP):**

Osmotic agents (mannitol, hypertonic saline).

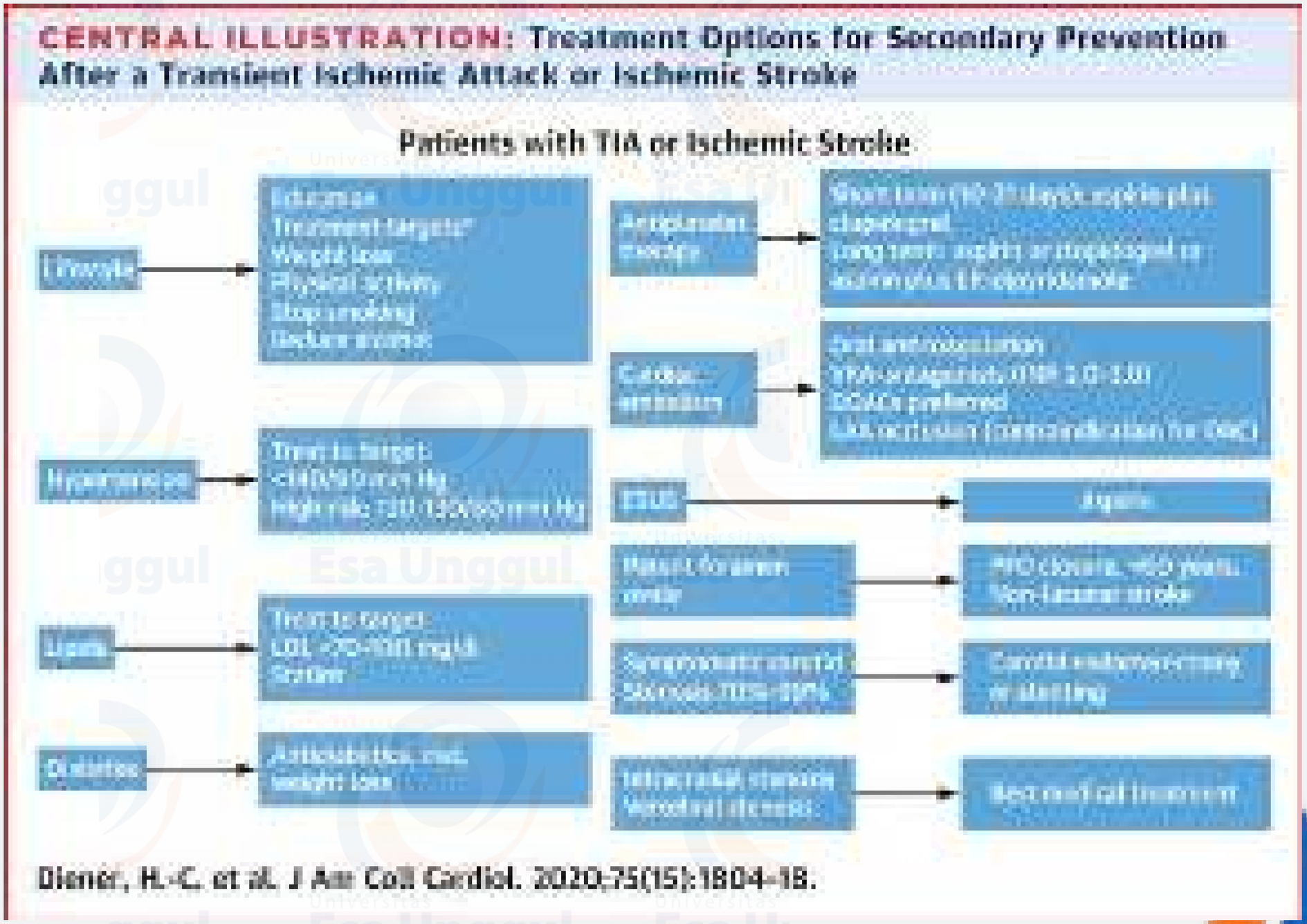
- Hemostatic Therapy

Vitamin K, prothrombin complex concentrates (PCCs), recombinant activated factor VII (rFVIIa), fresh frozen plasma (FFP)

- Antiepileptic Therapy
- Surgery
- Cerebroprotection

Pioglitazone, misoprostol, and celecoxib are tried to reduce inflammatory damage. Edaravone, flavanoid, and nicotinamide mononucleotide can reduce oxidative stress. The iron chelator deferoxamine is also in the experimental phase.

Rehab/ maintenance management



Rise your hand!

any question?

PSF316

Farmakoterapi Gagal Jantung

Sesi Ke 3

Topik Sesuai RPS:
Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi Penyakit Gagal Jantung

Dosen Pengampu:

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patofisiologi dan farmakoterapi Aritmia

Sesi 6

patofisiologi dan farmakoterapi gagal ginjal akut

Sesi 7

patofisiologi dan farmakoterapi gagal ginjal kronis

Ujian Tengah Semester

Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

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patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

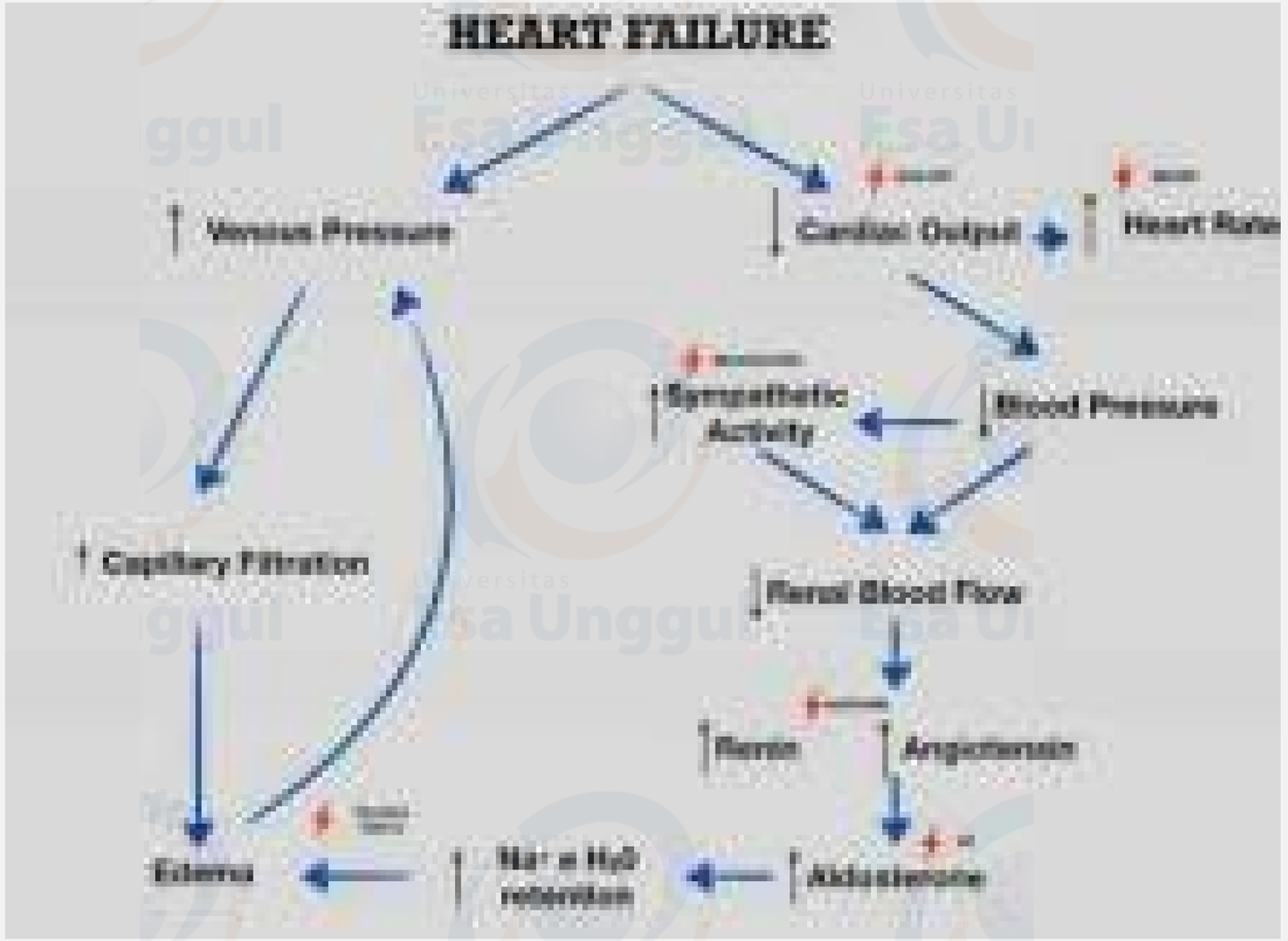
patofisiologi dan farmakoterapi rheumatoid arthritis

Sesi 14

patofisiologi dan farmakoterapi SLE

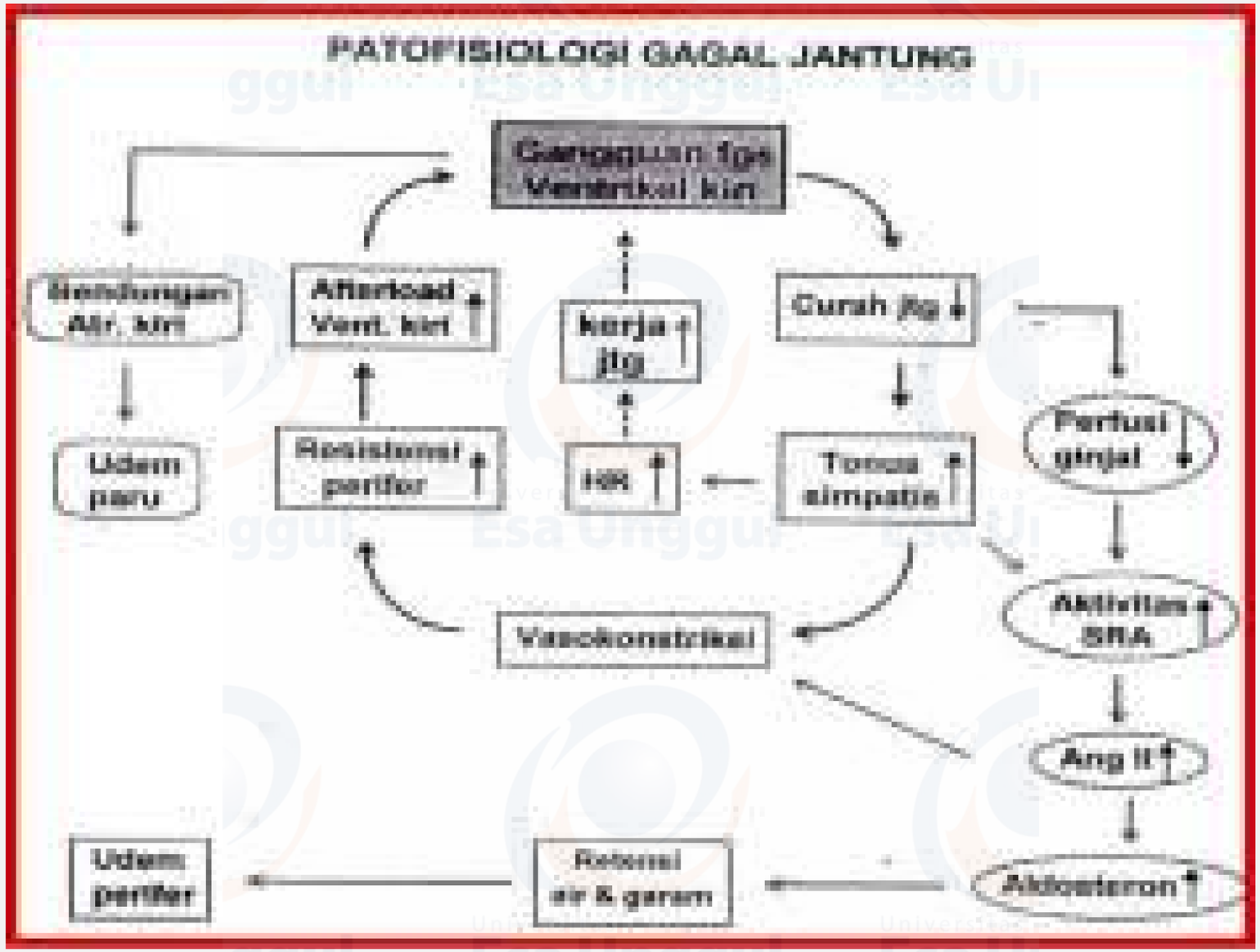
Ujian Akhir Semester

Apa itu Gagal Jantung/ HF?



Gangguan fungsi jantung sehingga tidak mampu memompakan darah dalam jumlah yang cukup untuk memenuhi perfusi jaringan

Apa itu Gagal Jantung/ HF?



manifestasi Klinis

Mekanisme	Jangka pendek, adaptif	Jangka panjang, maladaptif
Retensi air dan garam	Preload Mempertahankan curah jantung	Kongesti paru, anasarkaKongesti paru
Vasokonstriksi	Afterload Mempertahankan tekanan darahMempertahankan curah jantung	Curah jantung Pemakaian enersi jantung Nekrosis jantung
Stimulasi jantung	Kontraktilitas Relaksasi Laju jantung	Kalsium sitoplasma Pemakaian enersi jantung Nekrosis jantungAritmia, kematian mendadak

Penyebab Gagal Jantung

- Kelainan Otot Jantung:
  - Kardiomiopati
  - infark miokardium
- Beban Hemodinamik:
  - Hipertensi
  - Tirotoksisitas
  - Anemia Berat
- Gangguan input (load) jantung
  - Kelainan kaput (kongenital)
  - Defect septum
  - Perikarditis
  - Endomiocardial fibrosis
  - pericardial effusion

KLASIFIKASI GAGAL JANTUNG

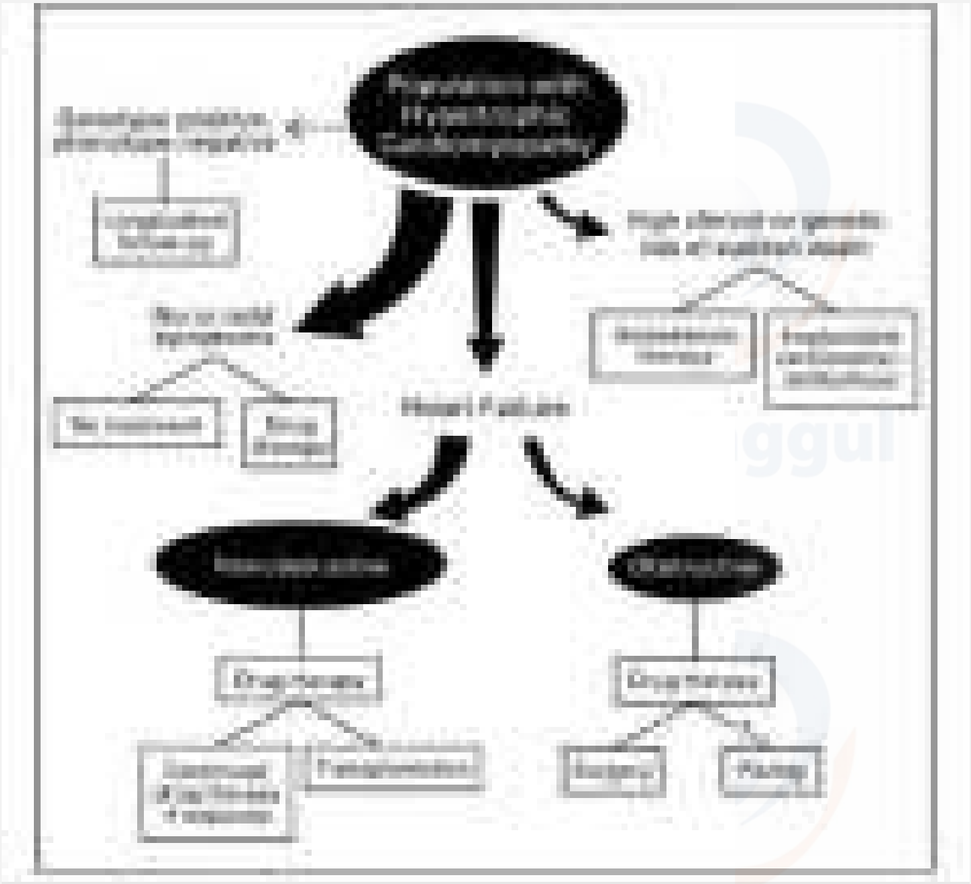
Klasifikasi berdasarkan kelainan struktural jantung	Klasifikasi berdasarkan kapsitas fungsional (NYHA)
Stadium A-Memiliki risiko tinggi untuk berkembang menjadigagal jantung.-Tidak terdapat gangguan struktural atau-fungsional jantung, tidak terdapat tanda atau gejala	Kelas I-Tidak terdapat batasan dalam melakukan aktifitasfisik.-Aktifitas fisik sehari-hari tidak menimbulkankelelahan, palpitasi atau sesak nafas
Stadium B-Telah terbentuk penyakit struktur jantung yang berhubungan dengan perkembangan gagaljantung,-Tidak terdapat tanda atau gejala	Kelas II-Terdapat batasan aktifitas ringan.-Tidak terdapat keluhan saat istrahat, namunaktifitas fisik sehari-hari menimbulkankelelahan, palpitasi atau sesak nafas
Stadium CGagal jantung yang simtomatikberhubungan dengan penyakit strukturaljantung yang mendasari	Kelas III-Terdapat batasan aktifitas bermakna.-Tidak terdapat keluhan saat istrahat, tetapi aktfitasfisik ringan-menyebabkan kelelahan, palpitasi atau sesak
Stadium DPenyakit jantung struktural lanjut serta gejala gagal jantung yang sangat bermakna saat istrahat walaupun sudahmendapat terapi medis maksimal (refrakter)	Kelas IV-Tidak dapat melakukan aktifitas fisik tanpakeluhan.-Terdapat gejala saat istrahat.-Keluhan meningkat saat melakukan aktifitas

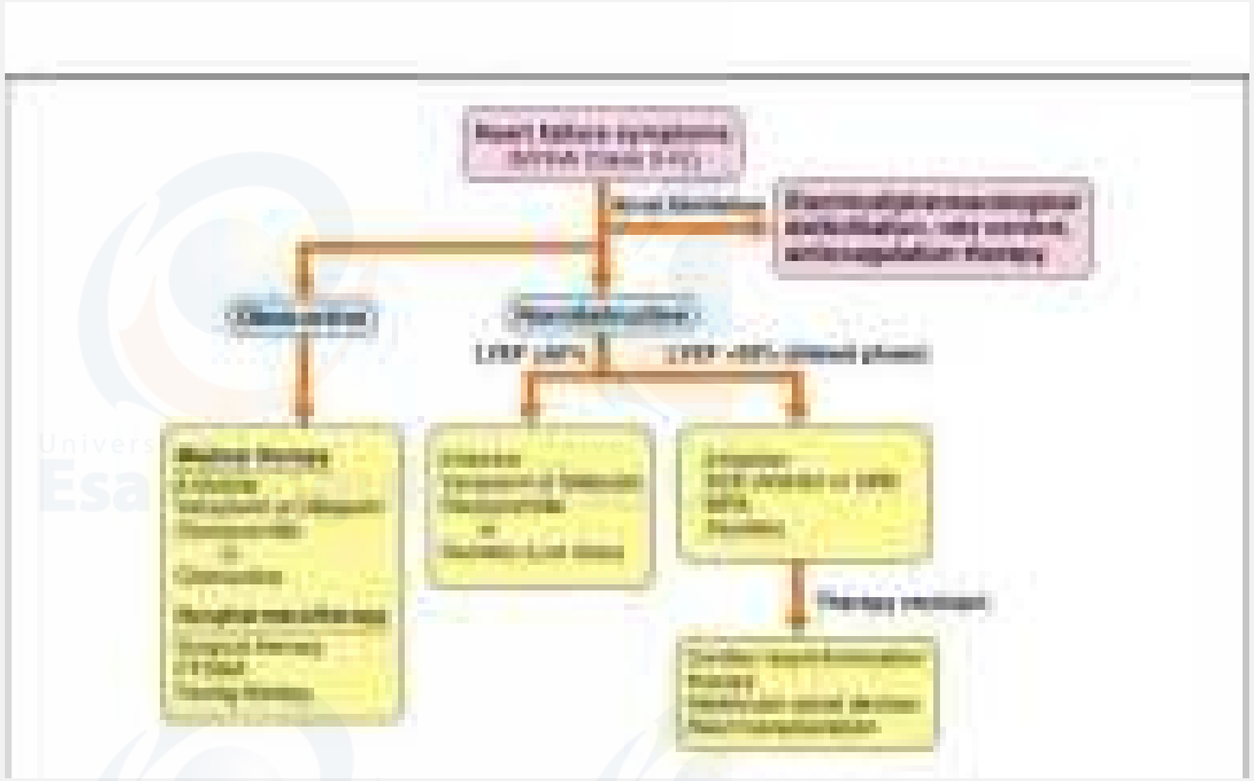
Algoritma Terapi HF

Principles in selecting appropriate medications

- Reduction in
  - Pre-load: Diuretics
  - After-load: ACE Inhibitors
  - Filling pressures: Nitrates
- Restoring perfusion
  - Inotropic agents
    - Beta adrenergic receptor agents; Dobutamine
    - Phosphodiesterase inhibitors: Milrinone

Algoritma Terapi Gagal Jantung





Farmakoterapi combine with surgery

Algoritma Terapi Gagal Jantung

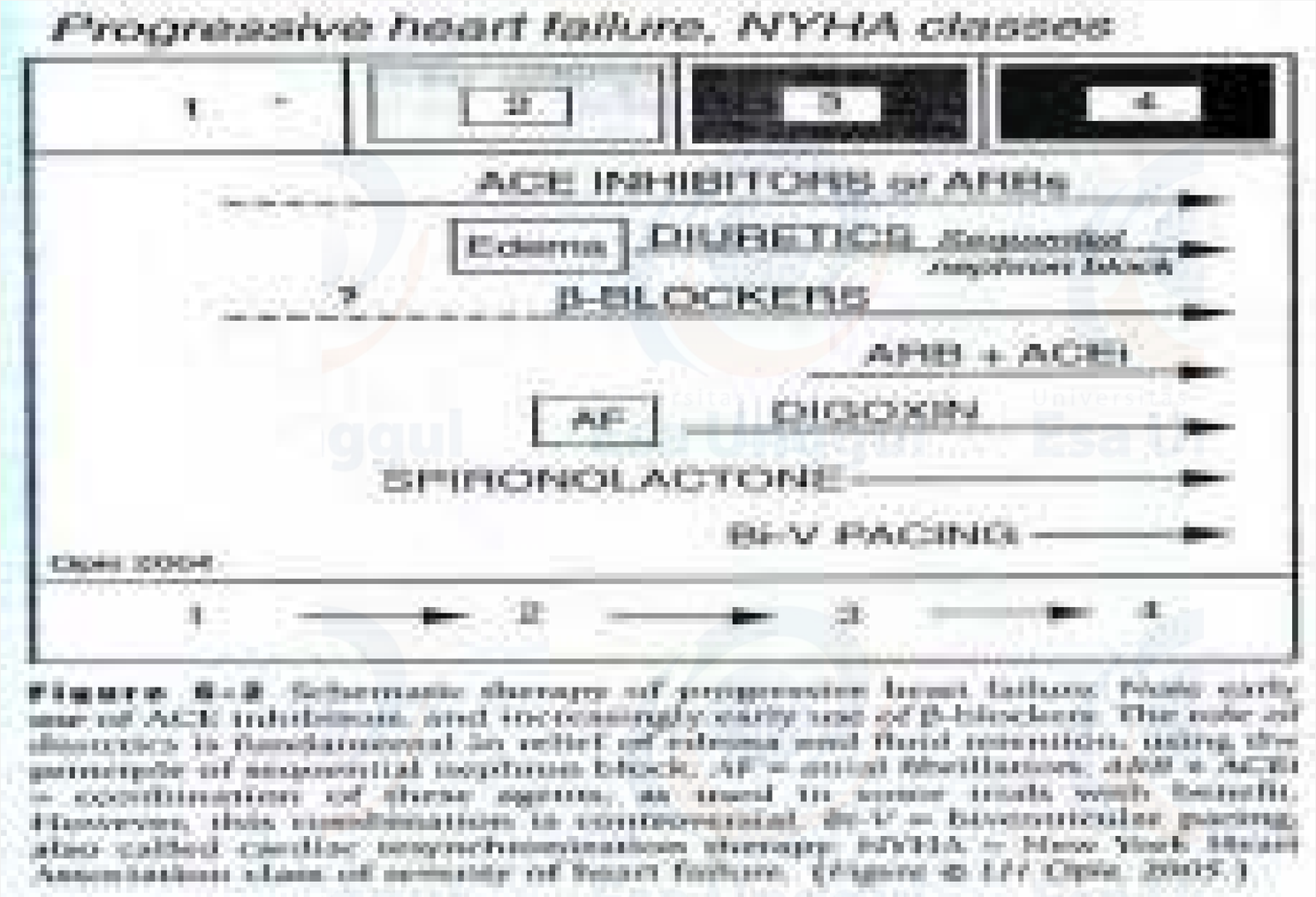
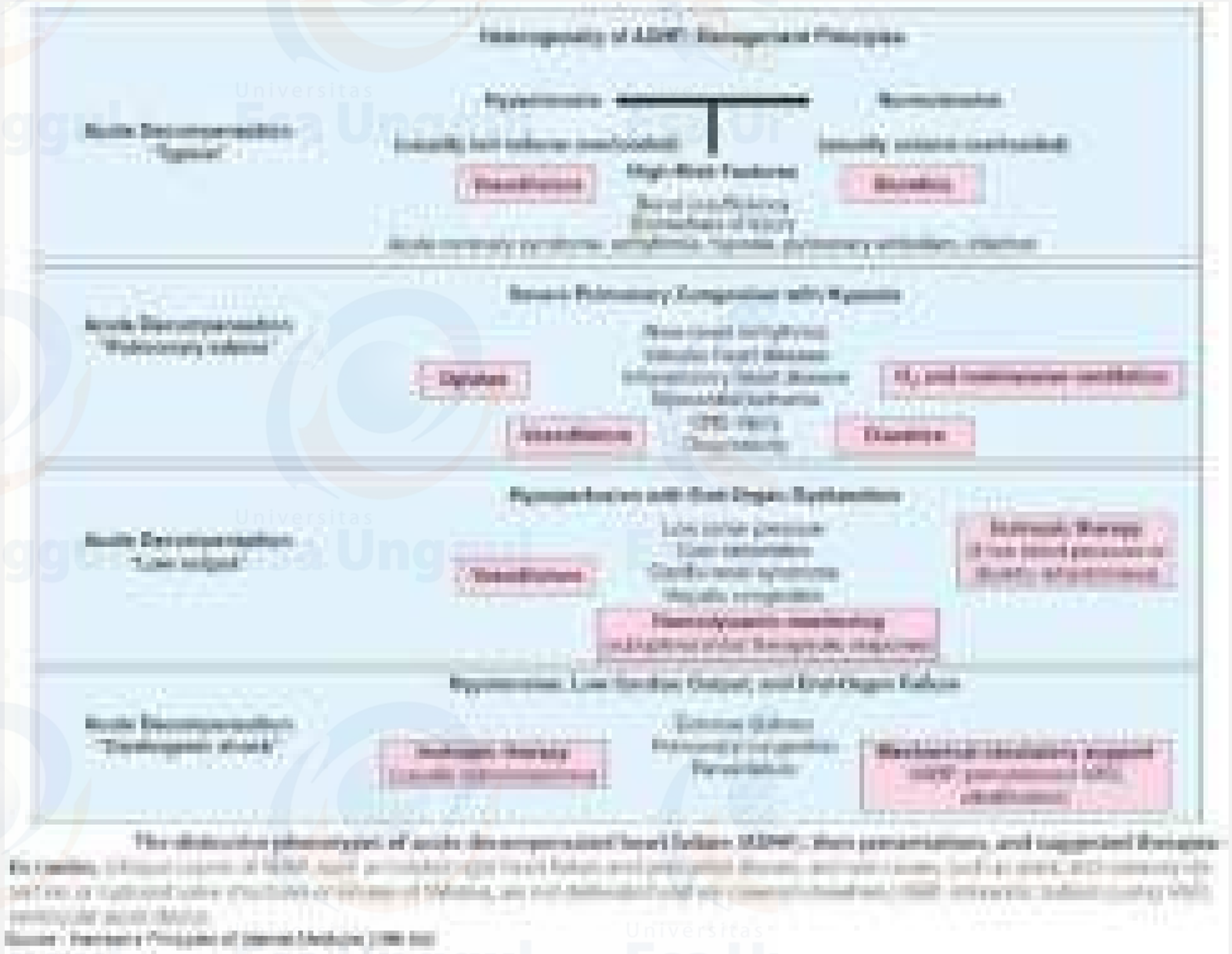


Figure 6-8 Schematic therapy of progressive heart failure. Note early use of ACE inhibitors and increasingly early use of β-blockers. The role of diuretics is fundamental in relief of edema and fluid retention, using the principle of sequential nephron block. AF = atrial fibrillation. ARB + ACEI = combination of these agents, as used in some trials with benefit. However, this combination is controversial. Bi-V = biventricular pacing, also called cardiac resynchronization therapy. NYHA = New York Heart Association class of severity of heart failure. (Figure 6-11 Opie, 2005.)

Farmakoterapi Gagal Jantung

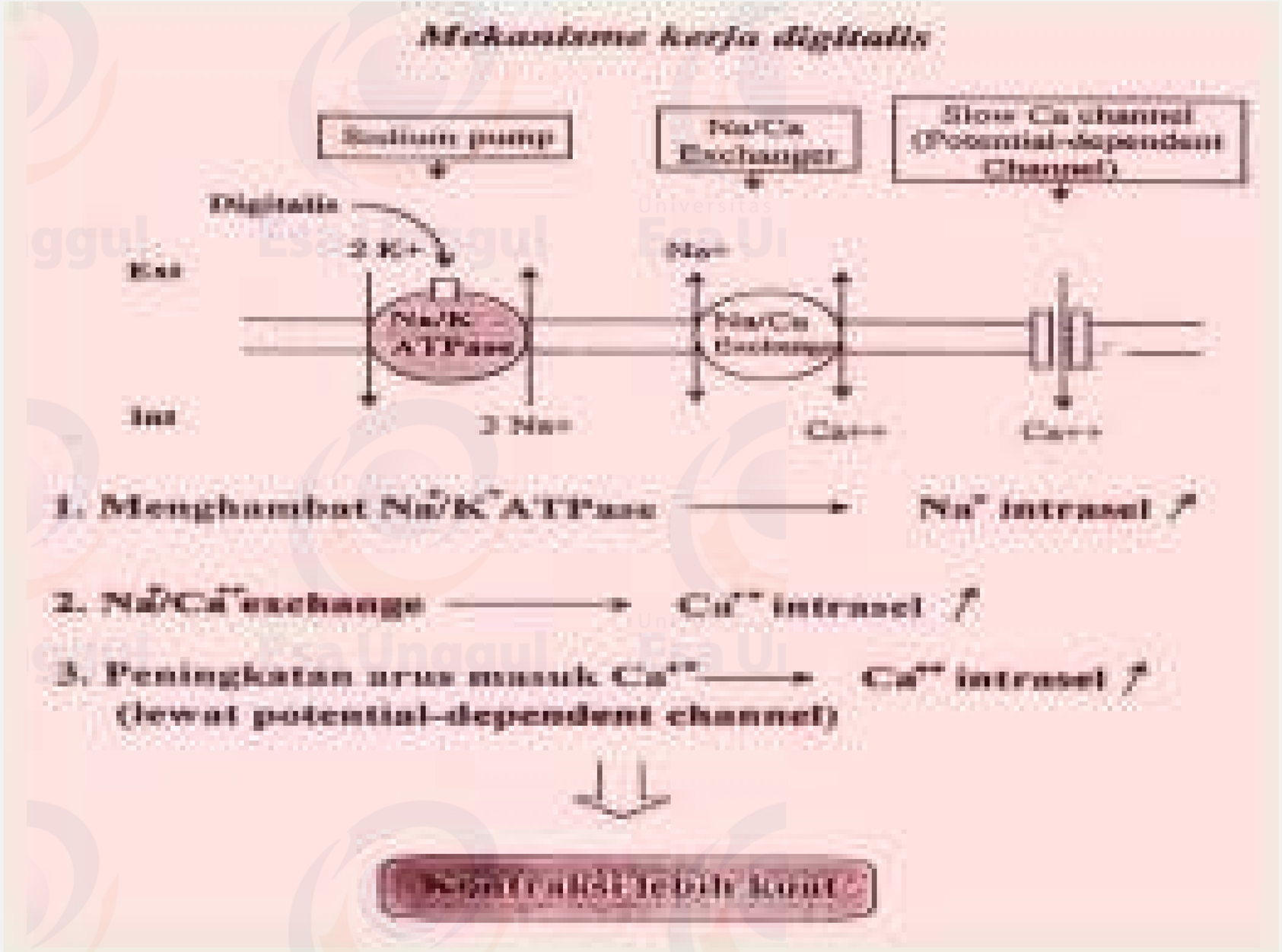
Agent of HF

- Diuretik
- Vasodilator
- ACEI /ARB
- Nitrat organik
- Hidralazin
- Penghambat alfa 1
- Obat inotropik



Efek Farmakologi:

- Curah jantung menurun -- bendungan sirkulasi paru menurun -- sesak nafas berkurang
- Sirkulasi ginjal membaik -- diuresis bertambah -- udem hilang
- Aktivitas RAA membaik -- angiotensin & aldosteron menurun, resistensi perifer dan udem hilang
- Aktivitas simpatis membaik -- fungsi jantung membaik



Inotropik

1. **Adrenergik**

Dopamin :

- Reseptor Beta 1 → inotropik (+)
- Reseptor D1 di ginjal & mesenterium → vasodilatasi → diuresis
- Reseptor alfa 1 dosis besar → vasokonstriksi
- Merangsang sekresi NE dan EPI

– Indikasi : syok kardiogenik& gagal jantung kronik refrakter

Dobutamin

- Reseptor Beta 1 → inotropik (+)
- Efek alfa 1 <<< dari dopamin
- Tidak merangsang sekresi NE dan epi
- Dosis besar : takikardi

– Indikasi : Gagal jantung refrakter (pengobatan jangka pendek)

Dopamin & Dobutamin

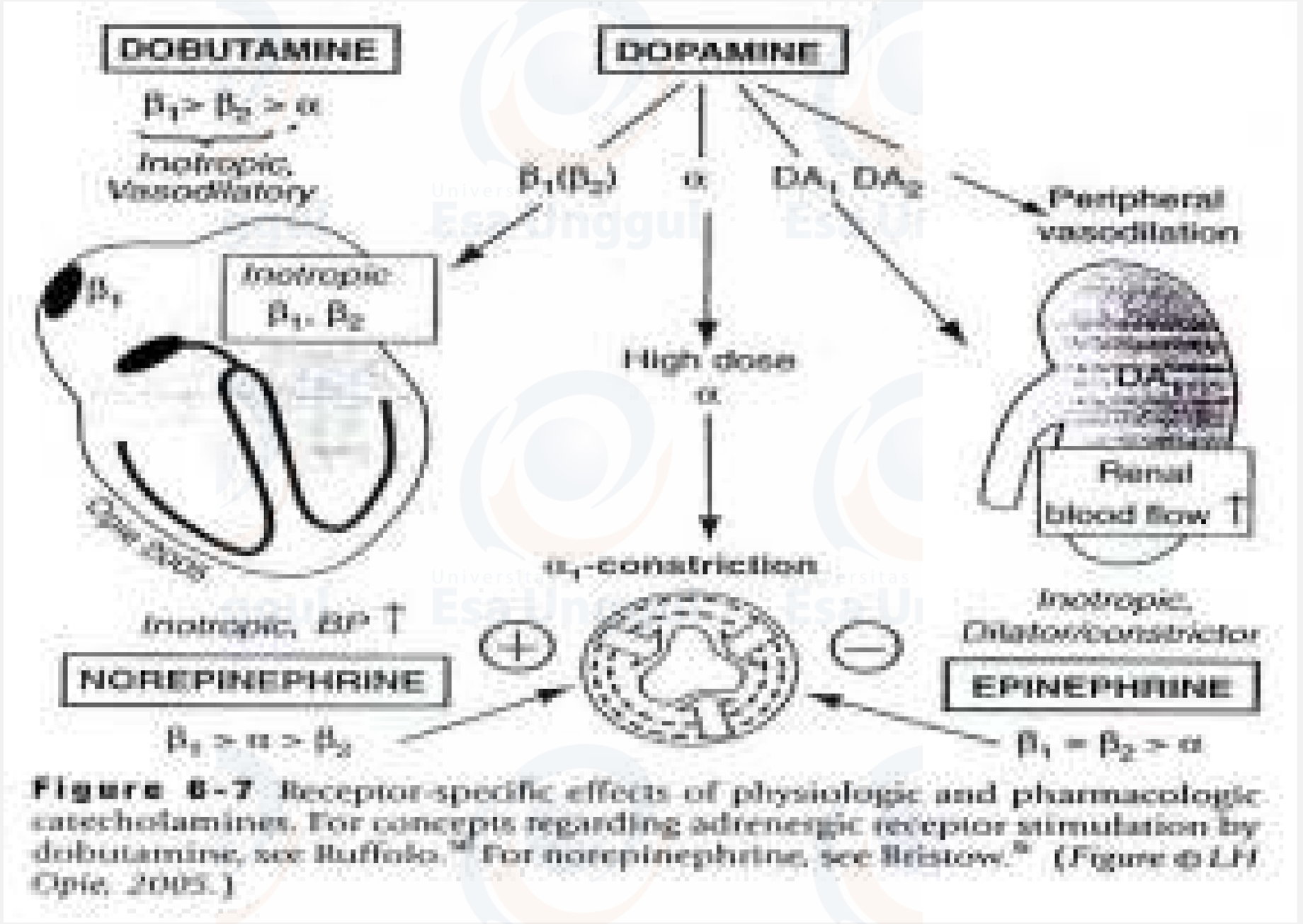
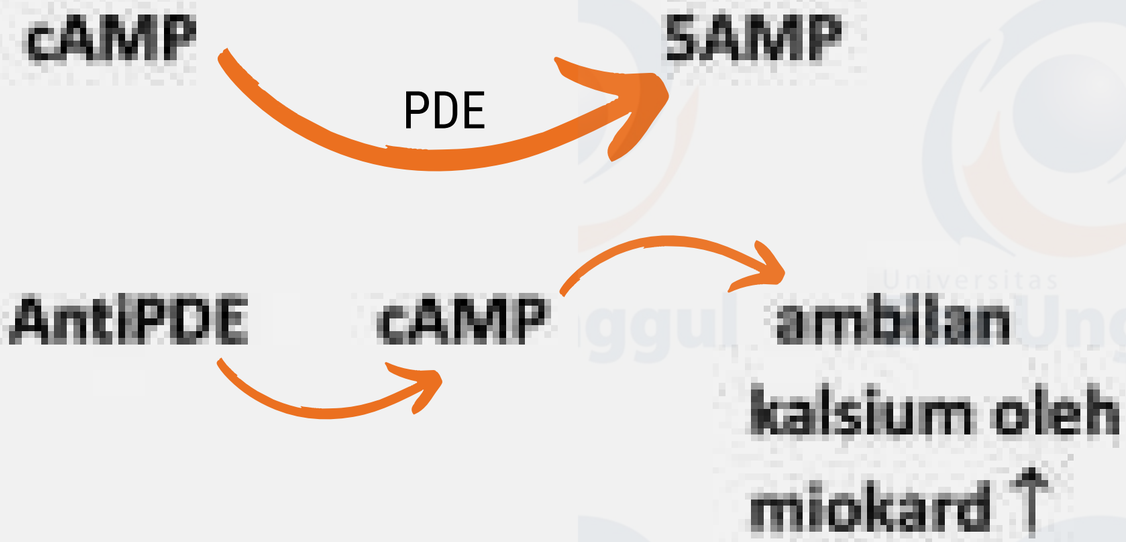


Figure 6-7 Receptor-specific effects of physiologic and pharmacologic catecholamines. For concepts regarding adrenergic receptor stimulation by dobutamine, see Ruffolo.[34] For norepinephrine, see Bristow.[35] (*Figure 6 LH Opie, 2005.*)

Inotropik

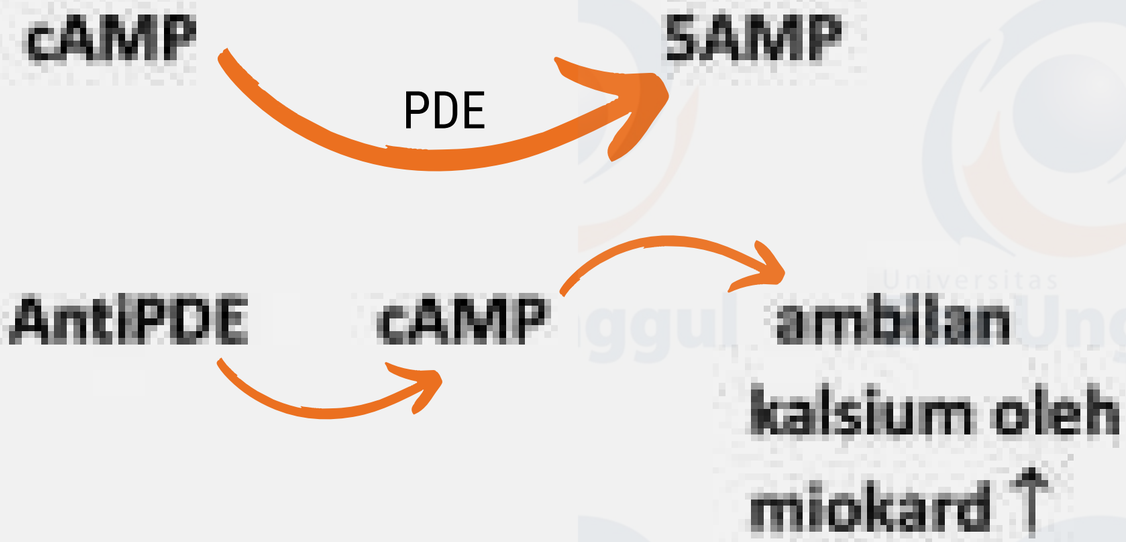
2. Antifosfodiesterase



Contoh : amrinon, milrinon

Inotropik

2. Antifosfodiesterase



Contoh : amrinon, milrinon

Beta blocker

Table 1 Possible beneficial actions of beta-blockers in CHF

Reduce sympathetic tone	Normalize high phosphorus energetic imbalance
Increase vagal tone	Reduce renin release
Improve force-frequency relationship	Reduce endothelin production and release
Improve myocardial work/oxygen consumption ratio	Increase norepinephrine re-uptake
Reduce subendocardial ischaemia	Upregulate beta-adrenergic receptors
Increase heart rate variability	Reduce inflammatory cytokines
Reduce QT-dispersion	Antagonize autoantibodies against $beta_1$-receptors
Reverse deterioration in heart rate variability	Antioxidant effect

Modified from Waagstein.[11]

Rise your hand!

any question?

PSF316

Farmakoterapi Sindrom Koroner Akut

Sesi Ke 4

Topik Sesuai RPS:
Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi Penyakit Sindrom Koroner Akut

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Topik Sebelum UTS

Sesi 1

Pendahuluan: jenis penyakit kardiovaskular dan pemeriksaan labolatorium

Sesi 2

Patofisiologi dan farmakoterapi **stroke**

Sesi 3

patofisiologi dan farmakoterapi gagal jantung

Sesi 4

patofisiologi dan farmakoterapi sindrom koroner akut

Sesi 5

patofisiologi dan farmakoterapi Aritmia

Sesi 6

patofisiologi dan farmakoterapi gagal ginjal akut

Sesi 7

patofisiologi dan farmakoterapi gagal ginjal kronis

Ujian Tengah Semester

Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

patofisiologi dan farmakoterapi epilepsi

Sesi 12

patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

patofisiologi dan farmakoterapi rheumatoid arthritis

Sesi 14

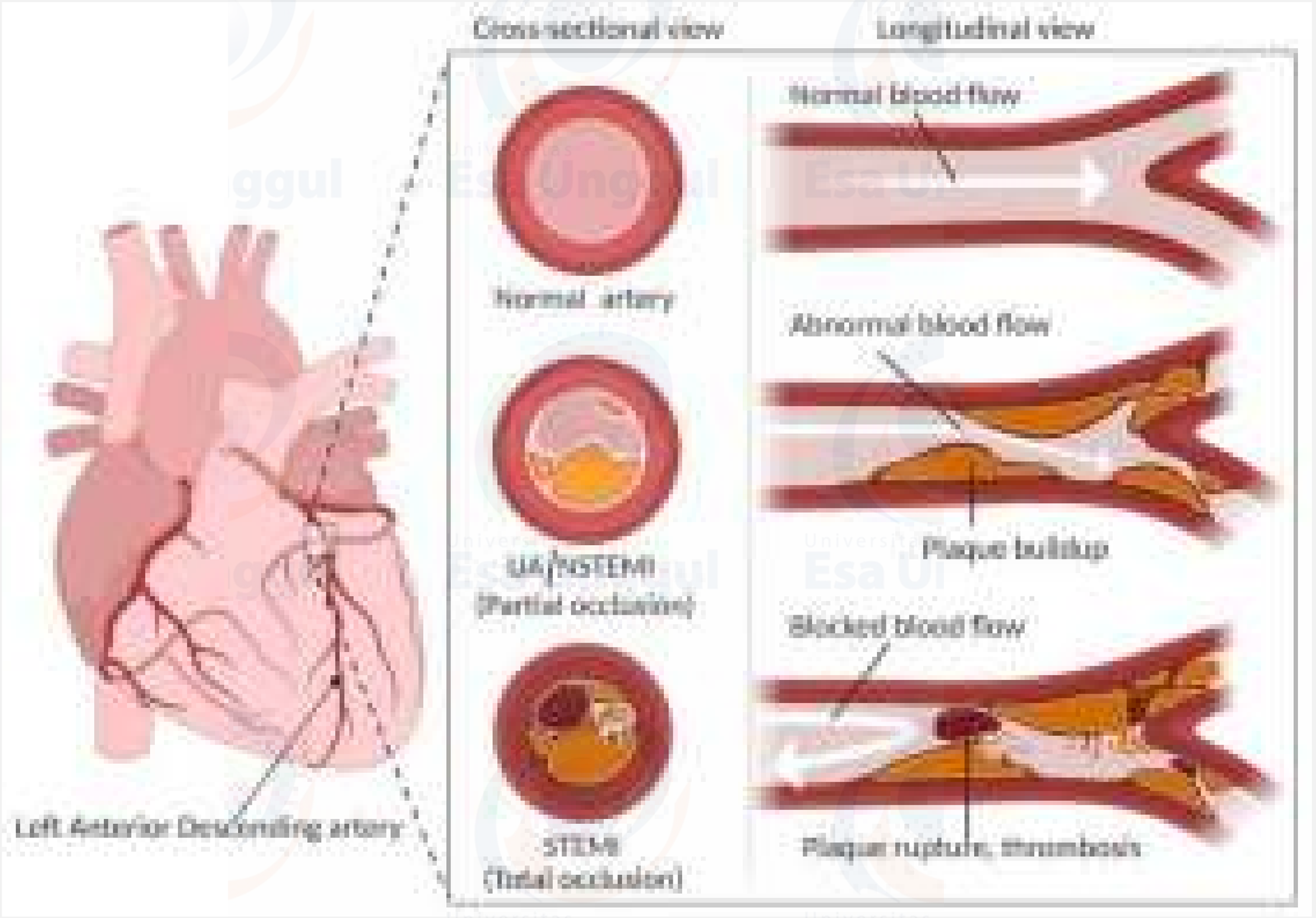
patofisiologi dan farmakoterapi SLE

Ujian Akhir Semester

Apa itu Sindrom Koroner Akut

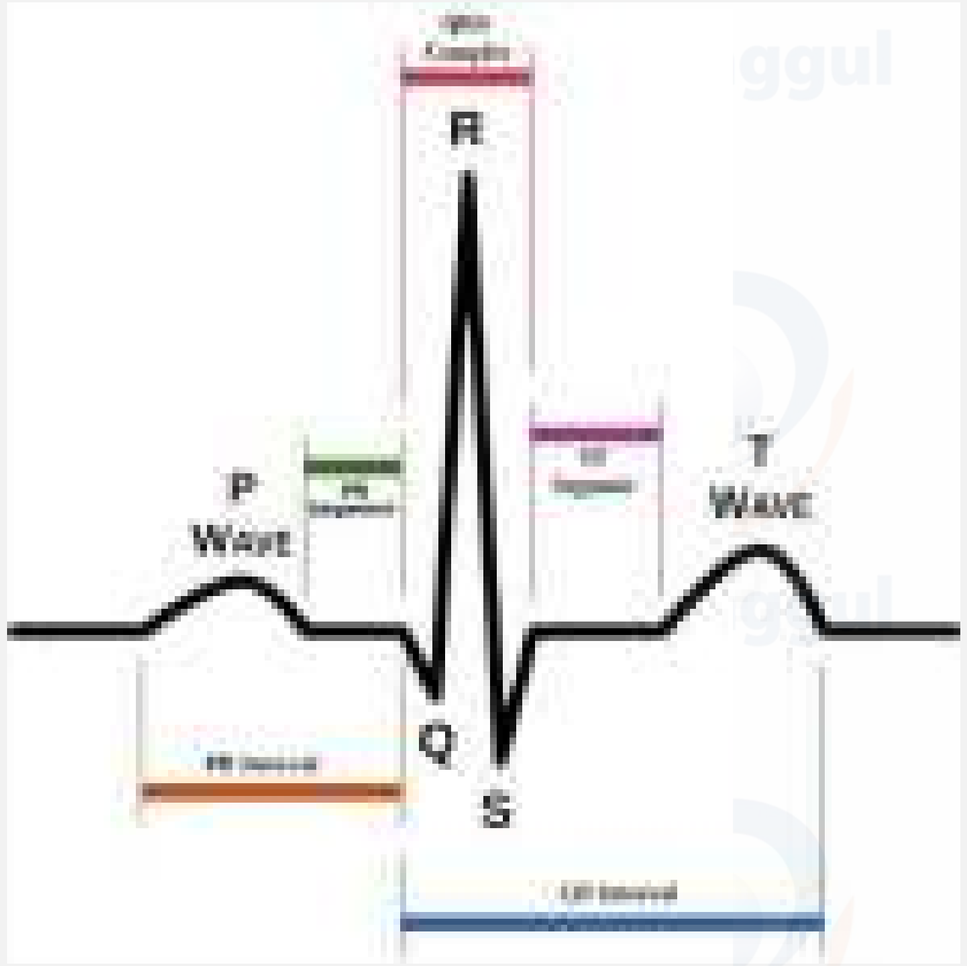
a range of conditions related to sudden, reduced blood flow to the heart.

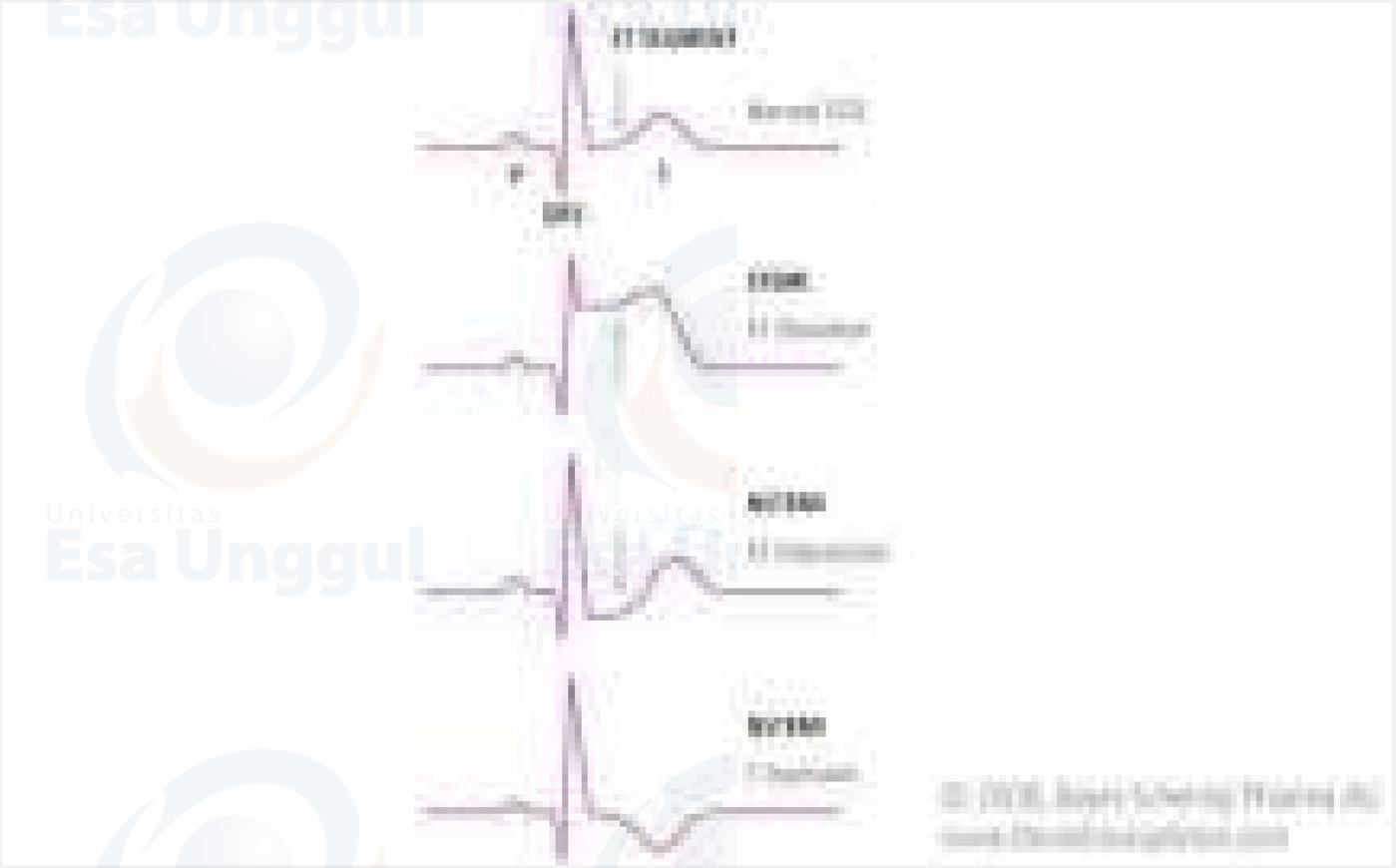
berkaitan dengan aterosklerosis


Cross-sectional view
Longitudinal view
Normal blood flow
Normal artery
Abnormal blood flow
UA/NSTEMI
(Partial occlusion)
Plaque buildup
Blocked blood flow
STEMI
(Total occlusion)
Plaque rupture, thrombosis
Left Anterior Descending artery

Gejala koroner akut?

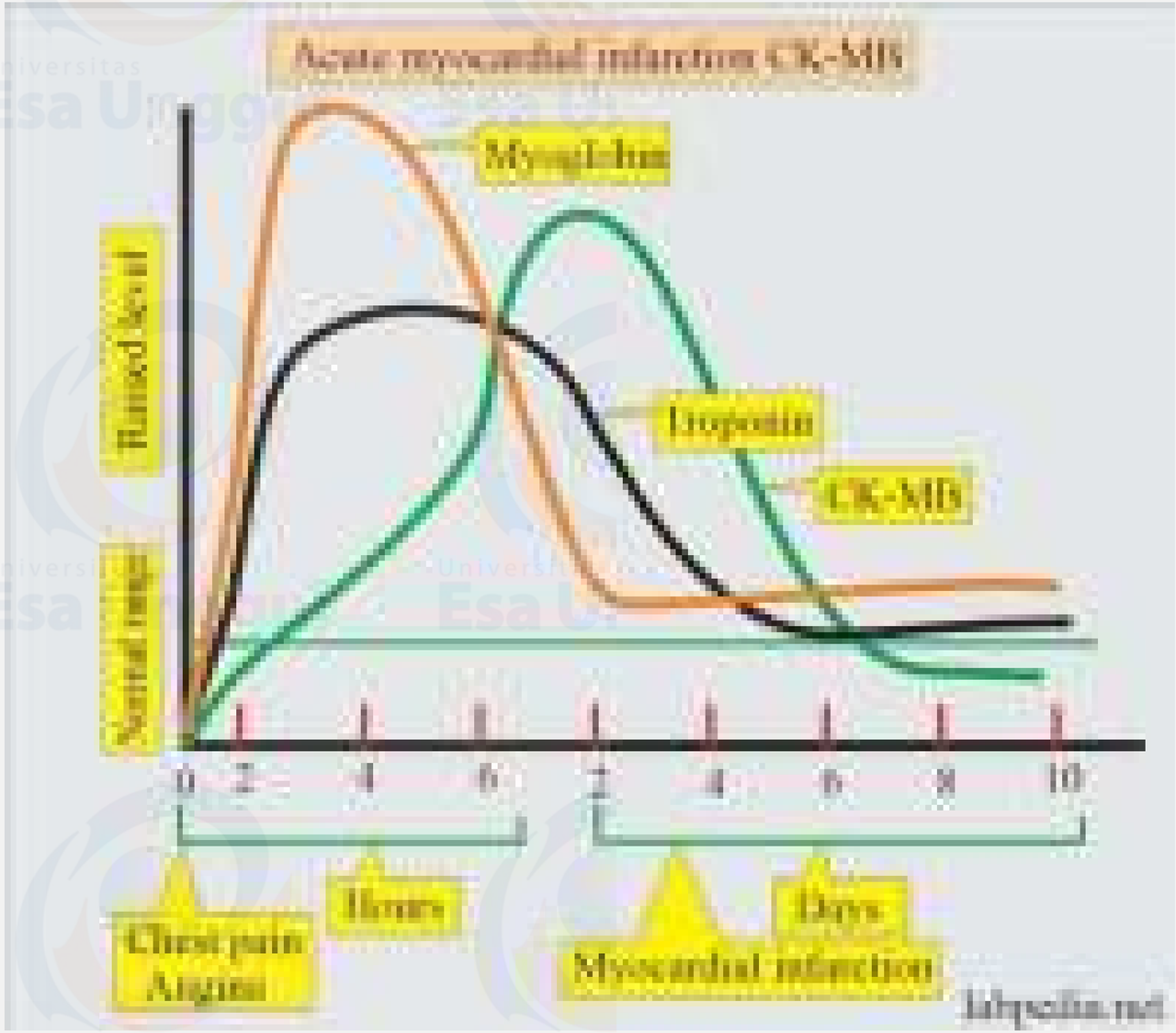
Pemeriksaan elektrokardiogram (EKG) dan pemeriksaan enzim jantung perlu dilakukan untuk membedakan jenis serangan sindroma koroner akut karena tata laksana lanjutan dan prognosisnya berbeda antara STEMI dan NSTEMI



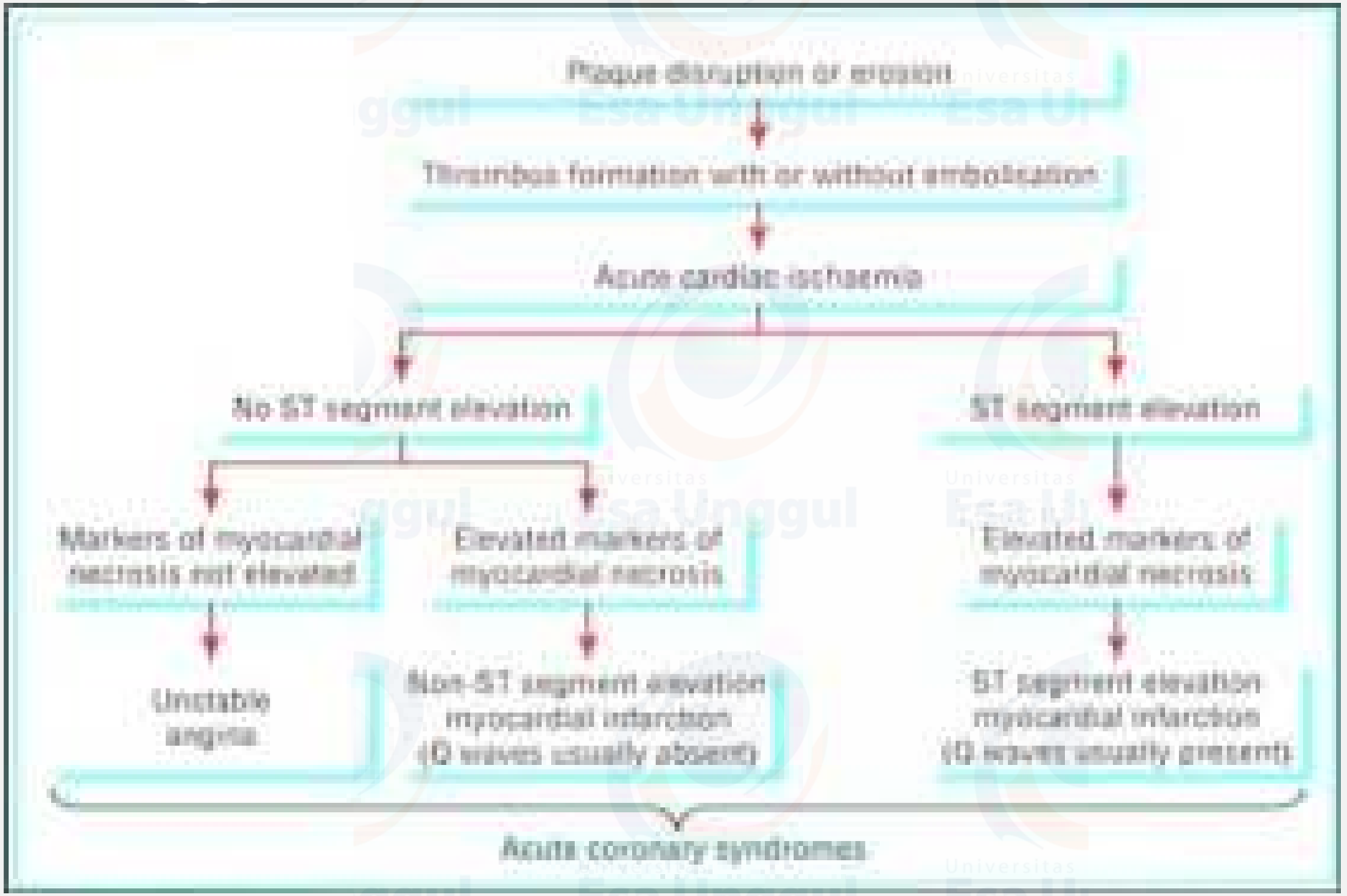


Pemeriksaan marka jantung

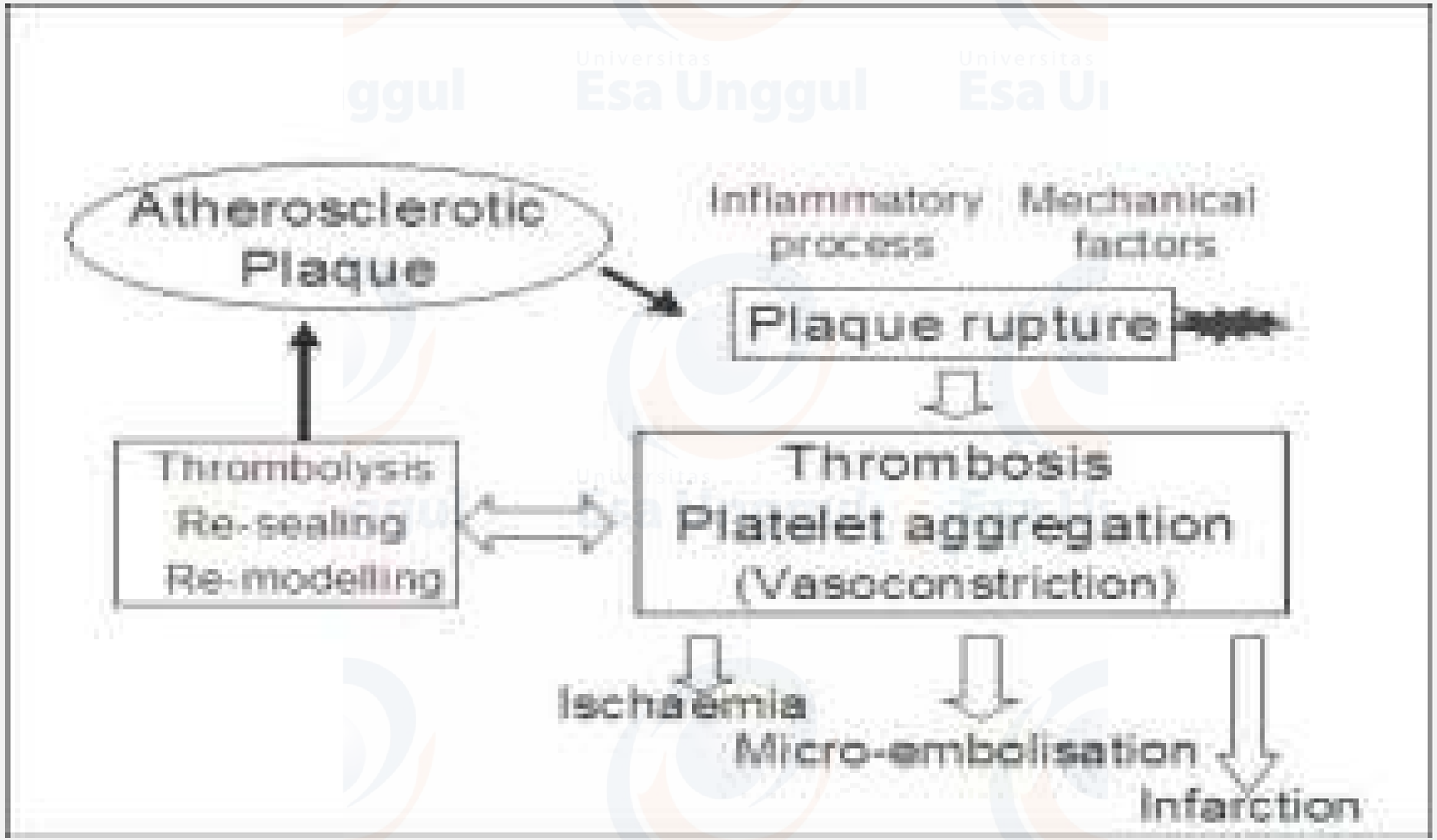
- **Kreatinin kinase-MB (CK-MB) atau troponin I/T** merupakan marka nekrosis miosit jantung dan menjadi marka untuk diagnosis infark miokard.
- **Troponin I/T** sebagai marka nekrosis jantung mempunyai sensitivitas dan spesifisitas lebih tinggi dari CK-MB.
- Peningkatan marka jantung hanya menunjukkan adanya nekrosis miosit, namun tidak dapat dipakai untuk menentukan penyebab nekrosis miosit tersebut (penyebab koroner/nonkoroner).



Patofisiologi



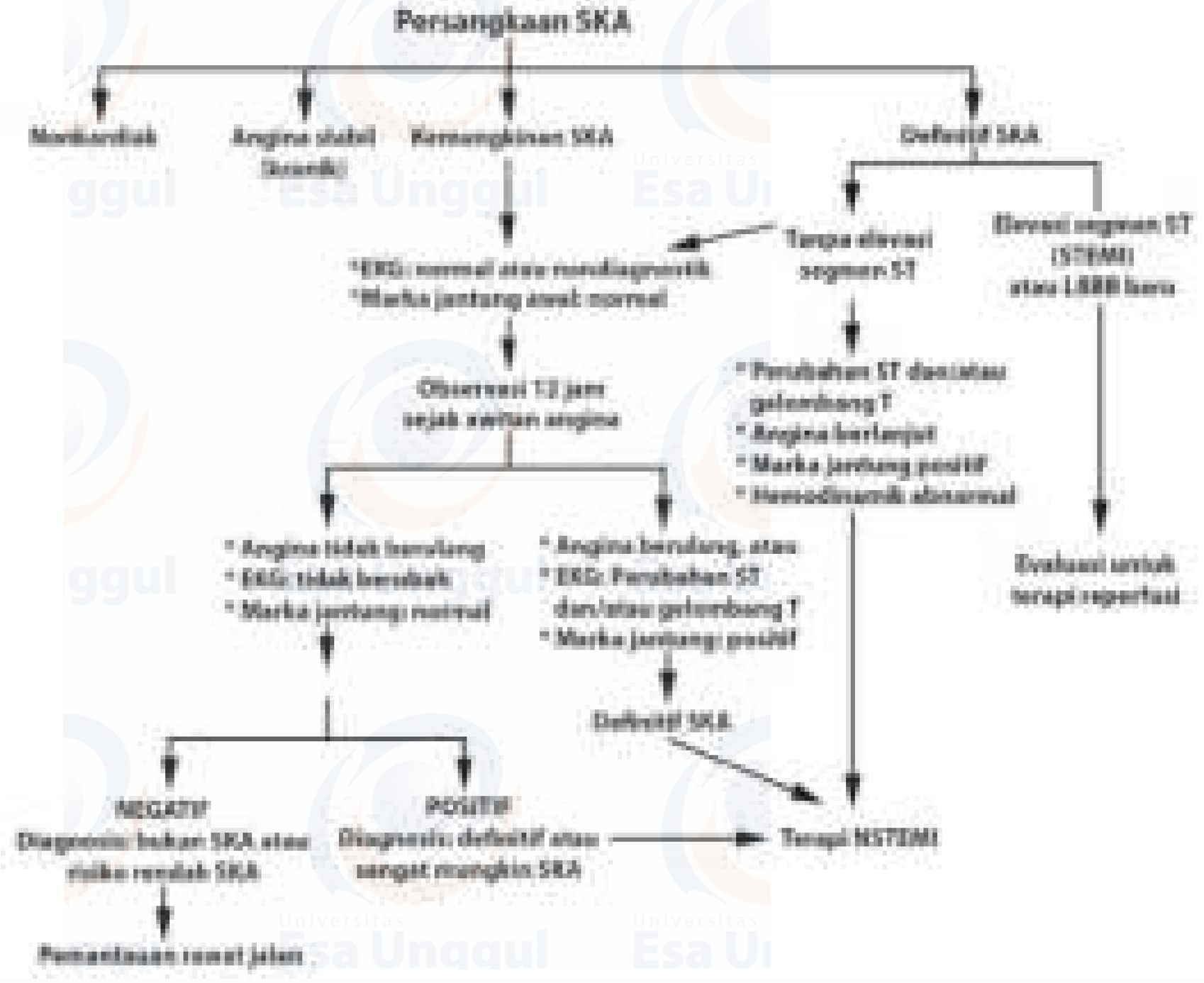
Patofisiologi



Resume perbedaan jenis SKA

EXTENT OF OCCLUSION	ECG	TROPONIN
Total occlusion	ST elevation New LBBB	RAISED
Incomplete occlusion	Other ischaemic changes / none	RAISED
Incomplete occlusion	Other ischaemic changes / none	NORMAL

Algoritma Terapi SKA



PRINSIP INISIAL TERAPI

PRINSIP INISIAL TERAPI

TERAPI	KETERANGAN
SUPLEMENTASI OKSIGEN	DIBERIKAN JIKA SATURASI O2 DIBAWAH 95% ATAU ADANYA DISTRESS RESPIRASI (SELAMA 6 JAM PERTAMA)
PEMBERIAN ASPIRIN DOSIS KECIL (160-320MG)	DIBERIKAN SEGERA TERHADAP SELURUH PASIEN (HARUS DIKETAHUI INTOLERANSI DAN ALERGI) TERHADAP ASPIRIN. DIBERIKAN SEBAIKNYA SUBLINGUAL
BLOCKER ADP: TICAGRELOR, CLOPIDOGREL	DOSIS TICAGRELOR 180MG, MAINT: 2 X 90 MG (KEC. PASIEN STEMI REPERFUSI DG FIBRINOLIITIK) DOSIS CLOPIDOGREL 300MG, MAINT: 75MG/HARI (REKOMENDASI DILANJUTKAN MESKI DENGAN FIBRINOLITIK)

PRINSIP INISIAL TERAPI

TERAPI	KETERANGAN
VASODILATOR: NTG/ ISDN	SPRAY/ TAB SUBLINGUAL UNTUK PASIEN NYERI DADA SAAT DI IGD, DAPAT DIULANG SETIAP 5 MENIT, MAKSIMAL 3 X, IV DAPAT DIBERIKAN JIKA NONRESPONSIF 3 DOSIS, ISDN DAPAT DIGUNAKAN SEBAGAI PENGGANTI
ANALGESIK KUAT: MORFIN SULFAT	1-5MG IV MORFIN DAPAT DIULANG SETIAP 10-30 MENIT JIKA TIDAK RESPONSIF NTG 3 DOSIS/ ISDN

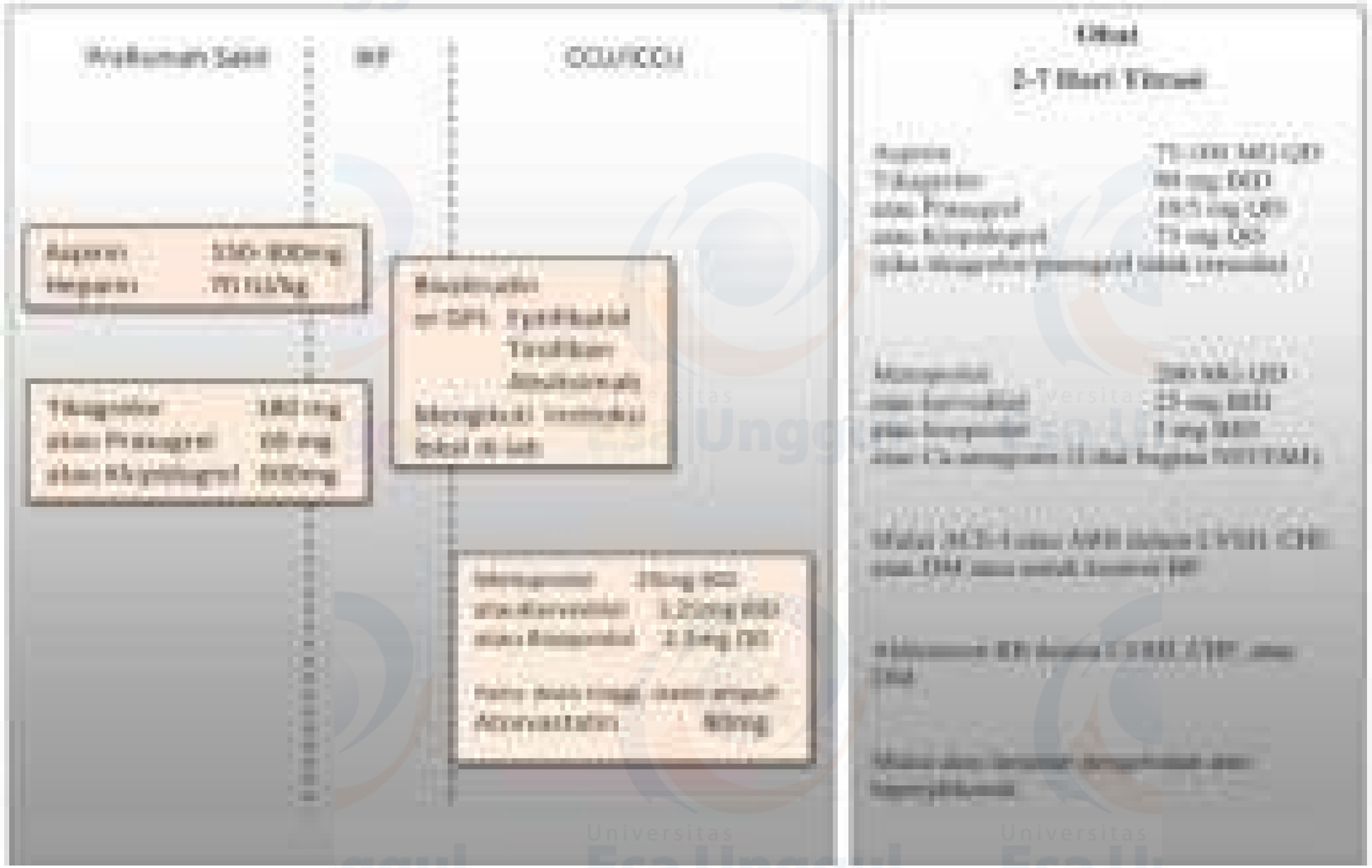
Pengobatan STEMI

If PCI is unable to be performed within 120 minutes then fibrinolytic agents should be considered (e.g. alteplase) while arranging transfer to a PCI centre.

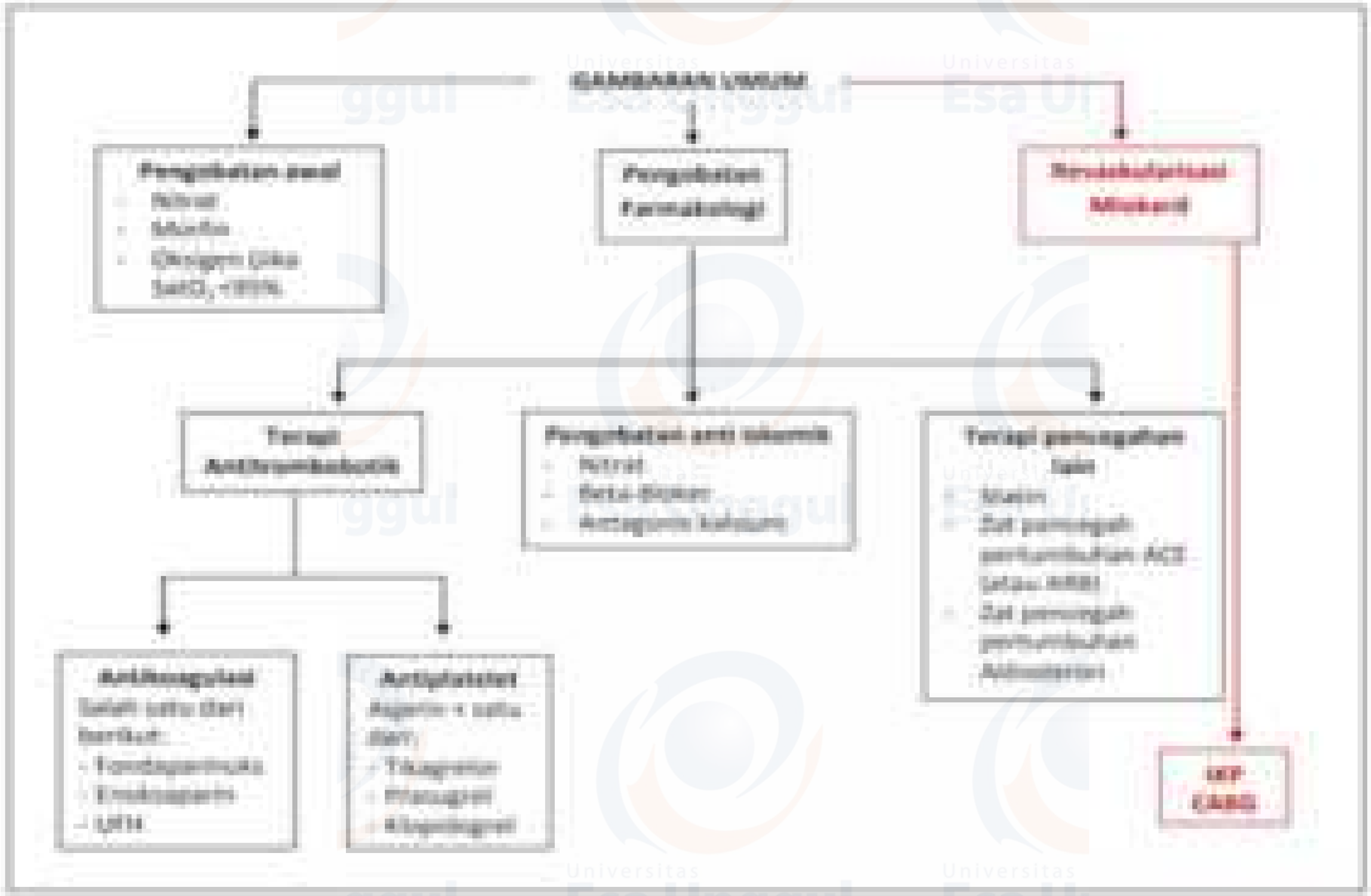
Anti platelet: aspirin and a second anti-platelet drug prior to PCI. This is usually ticagrelor 180 mg loading, following by 90 mg BD as a regular dose. Other options include clopidogrel (600 mg loading), particularly if there is a high bleeding risk, or Prasugrel (60 mg loading). The combination of aspirin and a second anti-platelet agent is referred to as dual anti-platelet therapy (DAPT) and this should be continued for 12 months post-PCI.

Antithrombotic therapy: using unfractionated heparin or low molecular weight heparin (LWMH). This is usually given at the time of PCI. Additional agents including glycoprotein IIb/IIIa inhibitors (e.g. tirofiban) may be given at the time of PCI in the presence of a high thrombus burden.

Pengobatan STEMI-tatalaksana indonesia



Pengobatan NSTEMI & UA



Pengobatan NSTEMI & UA

Treatment summary

The management of patients with NSTEMI or UA can be remembered using the mnemonic BATMAN

- **B** - Beta-blockers (unless contraindicated)
- **A** - Aspirin (300 mg loading, then 75 mg once daily)
- **T** - Ticagrelor (180 mg loading, then 90 mg twice daily); alternatively clopidogrel if high bleeding risk
- **M** - Morphine (titrate for analgesia)
- **A** - Anticoagulant agent (Fondaparinux 2.5 mg subcutaneous unless contraindicated)
- **N** - Nitrates (sublingual nitrates to relief pain - consider infusion if ongoing pain)

Obat-obatan pada SKA

Medication and Class	Route	STEMI (With Primary PCI)	STEMI (With Fibrinolytic Therapy)	NSTE ACS	Notable Adverse Effects*
Antiplatelet Therapy					
Aspirin (COX-1 inhibitor)	Oral	✓	✓	✓	—
Clopidogrel ($P2Y_{12}$ receptor antagonist)	Oral	✓	✓	✓	TTP; avoid concomitant omeprazole or esomeprazole
Prasugrel ($P2Y_{12}$ receptor antagonist)	Oral	✓	No specific recommendation	No specific recommendation	TTP; hypersensitivity
Ticagrelor ($P2Y_{12}$ receptor antagonist)	Oral	✓	No specific recommendation	✓	Dyspnea
Cangrelor† ($P2Y_{12}$ receptor antagonist)	IV	✓	No specific recommendation	✓	Hypersensitivity, decreased renal function, dyspnea
Abciximab (GP IIb/IIIa receptor antagonist)	IV	✓	No specific recommendation	✓	Allergic reactions, thrombocytopenia
Tirofiban (GP IIb/IIIa receptor antagonist)	IV	✓	No specific recommendation	✓	Thrombocytopenia
Eptifibatide (GP IIb/IIIa receptor antagonist)	IV	✓	No specific recommendation	✓	Thrombocytopenia, hypotension

Obat-obatan pada SKA

Anticoagulant Therapy					
Unfractionated heparin (anticoagulant)	IV	✓	✓	✓	Thrombocytopenia, HIT/HITTS, injection-site irritation, hypersensitivity, aminotransferase elevation, benzyl alcohol toxicity
Bivalirudin (direct thrombin inhibitor)	IV	✓	May use if patient develops HIT and requires continued anticoagulation	✓	Headache, thrombocytopenia, fever, acute stent thrombosis, coronary artery brachytherapy, INR interference
Enoxaparin (LMWH)	IV/SC	No specific recommendation	✓	✓	HIT with or without thrombosis, anemia, thrombocytopenia, aminotransferase elevation, diarrhea, nausea, ecchymosis, fever, edema, peripheral edema, dyspnea, confusion, injection-site pain
Fondaparinux (factor Xa inhibitor)	IV/SC	Not recommended as sole anticoagulant	✓	✓	Spinal or epidural hematomas, thrombocytopenia

Obat-obatan tambahan pada SKA

Additional Routine Medical Therapies Used in ACS

Therapy	Usage Recommendations	Avoid With	Caution With
Oxygen	Oxygen saturation <90%	—	COPD; CO_2 retention
Morphine	Ongoing chest pain (SL); persistent ischemia (IVTA); HF (IV)	Hypotension; recent PDE inhibitor use	RV infarction
IV morphine	STEMI; pain; NSTE-ACS; persistent chest pain despite anti-ischemic therapy	Cardiogenic hypotension; bradycardia	—
Beta-blocker	Within first 24 h in absence of HF, low-output state, risk of cardiogenic shock, other contraindications	RAD; signs of HF, low-output state, other contraindications to beta blockade	Increased risk of cardiogenic shock, RV infr
Non-DHP calcium channel blocker (e.g., verapamil or diltiazem)	For ischemic symptoms when beta-blockers are unsuccessful, are contraindicated, or cause unacceptable adverse effects	LV dysfunction, increased risk of cardiogenic shock, PR interval >0.24 s, or 2nd- or 3rd-degree AV block without pacemaker; the DHP nifedipine IR (use only in NSTE-ACS with beta-blocker)	—
ACE inhibitor (ARB, if intolerant)	Within first 24 h if LVEF <0.40, HF, STEMI, with anterior infarction, absence of contraindications	Hypotension, shock, bilateral renal artery stenosis, renal failure	—
High-intensity statin	All patients	—	CYP3A4 interactions/rhabdomyolysis, fibrates, myopathy (gemfibrozil), hepatic toxicity

Obat-obatan preventive pada SKA

Pharmacological agents

Following an ACS, several medications should be initiated to help in the secondary prevention of major cardiovascular events and to help prevent abnormal remodelling of the heart:

- **Dual anti-platelet therapy** (e.g. aspirin and clopidogrel) should be continued for one year, unless it is at risk of bleeding to prevent in-stent thrombosis.
- **Beta-blockers** (e.g. bisoprolol)
- **High dose statin** (e.g. atorvastatin 80 mg)
- **ACE inhibitor** (e.g. ramipril). Angiotensin receptor blocker can be an alternative if side-effects or intolerance to ACE inhibitor.
- **Consider mineralocorticoid antagonist** reserved for patients with LV dysfunction (i.e. heart failure) following MI.

Common Medications for Secondary Prevention of ACS

Medication or Class	Indicated Patients	Typical Treatment Length
Aspirin	All	Indefinitely
ACE inhibitor (ARB if intolerant)	All	Indefinitely
High-intensity statin	All	Indefinitely
Beta blocker	LVEF <40 with HF/prior MI symptoms Normal LV function: all	Indefinitely >3 y
$P2Y_{12}$ inhibitor	STEMI and NSTE-ACS receiving medical management	Minimum of 1 y

Rise your hand!

any question?

PSF316

Farmakoterapi Aritmia

Sesi Ke 5

Topik Sesuai RPS:
Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi Penyakit Aritmia

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Topik Sebelum UTS

Sesi 1

Pendahuluan: jenis penyakit kardiovaskular dan pemeriksaan labolatorium

Sesi 2

Patofisiologi dan farmakoterapi **stroke**

Sesi 3

patofisiologi dan farmakoterapi gagal jantung

Sesi 4

patofisiologi dan farmakoterapi sindrom koroner akut

Sesi 5

patofisiologi dan farmakoterapi Aritmia

Sesi 6

patofisiologi dan farmakoterapi gagal ginjal akut

Sesi 7

patofisiologi dan farmakoterapi gagal ginjal kronis

Ujian Tengah Semester

Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

patofisiologi dan farmakoterapi epilepsi

Sesi 12

patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

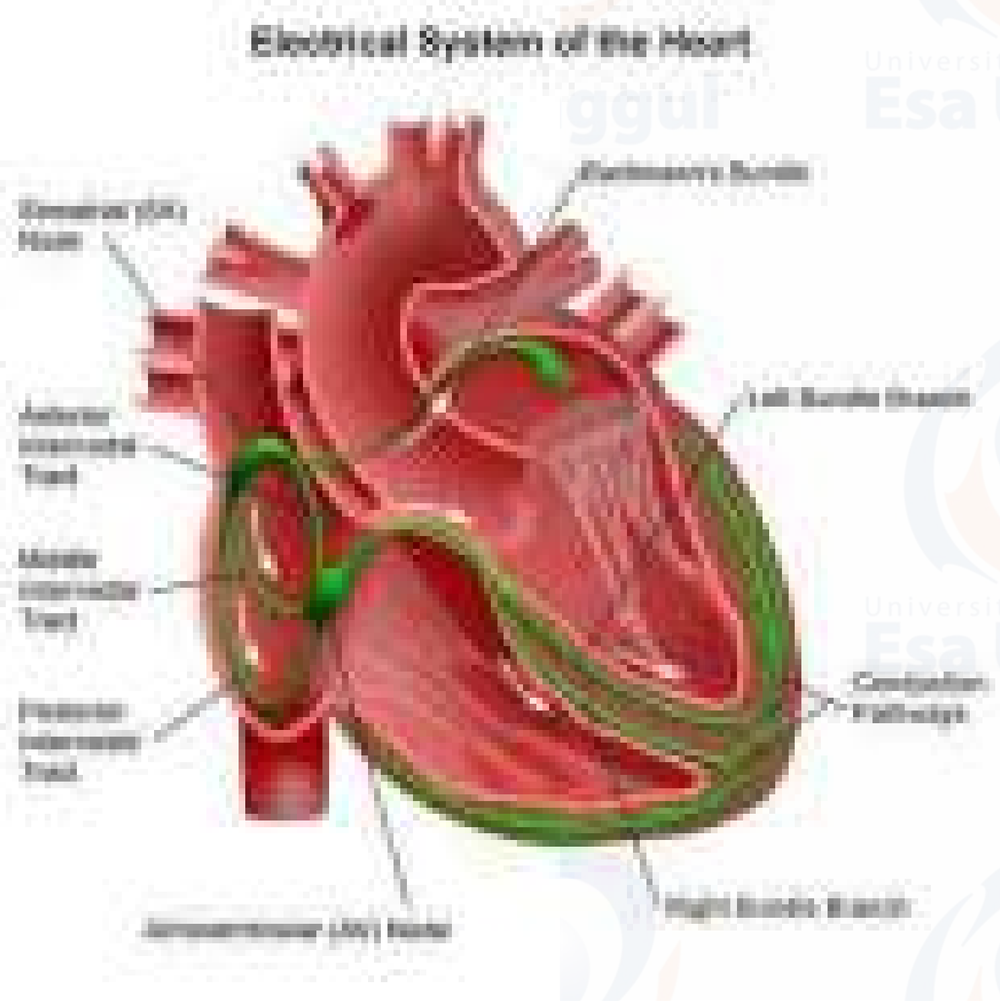
patofisiologi dan farmakoterapi rheumatoid arthritis

Sesi 14

patofisiologi dan farmakoterapi SLE

Ujian Akhir Semester

what is arrythmias

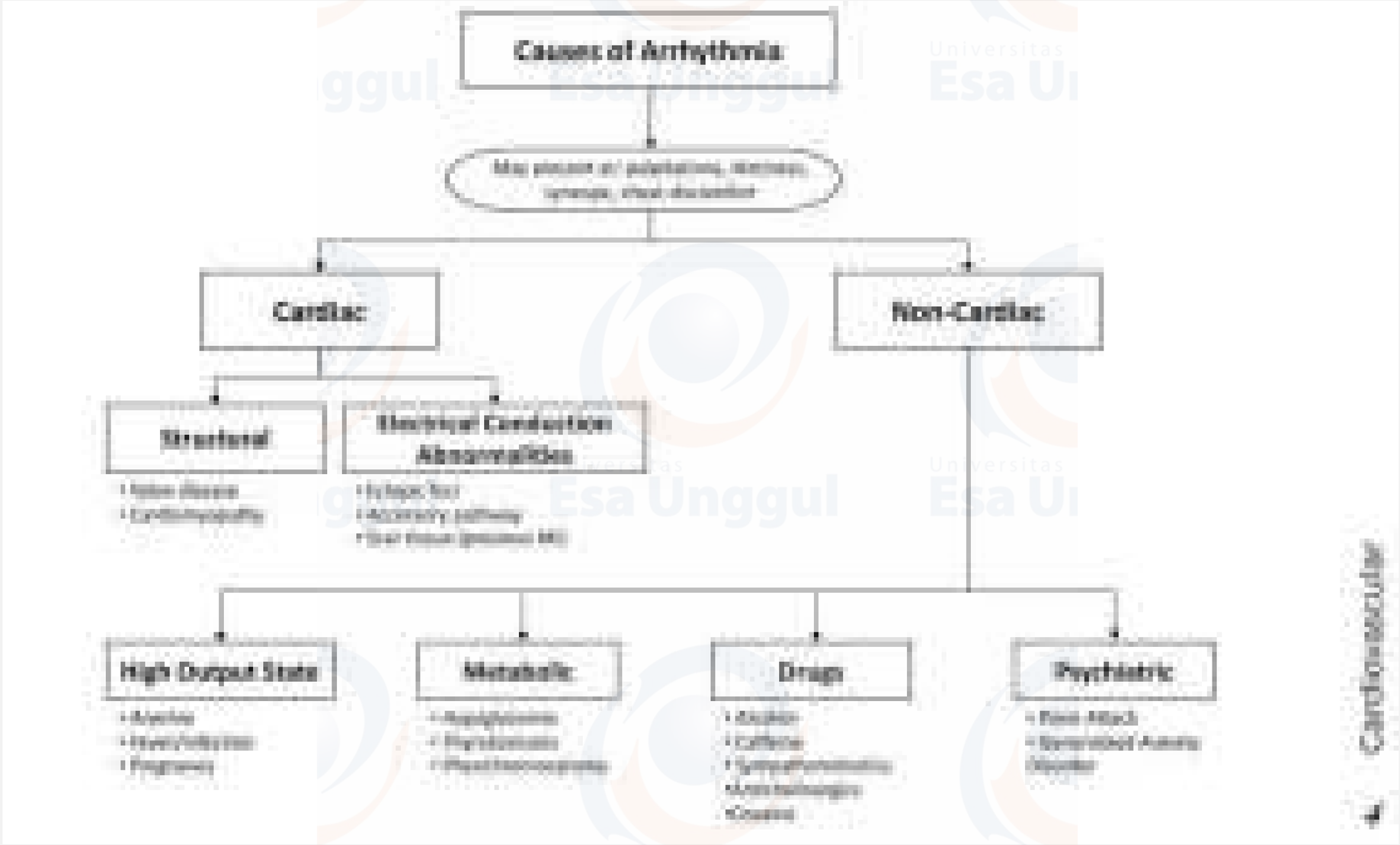


1. Pacemaker (nodus SA) menghasilkan irama yang abnormal
2. Adanya gangguan pada jalur konduksi normal
3. Bagian jantung selain nodus SA mengambil alih sebagai pacemaker

Perubahan/ gangguan irama jantung:
perubahan mekanisme penjalaran impuls listrik jantung

Sign and Symptomps

Etiology


Causes of Arrhythmia
Cardiac
Non-Cardiac
Structural
Electrical Conduction Abnormalities
High Output State
Metabolic
Drugs
Psychiatric
Cardiovascular

Types of Arrythmias

>100x/menit
<60x/menit

Arrhythmia is broadly categorized into bradyarrhythmias and tachyarrhythmia based on the heart rate. They are further divided according to the origin, means of transmission, and syndromes associated with it.

	origin of the arrythmias	definition	class
Tachiarrhtmia	Supraventricular takikardia (SVT)	originating from above AV node (atrial origin)	Atrial Fibrillation Atrial Flutter Atrial Tachycardia Atrial Premature Complex AV nodal reentrant tachycardia AV reentrat tachycardia AV junctional extrasystole
	Ventricular Tachycardia (VT)	below the AV node (ventricular origin)	Ventricular Fibrillation Ventricular Premature Beats Ventricular Tachycardia
Bradikardia	sinus bradycardia	increased vagal tone delay atrial impulse	
	Atrioventricular block		first degree AV block Second degree AV block Third degree/ complete AV block
	Sinus node dysfunction	SA node impulse generation at slower rate	

Ventrikel Takikardi

- Merupakan salah satu aritmia lethal (berbahaya) karena mudah berkembang menjadi ventrikel fibrilasi dan dapat menyebabkan henti jantung **(cardiac arrest).**
- Ventrikel takikardi disebabkan oleh keadaan yang mengganggu sistem konduksi jantung, seperti: **kurangnya asupan oksigen, kardiomiopati, HF, toksisitas digitalis.**

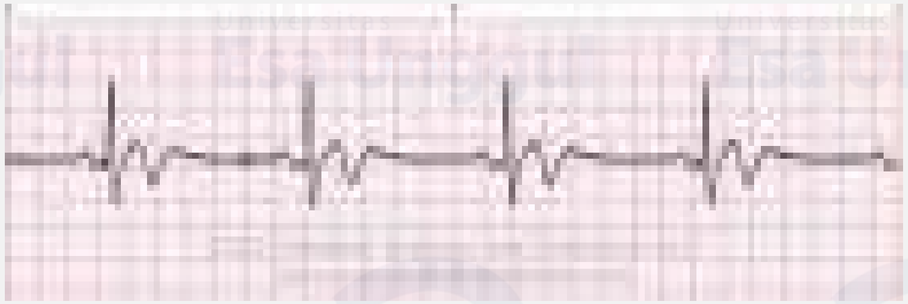
Ventrikel Fibrillation

- Jantung tidak lagi berdenyut melainkan hanya bergetar sehingga jantung tidak dapat memompa darah dengan efektif -final manifestasi Klinis: **cardiac arrest**
- Ventrikel takikardi disebabkan oleh keadaan yang mengganggu sistem konduksi jantung, seperti: **kurangnya asupan oksigen, kardiomiopati, HF, toksisitas digitalis.**

Ventrikular extrasystole - AV extrasystole

- Gangguan irama jantung dimana denyut jantung premature berasal dari 1 atau lebih fokus di ventrikel
- Jenis aritmia paling tinggi kasusnya, manifestasi Klinis: **iskemik miokardium, infark miokardium, HF**

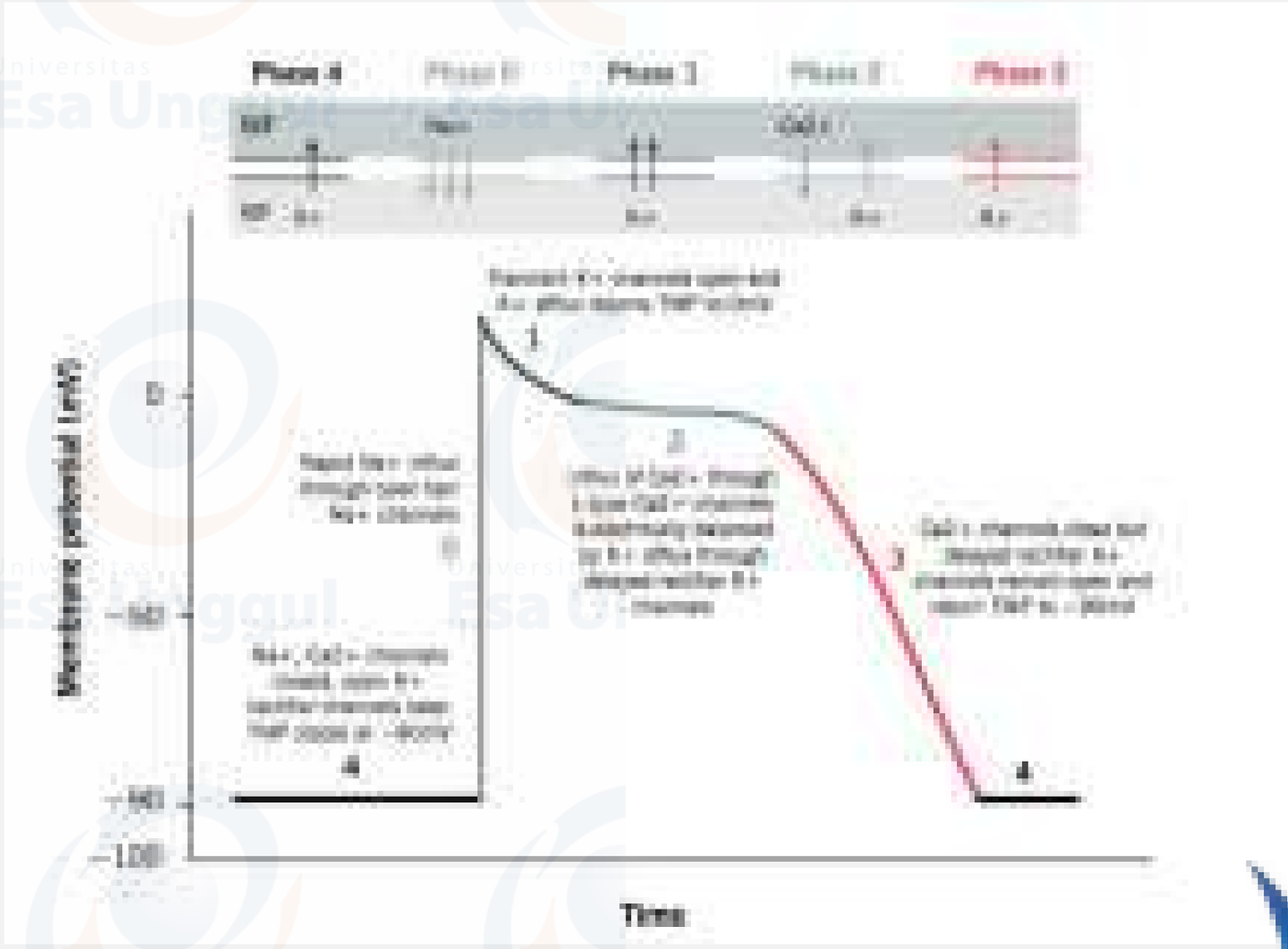
Bradikardia



- Adanya gangguan nodus SA, gangguan konduksi jantung, gangguan metabolik (hipotiroidisme)
- kerusakan jantung akibat HF atau CVD lainnya
- efek samping antihipertensi (beta bloker dsb)

Elektrofisiologi Jantung

- Fase 0 : depolarisasi cepat
- Fase 1 : repolarisasi awal cepat
- Fase 2 : repolarisasi lambat (plateau)
- Fase 3 : repolarisasi diastolik
- Fase 4 : depolarisasi lambat spontan



Resting potential (Em) : -80 sampai - 90 mv
Threshold potential (Et) = - 60 mv

Elektrofisiologi Jantung

- **Absolute Refractory Periode (ARP)**

Otot jantung tidak dapat dirangsang lagi untuk potensial aksi karena dalam kondisi kanal ion sudah terbuka.

- **Effective Refractory Periode (ERP)**

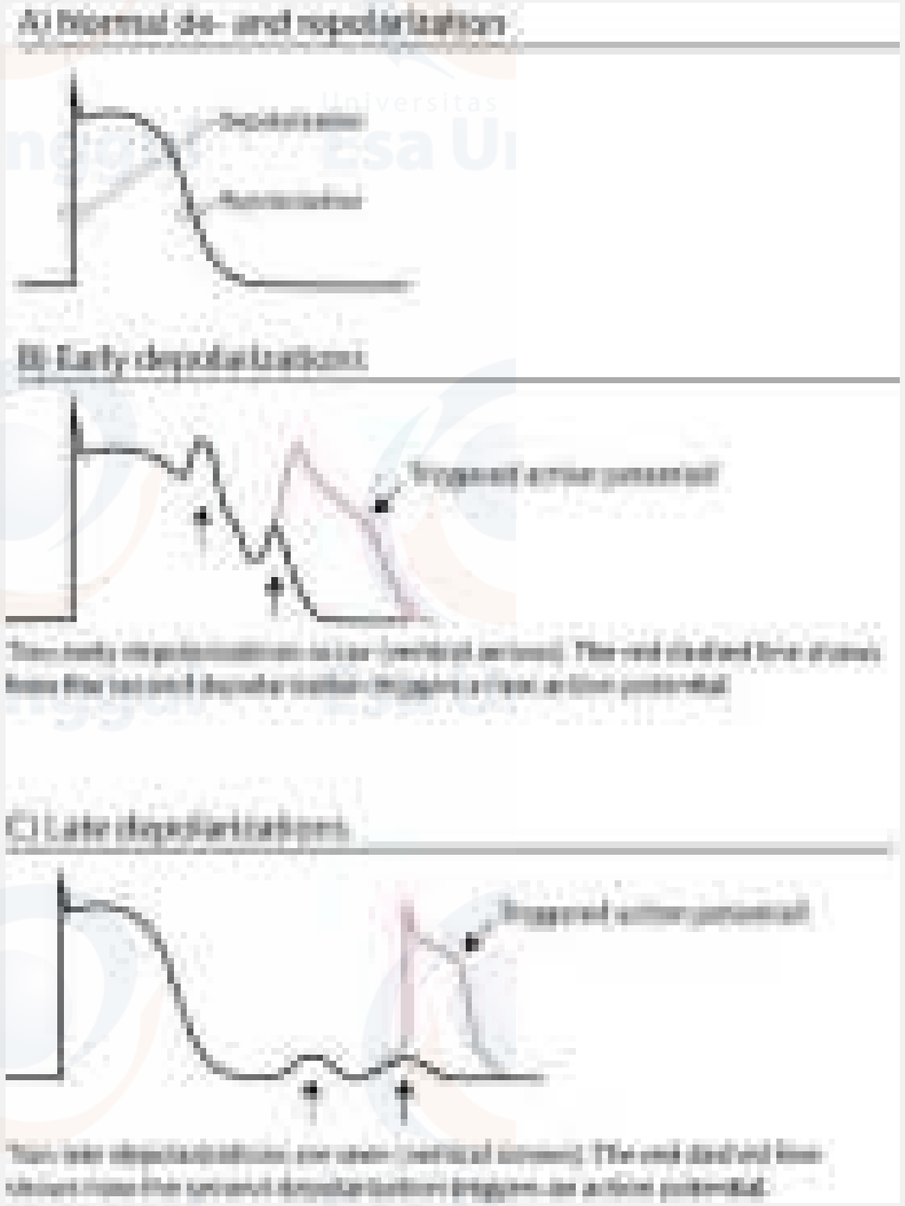
Sedang terjadi potensial aksi yang kecil/ lemah dan tidak dapat di propagasi. Saat ARP + fase 2 berubah menjadi

- **Relative Refractory Periode (RRP)**

Ketika fase 3 lemah dan membutuhkan stimulus yang lebih besar.

Arrythmias Mechanism

- Depolarisasi spontan (fase 4) dipercepat
- Resting potential dan treshold potential menurun (konduksi menurun):
  - Impuls baru terjadi sebelum repolarisasi sempurna dari impuls sebelumnya
  - Impuls terjadi saat depolarisasi spontan (fase 4)
  - Penurunan kecepatan potensial aksi (karena jaringan mengalami kerusakan) -- konduksi lambat
- Perubahan kecepatan repolarisasi

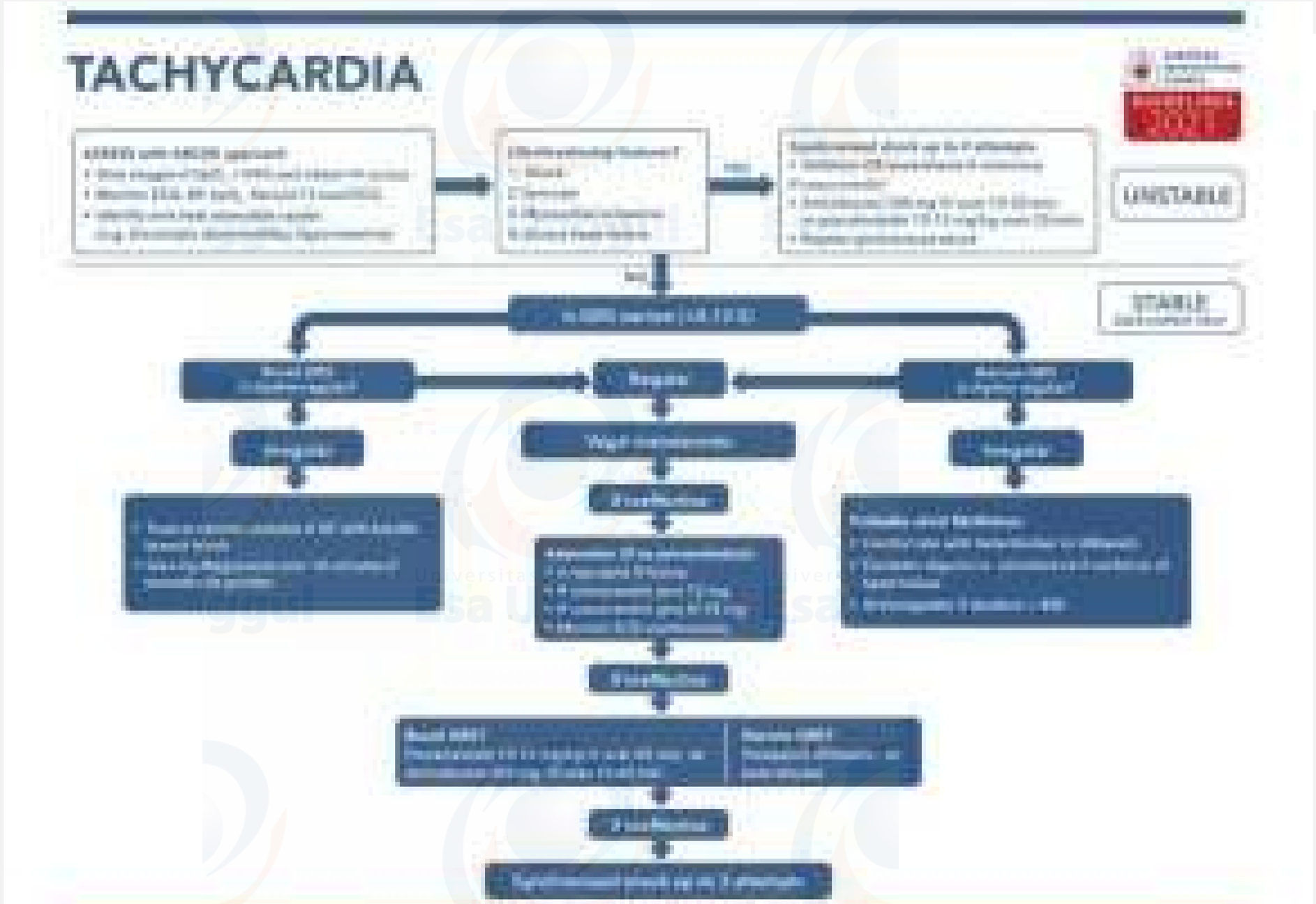


Golongan Obat anti-Aritmia

Kelas	Karakteristik	Contoh
I: Penghambat kanal Natrium	Menghambat kanal ion natrium cepat, menurunkan konduksi ventrikel dapat menghambat aktivitas ektopik ventrikel untuk mencegah VF. IA: mengurangi kecepatan depolarisasi, memperpanjang durasi potensial aksi. Memperlambat konduksi jantung, memperpanjang periode refrakter. IB: mengurangi laju depolarisasi secara lemah pada sel yang normal. Memperpendek durasi aksi potensial bisa sedikit memperpendek periode refrakter. IC: secara signifikan mengurangi laju depolarisasi, mengurangi konduksi jantung secara signifikan, meningkatkan sedikit periode refrakter.	IA: quinidine, procainamide, disopyramide IB: lignocaine, mexiletine IC: flecainide, propafenone
II: Agen simpatolitik	Antagonis β-adrenoseptor, menekan AV node	Bisoprolol
III: Penghambat repolarisasi	Menghambat kanal kalium, mengurangi laju efluks kalium. Mencegah aritmia reentran baik atrium maupun ventrikel, lebih baik dalam mempertahankan ritme sinus setelah kardioversi dari AF.	Sotalol (memiliki sifat β-blocker), amiodaron, [illegible]
IV: Antagonis kalsium	Menghambat respon ventrikel pada AF dan mencegah aritmia reentran AV. Adenosin juga mencegah aritmia akibat early after depolarizations...	Diltiazem, verapamil

Golongan Obat anti-Aritmia

- Menekan automatisitas di luar nodus SA
- Memperpanjang masa refrakter sehingga jaringan tidak bisa dirangsang

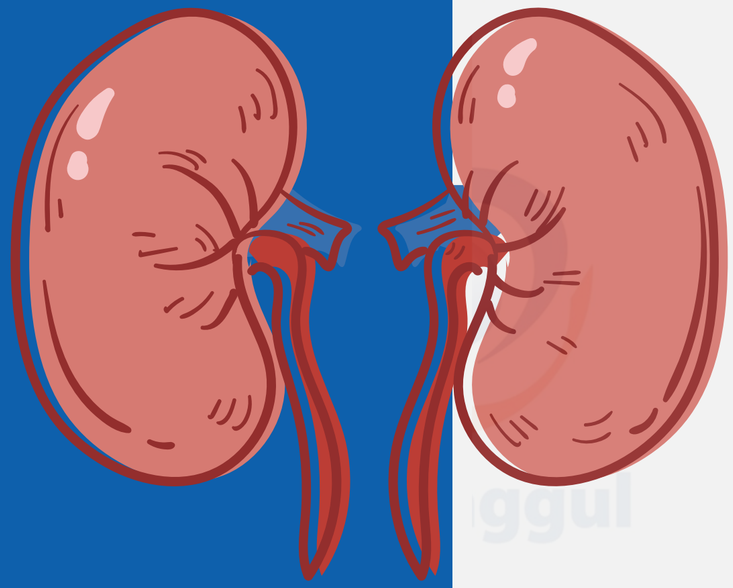


Tachycardia algorithm. ABCDE: airway, breathing, circulation, disability, exposure; BP: blood pressure; DC: direct current; ECG: electrocardiogram; IV: intravenous; SpO_2: arterial oxygen saturation; VT: ventricular tachycardia


BRADYCARDIA

Rise your hand!

any question?



PSF316

Farmakoterapi Gagal Ginjal Akut dan Kronis

Sesi Ke 6 dan 7

Topik Sesuai RPS:
Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi Gagal Ginjal Akut dan Kronis

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Topik Sebelum UTS

Sesi 1

Pendahuluan: jenis penyakit kardiovaskular dan pemeriksaan labolatorium

Sesi 2

Patofisiologi dan farmakoterapi **stroke**

Sesi 3

patofisiologi dan farmakoterapi gagal jantung

Sesi 4

patofisiologi dan farmakoterapi sindrom koroner akut

Sesi 5

patofisiologi dan farmakoterapi Aritmia

Sesi 6

patofisiologi dan farmakoterapi gagal ginjal akut

Sesi 7

patofisiologi dan farmakoterapi gagal ginjal kronis

Ujian Tengah Semester

Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

patofisiologi dan farmakoterapi epilepsi

Sesi 12

patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

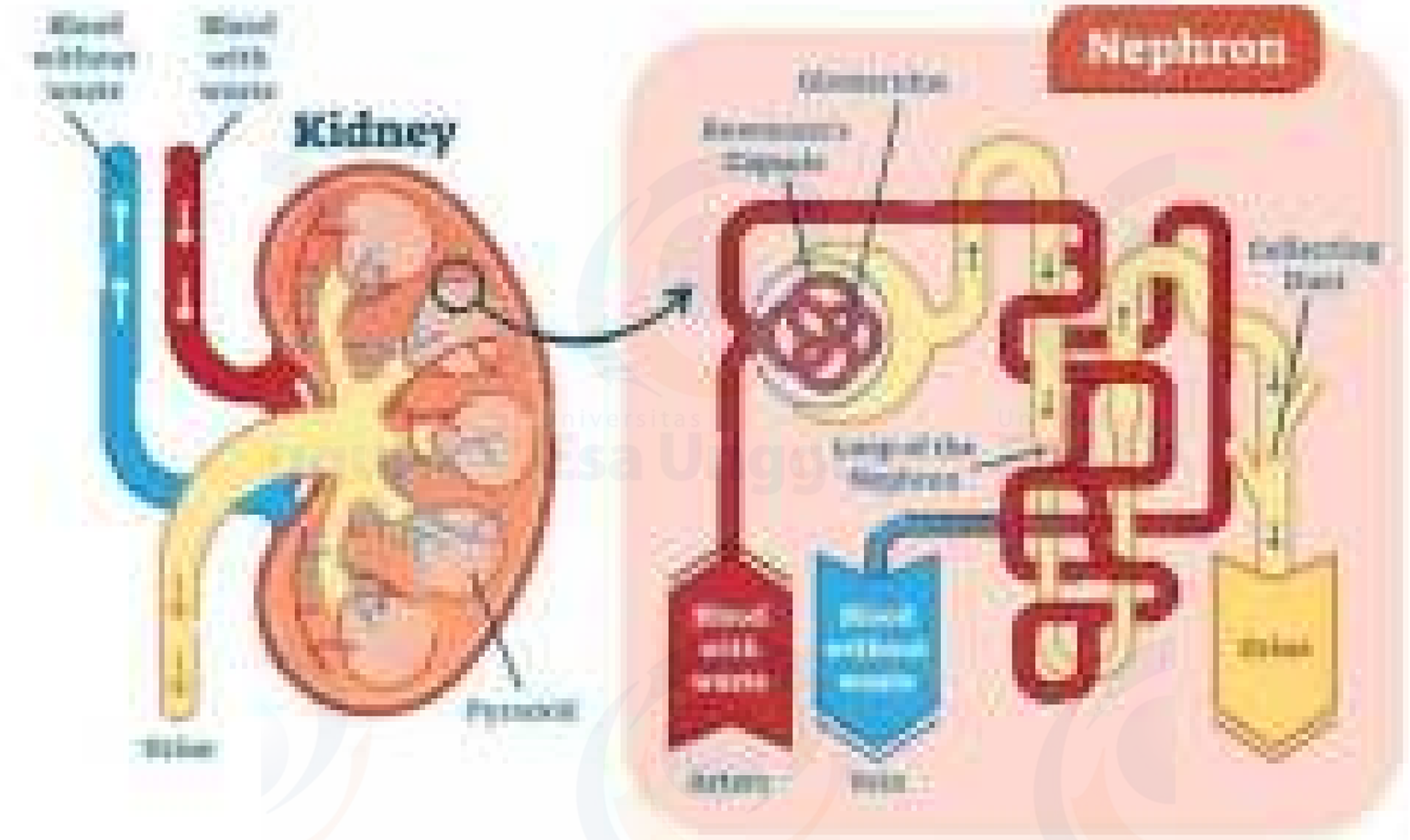
patofisiologi dan farmakoterapi rheumatoid arthritis

Sesi 14

patofisiologi dan farmakoterapi SLE

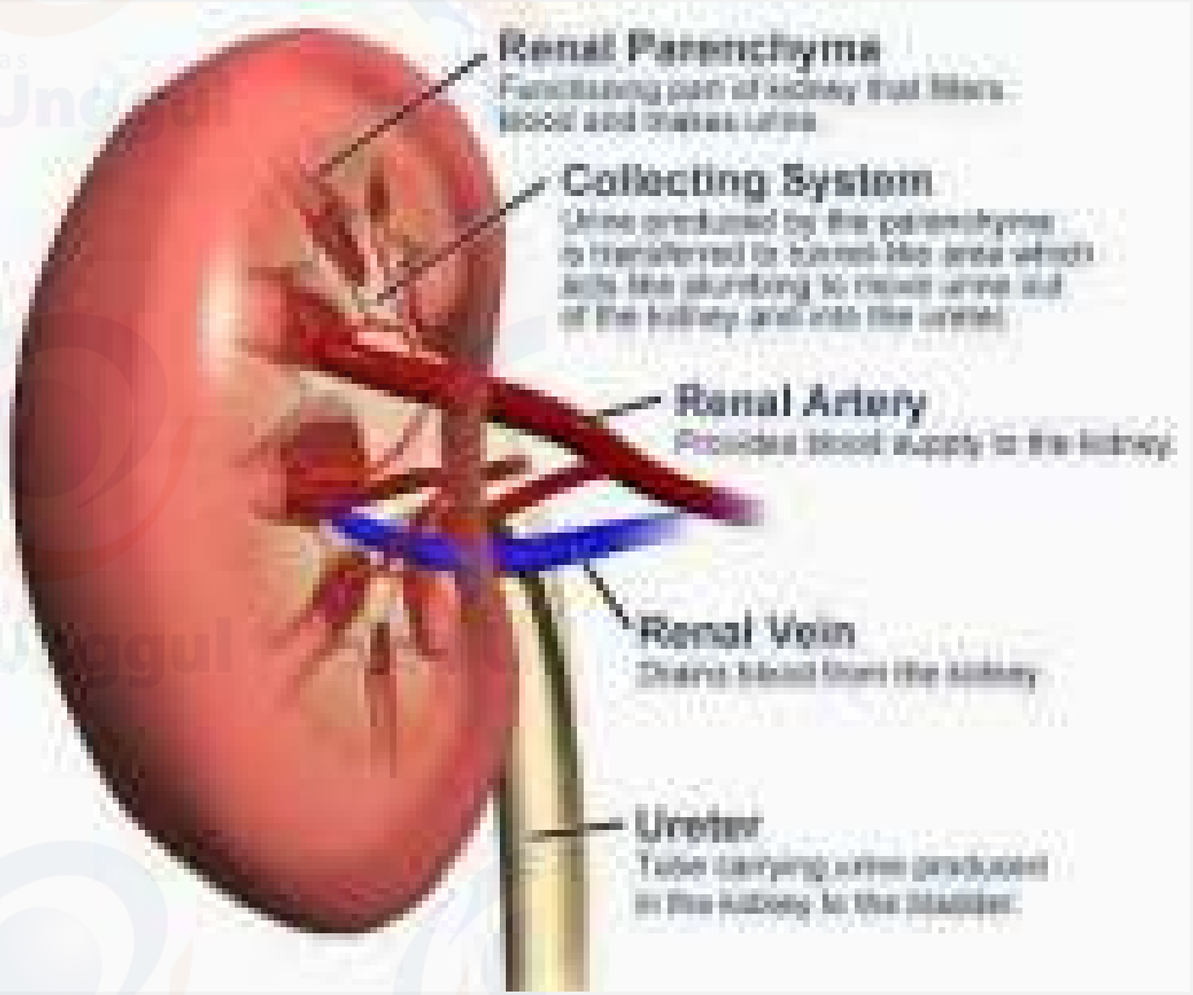
Ujian Akhir Semester

Renal Anatomy

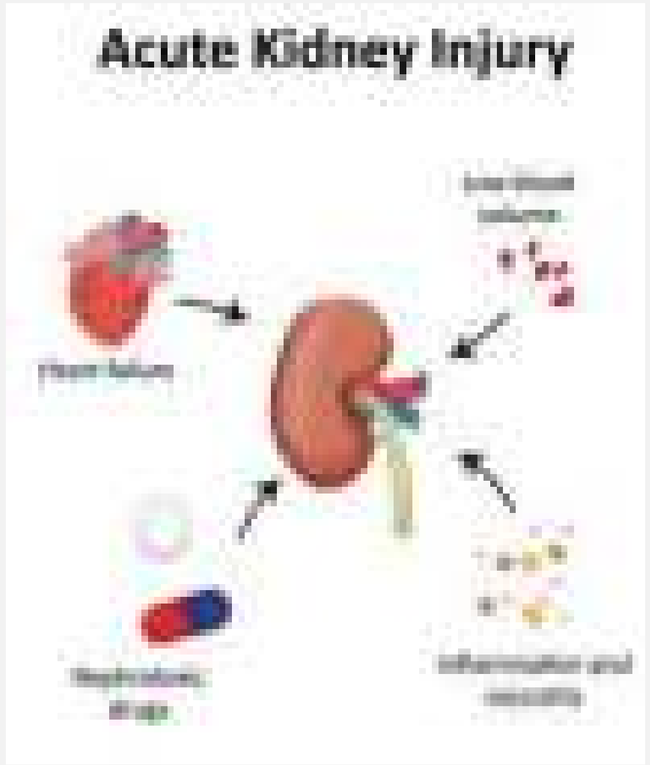


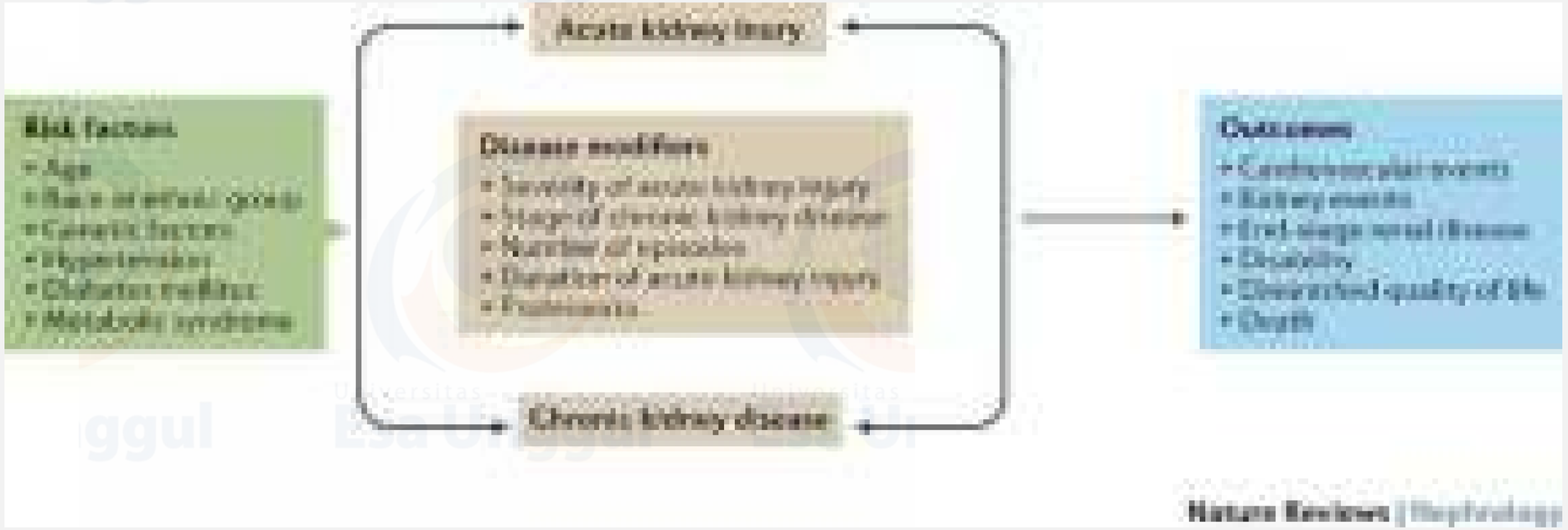
Renal Function

1. Untuk menjaga keseimbangan cairan dlm tubuh (Fluid Balance)
2. Pembentukan urin
3. Keseimbangan garam dan elektrolit (Electrolyte Balance)
4. Eliminasi produk akhir nitrogen dari metabolisme protein (terutama urea, asam urat & kreatinin
5. Mengeliminasi kelebihan asam dalam darah & mempertahankan kadar bikarbonat dalam batas normal (Acid-Base Balance)
6. Sintesis prostaglandin
7. Fungsi hormon
8. Sistem Renin-Angiotensin
9. Erythropoiesis : stimulasi produksi sel darah merah dalam sum-sum tulang
10. Aktivasi Vitamin D



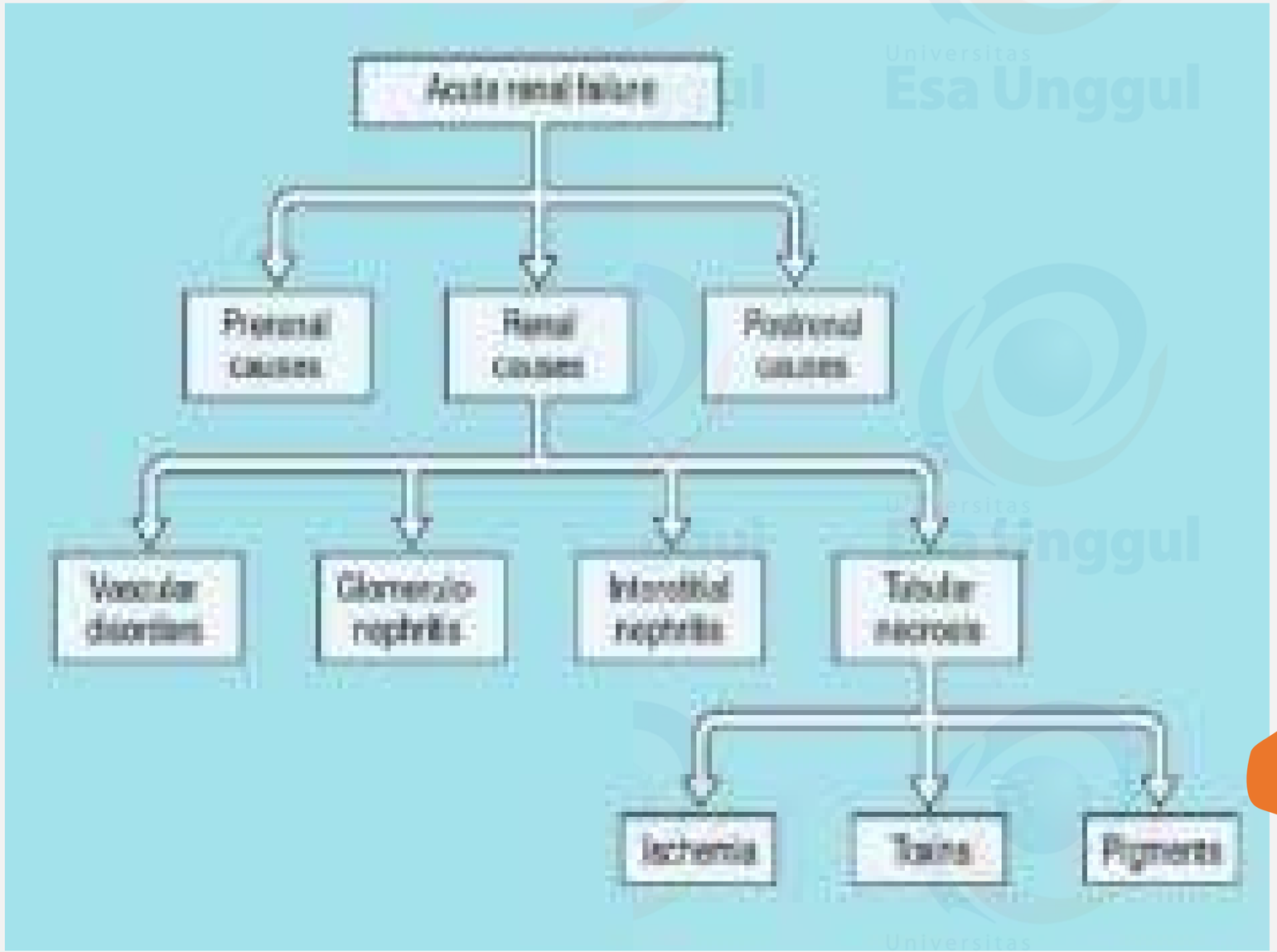
Renal Failure

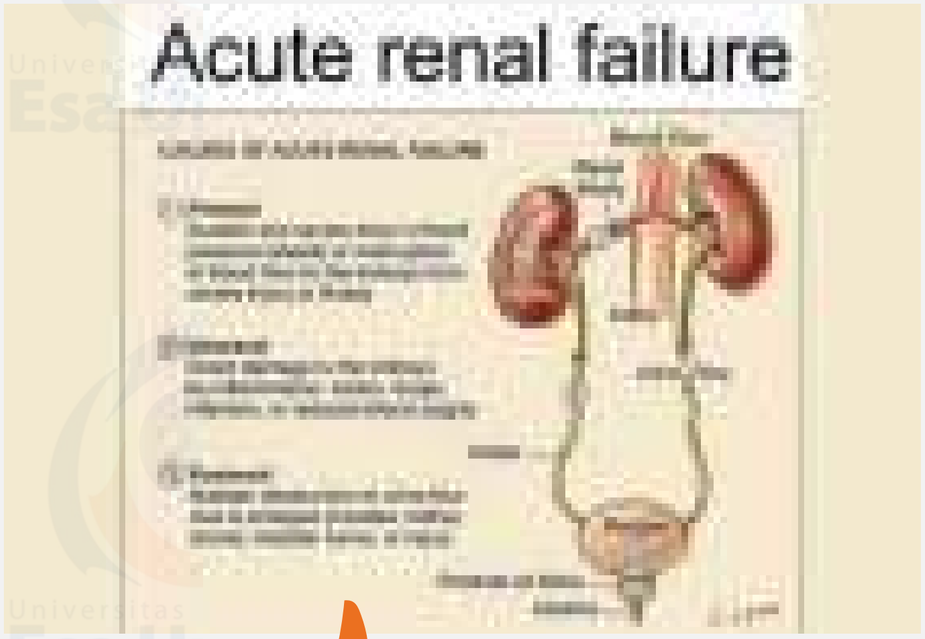




- **Akut:** berkembang dlm beberapa hari atau beberapa minggu
- **Kronis:** perkembangan Gagal ginjal yg progresif & lambat, biasanya berlangsung beberapa tahun

Acute Renal Failure





Pre-renal Azotemia/ uremia

- Penyebab GGA dengan prevalensi tertinggi
- Penurunan perfusi renal dan vasokonstriksi arterial aferen: penurunan RBF (normal value: 1200 ml/menit) dan GFR (normal value: 90 to 120 mL/min/1.73 m2)
- Tidak terjadi kerusakan seluler, GFR reversible

Post-renal

- **Obstruksi Ureter**
  - ureter bilateral intra-ureter (emboli, batu, kristal)
  - ekstra ureter (tumor, peritonial fibrosis)
  - papilliary necrosis (acute pyelonephritis)
- **Obstruksi Kandung Kemih**
  - mekanik (hipertropi prostat,malignansi, infeksi)
  - fungsional (anticholinergic effect, blocker ganglion, neuropathy)
  - Obstruksi uretra

GGA intrinsik

- Penyebab penurunan **fungsi ginjal** pada GGA intriksik:
  - Iskemik berat
  - mekanisme toksik/ imunologi
  - Kerusakan struktural pada glomerulus, tubulus, supply vaskuler, maupun jaringan interstitial
- **Acute Tubular Necrosis -** karena agen terapi
  - Antibiotik (aminoglikosida, amfoterisin, sefalosporin)
  - Metal (mercury, cuprum -tembaga)
  - Kontras media (CT/ MRI)
  - NSAID
  - agen kemoterapi (cisplatin, siklosporin)
- **Acute Tubulointerstitial Disease** - karena agen terapi, adanya infiltrat seluler pada membran tubuler/ sel epitel tubulus
  - Antibiotik (penisilin, eritromisin, sefalosporin)
  - Antihipertensi (captopril, furosemide, thiazide)
  - NSAID
- **Glomerulonephritis -** kerusakan membran glomerulus - proteinuria
  - Allopurinol
  - Antibiotik (ampicilin, rifampin)
  - Kemoterapi agent (siklosfosfamid, dauno doxorubicin)

AKI- based on KDIGO

- HB normal
- Oliguric type
- Non oliguric type (30-60%) – prognosis lebih baik – causa AB / nephrotoxic agent
- Umumnya "reversible"
- Frekuensi : 5-15% pasien rawat

KDIGO definition of acute kidney injury

Stage	Creatinine Criteria	Urine Output Criteria
1	Cr 1.5-1.9 times baseline, OR Cr increase >0.3 mg/dL	< 0.5 ml/kg/hr x 6-12 hours
2	Cr 2-2.9x baseline	<0.5 ml/kg/hr for >12 hours
3	Cr > 3x baseline, OR Cr > 4 mg/dL, OR Initiation of dialysis	<0.3 ml/kg/hr for >24 hours, OR Anuria > 12 hours

Patients are staged based on the single most concerning feature

AKI- based on KDIGO

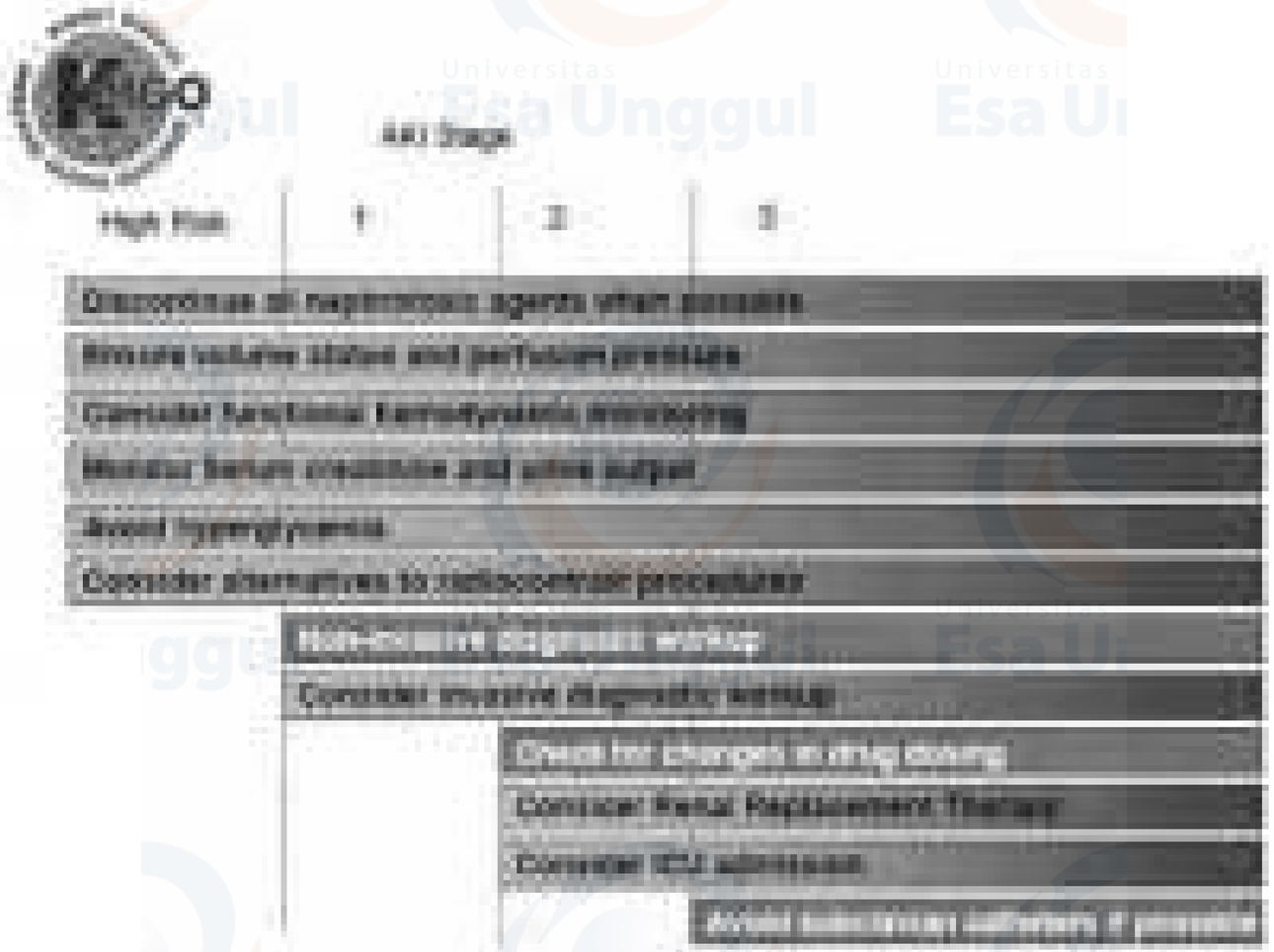


Figure 4 | Stage-based management of AKI. Shading of boxes indicates priority of action—solid shading indicates actions that are equally appropriate at all stages whereas graded shading indicates increasing priority as intensity increases. AKI, acute kidney injury; ICU, intensive care unit.

GFR and clearance

Rumus Cockcroft – Gault =

$$GFR = \frac{(140 - \text{usia}) \times \text{berat badan} \times 1{,}73}{72 \times Pcr \times A}$$

Pcr = kadar kreatinin darah (mg/dL)

A = luas permukaan tubuh (m^2)

Untuk wanita rumus tersebut dikalikan 0.85

Rumus MDRD (Modification of Diet in Renal Disease):

$$GFR\ (mL / mnt / 1{,}73\ m^2) = 186 \times (\text{kreatinin serum})^{-1{,}154} \times (\text{umur})^{-0{,}203} \times (0{,}742) \times (1{,}210)$$

Creatinine clearance calculation

$$\frac{\text{Kreatinin urine (mg/dL) X volume urine (ml/menit) X 1,73}}{\text{Kreatinin serum (mg/dL) X A } (m^2)}$$

A= luas permukaan tubuh
satuan: ml/menit

- Klirens kreatinin secara konvensional memerlukan pengumpulan urine 24 jam.
- Untuk menghindari kesalahan penilaian karena pengumpulan urine, digunakan rumus bersihan tanpa pengukuran kadar kreatinin urine yakni rumus Cockcroft-Gault

Tujuan dan prinsip terapi

- Menghilangkan Penyebab Utama
- Mencegah Kerusakan Lebih Lanjut
- Mengembalikan Fungsi Ginjal Secepat Mungkin

- Meningkatkan output urine & RBF
- Menjaga keseimbangan cairan & elektrolit
- Menghilangkan sampah metabolit
- Meminimalkan nephrotoxic injury lebih lanjut

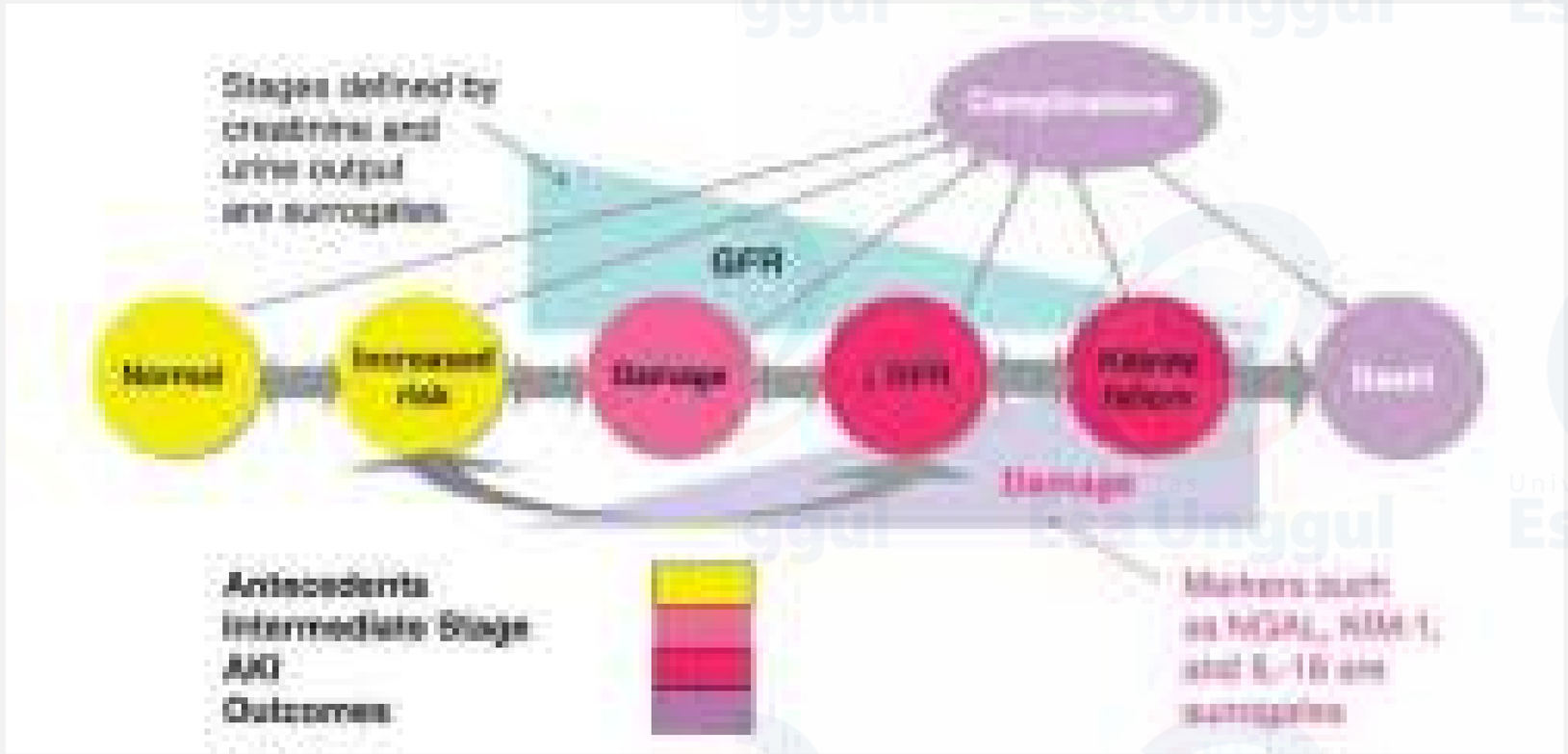
Farmakologi dan Non-Farmakologi

Non-Farmakologi	Farmakologi
• Kontrol Volume: pasien oliguria --- resusitasi cairan tepat ◦ perbaikan perfusi ginjal ◦ cegah hipoxia tubulus ◦ cegah nekrosis tubular • mencegah euvolemia perfusi jaringan dan keseimbangan elektrolit • hindari nefrotoxin agent	• Diuretik - output urin, meningkatkan RBF (1st: loop diuretik, mannitol) • Vasoactive -kenaikan RBF, perbaikan CrCl tanpa meningkatkan output urin (dobutamin) • Elektrolit (K+, Mg+, PO4-) • Hemodialisis (indikasi: uremia, hiperkalemia berat, CHV/ edema pulmonary, toksisitas obat/agen lainnya.

AKI VS CKD


KEY DIFFERENCE BETWEEN
CKD AND AKI
AKI
occurs when the kidneys suddenly fail due to an injury, medication, or illness.
VS
CKD
is the gradual loss of kidney function mainly caused by high blood pressure, diabetes, and an inflammatory condition known as glomerulonephritis.

Progression of AKI to CKD



AKI and CKD

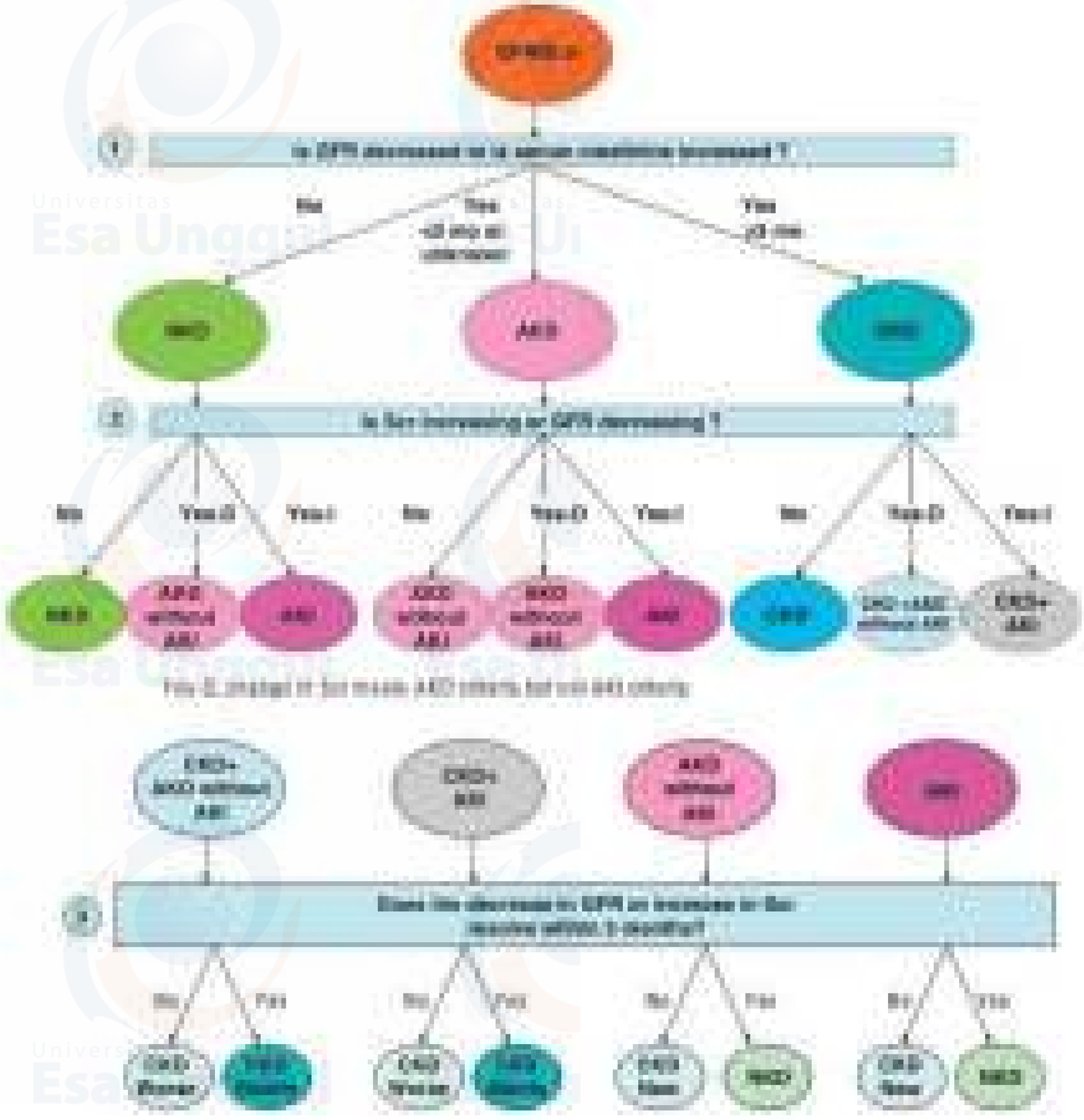
Table 11 | Definitions of AKI, CKD, and AKD

	Functional criteria	Structural criteria
AKI	Increase in SCr by 50% within 7 days, OR Increase in SCr by 0.3 mg/dl (26.5 μmol/l) within 2 days, OR Oliguria	No criteria
CKD	GFR <60 ml/min per 1.73 m^2 for >3 months	Kidney damage for >3 months
AKD	AKI, OR GFR <60 ml/min per 1.73 m^2 for <3 months, OR Decrease in GFR by ≥35% or increase in SCr by >50% for <3 months	Kidney damage for <3 months
NKD	GFR ≥60 ml/min per 1.73 m^2 Stable SCr	No damage

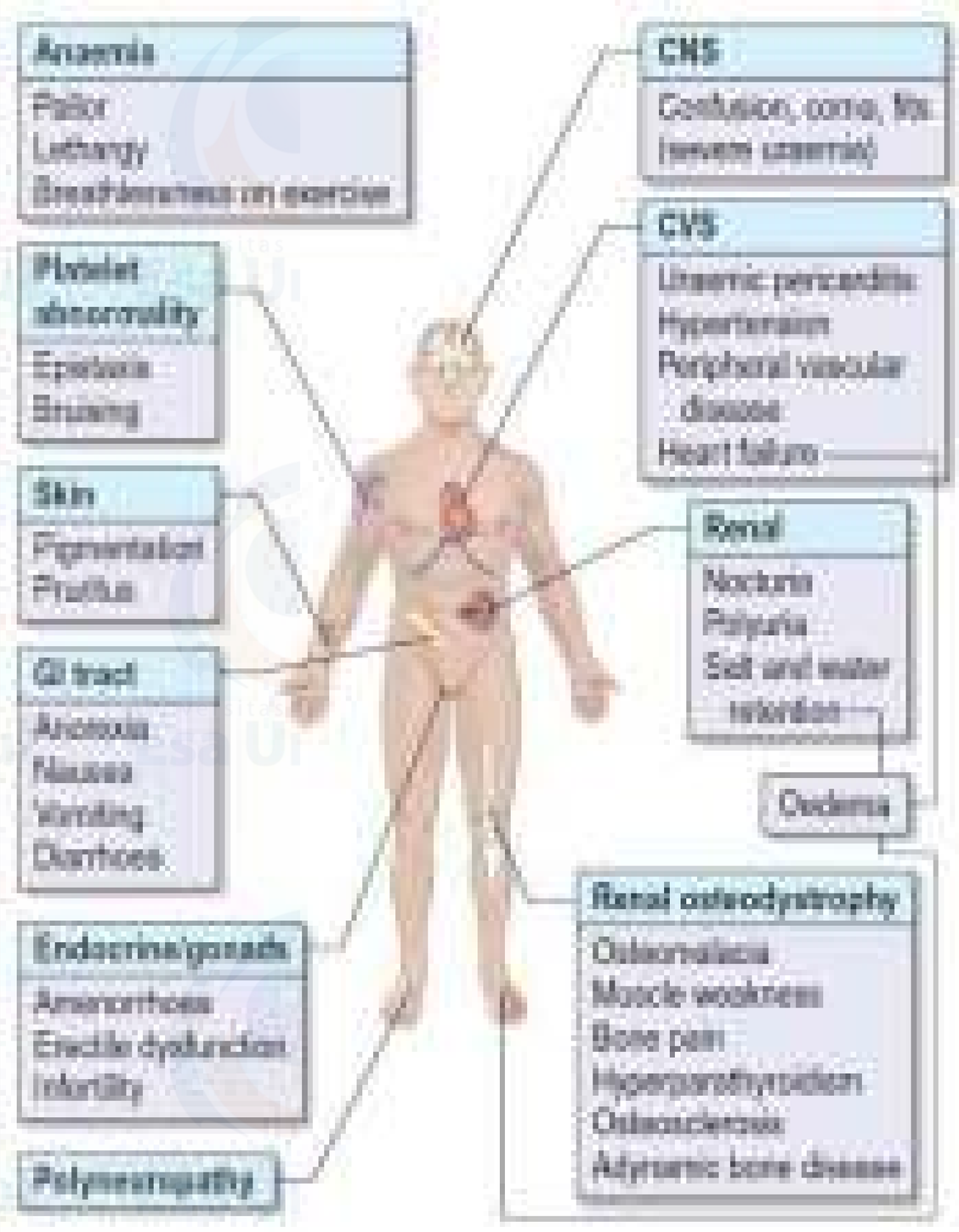
Table 12 | Examples of AKI, CKD, and AKD based on GFR and increases in SCr

Baseline GFR (ml/min per 1.73 m^2)	Increase in SCr during 7 consecutive days	GFR during next 3 months	Diagnosis
>60	>1.5 ×	NA	AKI
>60	<1.5 ×	<60	AKD without AKI
>60	<1.5 ×	>60	NKD
Baseline GFR (ml/min per 1.73 m^2)	**Change in SCr during next 7 days**	**GFR during next 3 months**	**Diagnosis**
<60	>1.5 ×	NA	AKI + CKD
<60	<1.5 ×	>35% decrease	AKD without AKI + CKD
<60	<1.5 ×	<35% decrease	CKD

AKI and CKD



Clinical sign and symptomp of CKD



Staging CKD & etiology

- Glomerulonelritis (25%)
- Diabetes melitus (23%)
- Hipertensi (20%)
- Ginjal polikistik (10%)

Klasifikasi

- Stadium 1 (glomerulo filtrasirate/GFR normal (> 90 ml/min)
- Stadium 2 (penurunan GFR ringan atau 60 s/d 89 m/min)
- Stadium 3 (penurunan GFR moderat atau 30 s/d 59 m/min)
- Stadium 4 (penurunan GFR parah atau 15-29 ml/min)
- Stadium 5 (penyakit ginjal stadium akhir/ terminal atau GFR < 15 ml/min)

Algoritma CKD

Derajat	LFG (ml/mnt/1,73m2)	Rencana Tatalaksana
1	≥ 90	Terapi penyakit dasar, kondisi komorbid,evaluasi perburukan fungsi ginjal, memperkecil resiko kardiovaskular.
2	60-89	Menghambat perburukan fungsi ginjal
3	30-59	Evaluasi dan terapi komplikasi
4	15-29	Persiapan terapi pengganti ginjal
5	< 15	Terapi pengganti ginjal

Terapi symptomatic - based on clinical manifestation

1. **Koreksi asidosis metabolic**
   - Asidosis metabolik harus dikoreksi karena meningkatkan serum kalium (hiperkalemia).
   - Untuk mencegah dan mengobati asidosis metabolik dapat diberikan suplemen alkali.
   - Terapi alkali (sodium bicarbonat) harus segera diberikan intavena bila pH < 7,35 atau serum bikarbonat < 20 mEq/l.

2. **Anemia**
   - Transfusi darah misalnya *Packed Red Cell* (PRC) merupakan salah satu pilihan terapi alternative
   - Terapi pemberian transfusi darah harus hati-hati karena dapat menyebabkan kematian mendadak
   - Preparat **besi, asam folat, nandrolon dekanoat, hormon anabolik untuk menstimulasi eritropoetin**

Terapi symptomatic - based on clinical manifestation

3. **Mengurangi gejala uremia:**
   a. GIT: kadang membaik dengan diet TKRP, memperbaiki asidosis dengan NaHCO3, obat anti muntah.
   b. Neuromuskular: vit.B1, B6, B12 dosis tinggi, diazepam
   c. Osteodistrofi renal: koreksi asidosis, obat pengikat fosfat, suplementasi kalsium, vitamin D3.

Replacement Therapy - for ESRD

- Dilakukan pada penyakit gagal ginjal kronik stadium 5, yaitu pada LFG / GFR kurang dari 15 mtmenit.
- Terapi tersebut dapat berupa:
  - Hemodialisis
  - Dialisis peritoneal
  - Transplantasi ginjal

Indikasi

a. Uremia – azotemia
b. Hyperkalemia berat
c. Kelebihan Volume – biasanya pada pasien CHV (pulmonary edema)
d. Menghilangkan toksin : keracunan ethylene glycol , overdosis theophylline .

Rise your hand!

any question?

PSF316

Farmakoterapi Diabetes

Sesi Ke 8

Topik Sesuai RPS:
Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi Diabetes

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Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

patofisiologi dan farmakoterapi epilepsi

Sesi 12

patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

patofisiologi dan farmakoterapi rheumatoid arthritis

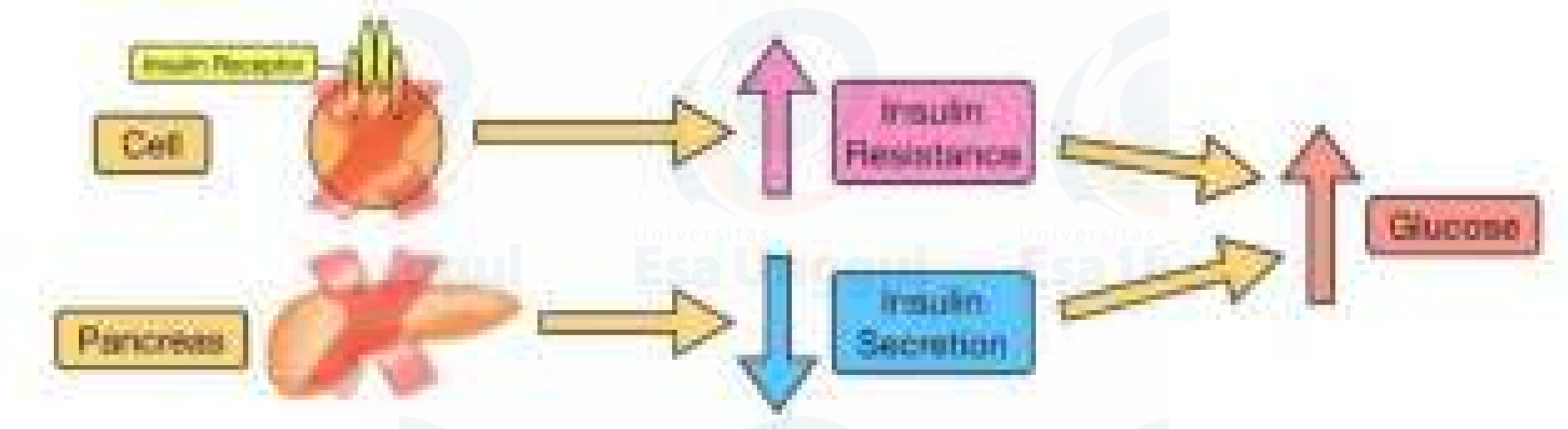
Sesi 14

patofisiologi dan farmakoterapi SLE

Ujian Akhir Semester

Diabetes on WHO definition

a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces.



Diabetic Types

DIABETES MELLITUS

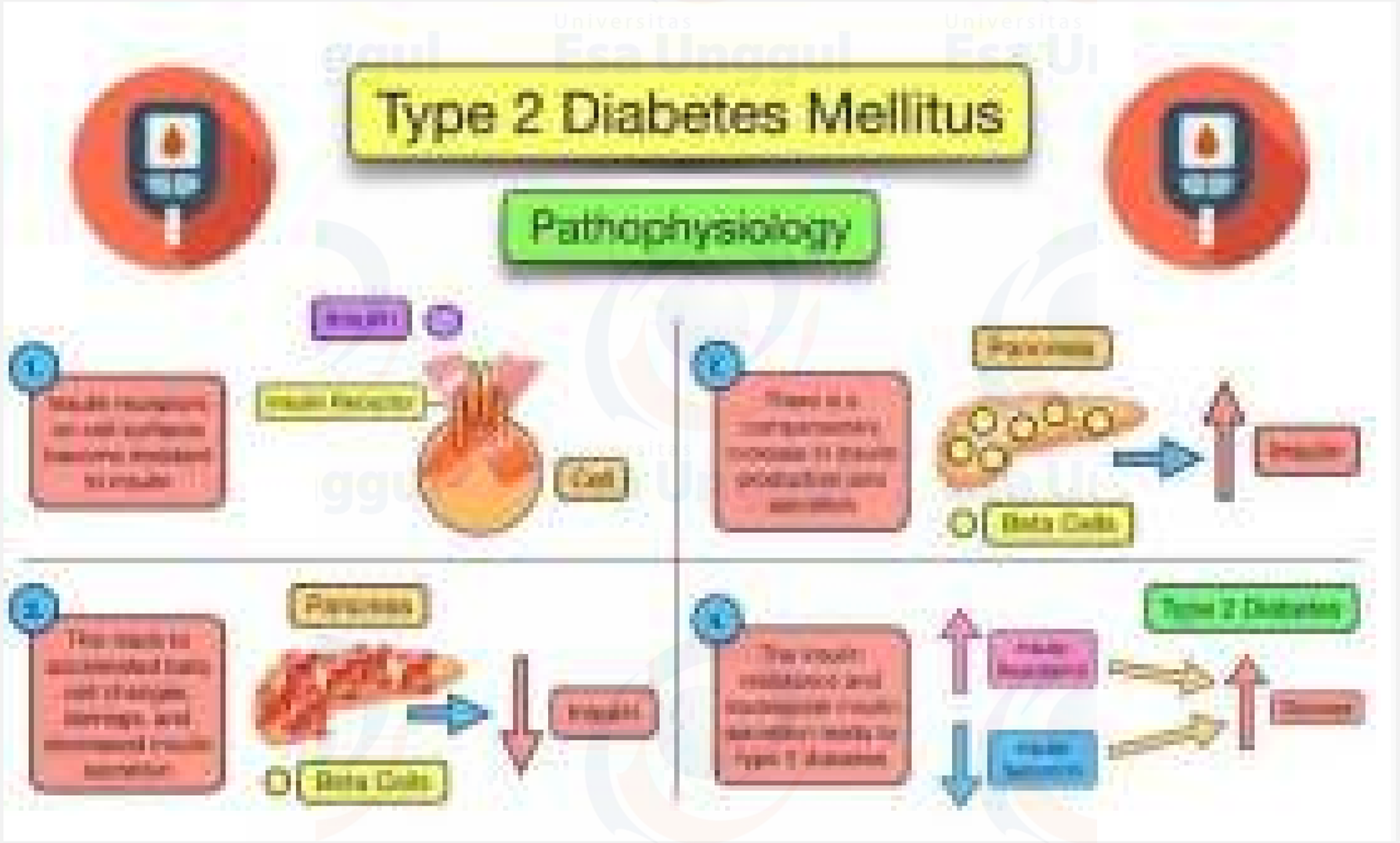
TYPE 1 VS TYPE 2

• Occurs when the pancreas is unable to produce enough insulin • Tends to develop at a young age • Cannot be prevented • Requires insulin therapy	• Occurs due to insulin resistance (i.e. when the body does not respond well to insulin) • Tends to develop at an older age • Can be prevented with lifestyle changes • Can be managed with lifestyle modifications alone if diagnosed early

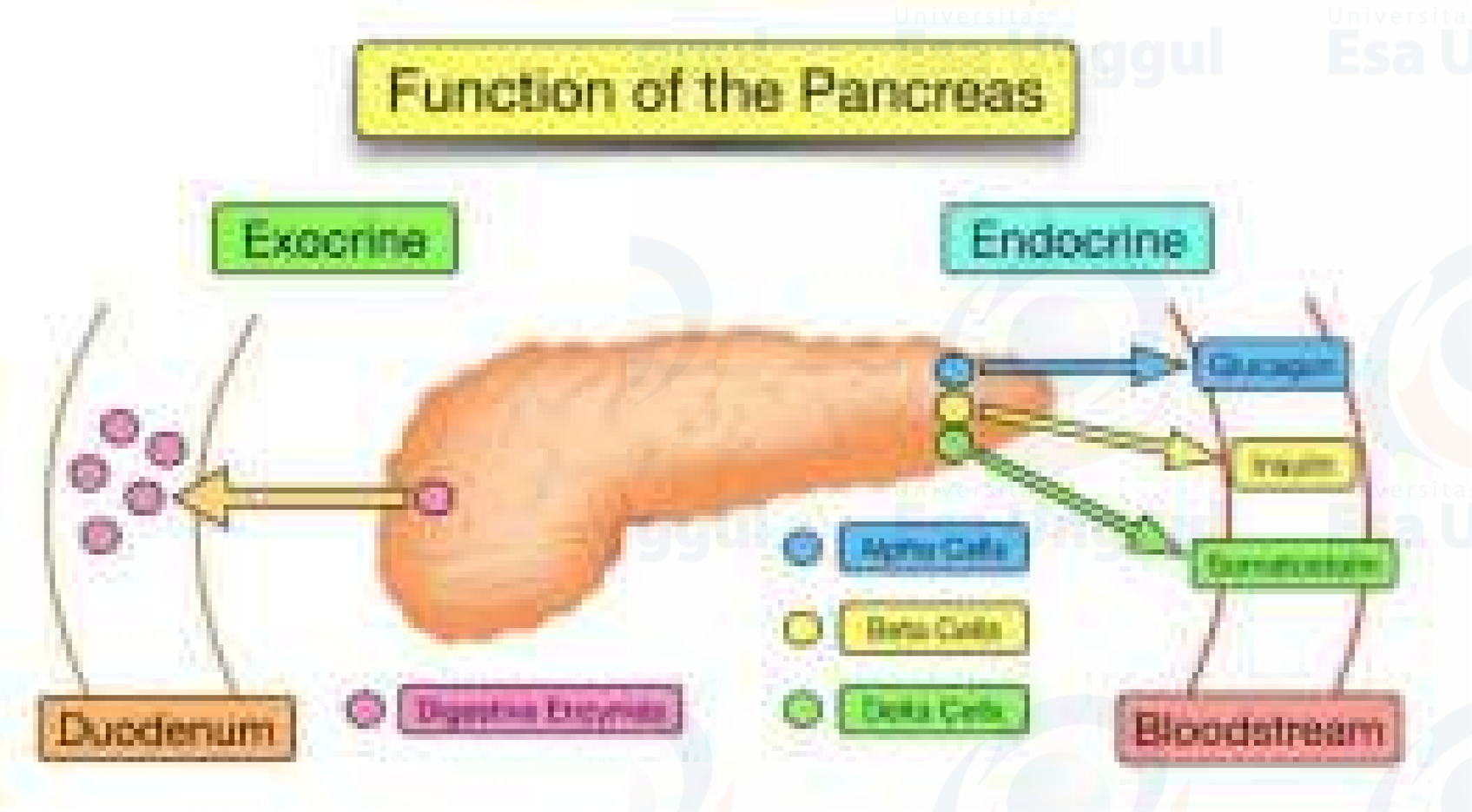
• Both share symptoms of frequent urination, increased thirst, extreme hunger, unintentional weight loss, fatigue, blurry vision, slow-healing sores or wounds that heal slowly, and numbness and tingling, sensation in hands and feet.

• Both can benefit from lifestyle modifications such as a healthy diet, physical activity, blood sugar level monitoring, and management of stress and other existing health conditions.

patophysiology of diabetes

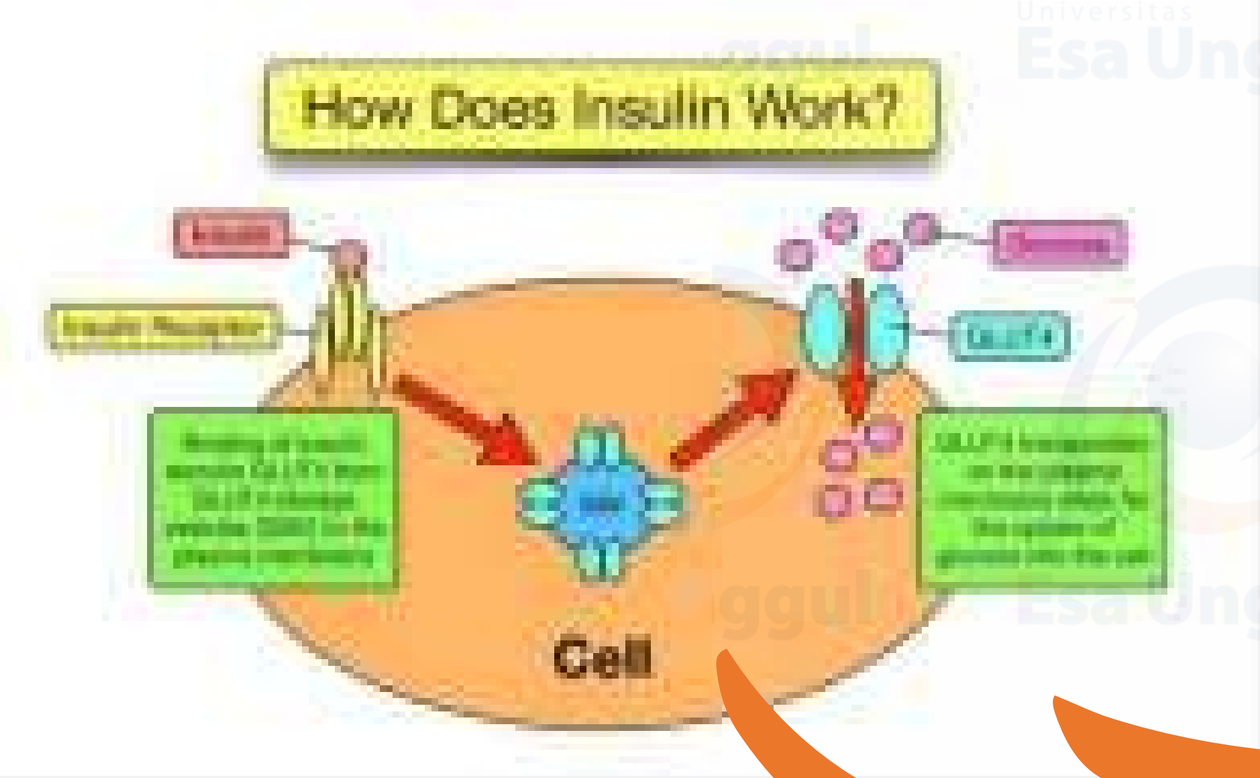


Role of Pancreas



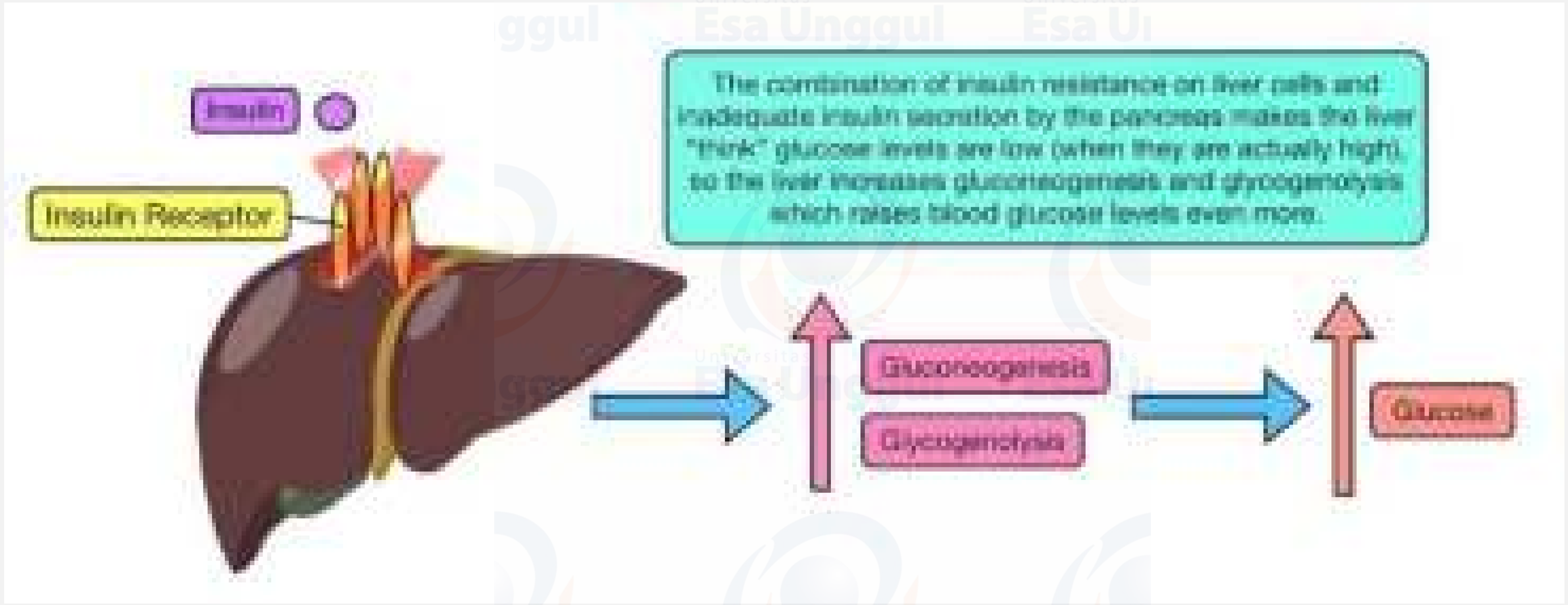
- Glucagon: is a hormone that your pancreas makes to help regulate your blood glucose (sugar) levels- increases your blood sugar level
- Insulin: hormone your pancreas makes that's essential for allowing your body to use sugar (glucose) for energy
- somatostatin: to prevent the production of other hormones in your endocrine system and certain secretions in your exocrine system.

Role of Insulin on glucose

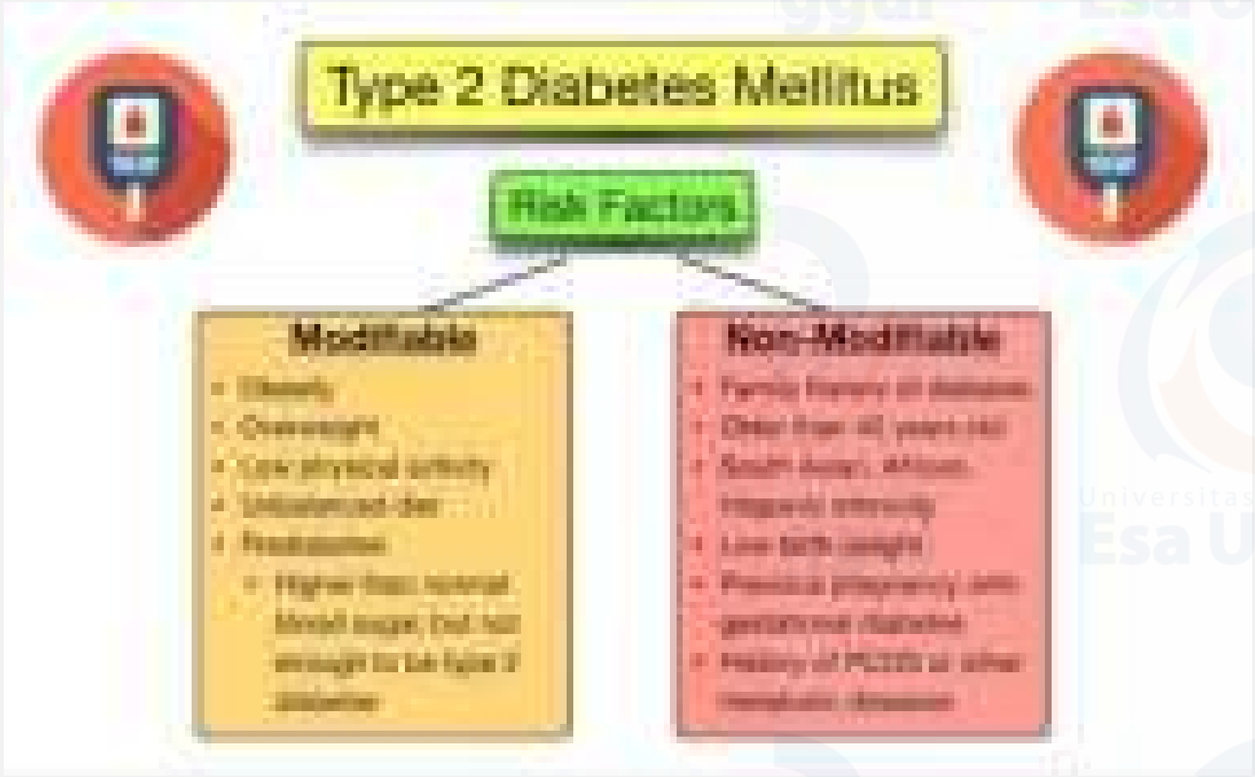


Insulin receptor signaling pathway: Insulin binds to insulin receptors which increases the recruitment of GLUT4 glucose transporters to the plasma membrane. GLUT4 allows for glucose uptake into the cell

Impact to the liver - higher glucose



Sign, symptomp and risk factor



Glucose value (USA Guidelines)

	Hemoglobin A1C (HbA1c)	Fasting Blood Sugar Test	Oral Glucose Tolerance Test	Random Blood Sugar Test
Normal	< 5.7%	< 100 mg/dL	< 140 mg/dL	N/A
Prediabetes	5.7 - 6.4%	100 - 125 mg/dL	140 - 199 mg/dL	N/A
Diabetes	≥ 6.5%	≥ 126 mg/dL	≥ 200 mg/dL	≥ 200 mg/dL

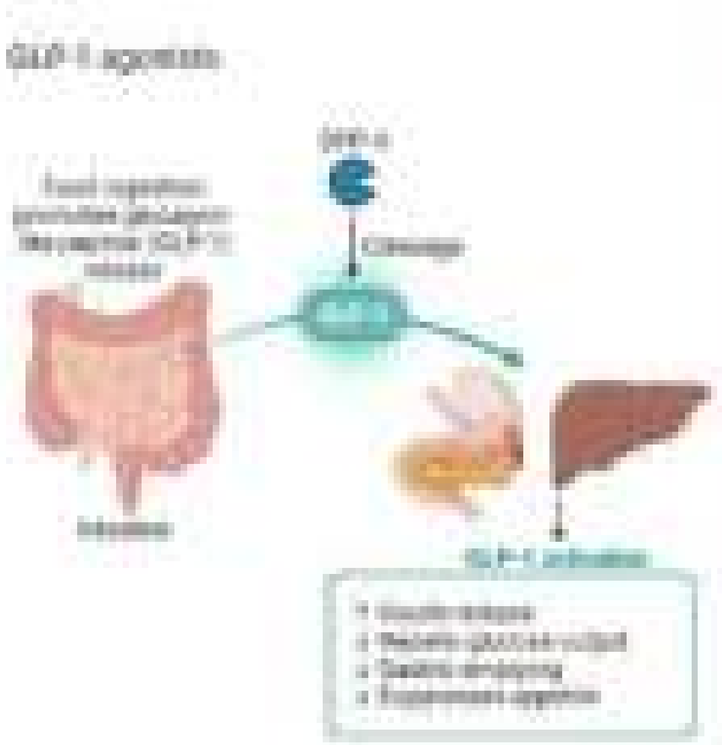
Anti - diabetic Agent

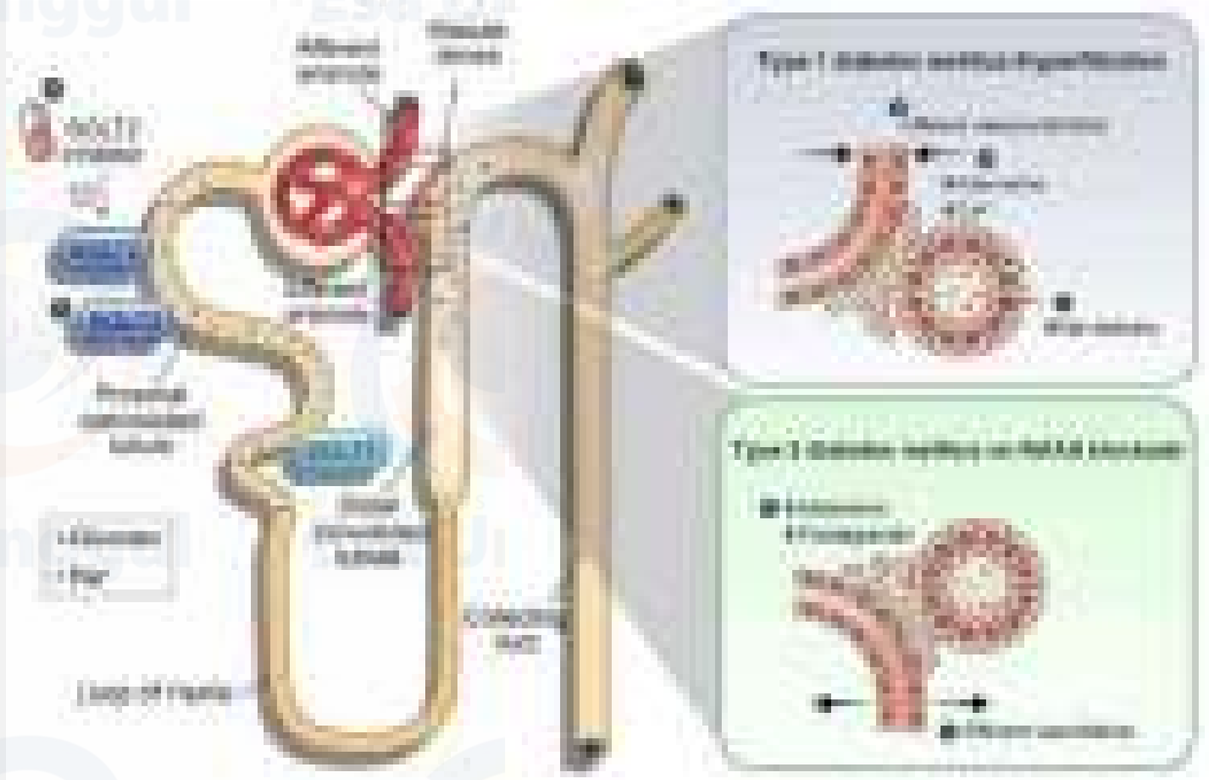
Type 2 Diabetes Medications

*ROH = Risk of Hypoglycemia

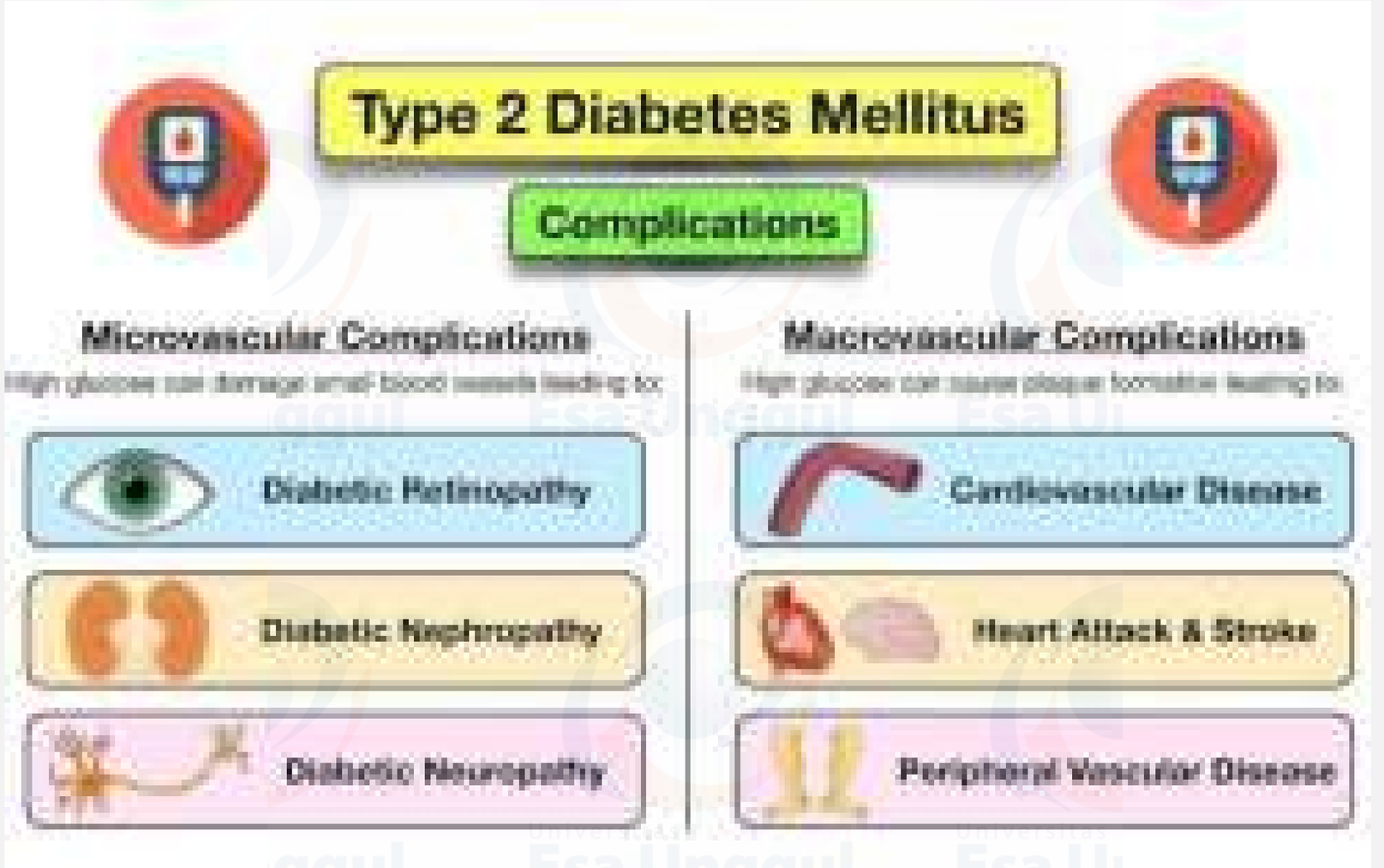
Drug Class	Examples	Mechanism of Action	Side Effects	ROH*	Contraindications
Biguanides	Metformin	Increase insulin sensitivity; Decrease hepatic gluconeogenesis	Nausea, vomiting, diarrhea, vitamin B12 deficiency, lactic acidosis (rare)	No	CKD, heart disease, liver disease, metabolic acidosis
Thiazolidinediones	Pioglitazone	Increase insulin sensitivity; Decrease hepatic gluconeogenesis	Weight gain, fluid retention, heart failure, bladder cancer risk, fractures, increase HDL	No	Heart failure, osteoporosis, history of bladder cancer
Sulfonylureas	Glipizide	Stimulate insulin secretion by inhibiting/closing beta cell ATP-sensitive K+ channels	Hypoglycemia, weight gain	Yes	CKD, hepatic impairment
SGLT-2 Inhibitors	Dapagliflozin	Decrease glucose reabsorption in the kidney; increase glucose excretion	Weight loss, thirst, increased urination, UTI risk, AKI	No	Renal impairment
DPP-4 Inhibitors	Sitagliptin	Increase GLP-1, which increases insulin secretion	Dizziness, headaches, URIs, joint pain, risk of pancreatitis	No	Pancreatitis, heart failure, angioedema, DKA
GLP-1 Mimetics	Exenatide	Increase insulin secretion; inhibit glucagon secretion	Nausea, vomiting, diarrhea, pancreatitis, weight loss, AKI	No	Pancreatitis, CKD, medullary thyroid cancer, gastroparesis
Insulin	"Basal"	Exogenous insulin provided	Weight gain	Yes	Hypokalemic drugs, dose adjusted for renal/liver failure

Anti - diabetic Agent

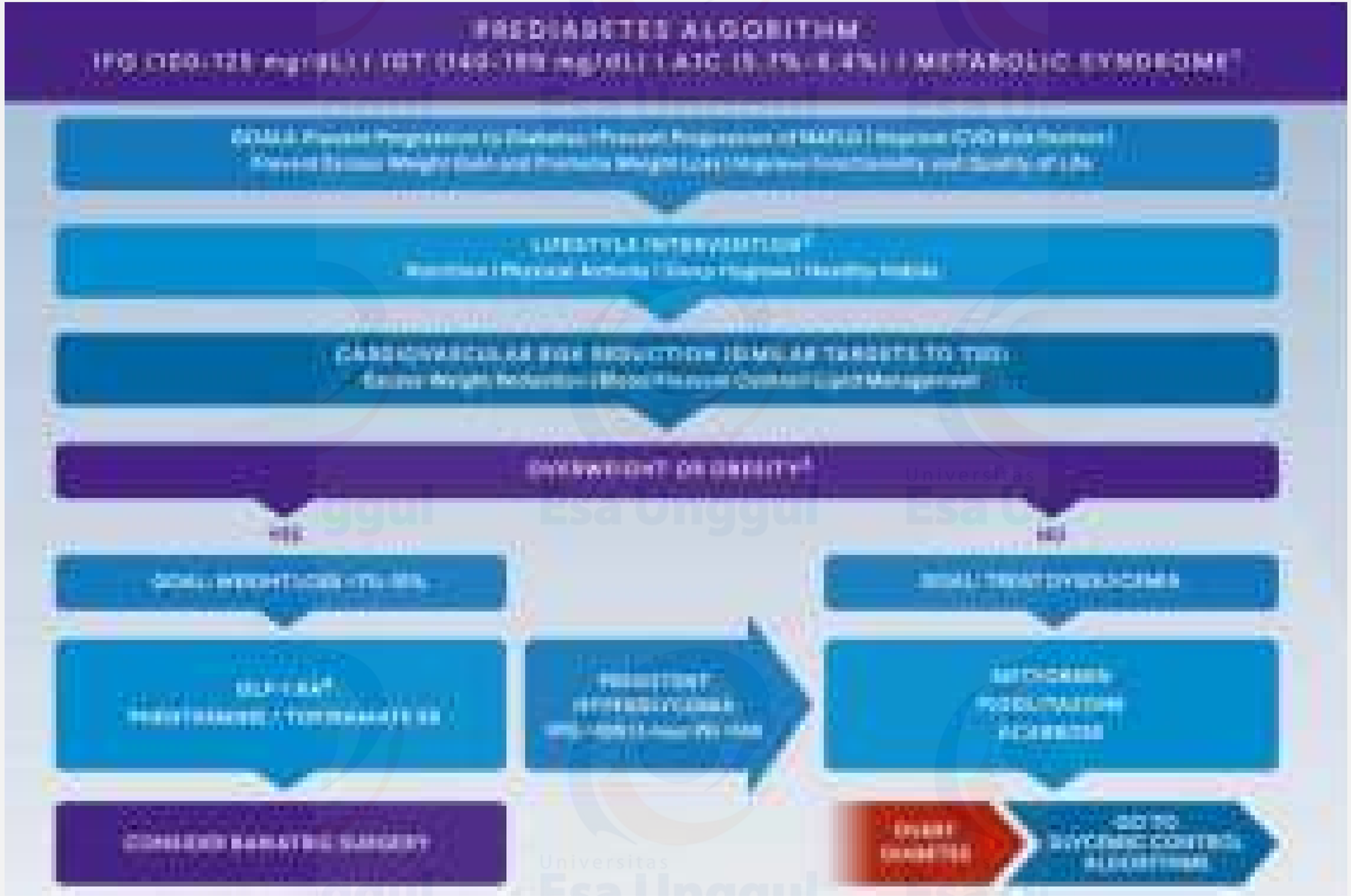




Clinical Manifestation - risk of Complication

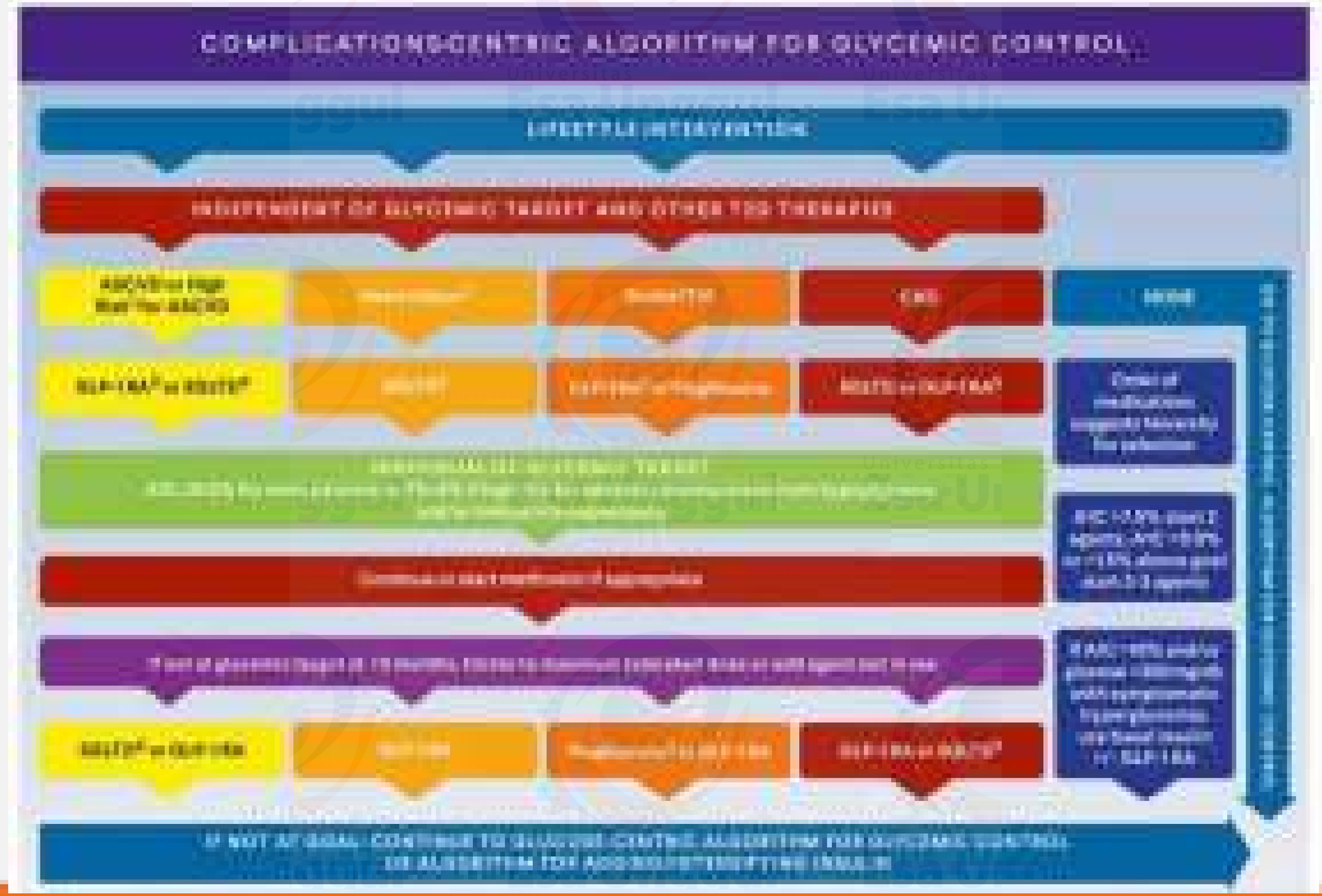


Pre-diabetic Algorithm



Diabetic Algorithm (without comorbid)

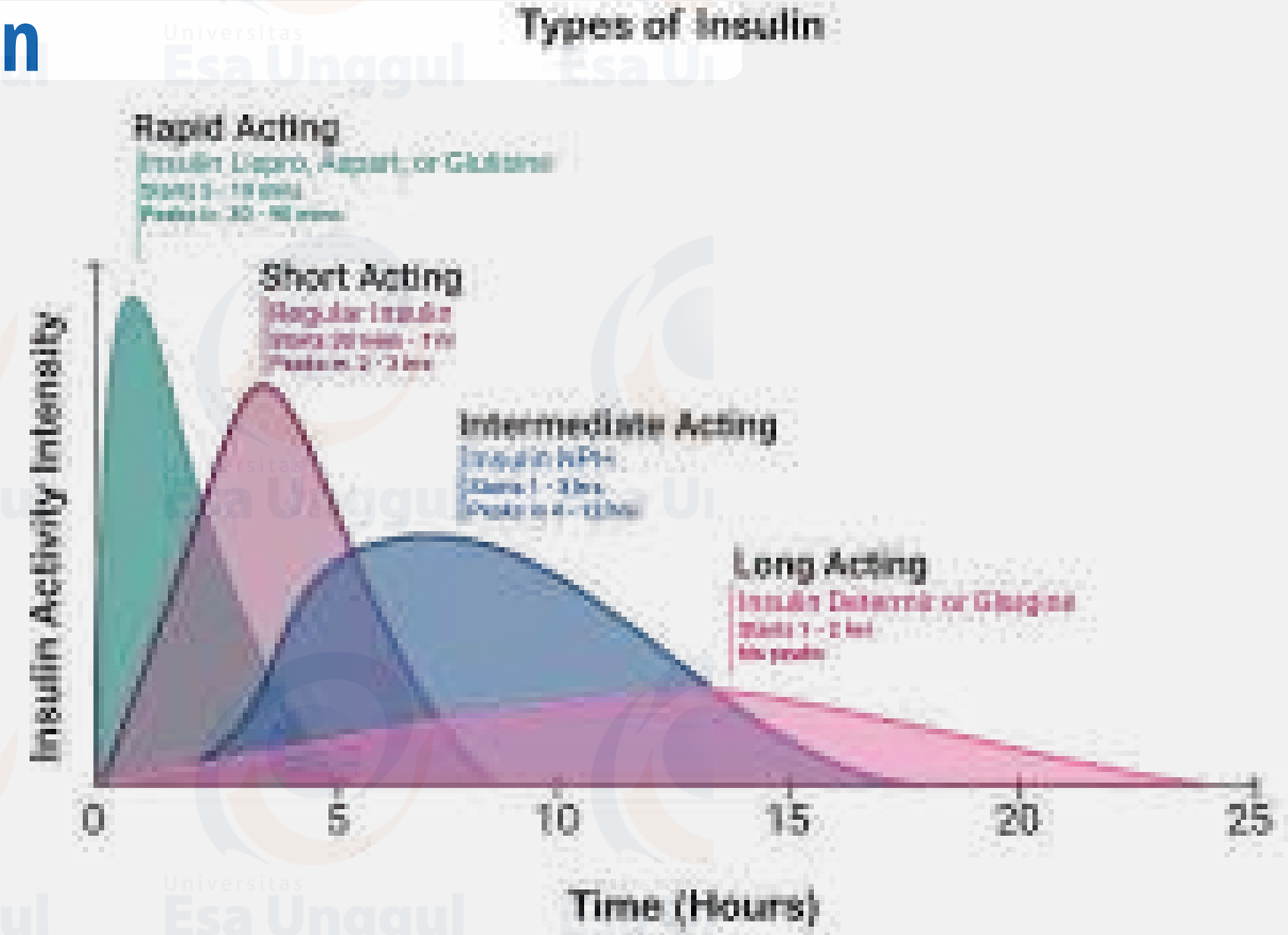
Diabetic Algorithm (with comorbid)



Adding Insulin Algorithm

- Basal insulin suppresses glucose production by the liver (gluconeogenesis) between meals and overnight.
- Prandial (bolus) insulin covers increases in blood glucose levels following meals.

types of insulin



Rise your hand!

any question?

PSF316

Farmakoterapi Tiroid

Sesi Ke 9

Topik Sesuai RPS:
Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi Tiroid

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Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

patofisiologi dan farmakoterapi epilepsi

Sesi 12

patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

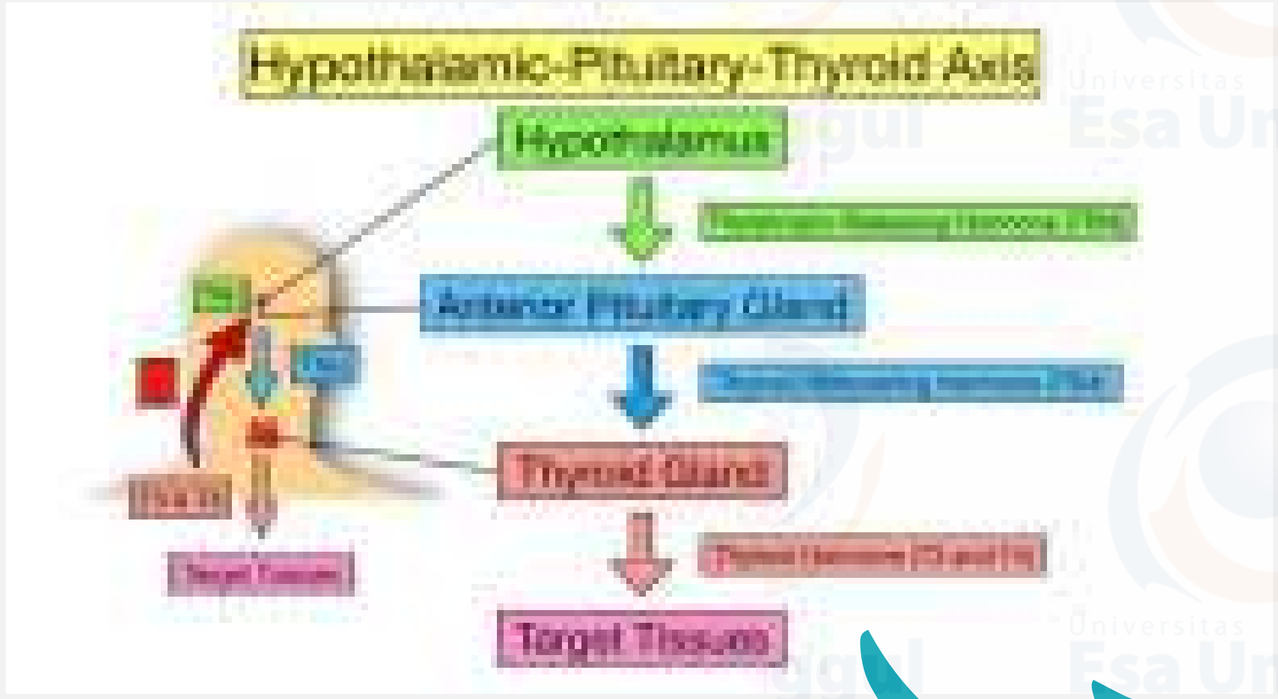
patofisiologi dan farmakoterapi rheumatoid arthritis

Sesi 14

patofisiologi dan farmakoterapi SLE

Ujian Akhir Semester

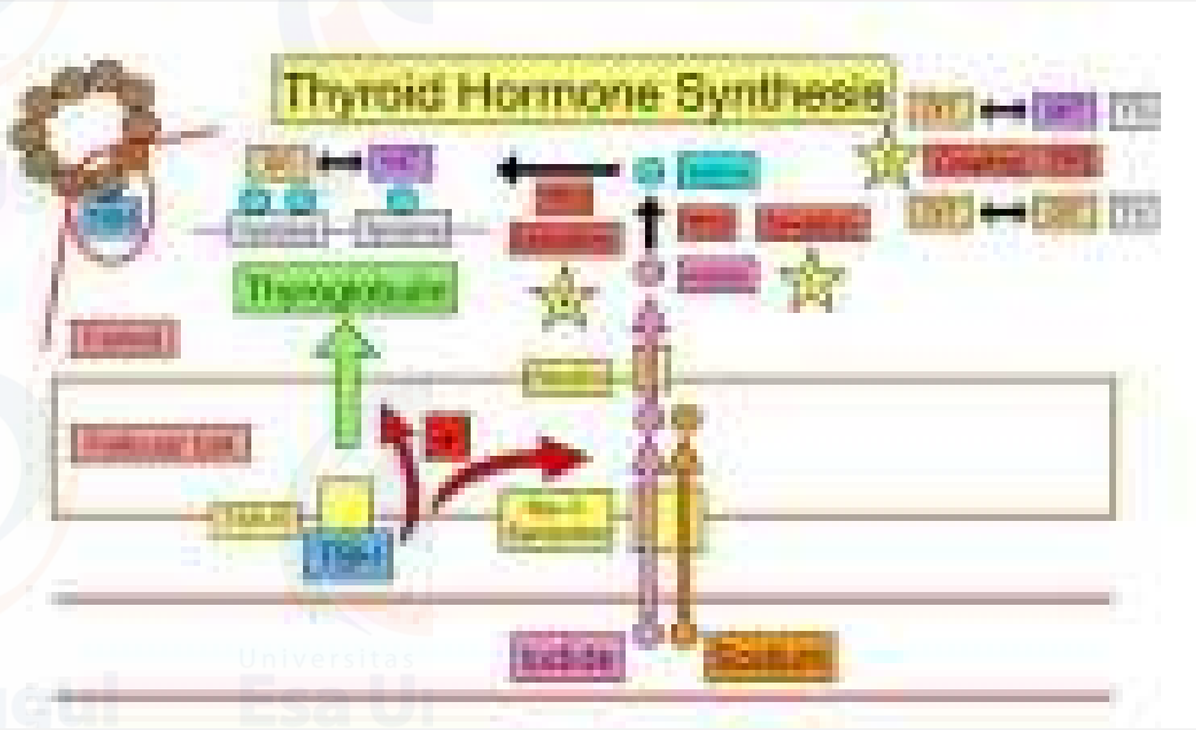
Tyroid Hormon Synthesis



- The thyroid follicular cells produce a protein called thyroglobulin - Thyroglobulin is an important precursor for thyroid hormone
- The production of thyroid hormone requires 2 main ingredients: Thyroglobulin and Iodine (from blood stream iodine - iodide)
- Iodide - iodine (by TPO)
- Iodine combine with thyroglobulin = DIT and MIT
- MIT DIT coupling (by TPO) = T3 and T4

Synthesis pathway includes the following steps:

1. **TRH Release (Hypothalamus)**
2. **TSH Release (Anterior Pituitary Gland)**
3. **Thyroid Hormone Synthesis (Thyroid Gland)**
    a. **Thyroglobulin Production**
    b. **Iodide Uptake**
    c. **Iodide Oxidation**
    d. **Thyroglobulin Iodination**
    e. **MIT/DIT Coupling**
    f. **Thyroglobulin Proteolysis**
4. **Thyroid Hormone Release (Thyroid Gland)**



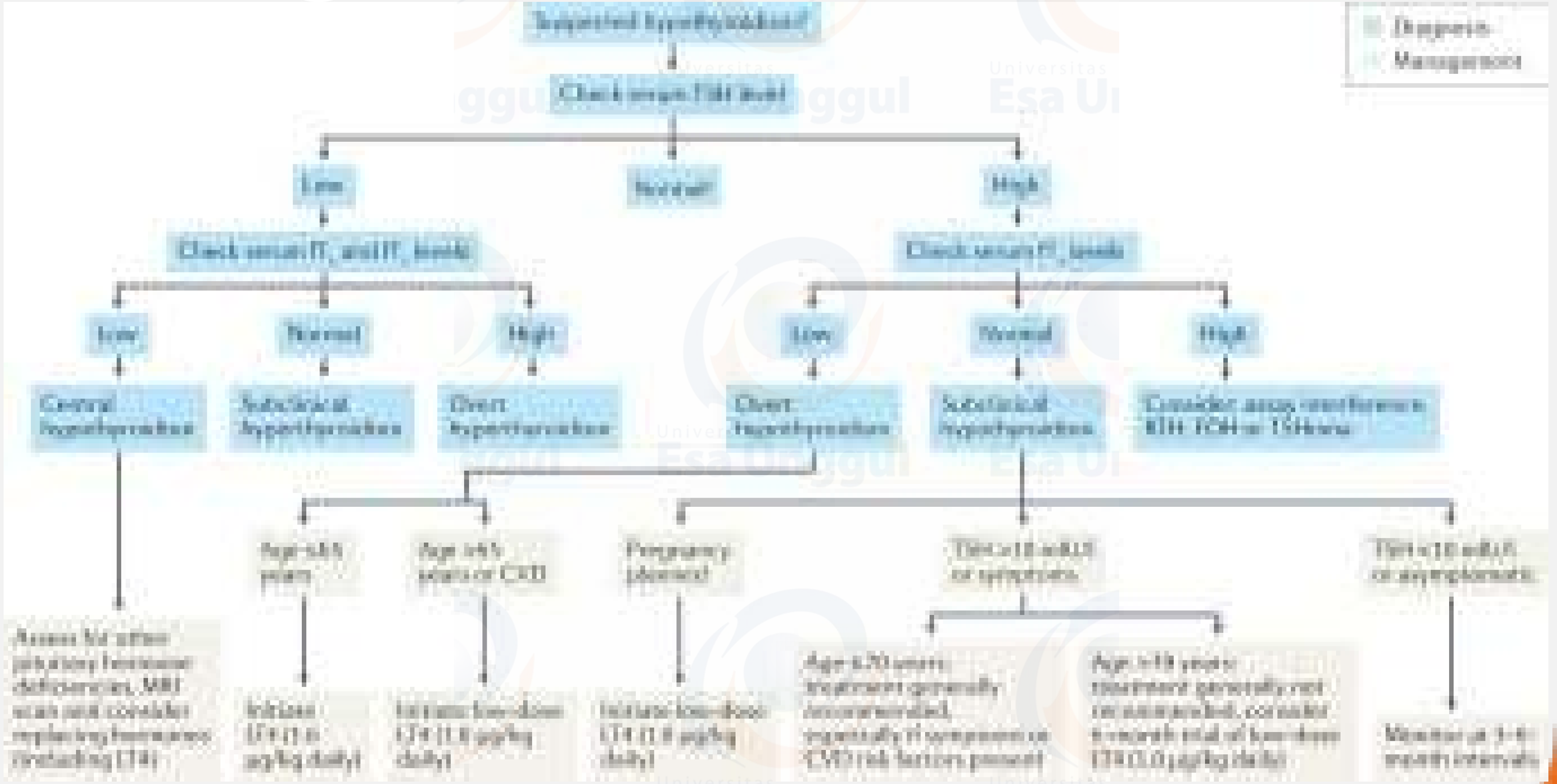
Tyroid Disease

- Kadar tiroid terlalu tinggi- manifestasi klinis tirotoksisitas
- hiperaktivitas kelenjar tiroid

Hyperthyroidism	Hypothyroidism
Weight Loss	Weight Gain
Increased Appetite	Decreased Appetite
Heat Intolerance Increased Sensitivity to Heat	Cold Intolerance Increased Sensitivity to Cold
Tachycardia, Palpitations, Arrhythmias	Bradycardia
Diarrhea	Constipation
Anxiety, Nervousness, Irritability, Insomnia, Tremors	Fatigue, Depression, Impaired Memory, Impaired Concentration, "Mental Fog"
Increased Hair and Nail Growth Increased Sweating	Hair Loss and Thin Nails Dry Skin

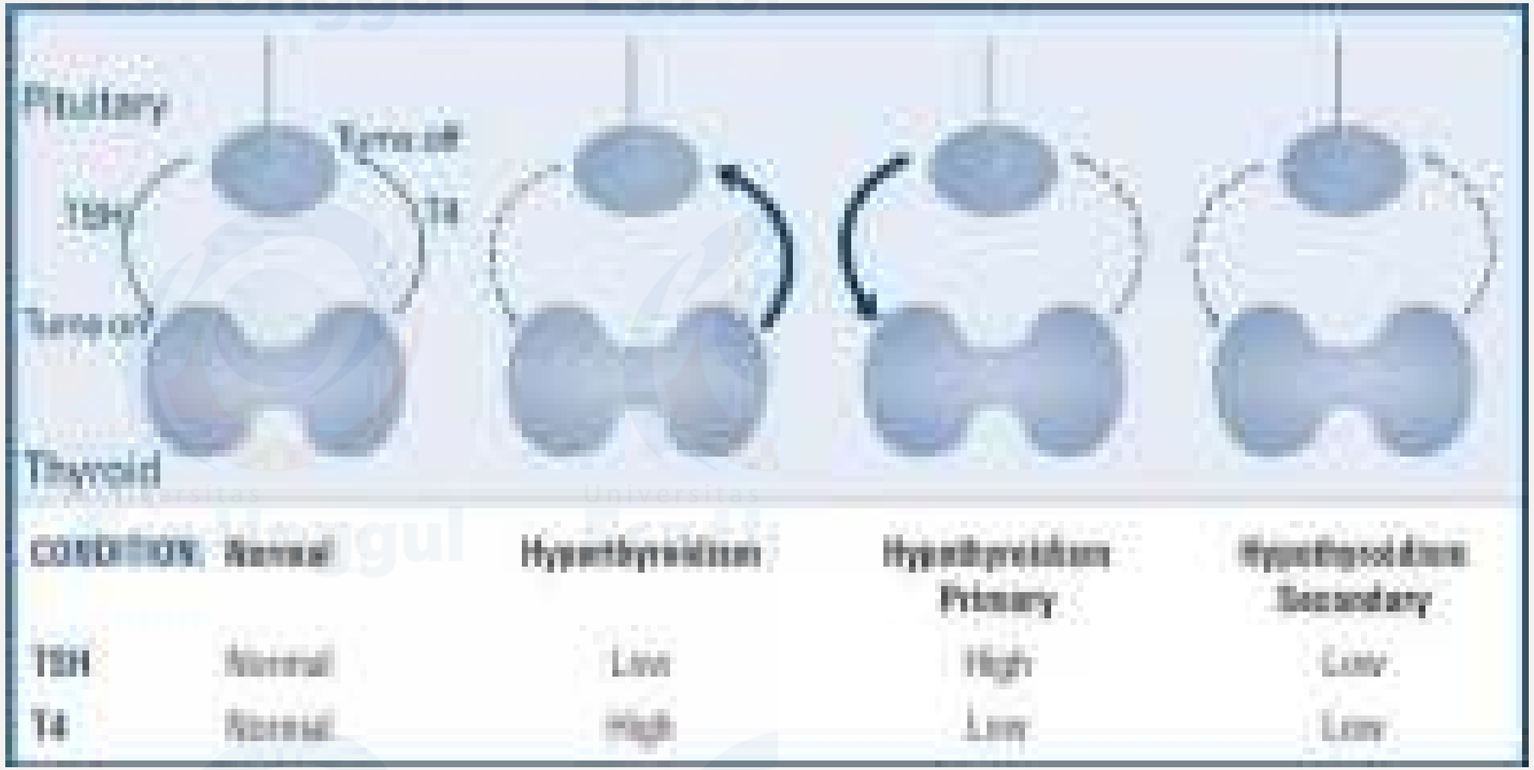
- Defisiensi hormon tiroid, yang kemudian mengakibatkan perlambatan proses metabolik.
- Pada bayi dan anak-anak terjadi perlambatan pertumbuhan dan perkembangan, serta retardasi mental
- Terapi hipotiroid pada dewasa bersifat reversible

Algorithm of Tyroid Disease



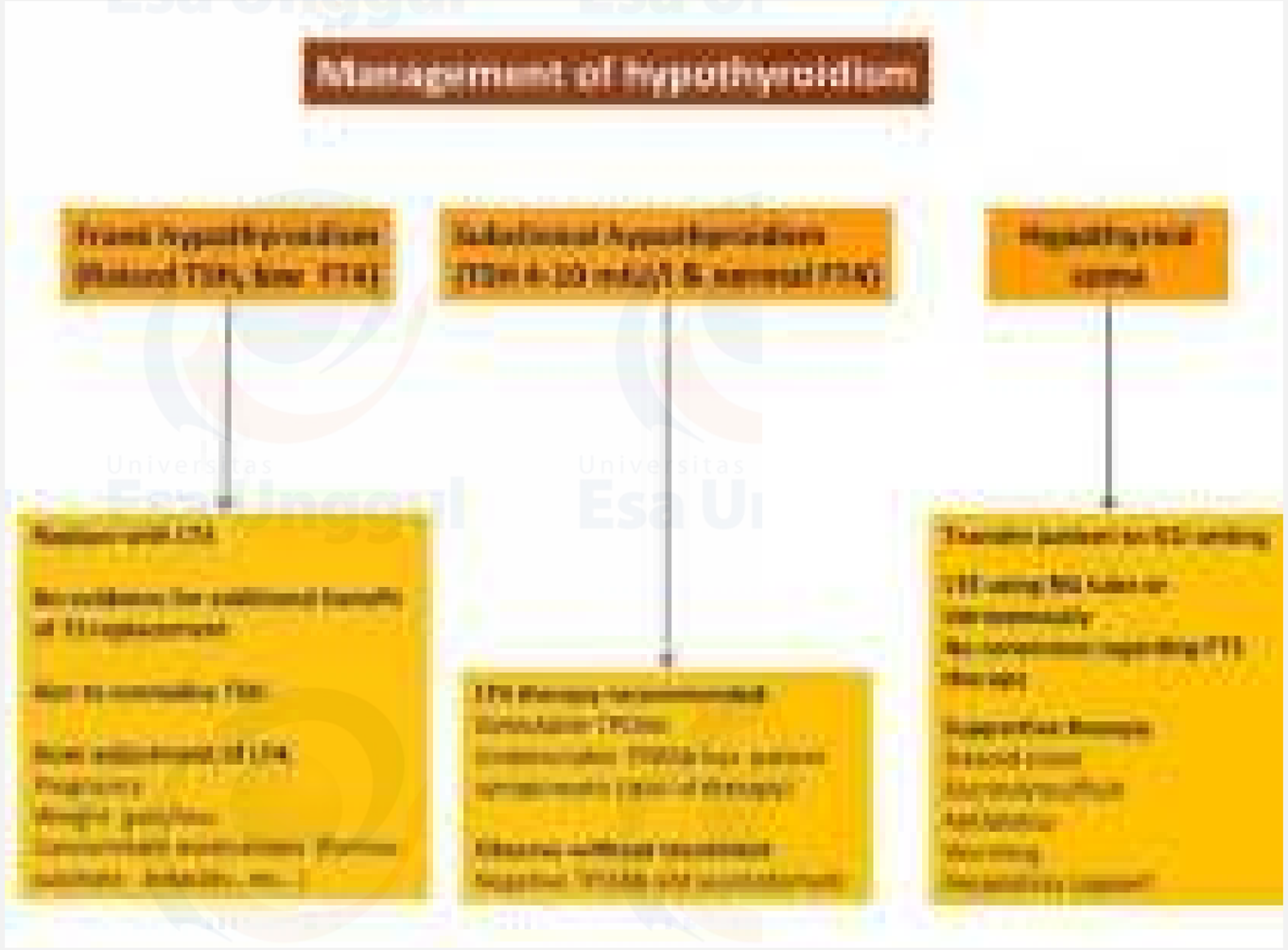
Value of T3 T4 and TSH

Optimal Reference Ranges for Top Thyroid Tests		
TEST NAME	STANDARD REFERENCE RANGE	OPTIMAL REFERENCE RANGE
TSH	0.4 - 5.5 µIU/mL	0.5 - 2 µIU/mL, 0.5 - 2.5 µIU/mL in elderly
Free T4	9 - 23 pmol/L	15 - 23 pmol/L
Free T3	3 - 7 pmol/L	5 - 7 pmol/L
Reverse T3	11 - 21 ng/dl	11 - 14 ng/dl
TPO Antibodies	<35 IU/mL	<2 IU/mL
TG Antibodies	<35 IU/mL	<2 IU/mL



Tatalaksana Hipotiroid

- Levotiroksin (T4), yang terdapat dalam bentuk murni dan stabil
- Levotiroksin dikonversi menjadi T3 di intraselular
- Waktu paruh levotiroksin kira-kira 7 hari, jadi hanya perlu diberikan sekali sehari.
- Preparat ini diabsorpsi dengan, kadar dalam darah
- Diberikan 30 menit sebelum makan, dan dosis harian levotiroksin sebaiknya diminum pagi hari untuk menghindari gejala-gejala insomnia yang dapat timbul bila diminum malam hari.
- Mulai dengan dosis rendah, tingkatkan bertahap 1 x sehari
- Pemberian umumnya seumur hidup



Tatalaksana Hipotiroid

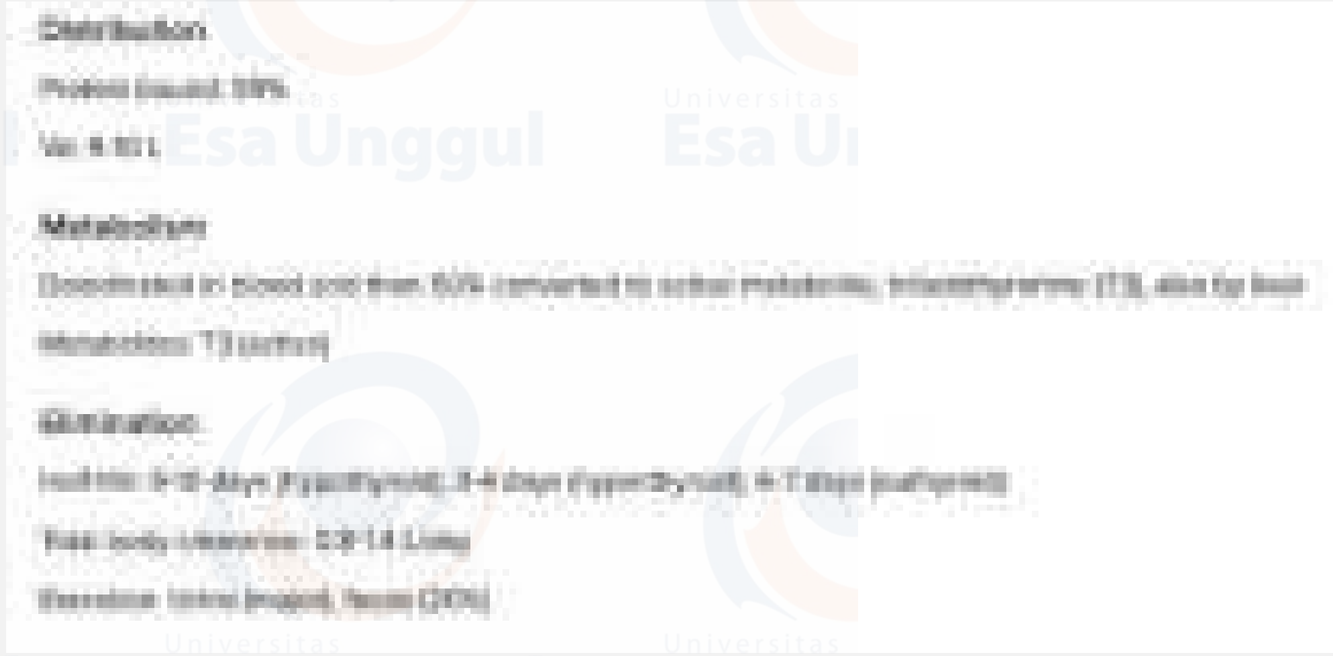
Berat Badan	Indeks Massa Tubuh	Status Kehamilan	Penyebab Hipotiroidisme
Nilai TSH	Usia	Kondisi Umum	Penyakit lain

Faktor penentu dosis Levotirosin

Euthyrox® – Dosis Rekomendasi

Indikasi	Dosis Harian
• Goiter Eutiroid	
• Dewasa	75-200 µg
• Remaja	50-150 µg
• Pencegahan rekuren setelah operasi goiter eutiroid	75-200 µg
• Substitusi terapi pada hipotiroid (dewasa)- inisial	25-50 µg Naikkan 25-50µg tiap 2-4 minggu
• Substitusi terapi pada hipotiroid (dewasa)- pemeliharaan	100-200 µg
• Substitusi terapi pada hipotiroid (lansia)- inisial • Dengan penyakit jantung • Dengan riwayat hipotiroid lama	Mulai dengan dosis 12.5 µg/hari Naikkan perlahan (mis. 12.5 µg/hari dinaikkan tiap 2 minggu)
• Terapi kombinasi dengan terapi hipertiroid	50-100 µg
• Terapi supresi pada kanker tiroid	150-300 µg
• Tes thyroid suppression untuk diagnostik	200 µg

Pharmacokinetics and interactions



Interactions	AGENT	INSTRUCTION AND EXPLANATIONS
Major	Sodium iodide I-131	Contraindicated. Use of thyroid products or iodine before and during treatment with sodium iodide I-131 decreases uptake of sodium iodide I-131 by the thyroid gland
Serious	Anticoagulant, fibrinolitik	Levothyroxine increases effects of other agent with pharmacodynamic synergism. Avoid or Use Alternate Drug.
Monitor Closely	Antidiabetic	Levothyroxine decreases effects of metformin by pharmacodynamic antagonism. Patient should be closely observed for loss of blood glucose control

side effect and contraindication

Angina pectoris
Arthralgia
Congestive heart failure
Flushing
Increased pulse
Myocardial infarction
Palpitations
Arrhythmias
Cramps
Diarrhea
Nervousness
Anxiety

Warnings

Black Box Warnings

Thyroid hormones, either alone or with other therapeutic agents, should not be used for the treatment of obesity or for weight loss.

In euthyroid patients, doses within the range of daily hormonal requirements are ineffective for weight reduction. Larger doses may produce serious or even life-threatening manifestations of toxicity, particularly when given in association with sympathomimetic amines such as those used for their anorectic effects.

Contraindications

Hypersensitivity to thyroid hormone or other ingredients

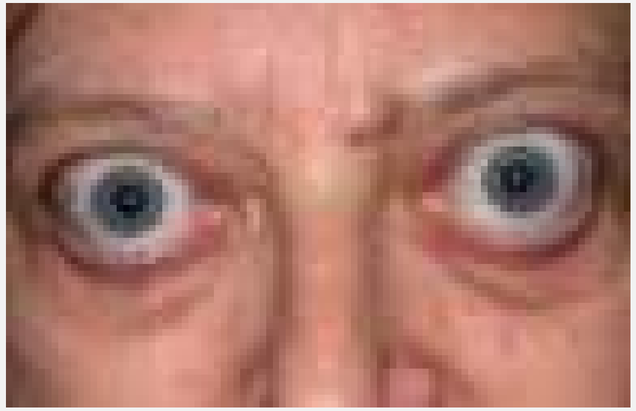
Uncorrected adrenal insufficiency

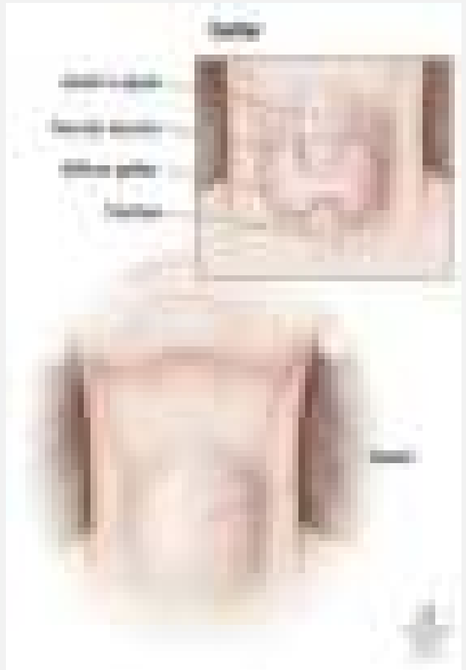
- Levotiroksin dapat digunakan pada pasien hipertiroid dengan Catalan\
  - Sebagai terapi konkomitan bersama dengan obat antitiroid pada hipertiroid setelah fungsi normal tercapai (kecuali untuk Ibu hamil)

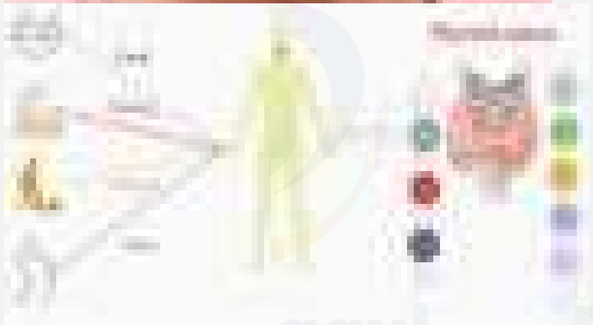
Converting Brands

- Perubahan merek atau formulai dapat mempengaruhi **bioavailabiltas** suatu produk
- Jika peralihan levotiroksin dari satu merek ke merek lain atau ke levotiroksin generic, yg harus dipilih adalah produk levotiroksin yg sdh **memiliki hasil bioekivalensi**, walaupun hasil studi BE tdk menjamin eutiroid akan tetap terjaga setelah perubahan merek levotiroksin
- Dianjurkan melakukan **test TSH darah 6 minggu** setelah peralihan

Etiology of hypertiroid

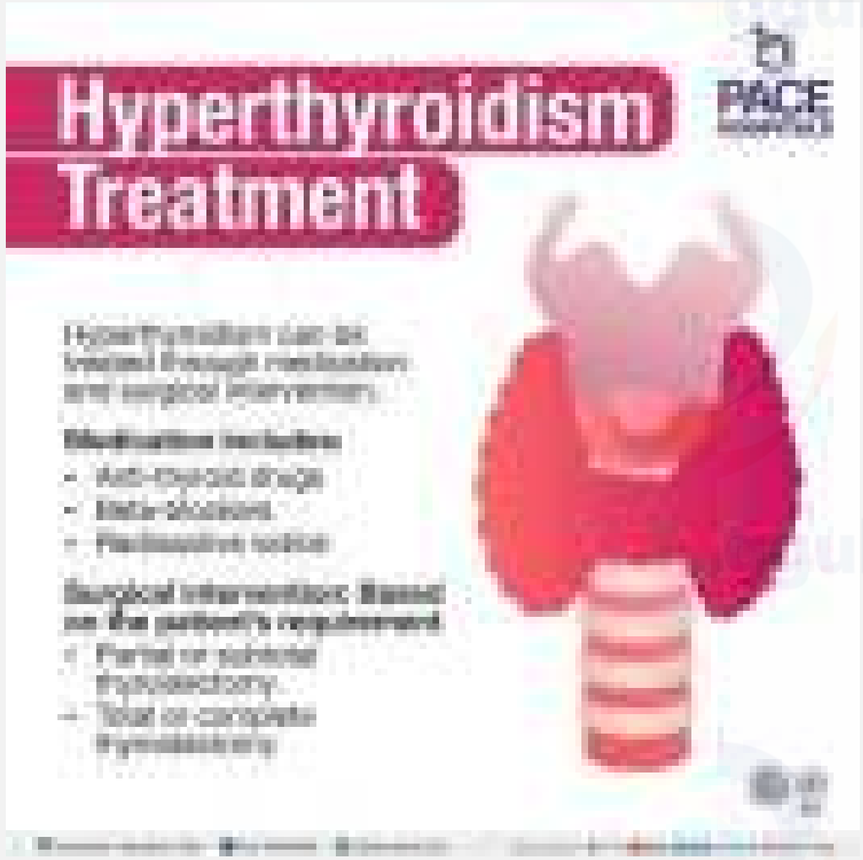


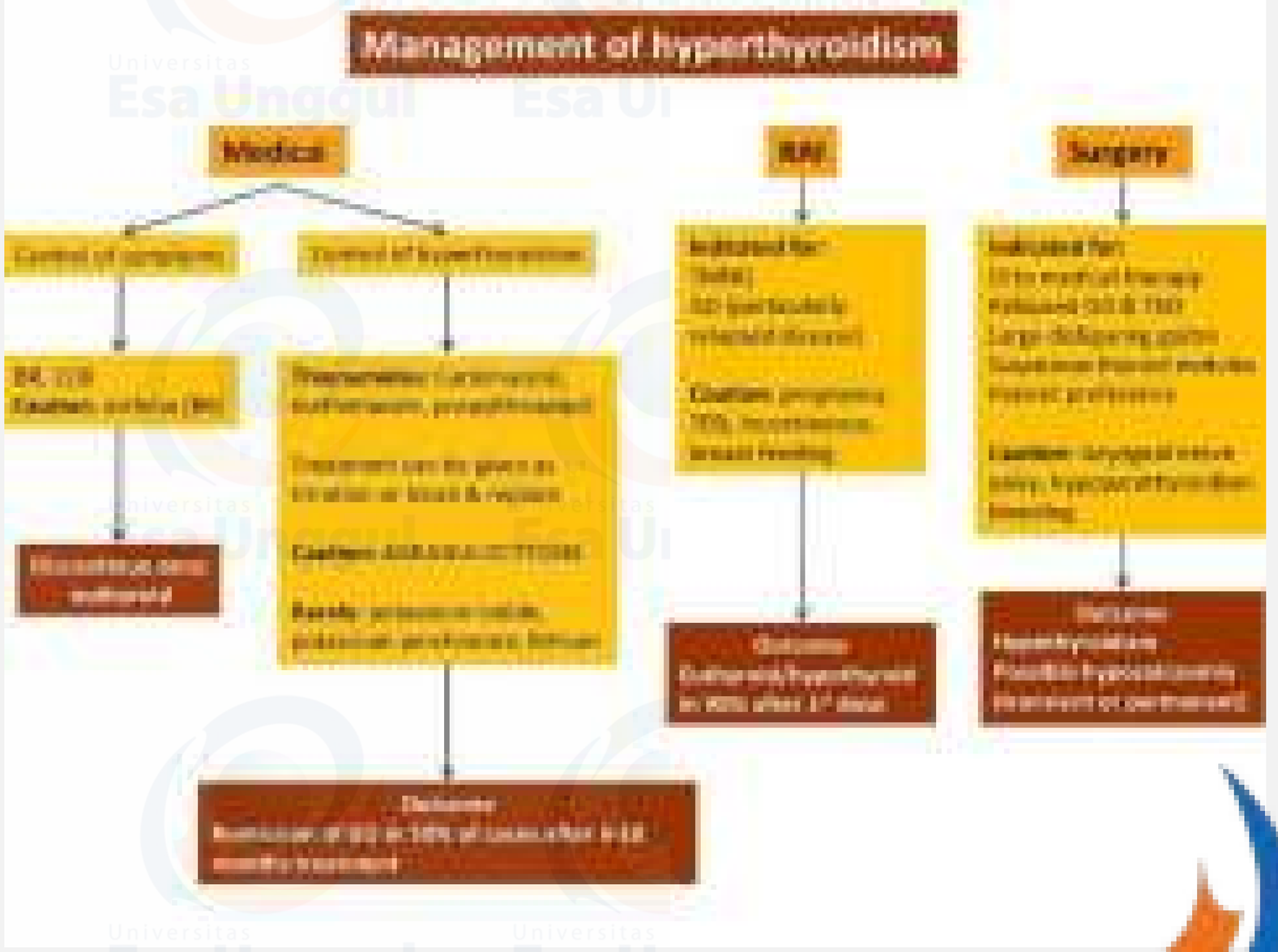




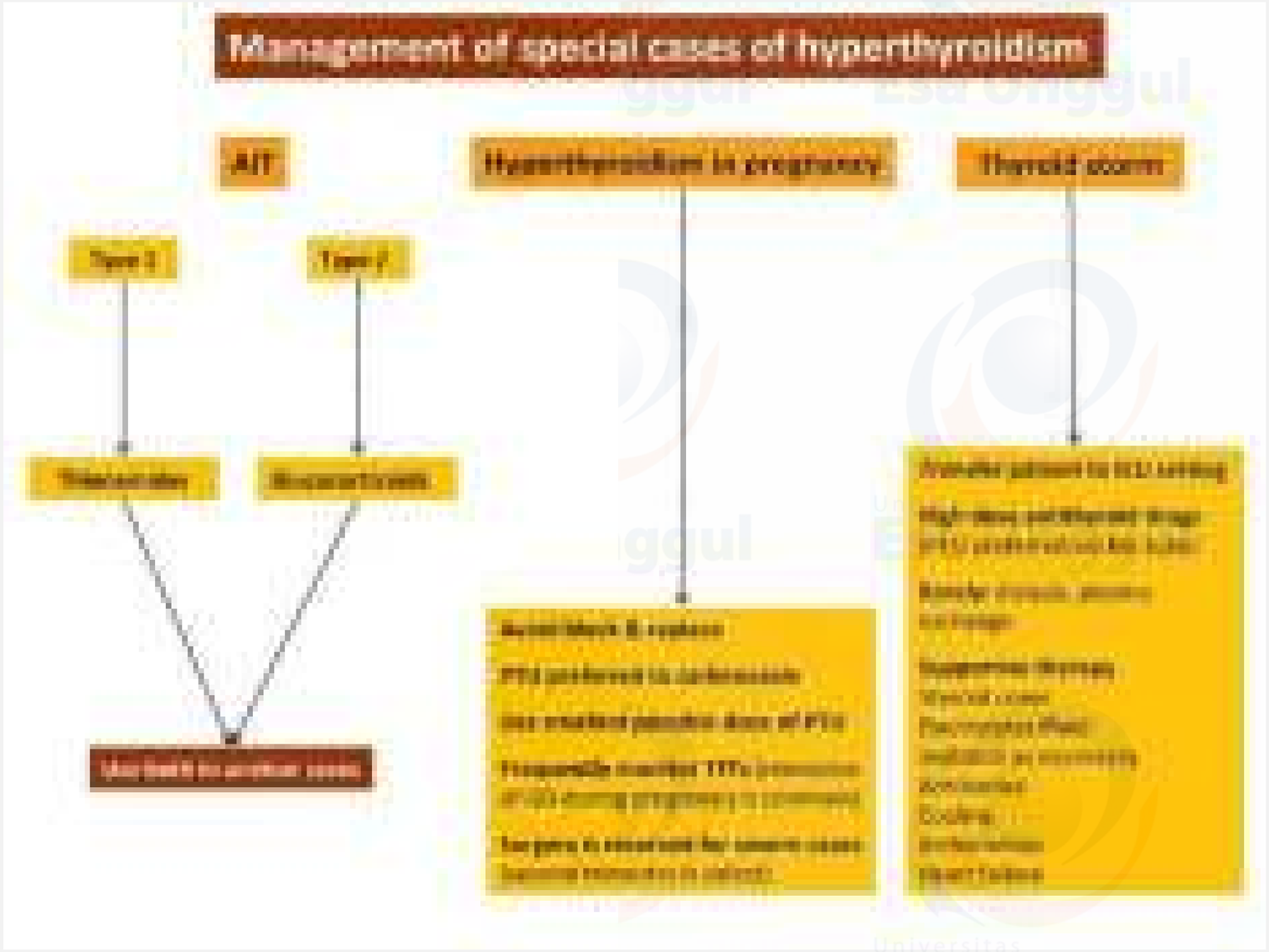
Cause of hyperthyroidism	Frequency and serology	Diagnosis
Graves' disease	80%, thyroid-stimulating antibodies	Clinical examination (thyroid goiter, extrathyroidal complications) Thyroid autoantibodies Thyroid uptake scan in diffuse cases
Toxic nodule or toxic multinodular goiter	15%, activating mutations in TSH receptor and its genes	Clinical examination Thyroid uptake scan
Thyroiditis	5%, autoimmune, viral, or drug-induced destruction	Clinical examination Thyroid uptake scan ESR
TSH-secreting tumors	<1%	Raised TSH and thyroid hormones Pituitary imaging
Exogenous thyroid hormone administration	Variable, excess ingestion of thyroid hormones	Clinical assessment
Hyperemesis gravidarum Choriocarcinoma	Rare, raised hCG	Clinical assessment Absence of thyroid autoimmunity Recent pregnancy Imaging of the pelvis
Metastasis	Rare, as signs may be due to thyroid tissue	Clinical assessment Thyroid uptake scan Imaging of the pelvis
Thyroid hormone resistance	Rare, pituitary resistance or thyroid resistance	Clinical assessment Family history

Tatalaksana Hipertiroid





Tatalaksana Hipertiroid

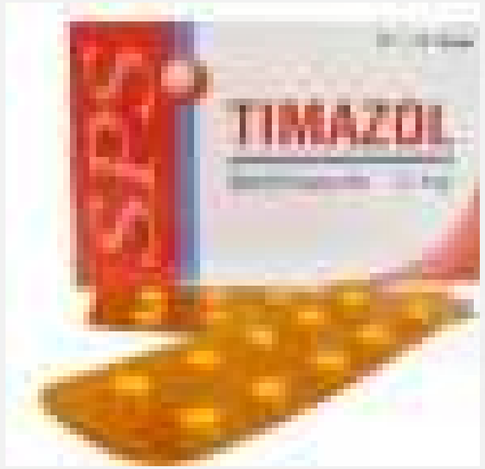


Hipertiroidisme – Terapi Anti-tiroid

Tiamazole	30–40 mg	2.5–10 mg	Paling poten
Carbimazole	30–40 mg	5–15 mg	Prodrug tiamazole
PTU	150–450 mg	50–150 mg	Alternatif pada kehamilan

- Di dalam tubuh,
- Carbimazole akan diubah menjadi Tiamazole 10 mg,
- Carbimazole + 6 mg MMI.

Converting agents



- Metimazol merupakan metabolit aktif Carbimazol, pasien sebelumnya juga sudah mendapatkan carbimazole. Maka dapat diberikan Carbimazole dengan konversi dosis :
  - Carbimazol 50 mg perhari ekivalen dengan methimazole 30 mg perhari (1 mg carbimazole =6/10 methimazole)
  - Aturan penggunaan methimazol 30 mg sehari (1x 3 tablet methimazol 10 mg)

	Thyrosol	PTU
Potensi relatif	10-50	1
Rute administrasi	Oral	Oral
Absorbsi GIT	Hampir seluruhnya	Hampir seluruhnya
T1/2 serum (jam)	6-8	1-2
Durasi aksi (jam)	>24	12-24
Transfer transplasenta	Ya	Ya
Ikatan dengan protein	Tidak	80-90%
Metabolit Aktif	Ya	Ya
Pemberian	Sekali sehari	2-3 kali sehari

	PTU	Thyrosol
Inhibisi konversi T4 menjadi T3	Ya	Tidak
Penyimpanan intra tiroid	Minor	Mayor
Waktu mencapai kadar tiroid normal dalam darah (minggu)	6-10	2-4
Kepatuhan pasien/compliance	Lebih buruk	Lebih baik
Toksisitas:		
- Tergantung dosis	Tidak	Ya
- Agranulositosis	Tidak tergantung dosis	Tergantung dosis
- Hepatotoksik	Kurang	Lebih sering

Thyrosol* memperlihatkan aktivitas tiroid lebih cepat dibanding PTU

Side effect and contraindications

Overdosis	Kontraindikasi

• Menyebabkan penurunkan goiter dan hipotiroidisme:
  ◦ Dosis Thyrocol® diturunkan
  ◦ Ditambah Euthyrox®
	• Hipersensitifitas terhadap thiamazole atau derivat thionamide.
	• Gangguan fetung jenis darah sedang sampai berat (granulositopenia).
	• Kolestasis yang telah disebabkan oleh hipertiroidisme.
	• Kerusakan sumsum tulang setelah terapi dengan tiamazol atau carbimazole.

Minor	Mayor

• Umum (1-5%)
  ◦ Rash.
  ◦ Urticaria.
  ◦ Arthralgia.
  ◦ Demam.
  ◦ Transient neutropenia.
• Jarang
  ◦ Arthritis.
	• Jarang (0,2-0,5%)
	  ◦ Agranulositosis.
	• Sangat Jarang
	  ◦ Hepatitis (PTU).
	  ◦ Aplastic anemia.
	  ◦ Trombositopenia.
	  ◦ Hepatitis Kolestatik.
	  ◦ Hipoglikemia.

Rise your hand!

any question?

PSF316

Farmakoterapi Osteoporosis

Sesi Ke 10

Topik Sesuai RPS:
Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi Osteoporosis

Dosen Pengampu:

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patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

patofisiologi dan farmakoterapi rheumatoid arthritis

Sesi 14

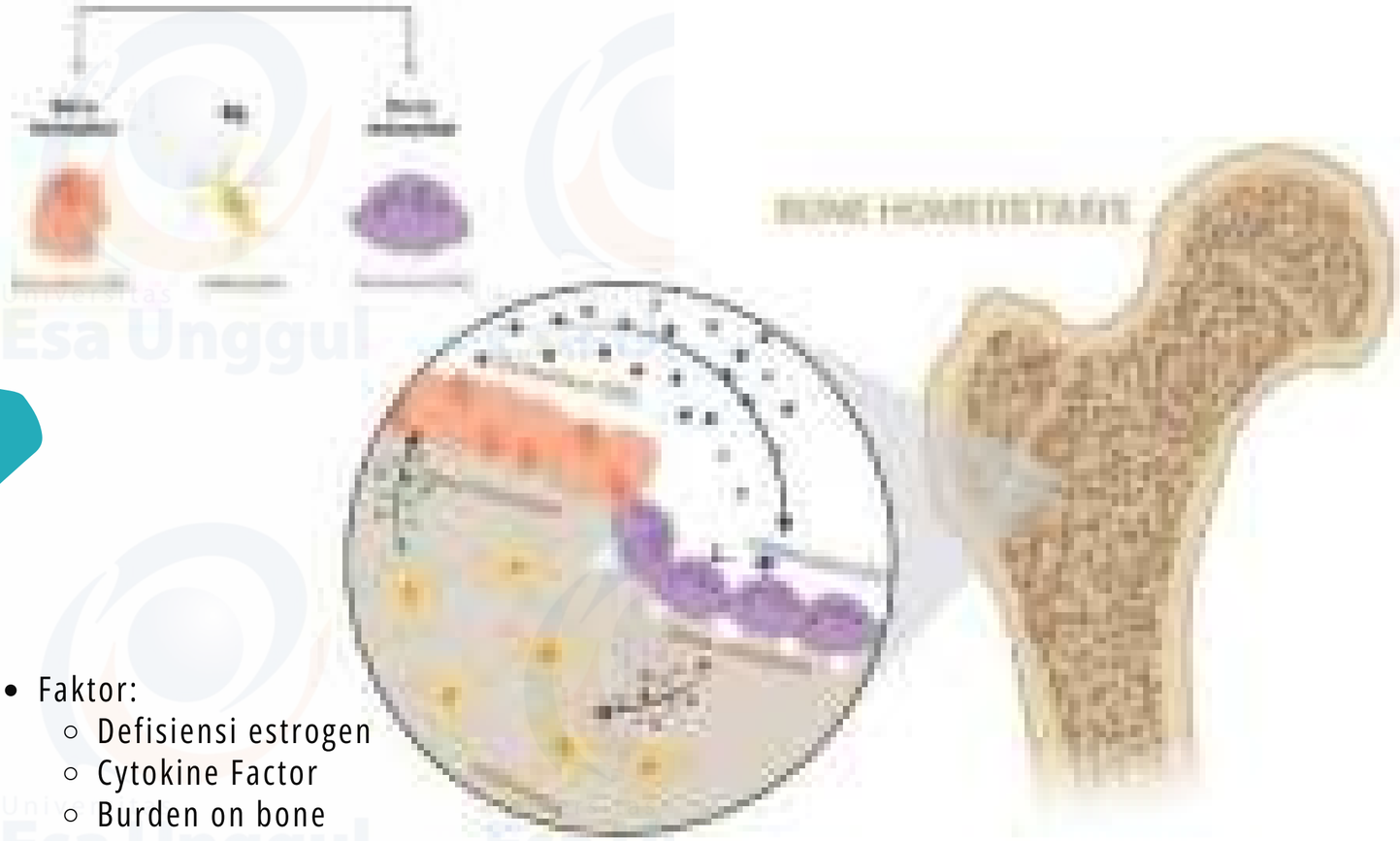
patofisiologi dan farmakoterapi SLE

Ujian Akhir Semester

Osteoporosis

Osteoporosis occurs when the creation of new bone doesn't keep up with the loss of old bone.

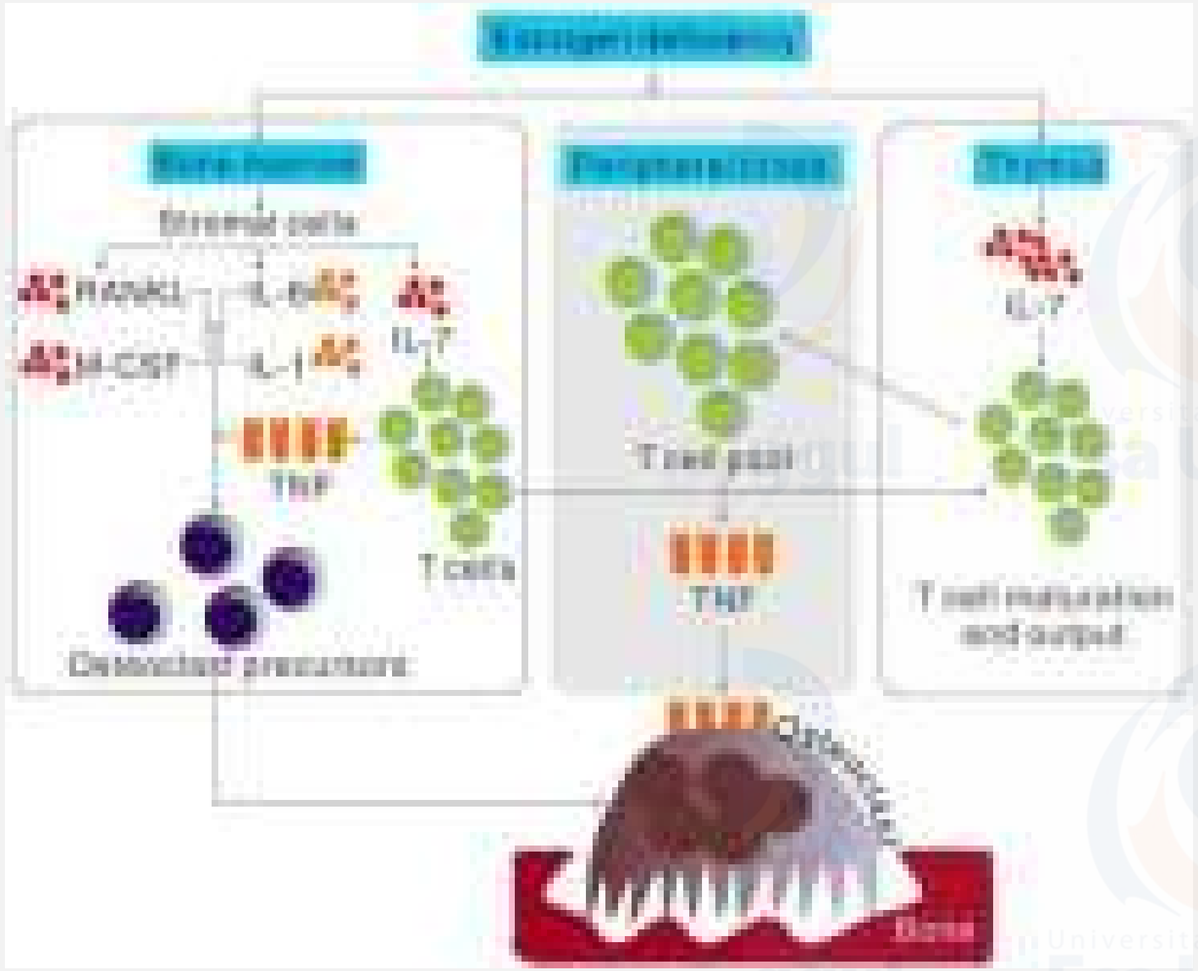
- Osteoporosis: imbalance/ abnormalitas bone turn-over - homeostasis
- Defisiensi hormon estrogen menstimulasi mediator yang berpengaruh terhadap aktivitas sel osteoklast (increased), dibandingkan dengan ketersediaan osteoblast.

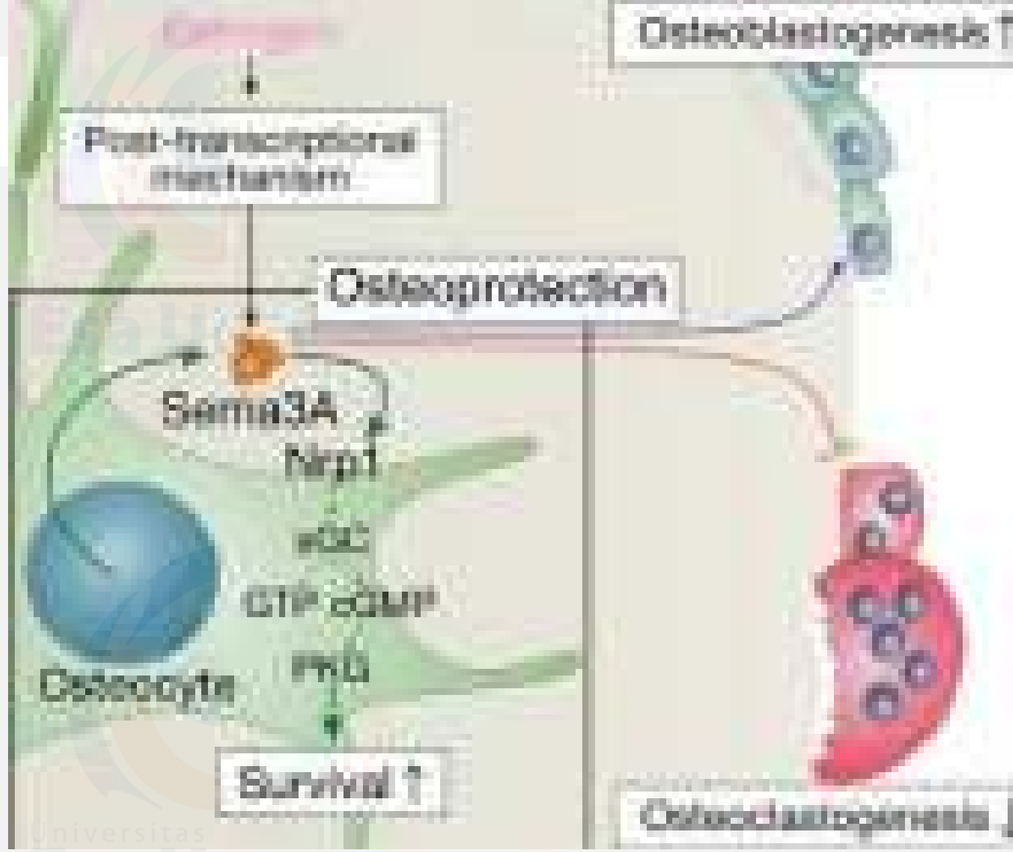


- Faktor:
  - Defisiensi estrogen
  - Cytokine Factor
  - Burden on bone

Bone metabolism

- Defisiensi estrogen menyebabkan ekspresi Sema3A menurun, maka fungsi osteoproteksi akan berkurang.
- Impact: **increased osteoclastogenesis, decreased osteoblastogenesis**





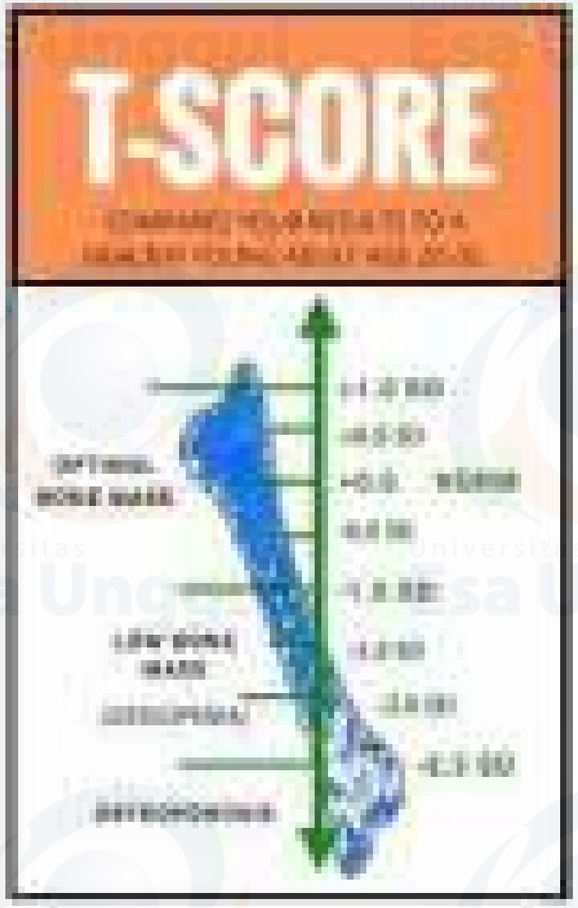
- Sitokin yang menstimulasi osteoklastgenesis: **IL1, IL6, IL7, TNF, MCSF (macrophage stimulating factor)**
- Sitokin yang menghambat osteoklastogenesis: **IL-4, IL-10,IL-18, dan interferon-g,**

- Pembebanan mekanik menimbulkan stress mekanik - resultant tissue deformation : osteoclast stimulation

Value of Bone Marker

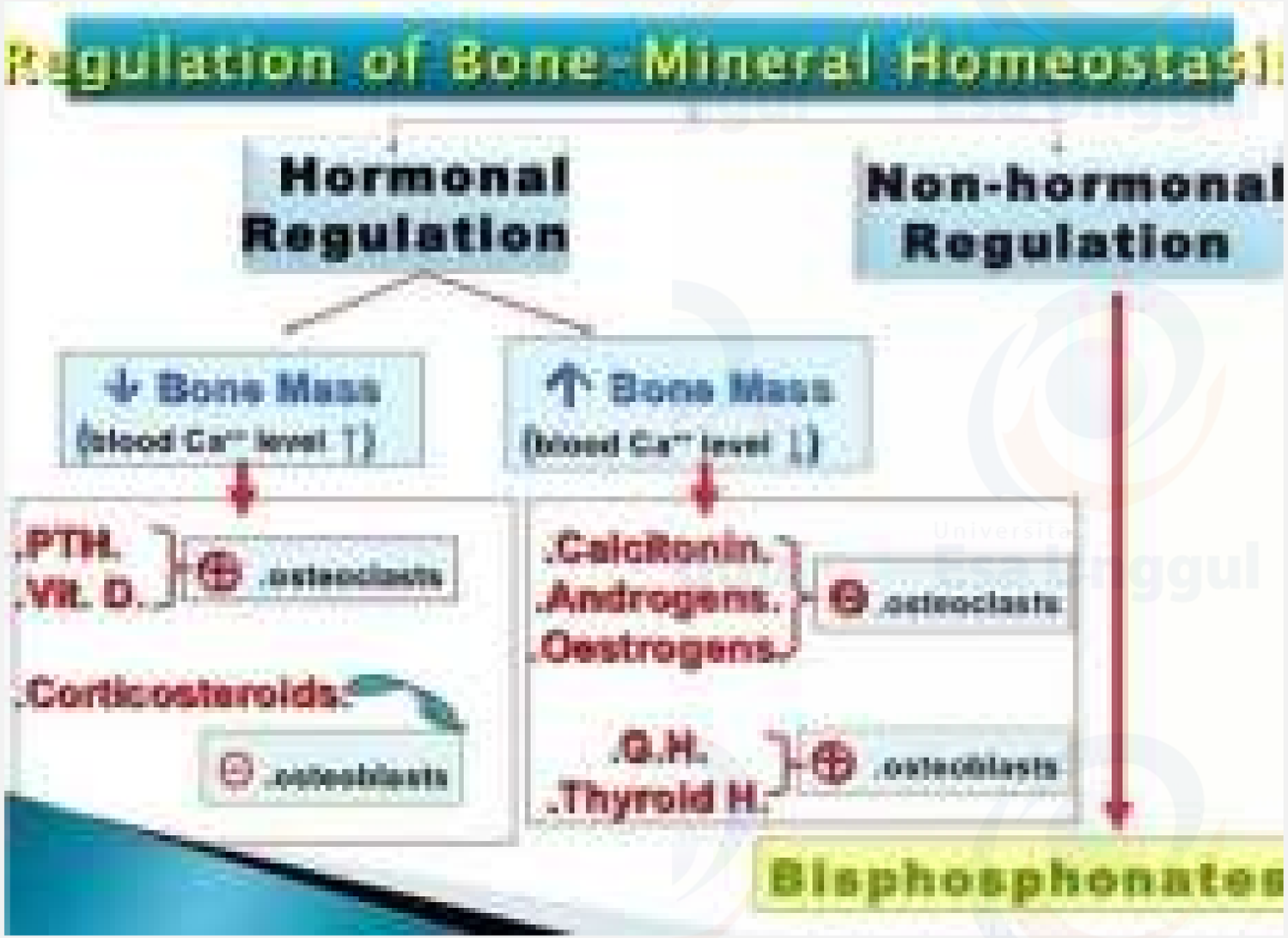
Table 1: Diagnostic criteria for osteoporosis according to WHO.

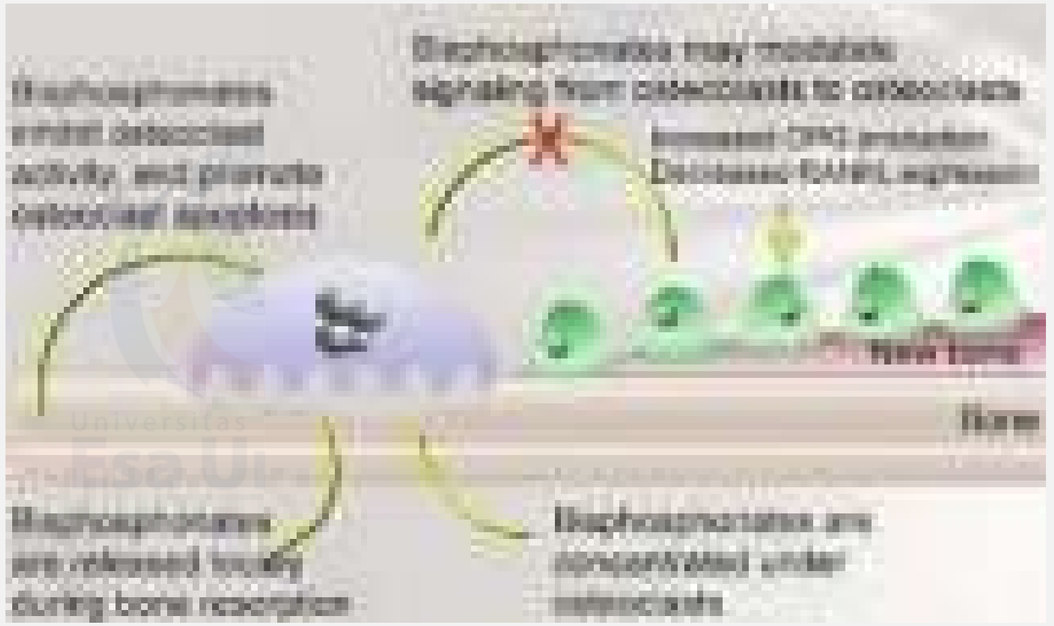
Diagnostic criteria	T – score range	Bone mineral density
Osteoporosis	T Score ≤-2.5	2.5 SD or more below that of the mean level for a young-adult reference population
Osteopenia	-2.5<T-Score -1.0	Between 1.0 and 2.5 SD below that of the mean level for a young-adult reference population
Severe Osteoporosis	T Score ≤-2.5 with fragility fracture	2.5 SD or more below that of the mean level for a young-adult reference population with fractures
Normal	T-Score ≥ – 1.0	Within 1 SD of the mean level for a young-adult reference population



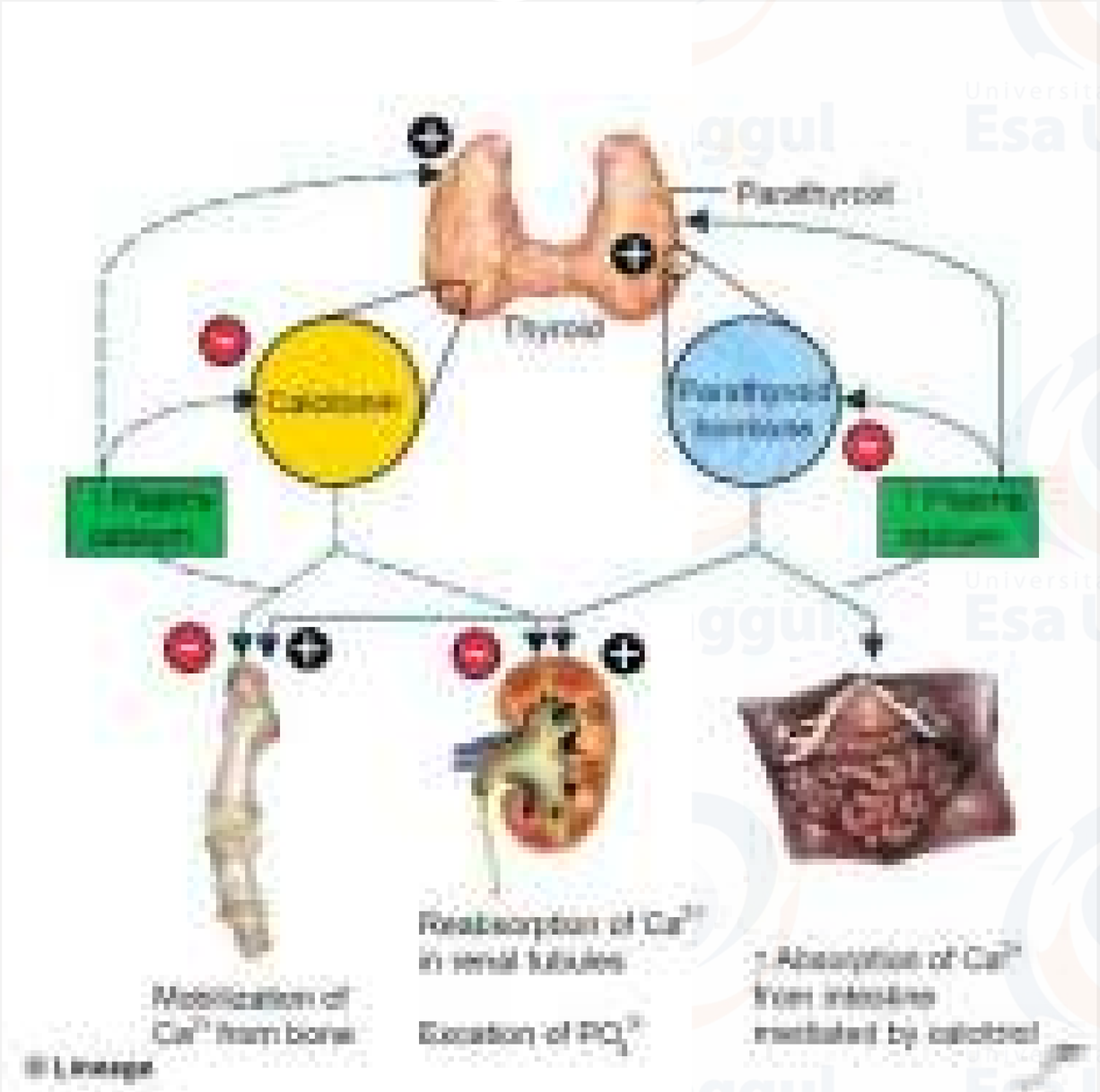
- Penentuan massa tulang secara radiologis, dengan densitometer DEXA (Dual Energy X-ray Absorptiometry)
- Pemeriksaan laboratorium berupa parameter biokimiawi untuk bone turnover, terutama mengukur produk pemecahan kolagen tulang oleh osteoklas.

Regulation bone mineral





Regulation bone related to thyroid

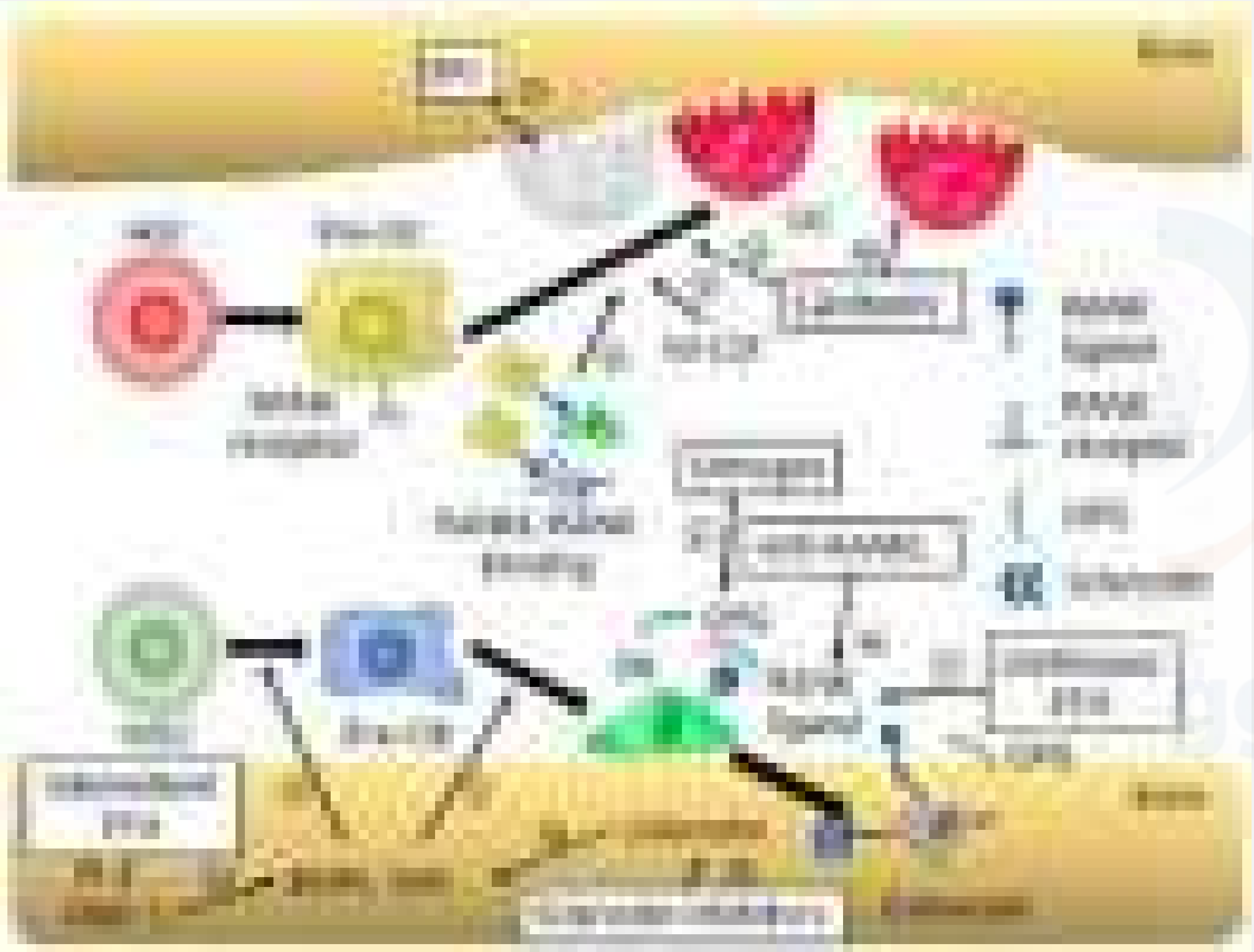


- Calcitonine: lower calcium levels in your blood (not your bones). It does this in two main ways:
  - Calcitonin inhibits (blocks) the activity of osteoclasts, which are cells that break down bone.
  - Calcitonin can decrease the amount of calcium that your kidneys reabsorb and release back into your bloodstream, thus causing lower blood calcium levels.
- PTH stimulates the release of calcium:
  - An indirect process through osteoclasts which ultimately leads to the resorption of the bones
  - regulate the renal reabsorption
  - absorbtion calcium from intestine

Osteoporosis Treatment

Antiresorptives:
Estrogen (raloxifene), kalsitonin, bisfosfonat, denosumab (anti RANK)

Anabolic agents:
Teriparatide



Summary of Evidence on Pharmacologic Treatments for Low BMD and Osteoporosis

Treatment	Effect on fracture risk in women with osteoporosis (evidence quality): Vertebral	Nonvertebral	Hip	Adverse effects (evidence quality)
Bisphosphonates				
Alendronate (Fosamax)	Improves (high)	Improves (high)	Improves (high)	Mild upper GI symptoms (high)
Ibandronate (Boniva)	Improves (high)	Unclear	Unclear	Mild upper GI symptoms (high) Myalgias, cramps, limb pain
Risedronate (Actonel)	Improves (high)	Improves (high)	Improves (high)	Mild upper GI symptoms (high)
Zoledronic acid (Reclast)	Improves (high) [illegible]	Improves (high)	Improves (high)	Mild upper GI symptoms, hypocalcemia, influenza-like symptoms (high) [illegible]
Denosumab (Prolia)	Improves (high)	Improves (high)	Improves (high)	Mild upper GI symptoms (high) Infection (moderate) Rash
Teriparatide (Forteo)	Improves (high)	Improves (high)	Unknown	Mild upper GI symptoms, headache, hypercalcemia (high) [illegible]
Raloxifene (Evista)	Improves (high)	No effect	No effect	Hot flashes, thromboembolic events (high) Pulmonary embolism, cerebrovascular death
Calcium and vitamin D	Unclear	Unclear	Unclear	[illegible]
Menopausal hormone therapy	Improves in postmenopausal women not selected for having osteoporosis [illegible] (high) [illegible]	Unclear	Improves in postmenopausal women not selected for having osteoporosis [illegible] (high)	Increased risk of cerebrovascular accidents and thromboembolic events (high)

Tatalaksana Osteoporosis

- In those with **no prior fragility fractures** or with moderate fracture risk:

First line: Alendronate, risedronate, zoledronic acid, or denosumab (Prolia, Amgen)
Second line: ibandronate and raloxifene are considered alternatives.

- In those with **prior fragility fractures** or indicators of high fracture risk

First Line: denosumab, teriparatide (Forteo, Lilly), and zoledronic acid are recommended
Second Line: alendronate and risedronate as alternatives.

- For those **unable to use oral therapy**

First Line: Teriparatide, denosumab, or zoledronic acid should be considered

- Initial therapy for **spine-specific efficacy**

Drugs of choice: Raloxifene or ibandronate may be used

Indicators of high fracture risk include advanced age, fragilty, glucocorticoids, very low T-scores, and increased fall risk.

Tatalaksana Osteoporosis

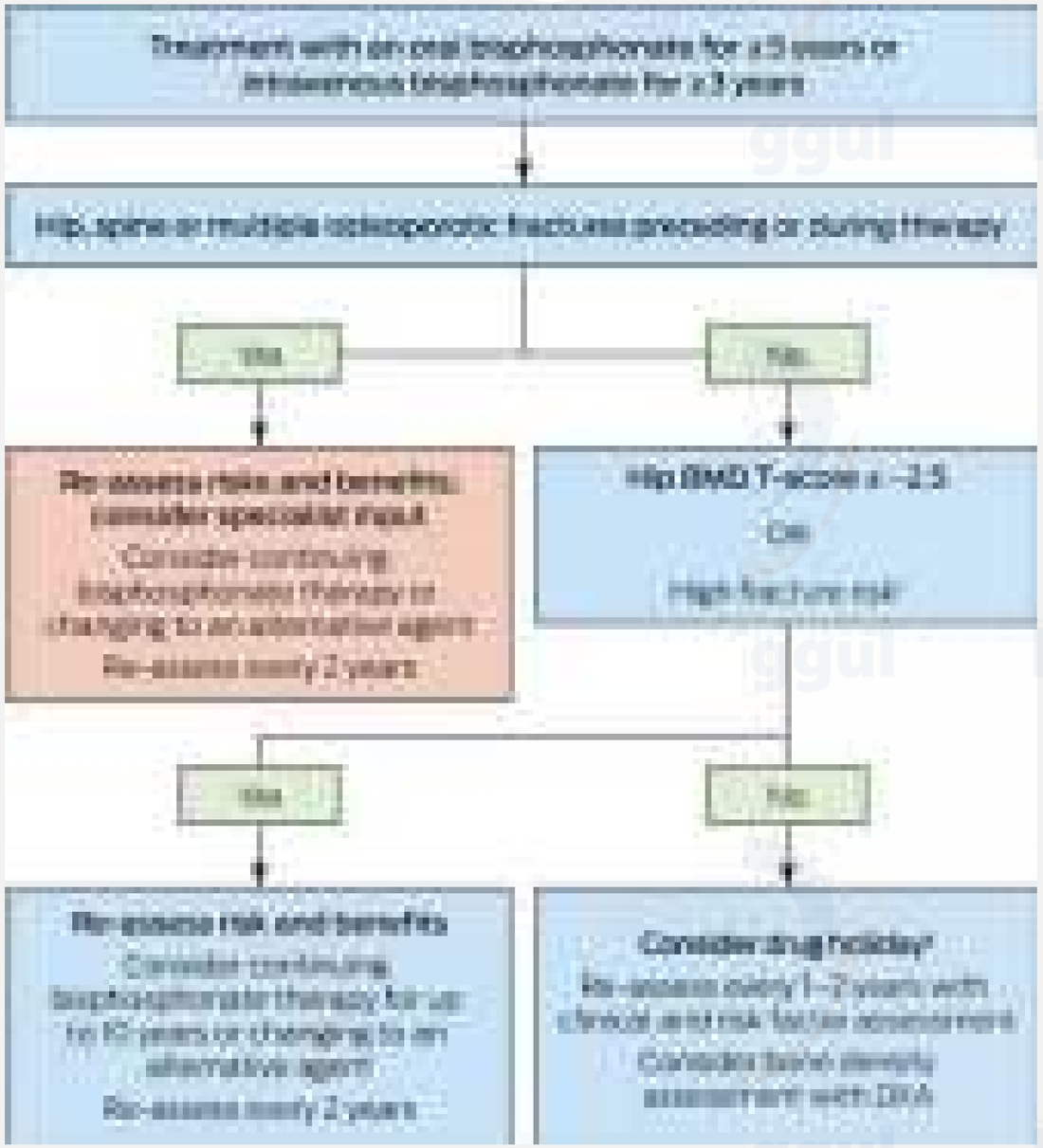


Table 3 Dose Recommendations for Bisphosphonates

Bisphosphonate	Prophylactic Dose	Treatment Dose	CrCl Recommendation
Alendronate	5 mg PO once daily or 35 mg PO once weekly	10 mg PO once daily or 70 mg PO once weekly	≥ 35 mL/min
Risedronate (IR)	5 mg PO once daily or 35 mg once weekly	5 mg PO once daily or 35 mg PO once weekly or 150 mg PO once monthly	≥ 30 mL/min
Zoledronic acid	5 mg IV every 2 years	5 mg IV once yearly	≥ 35 mL/min
Ibandronate	2.5 mg PO once daily or 150 mg PO once monthly	2.5 mg PO once daily or 150 mg PO once monthly or 3 mg IV every 3 months	≥ 30 mL/min

CrCl = creatinine clearance, IR = immediate release, IV = intravenous, PO = orally

Estrogen

- Estrogen sangat baik diabsorbsi melalui kulit, mukosa vagina, dan saluran cerna.
- Efek samping : nyeri payudara (mastalgia), retensi cairan, peningkatan berat badan, tromboembolisme, dan pada pemakaian jangka panjang dapat meningkatkan risiko kanker payudara.
- Kontraindikasi absolut : kanker payudara, kanker endometrium, hiperplasiendometrium, perdarahan uterus disfungsional, hipertensi, penyakit tromboembolik, karsinoma ovarium,dan penyakit hait yang berat

Bifosfonat

- Pemberian bisfosfonat secara oral akan diabsorpsidi usus halus dan absorpsinya sangat buruk
- Absorpsi terhambat bila diberikan bersama-sama dengan kalsium, kation divalen lainnya, dan berbagai minuman lain kecuali air.
- Idealnya diminum pada pagi hari dalam keadaan perut kosong.
- Setelah itu penderita tidak diperkenankan makan apapun minimal selama 30 menit, dan selama itu penderita harus dalam posisi tegak, tidak boleh berbaring.

Rise your hand!

any question?

PSF316

Farmakoterapi Epilepsi

Sesi Ke 11

Topik Sesuai RPS:
Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi Epilepsi

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Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

patofisiologi dan farmakoterapi epilepsi

Sesi 12

patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

patofisiologi dan farmakoterapi rheumatoid arthritis

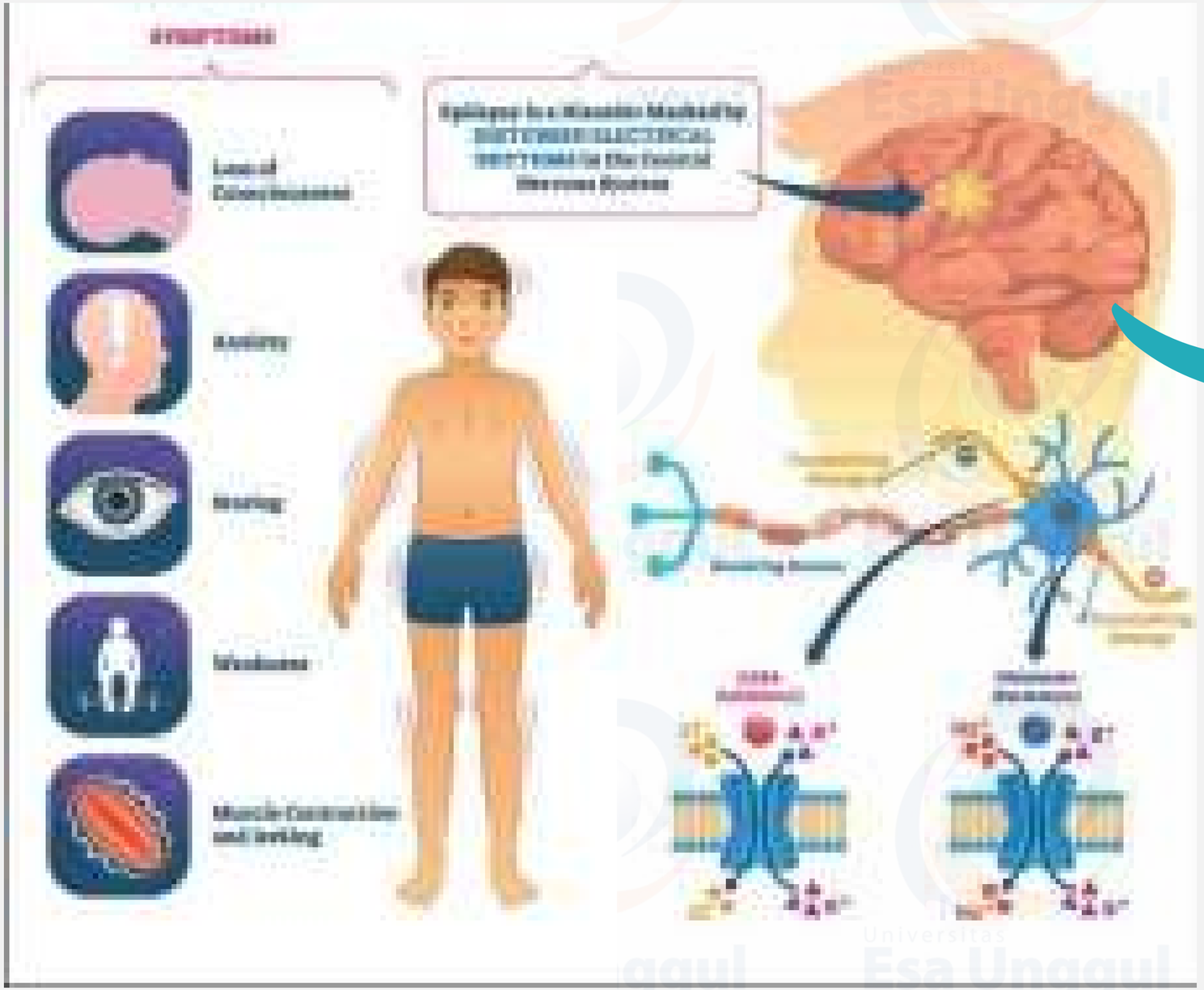
Sesi 14

patofisiologi dan farmakoterapi SLE

Ujian Akhir Semester

Epilepsi

Kejadian kejang kambuhan (repetitive - berulang - kronis)



- Manifestasi klinis dari aktivitas neuron yang berlebihan dalam korteks serebral
- Dampak yang tidak dapat diprediksi, sesuai dengan luas daerah otak fugsional yang terlibat

ETIOLOGI:

- Aktivitas saraf abnormal (patologis)
- Gangguan metabolik/ lesi mikro di otak (trauma/ cacat kongenital)
- Hipoksia
- Infeksi
- Febrile
- Tumor

Genetical Epilepsy

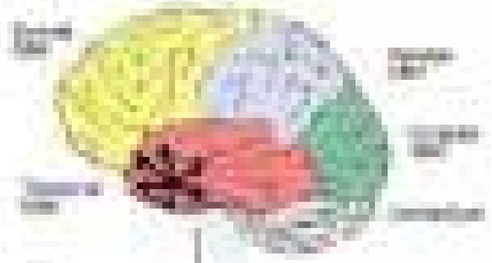
Table 1. Epilepsy Syndromes Associated with Single-Gene Mutations.

Epilepsy Syndrome	Gene	Gene Product*	Study
Generalized epilepsy with febrile seizures plus	SCN1B	Sodium-channel subunit	Wallace et al.[34]
	SCN1A	Sodium-channel subunit	Escayg et al.[35]
	SCN2A	Sodium-channel subunit	Sugawara et al.[36]
	GABRG2	$GABA_A$-receptor subunit	Baulac et al.[37]
Benign familial neonatal convulsions	KCNQ2	Potassium channel	Biervert et al.,[38] Singh et al.[39]
	KCNQ3	Potassium channel	Charlier et al.[40]
Autosomal dominant nocturnal frontal-lobe epilepsy	CHRNA4	Neuronal nicotinic acetylcholine-receptor subunit	Steinlein et al.[41]
	CHRNB2	Neuronal nicotinic acetylcholine-receptor subunit	Fusco et al.[42]
Childhood absence epilepsy and febrile seizures	GABRG2	$GABA_A$ receptor subunit	Wallace et al.[43]
Autosomal dominant partial epilepsy with auditory features	LGI1	Leucine-rich transmembrane protein	Kalachikov et al.[44]

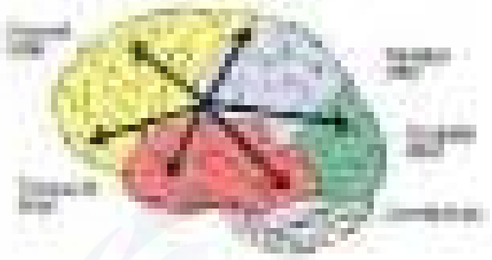
*$GABA_A$ denotes γ-aminobutyric acid type A.

Seizure Classification

Partial



Generalized



Simple

Dystonic posturing
- **Upper extremities (fencing)**
- **Lower extremities**

Complex

- **Automatisms (manual, oral)**
- **Frontal: fencing posture**
- **Amnesia for event and confusion often after event**

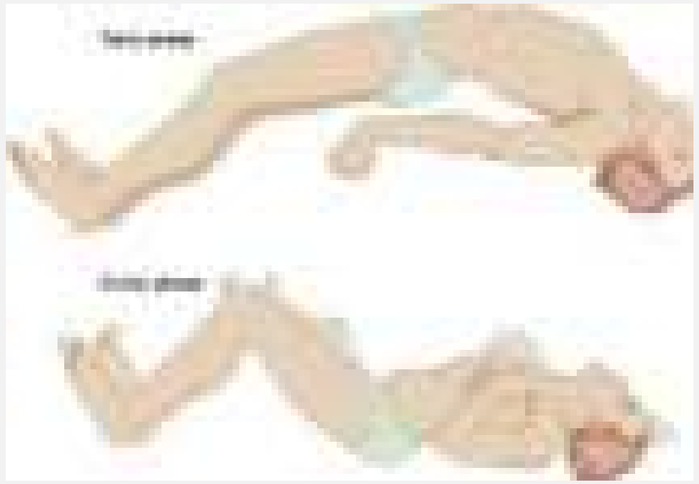
Tonic Clonic

Absence

Tonic or Atonic

Myoclonic

Type and symptomp of seizure



Tonic:

- Sudden muscle stiffening
- Impaired consciousness
- Failing to ground

Clonic:

- Rhytm jerking
- Involve arms, neck, phase

Atonic:
Muscles suddenly become limp

Absence:
Seizures that generally last just a few seconds, and are characterized by a blank or “absent” stare.

Fencing movements

Dystonia movement

Type of seizure

Status epileptikus

- Kejang umum yang terjadi selama 5 menit atau lebih atau kejadian kejang 2 kali atau lebih tanpa pemulihan kesadaran di antara dua kejadian tersebut

Tipe 1 (tidak ada lesi struktural)	Tipe 2 (Ada lesi struktural)
• Infeksi • Infeksi CNS • Gangguan metabolik • Turunnya level AED • Alkohol • Idiopatik	• Anoksia/hipoksia • Tumor CNS • CVA • Overdose obat • Hemorragi • Trauma

Seizure type	Symptoms	Approximate duration
Tonic–clonic	Initial loss of consciousness. In the tonic phase, the person will go still and may cry out as air in their lungs. In the subsequent clonic phase, they will make jerky movements, breathing may be affected, they may go blue around the mouth, and, in some cases, they may experience incontinence of their bladder and/or bowels.	1–3 minutes
Tonic	Instant loss of consciousness. Person goes still and falls to the ground – usually backwards.	Unknown
Atonic seizures	Muscles relax and the person goes floppy – usually fall forwards, potentially injuring themselves.	15 seconds
Absence seizures	Person may appear to pause and stare for a second during a very brief loss of consciousness. If they are speaking, they will stop briefly and then continue as if nothing has happened. More common in children but can occur in adults.	A few seconds; however, a person may have tens or even hundreds of absences throughout the day.
Myoclonic seizures (myoclonic jerks)	Very brief loss of consciousness leading to the person's arms and/or legs jerking sharply and uncontrollably. If the person is holding an object, they may drop it.	Fraction of a second but may occur in clusters.

Prinsip Umum Terapi Epilepsi

Monoterapi

- Mengurangi potensi ADRs
- Meningkatkan adherence

Minimalisir sedatif

- Efek toleransi
- Efek pada intelegensia, memori, kemampuan motorik

Therapy on type

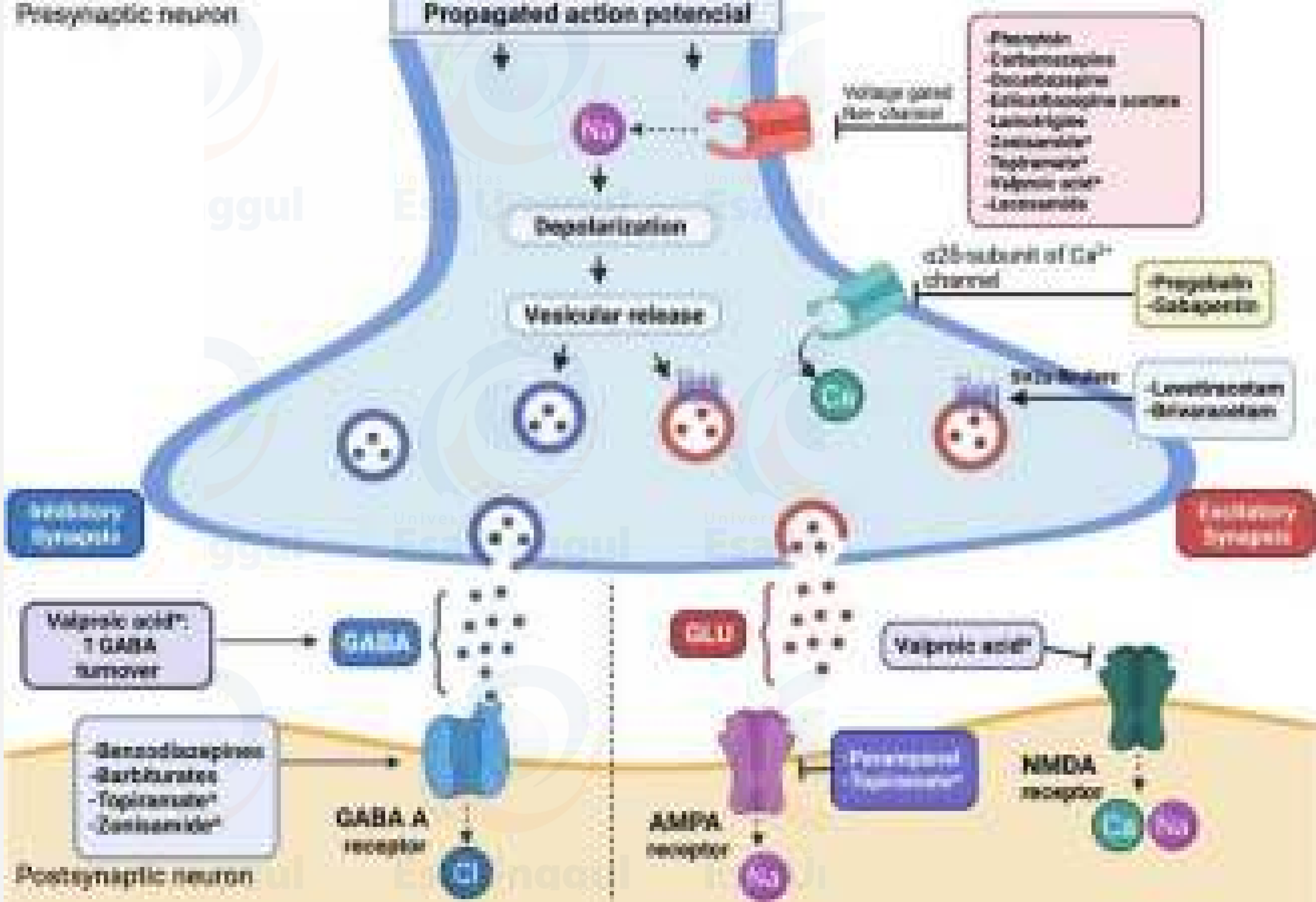
- Ketepatan diagnosa jenis epilepsi
- Pemilihan terapi berdasarkan jenis

Start low, Monitoring

- Penentuan dosis terendah, dan tappering on/ off
- Variasi respon individu - rutin evaluasi - ganti terapi (tetap monoterapi)

Class of therapy on Epilepsy

1. Inaktivasi Kanal Na+ - inhibisi depolarisasi
2. Aktivasi GABAergik - transmisi inhibitori
3. Inaktivasi Kanal Ca2+ - inhibisi depolarisasi
4. Inhibit NMDA - glutamate sites


Presynaptic neuron
Propagated action potencial
Depolarization
Vesicular release
Voltage gated Na+ channel
-Phenytoin
-Carbamazepine
-Oxcarbazepine
-Eslicarbazepine acetate
-Lamotrigine
-Lacosamide*
-Topiramate*
-Valproic acid*
-Lacosamide
α2δ subunit of Ca2+ channel
-Pregabalin
-Gabapentin
SV2A Protein
-Levetiracetam
-Brivaracetam
Inhibitory Synapse
Excitatory Synapse
Valproic acid*: ↑ GABA turnover
GABA
GLU
Valproic acid*
-Benzodiazepines
-Barbiturates
-Topiramate*
-Zonisamide*
GABA A receptor
AMPA receptor
Perampanel
NMDA receptor
Postsynaptic neuron

Antiepileptic drugs agent

Drugs	Mechanism of action	Side effects	Others notes
Carbamazepine	• Blocks Na+ channels, increasing their refractory period	• Hyponatremia (secondary to SIADH), especially in elderly • Characteristic rash • Stevens-Johnson syndrome • Blood dyscrasias: neutropenia, leukopenia, thrombocytopenia, pancytopenia, and anaemias • Dizziness and ataxia • Visual disturbances (e.g. diplopia) • Anaemia (hypersensitivity reaction)	• Cx: acute porphyrias, ↓ AV conduction abnormalities and history of bone marrow depression • Caution: cardiac disease • May exacerbate myoclonic and absence seizures • Withdraw immediately in cases of aggravated liver dysfunction or acute liver disease
Topiramate	• Blocks Na+ channel • Binds to GABAA receptor • Blocks high voltage Ca channel • Inhibits carbonic anhydrase and may act on glutamate (NMDA) when	• Paresthesia • Weight loss • Nervousness, anxiety depression • Glaucoma, oligohydrosis and hyperthermia secondary to decreased carbonic anhydrase activity • Teratogenic → cleft palate	• Caution: acute porphyrias, risk of metabolic acidosis, risk of nephrolithiasis
Sodium valproate	• Blocks Na+ channel • Blocks GABA transaminase • Blocks T type calcium channels	• Increased appetite and weight gain • Ataxia and tremor • Hepatitis and pancreatitis (rare) • Thrombocytopenia • Teratogenic • Hyponatremia	• Cx: acute porphyrias, personal or family history of severe hepatic dysfunction, known/ suspected mitochondrial disorders • Caution: SLE

Antiepileptic drugs agent

Drugs	Mechanism of action	Side effects	Other notes
Lamotrigine	• Blocks Na+ channel • Blocks high voltage dependent calcium channels	• Drowsiness and dizziness • Headache • Diplopia • Nausea • Steven Johnson syndrome • Aseptic/aseptic hypersensitivity syndrome	• Mal-associated myoclonic seizures and Parkinson's disease
Ethosuximide	• Block T-type voltage sensitive calcium channels	• Nausea and vomiting • Aggression • Sleep disturbance, drowsiness • Agranulocytosis • Steven Johnson syndrome • Depression, suicidal tendencies • Lupus like syndrome	• Avoid in acute porphyrias
Levetiracetam	• Precise mechanism of action is unknown	• Fatigue • Infection • Drowsiness, dizziness, agitation, anxiety and irritability • Depression, suicidal tendencies	

Antiepileptic drugs agent

Drugs	Mechanism of action	Side effects	Other notes
Phenytoin	• Blocks Na+ channel increasing their refractory period • Blocks voltage dependent calcium channels at very high concentration	• Acute dizziness, diplopia, nystagmus, slurred speech, ataxia, confusion, seizures • Gingival hyperplasia • Hirsutism • Megaloblastic anaemia (altered folate metabolism) • Peripheral neuropathy • Enhanced vitamin D metabolism causing osteomalacia • Steven-Johnson syndrome (SJS) • Anticonvulsant hypersensitivity syndrome • Teratogenic – cleft palate and congenital heart disease	• IV: acute porphyrias, second and third degree heart block, sinus bradycardia, sino-atrial block • May exacerbate absence, myoclonic and generalized seizures • Discontinue immediately if hepatotoxicity • Pre-treatment screening of HLA-B 1502 allele in Han Chinese or Thai Dogn - increased risk of SJS • Consider vitamin D supplements
Benzodiazepines • Lorazepam • Diazepam	• Binds to GABA inhibitory receptor	• Drowsiness, confusion • Addiction	• Withdrawal should be gradual as abrupt withdrawal may cause confusion, toxic psychosis, seizures or condition resembling delirium tremens
Ethosuximide	• Analogue of GABA • Unknown mode of action	• Mild drowsiness, dizziness • Ataxia • Weight gain • Diarrhoea	• Caution: diabetes mellitus, elderly • Not recommended if tonic, atonic, absence or myoclonic seizures present

Tatalaksana Epilepsi

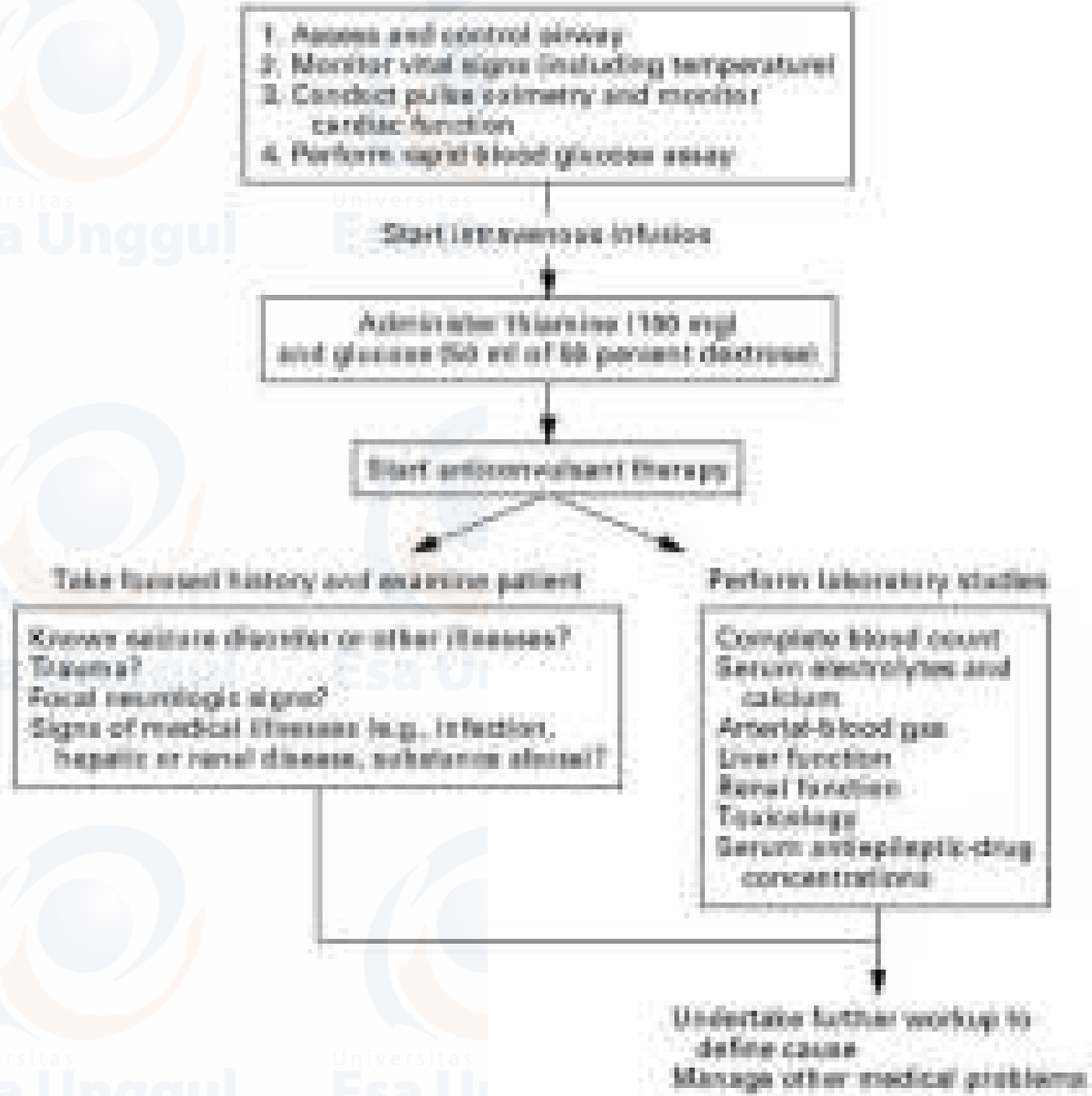
	Kejang parsial	Kejang Umum (generalized seizures)		
		Tonic-clonic	Absense	Myoclonic, atonic
Drug of choice	Karbamazepin Fenitoin Valproat	Valproat Karbamazepin Fenitoin	Etosuksimid Valproat	Valproat
Alternatives	Lamotrigin Gabapentin Topiramat Tiagabin Primidon Fenobarbital	Lamotrigin Topiramat Primidon Fenobarbital	Clonazepam Lamotrigin	Klonazepam Lamotrigin Topiramat Felbamat

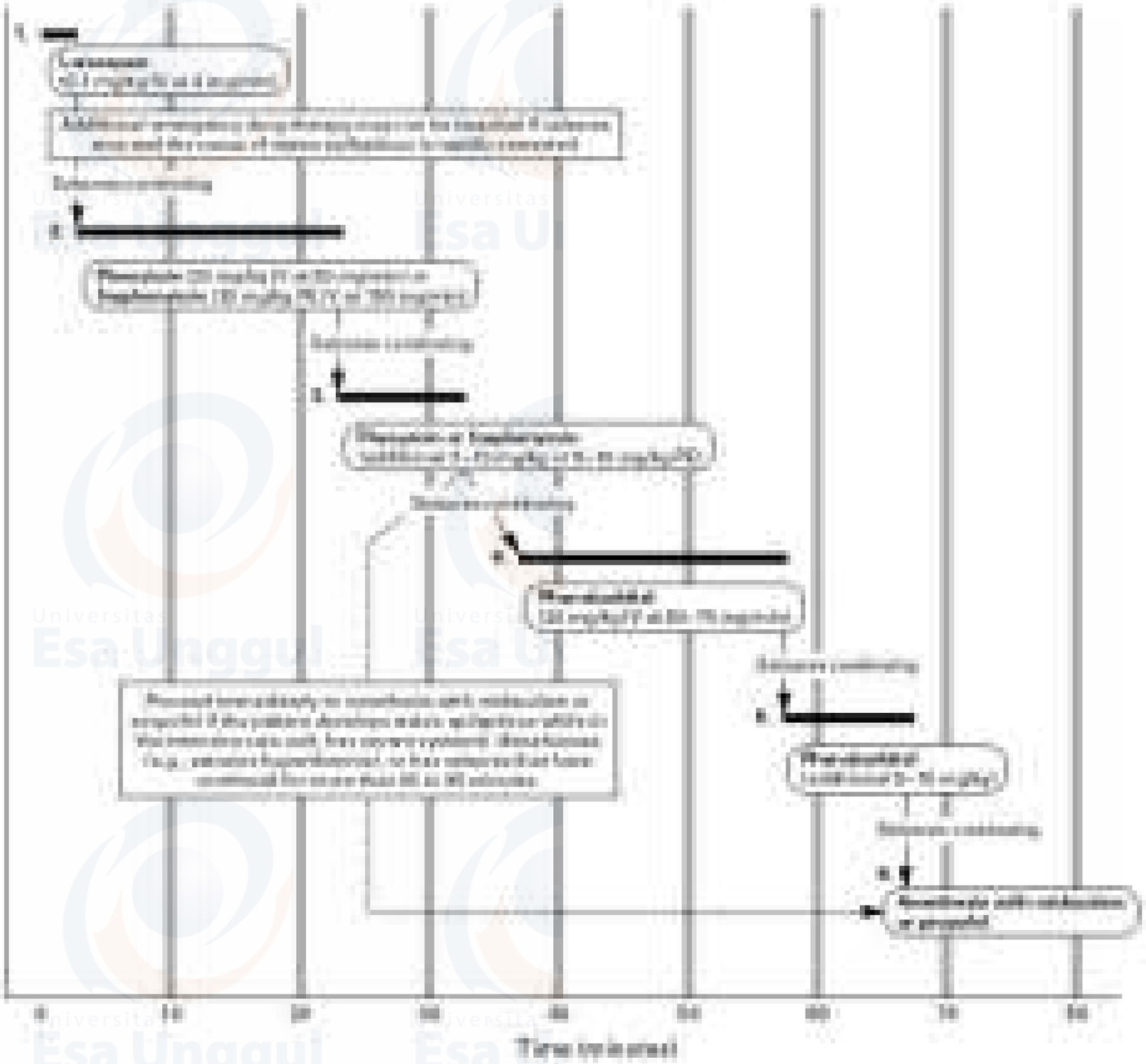
Algoritma Epilepsi


lanjutan
Lanjutkan terapi
Tidak kambuh Selama > 2 th ?
ya
tidak
Hentikan pengobatan
Kembali ke Assesment awal


Tidak berhasil
Efek samping dapat ditoleransi ?
Tidak
Ya
Hentikan AED yang tdk efektif, Tambahkan AED2 yang lain
Tingkatkan dosis AED2, cek interaksi, Cek kepatuhan
Sembuh ?
Ya
Tidak
Lanjutkan terapi
Rekonfirmasi diagnosis, Pertimbangkan pembedahan Atau AED lain

Tatalaksana Status Epileptikus




Time in minutes

Rise your hand!

any question?

PSF316

Farmakoterapi Penyakit Autoimun

SLE & RA

Sesi Ke 13 & 14

Topik Sesuai RPS:

Mahasiswa mampu menjelaskan Patofisiologi dan farmakoterapi SLE dan RA

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Topik Sebelum UAS

Sesi 8

patofisiologi dan farmakoterapi diabetes mellitus

Sesi 9

patofisiologi dan farmakoterapi penyakit tiroid

Sesi 10

patofisiologi dan farmakoterapi osteoporosis

Sesi 11

patofisiologi dan farmakoterapi epilepsi

Sesi 12

patofisiologi dan farmakoterapi kehamilan, laktasi dan PCOS

Sesi 13

patofisiologi dan farmakoterapi rheumatoid arthritis

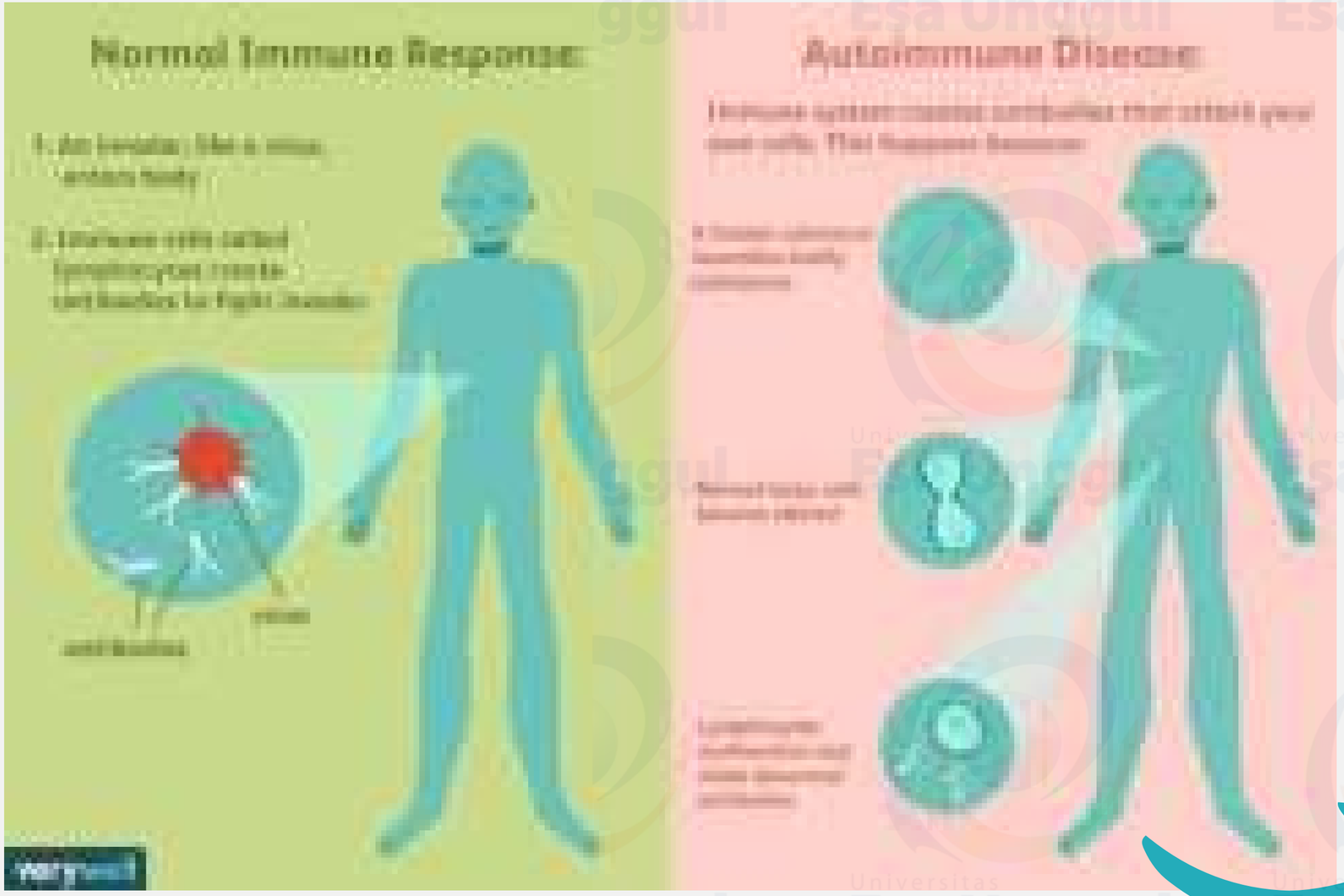
Sesi 14

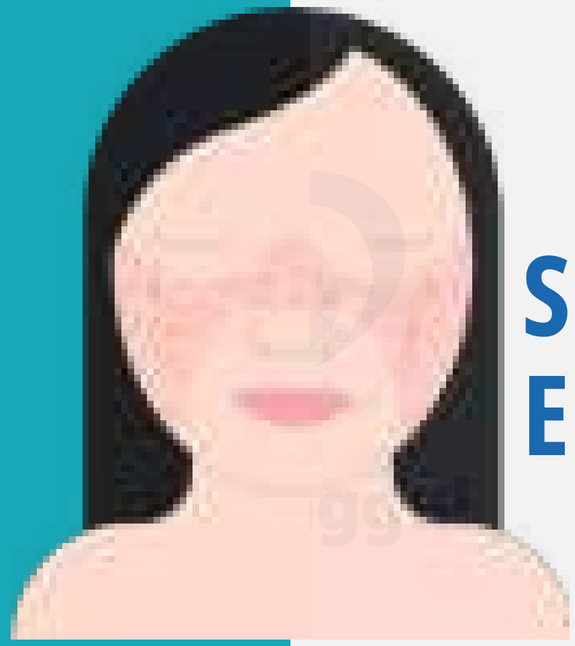
patofisiologi dan farmakoterapi SLE

Ujian Akhir Semester

Autoimmune:

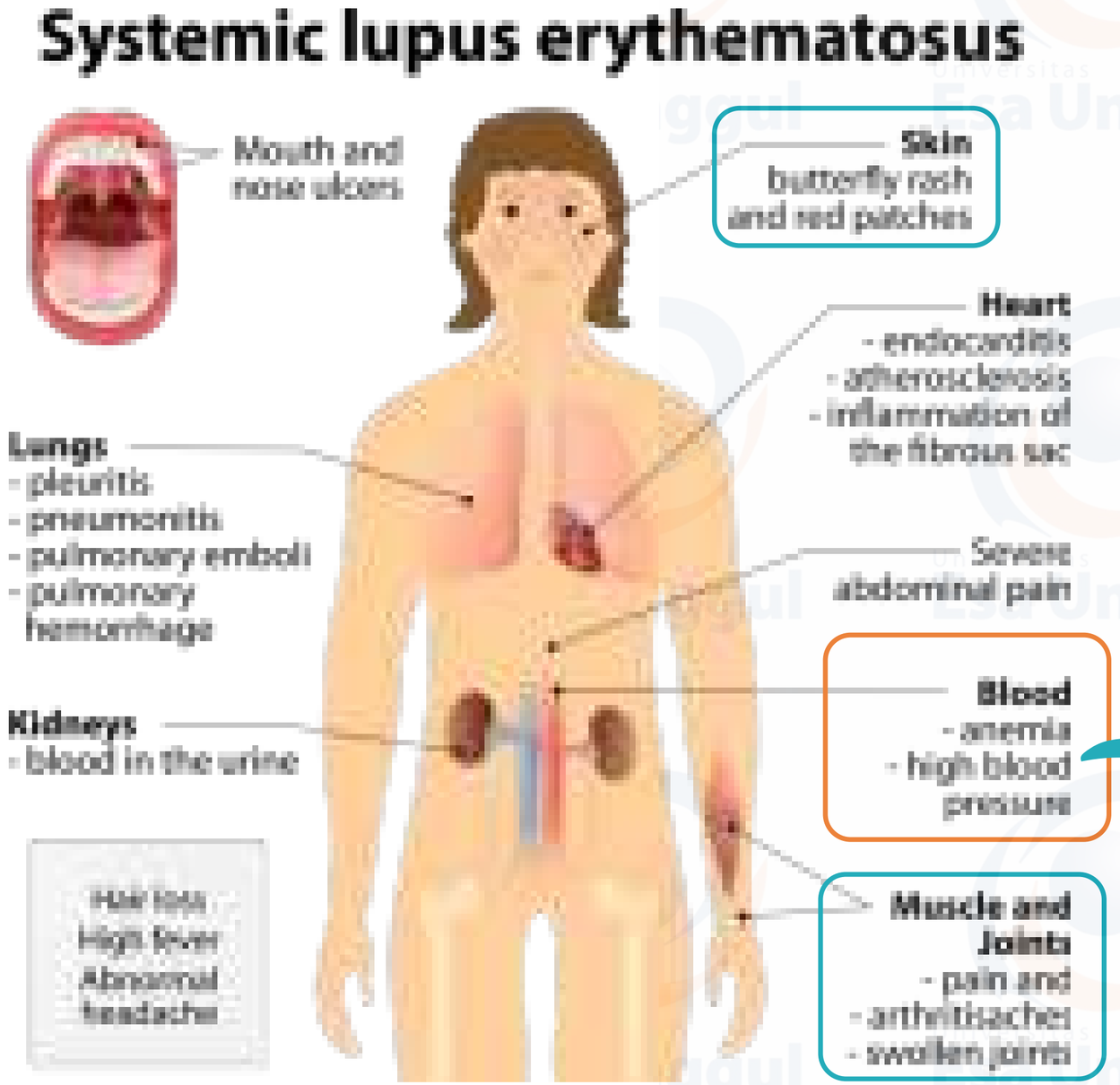
happens when the body's natural defense system can't tell the difference between your own cells and foreign cells, causing the body to mistakenly attack normal cells.





Systemic Lupus Erythematosus

SLE Inflamasi sistemik - kronis , multi-organ



SLE is a multisystemic disease with an unknown etiology. However, several factors play a role in the etiopathogenesis of SLE:

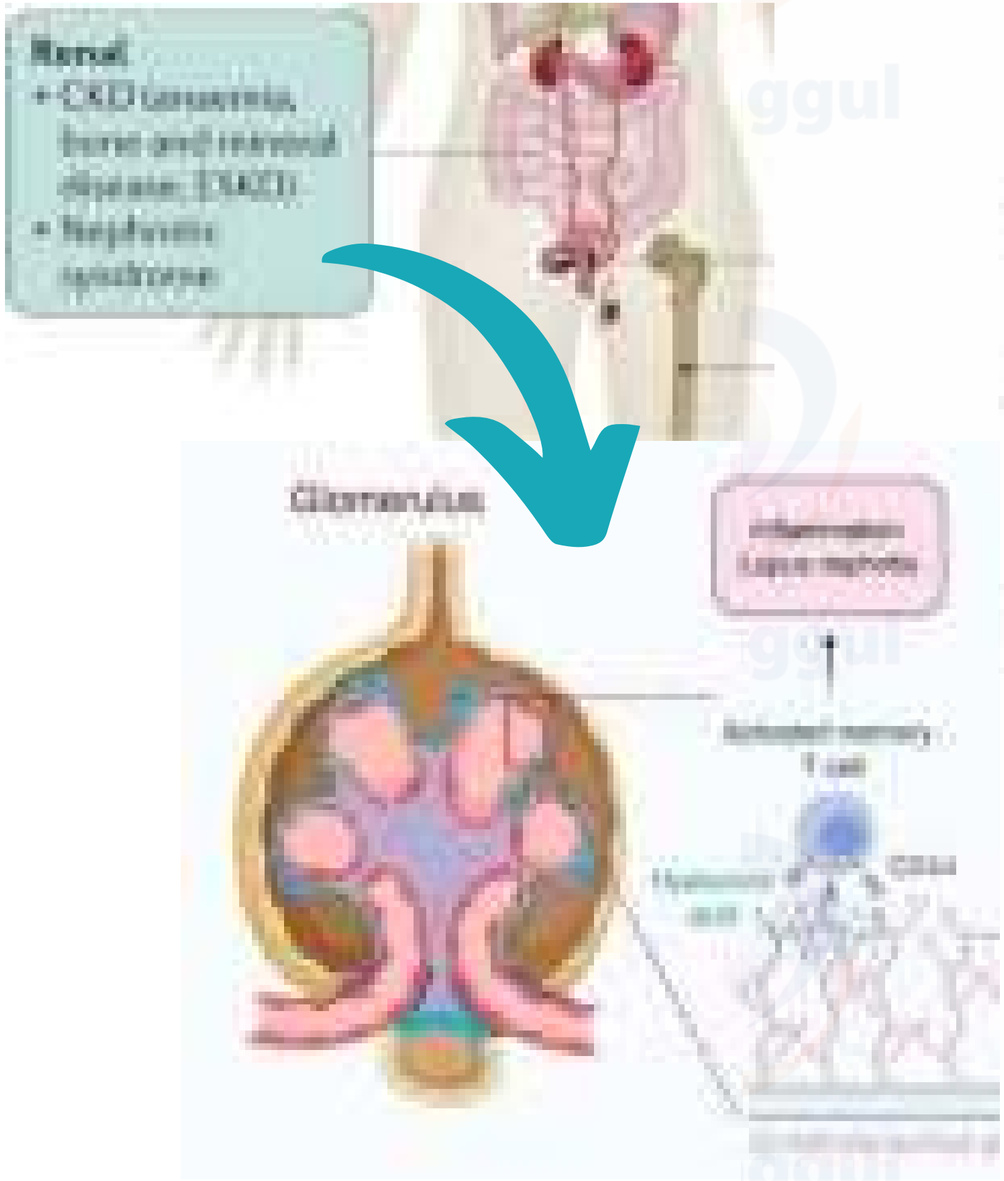
- Genetic
- Immunological
- Endocrine
- Environmental

Whos the most at risk?
Women in childbearing age (1:10)

Manifestasi klinis:
Trombositopenia, leukopenia, etc

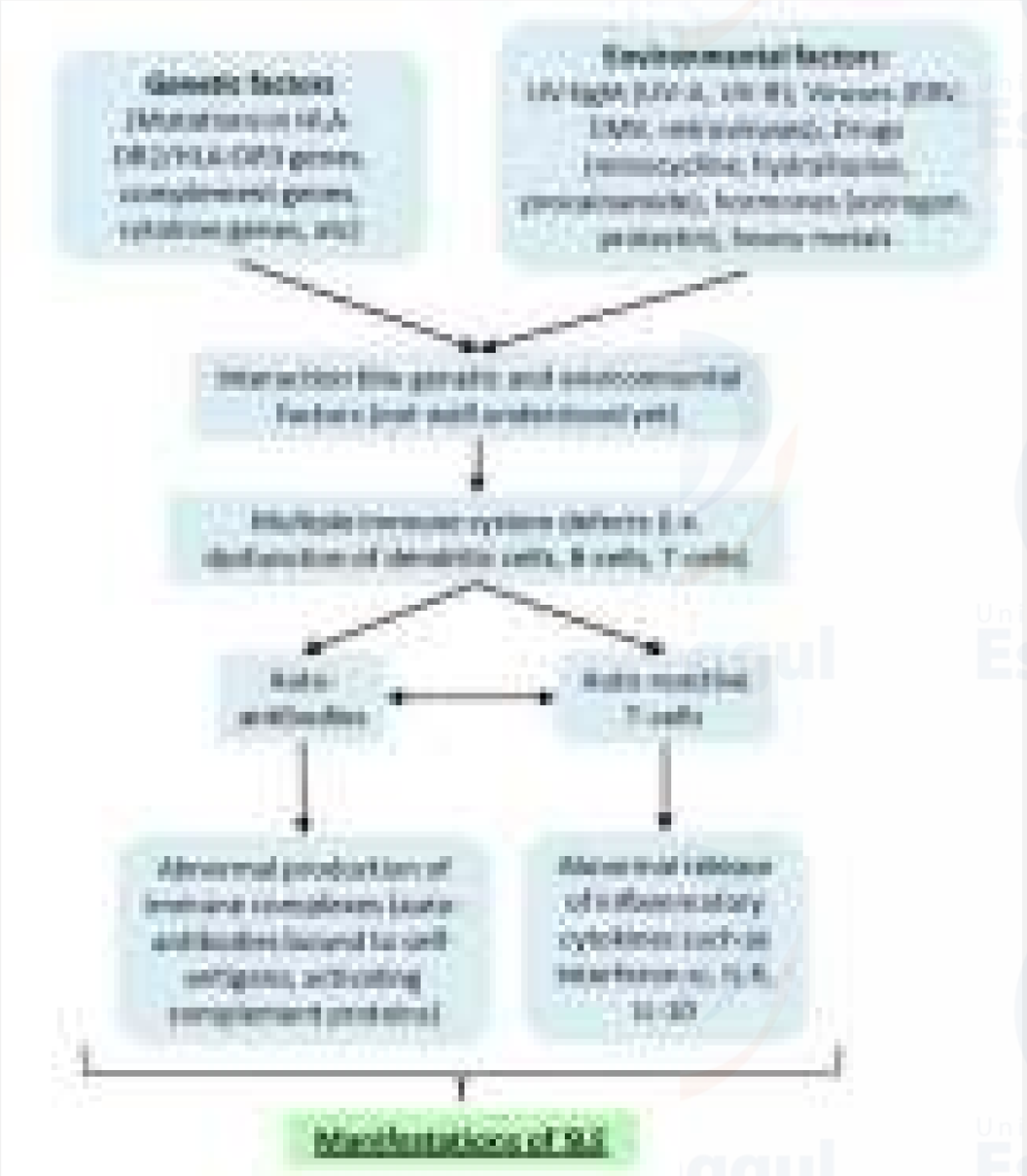
SLE

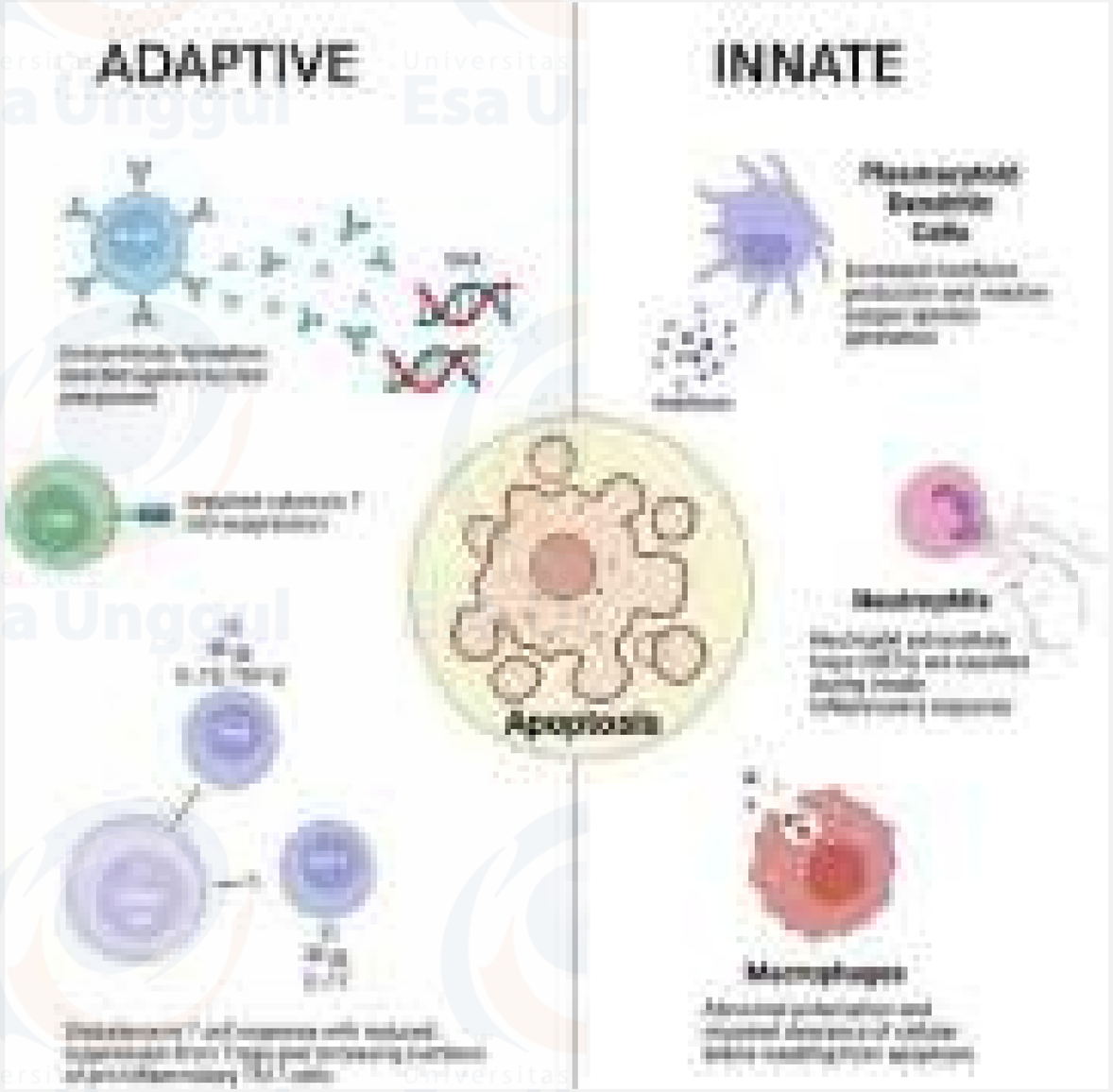
Final Manifestation - RENAL FAILURE



- Membutuhkan dialisis atau transplantasi ginjal.
- Sebagian besar penelitian menunjukkan keuntungan rituximab dalam mengobati lupus.
- Rituximab intra vena, yaitu memasukkan antibodi yang menekan sejumlah sel darah putih, sel B, dan menurunkan jumlahnya dalam sirkulasi.

Patophysiology





Principle of SLE- therapy

Treatment in SLE aims to prevent organ damage and achieve remission.

The choice of treatment is dictated by the organ system/systems involved

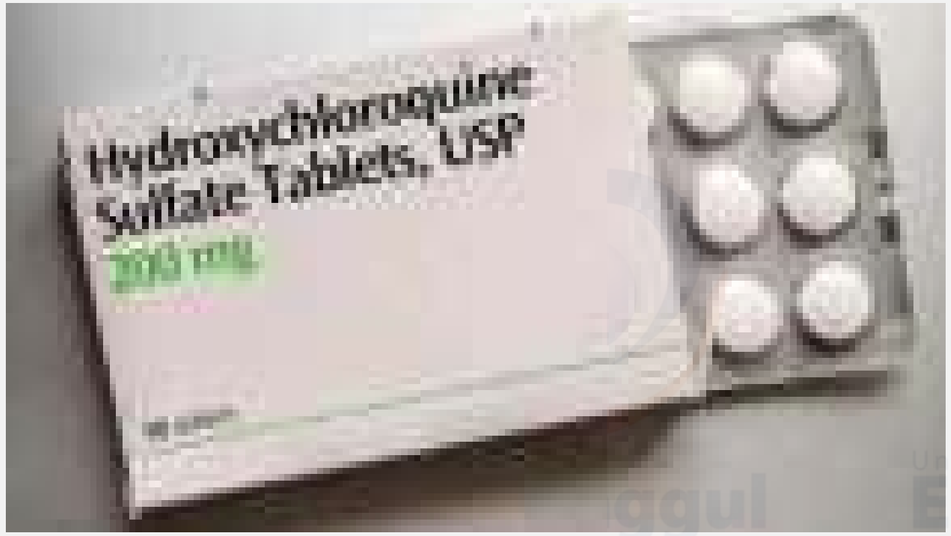
The severity of involvement and ranges from minimal treatment (NSAIDs, antimalarials) to intensive treatment (cytotoxic drugs, corticosteroids).

- Stress reduction techniques, good sleep hygiene, exercises, and emotional support shall be encouraged.
- Smoking can worsen SLE symptoms, and patients should be educated about the importance of smoking cessation.
- Dietary recommendations shall include avoiding alfalfa sprouts and echinacea and including a diet rich in vitamin D.
- Photoprotection is vital. All patients with SLE shall avoid direct sun exposure. using broad-spectrum (UV-A and UV-B) sunscreens with a sun protection factor (SPF) of 30 or more.

Principle of SLE- therapy

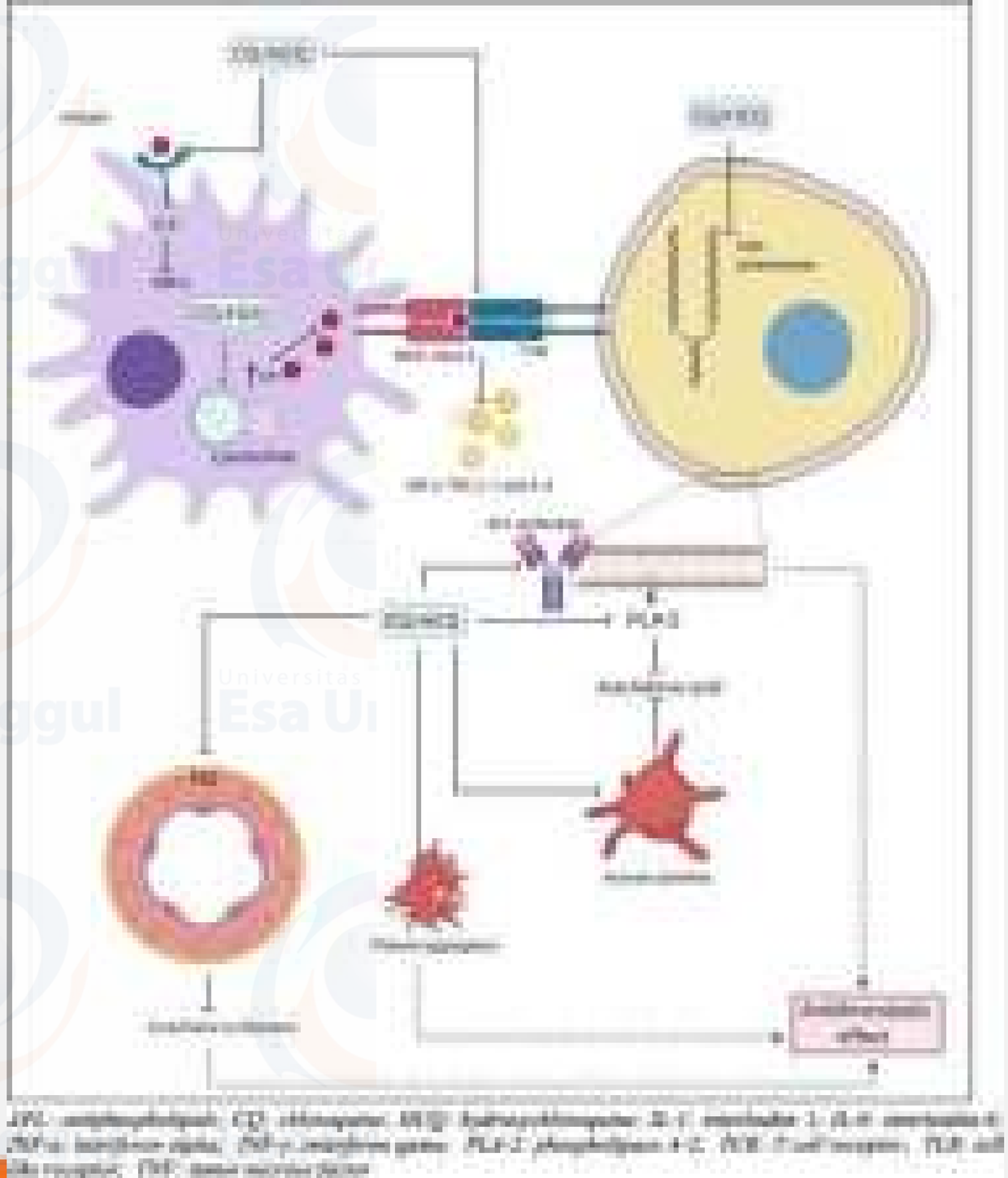
Kelas Terapi	Main Effect	Indication and contraindication
Antimalarials	inhibition of lysosomal activity and autophagy, inhibition of pro-inflammatory cytokine signaling and secretion, inhibition of T-cell proliferation, and blocking of Toll-like receptors	I: as the background therapy for all patients with SLE without contraindications to this drug CI: retinopathy and cardiomyopathy and relate to high doses of HCQ.
Immunosuppressant **Glucocorticoids**	GCs reduce the expression of cytokines and adhesion molecules, inhibit leucocyte traffic, and their access to inflammation sites, and interfere with leucocyte, fibroblast, and endothelial cell functions	I: Maintenance therapy and gold standard (low dose), and for severe or life-threatening conditions in which we need a rapid anti-inflammatory effect (high dose). CI: hypersensitive, and occur s-ADRS
Immunosuppressant **Non -Glucocorticoids**	Non-corticosteroid immunosuppressants target different B-cell populations.	I: Non-corticosteroid immunosuppressants constitute the basic therapy for reducing SLE activity. They are used to initiate and maintain therapy.
Biologics Agent	Antibody monoclonal - blocking their activity may help to normalize B cell activity in SLE.	Biologics should be considered in persistently active or recurrent SLE **belimumab and anifrolumab. Rituximab (RTX)** is used off-label

Hydroxychloroquine



Antimalarial - digunakan untuk SLE penyakit kulit (rash) dan sendi (arthritis).

- Efek samping: gangguan GI tract, perubahan pigmen mata
- Mengurangi frekuensi koagulasi abnormal akibat inflamasi
- Mengurangi intensitas flare pada SLE



Immuno-supressant (non-steroid)

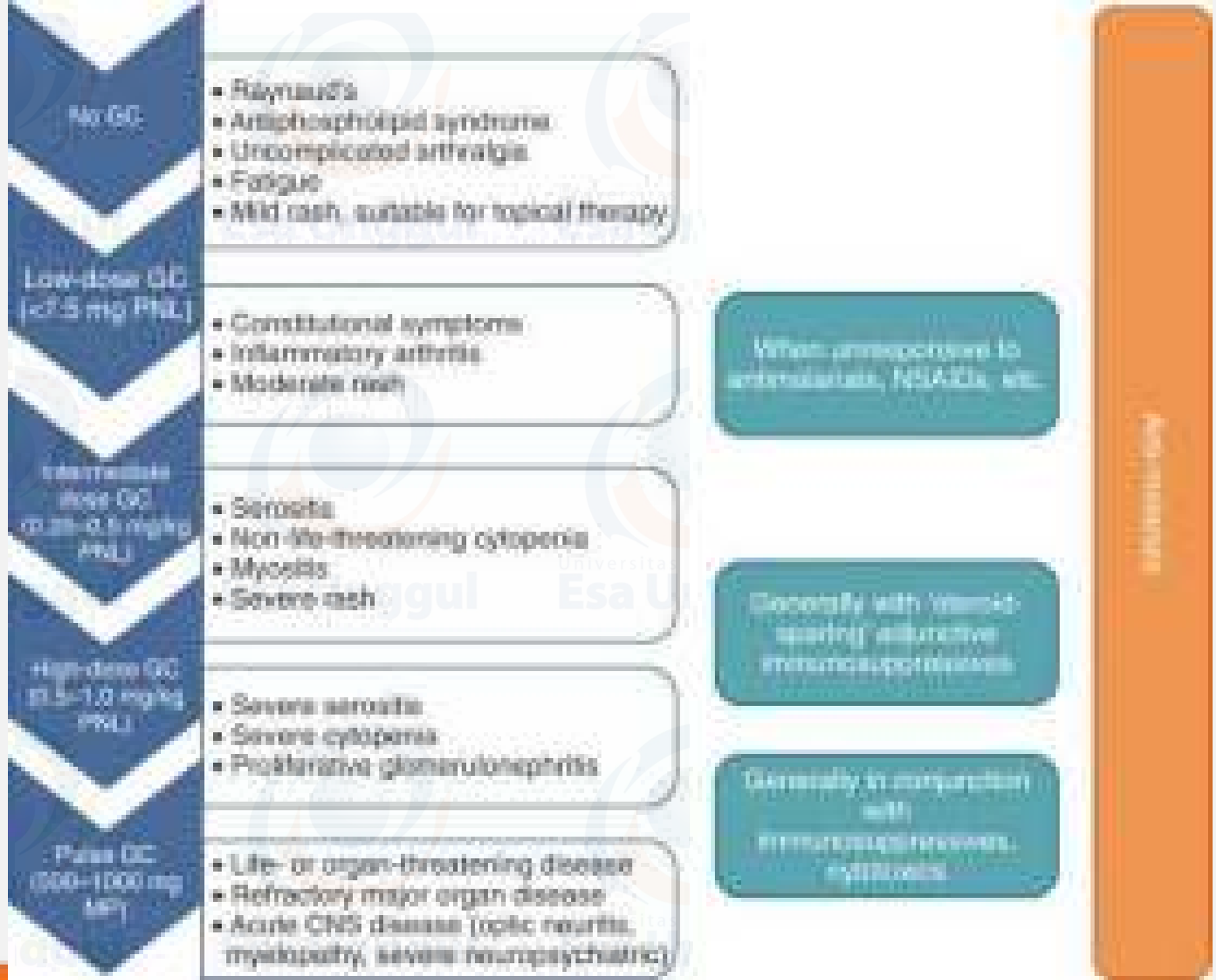
Kondisi SLE dengan manifestasi multiorgan berat

- Efek samping: hematotoksik, meningkatkan resiko infeksi, dan perdarahan

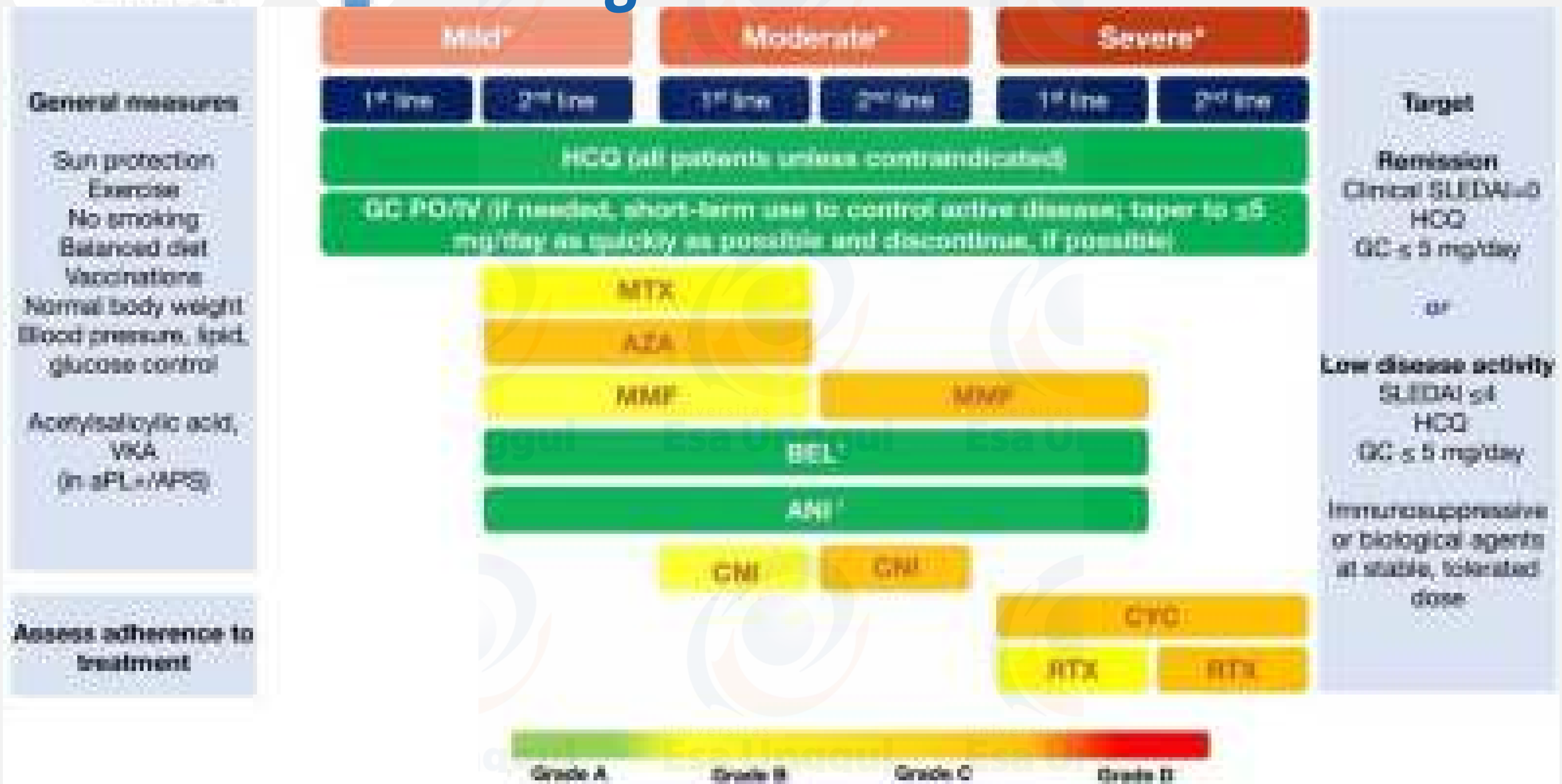
Table 3 Immunosuppressive agents in SLE

Immunosuppressive agent	Main indications	Safety issues
MTX (oral, subcutaneous)	• Musculoskeletal, cutaneous, seminal disease • Mild SC sparing effect	• Liver, gastrointestinal and haematological adverse events (reduced by co-administration of folic acid) • Avoid in elderly patients and/or in case of glomerular filtration rate <30 ml/min • Contraindicated during pregnancy and lactation
AZA (oral)	• Wide spectrum of manifestations, including constitutional, haematological, musculoskeletal and neurological disease • Maintenance of response following induction with CYC • Mild steroid-sparing effect	• Liver, gastrointestinal and haematological adverse events • Possible drug–drug interactions (avoid co-administration with allopurinol) • Safe to use during pregnancy and lactation (dose ≤3 mg/kg/day)
Calcineurin inhibitors (cyclosporine, tacrolimus, voclosporin)	• Used in combination with mycophenolate in selected cases of LN • Third-line option (when other options are unavailable or intolerable) in refractory cutaneous and haematological disease	• Metabolic (hypertension, dyslipidaemia, hyperglycaemia), renal (increased serum creatinine, hyperkalaemia) and gastrointestinal adverse events; gingival hyperplasia, tremor • Safe to use during pregnancy (continuous use of folic acid is recommended)
Mycophenolate (oral: mycophenolate mofetil; enteric-coated mycophenolic acid)	• First-line treatment of LN • Effective in a wide spectrum of manifestations, including moderate or severe haematological disease • Maintenance of response following induction with CYC	• Gastrointestinal, haematological (leukopenia less frequent than with AZA), infectious (especially when used at ≥3 g/day or with high-dose GCs) adverse events • Contraindicated during pregnancy and lactation
CYC (i.v., low dose: 500 mg biweekly ×4 times; high dose: 0.75–1 g/m² monthly ×6–7 times)	• First-line treatment of LN and severe (organ- or life-threatening or refractory manifestations including renal, neuropsychiatric, vascular, haematological disease • Low dose preferred in most settings; high dose may be indicated in particularly severe disease	• Haematological, infectious and bladder (cystitis) adverse events (especially high dose) • Gonadal toxicity (age- and dose-related) with high doses • Can be indicated during pregnancy (can be used during the second/third trimester in selected cases) and lactation

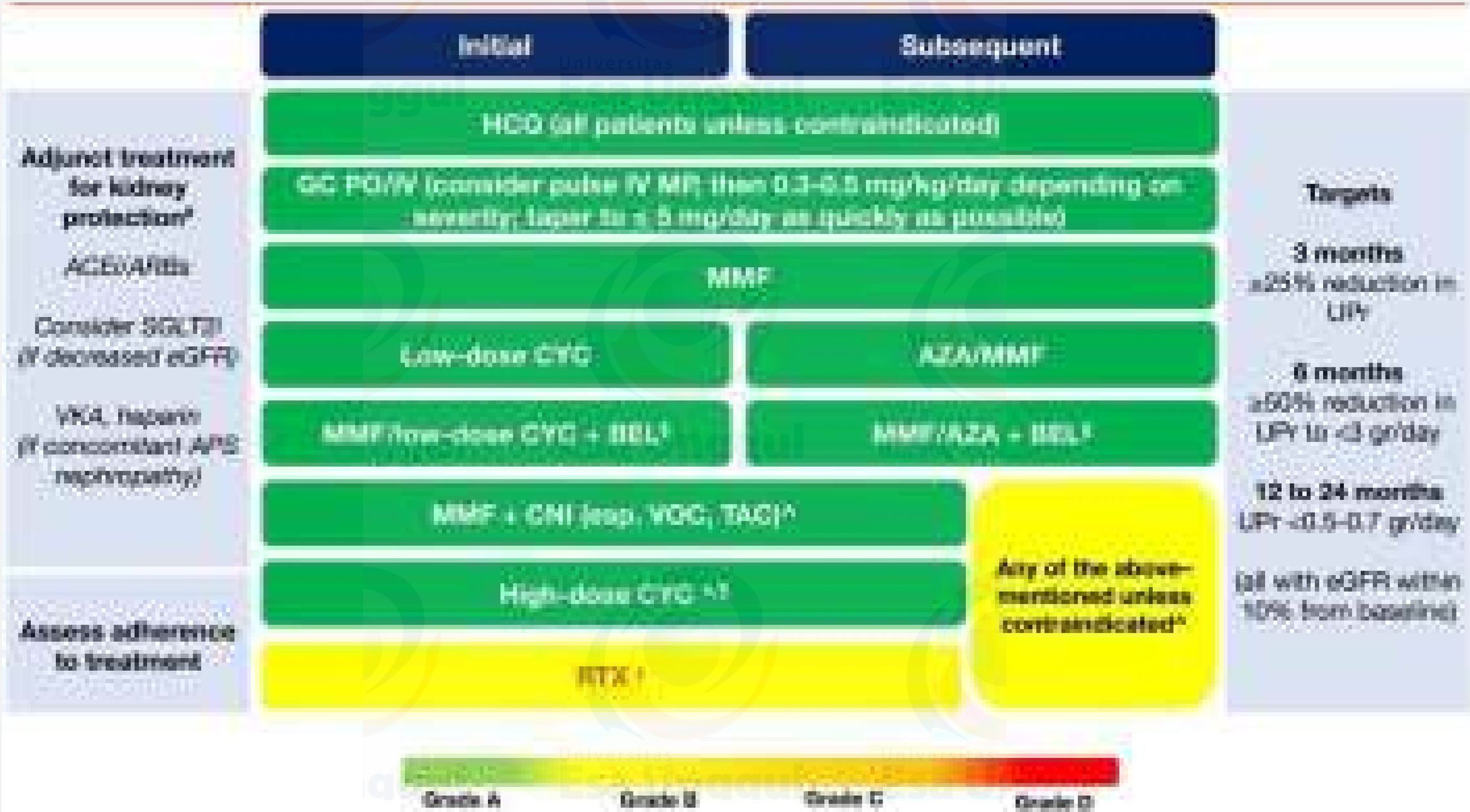
Immuno-supressant (Steroid)



SLE algorithm



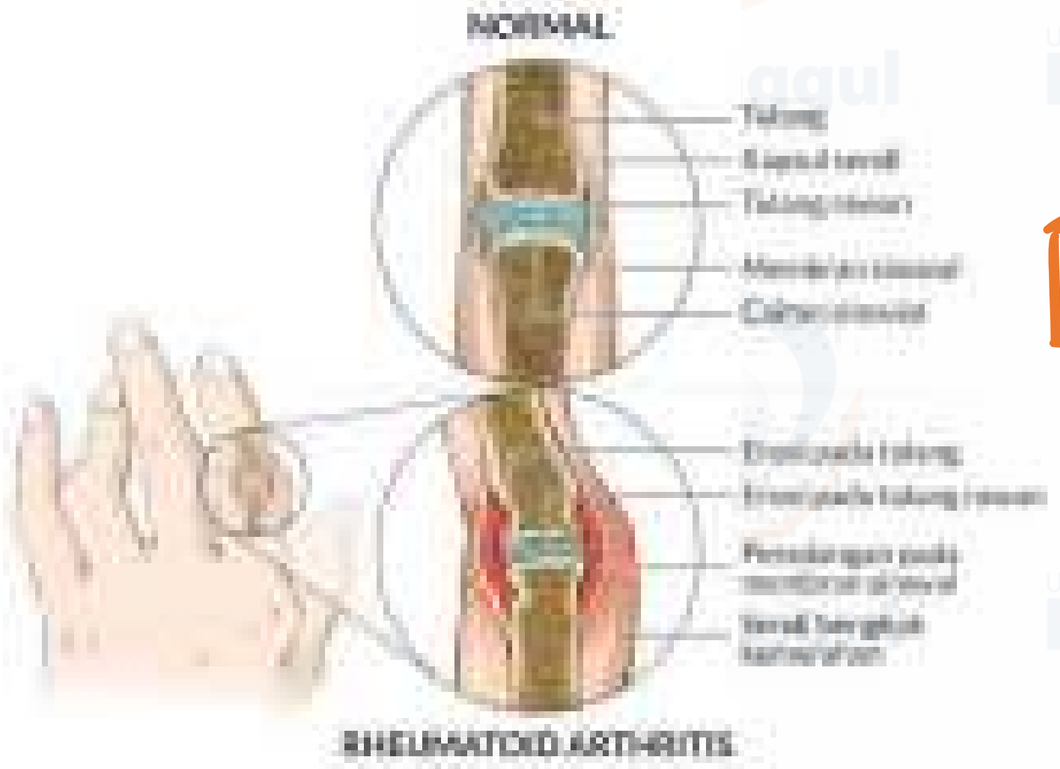
Lupus Nephritis Algorithm



Rheumatoid Arthritis

RA

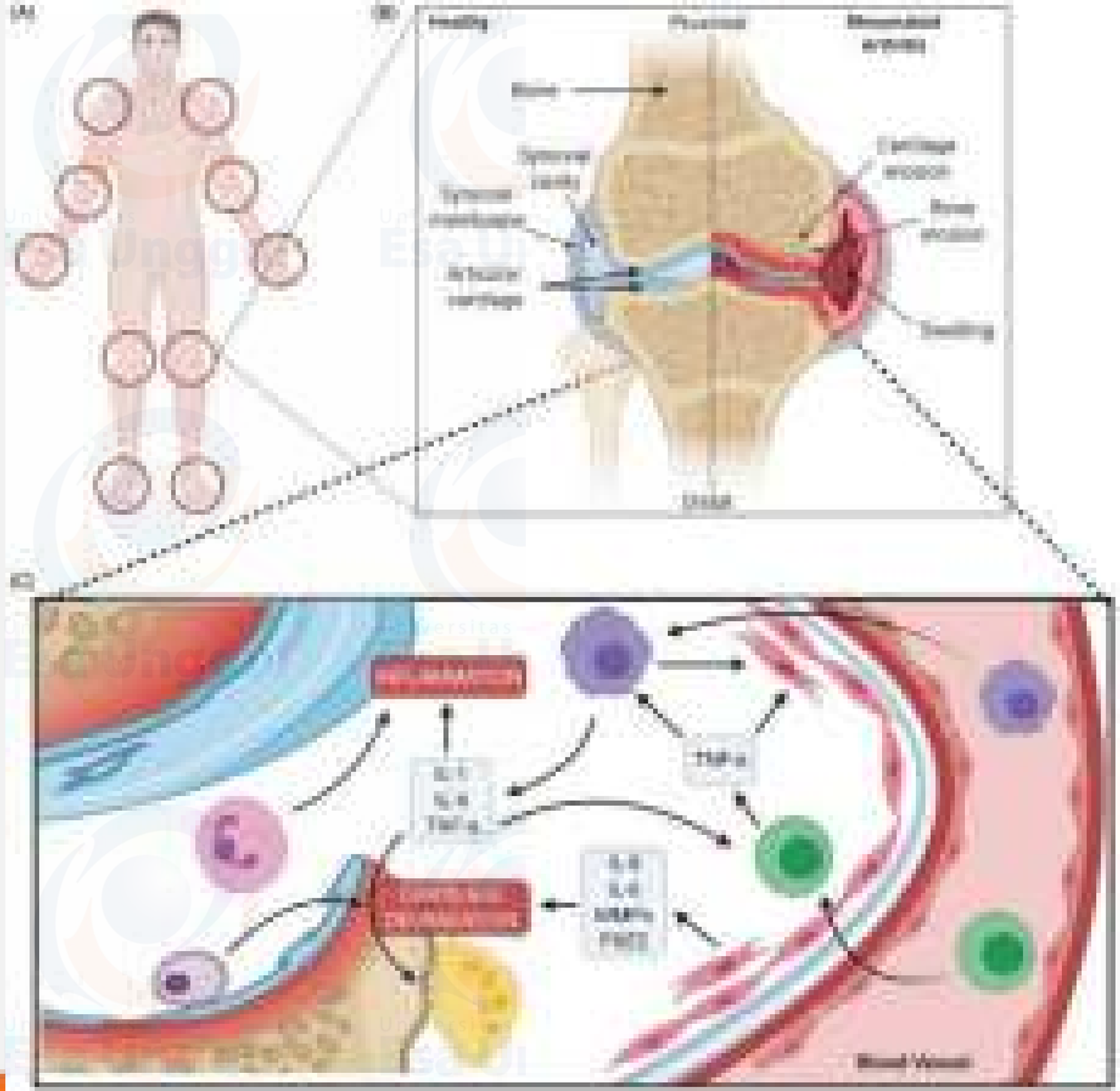
Inflamasi pada persendian (tangan dan kaki), peradangan - nyeri - kerusakan sendi



- Faktor predisposisi: mekanisme imunitas (antigen-antibodi), faktor metabolik, dan infeksi virus

Patophysiology

- TNF alpha impacts synoviocytes, macrophages/monocytes and osteoclasts;
- Inititating RA pathogenesis.
- Synoviocytes line the capsule and T-cells infiltrate the synovial membrane, initiating inflammation via TNF alpha.
- Joint degradation occurs via recruitment of macrophages and secretion of inflammatory cytokines.
- Bone erosion occurs by osteoclasts and inhibition of collagen secretion by synoviocytes



Risk Factor

Tidak dapat dimodifikasi:

- Genetik
- Usia: timbul antara usia 40 tahun sampai 60 tahun
- Jenis kelamin; lebih sering pada perempuan dibanding laki-laki dengan rasio 3:1.

Dapat dimodifikasi:

- Gaya hidup: merokok, diet, infeksi, jenis pekerjaan
- Hormonal: faktor reproduksi yang meningkatkan risiko RA yaitu pada perempuan dengan sindrom polikistik ovari, siklus menstruasi ireguler, dan menarche usia sangat muda.
- Bentuk tubuh : Risiko RA meningkat pada obesitas atau yang memiliki Indeks Massa Tubuh (IMT) lebih dari 30.

Principle Therapy of RA

NSAID → **Oral**

NSAID → **Topikal**

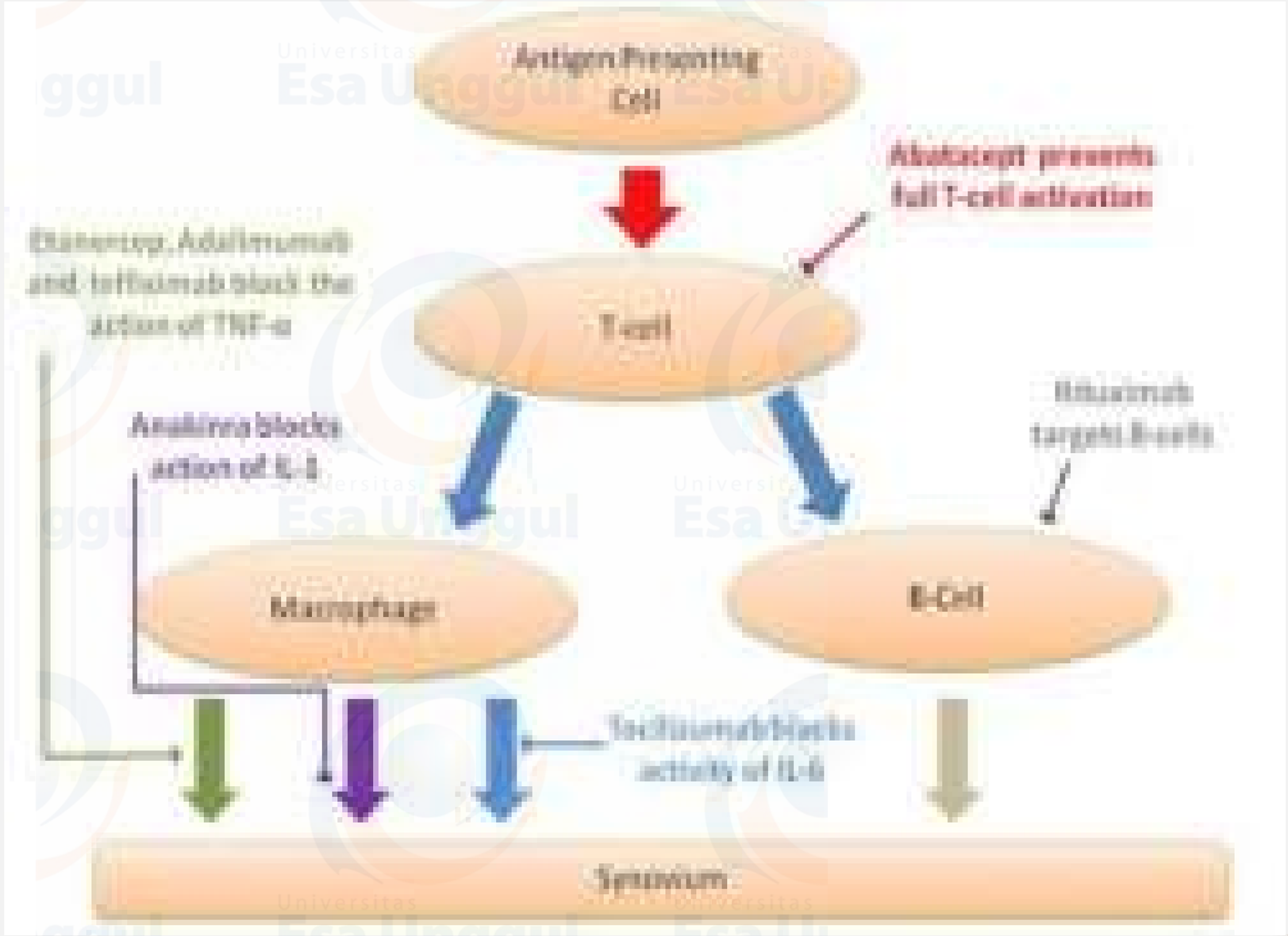
- Nyeri inflamasi yang dikeluhkan penderita rematik, bukan semata-mata akibat peningkatan mediator inflamasi prostaglandin.
- Berbagai mediator inflamasi lain (misalnya bradikinin) dan sitokin (TNF-alfa dan interleukin) turut serta dilepaskan dan berperan serta dalam mencetuskan nyeri inflamasi

Syarat dan Pertimbangan pemberian NSAID untuk RA:

1. **Terdistribusi ke sinovium**
2. **Mula kerja cepat**
3. **Masa kerja lama (panjang),**
4. **Efek samping minimal,**
5. **Mekanisme kerja multifactor**

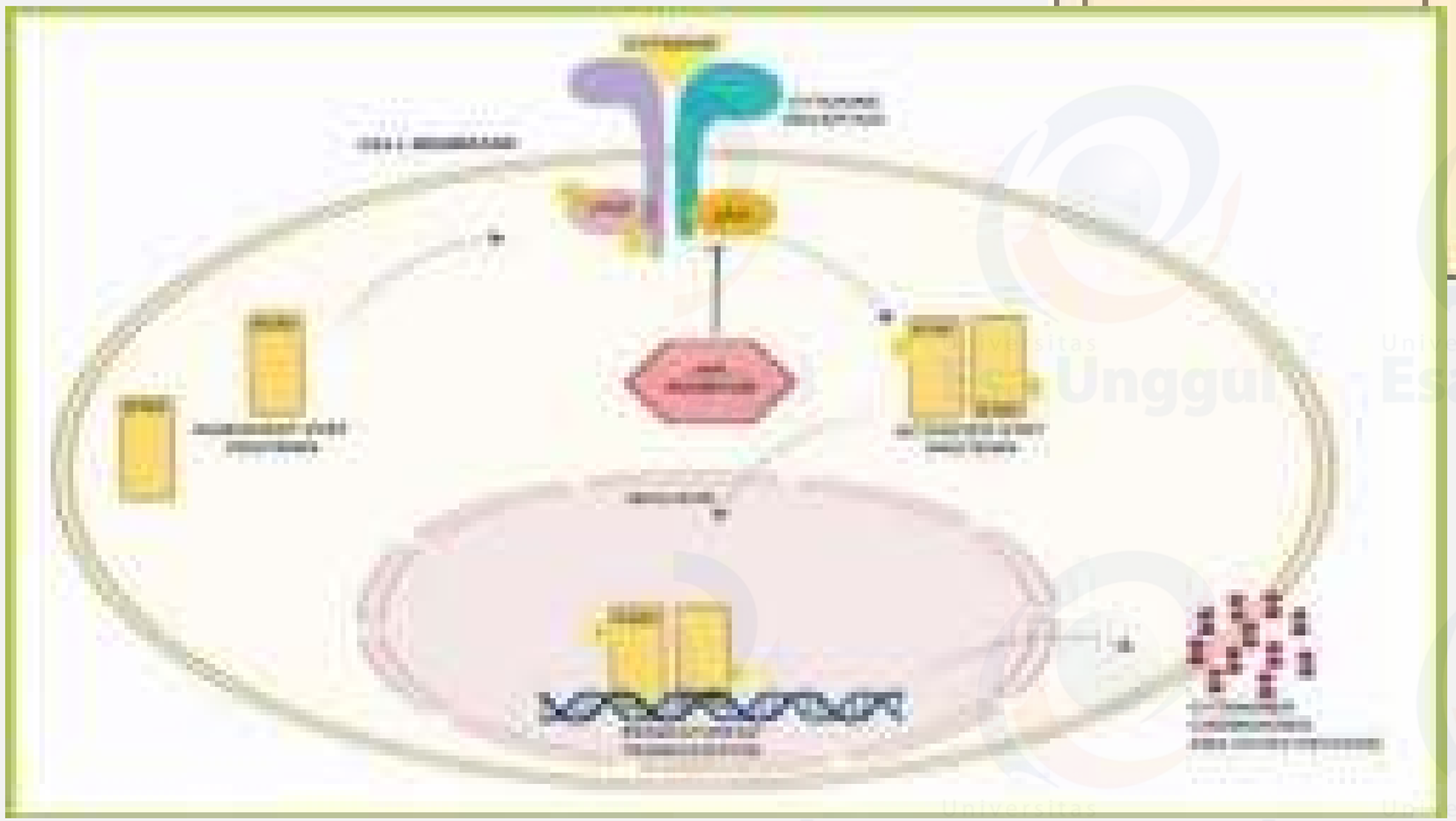
Biologics - anti cytokine

Anti-TNF alpha
- Etanercept
- Infliximab
- Adalimumab
- IL-1 receptor antagonist (Anakinra)

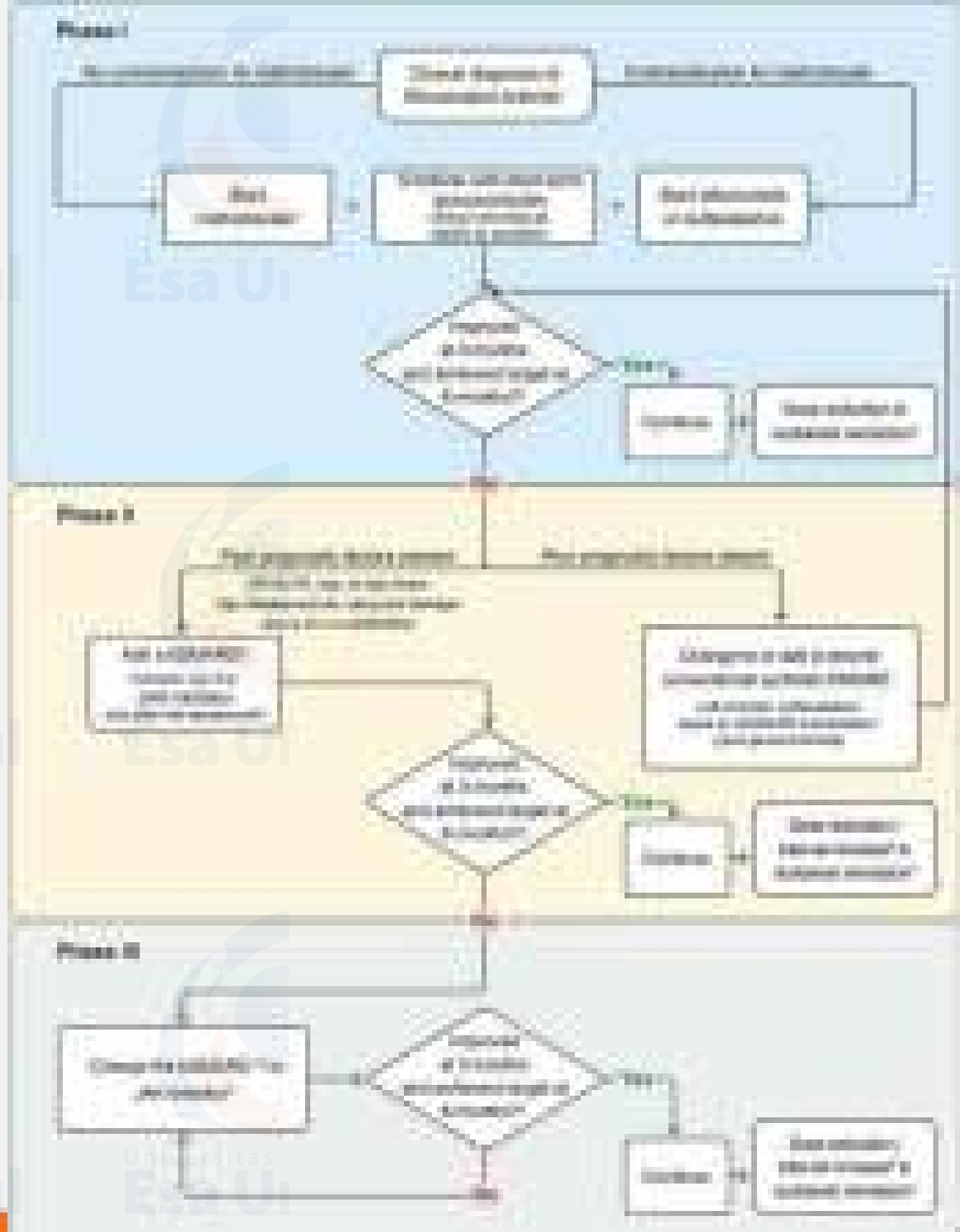


DMARDs

Conventional synthetic DMARDs	Biologics	Targeted synthetic DSMARDs
• Methotrexate • Leflunomide • Sulfasalazine • Hydroxychloroquine	• TNF-α inhibitors: Etanercept • anti-TNF monoclonal antibodies: Infliximab, Adalimumab, Golimumab, Certolizumab Pegol • B cell depletion: Rituximab • T cell co-stimulation: Abatacept • IL-6 inhibitors: Tocilizumab, Sarilumab	• Janus kinase inhibitors Baricitinib Tofacitinib Upadacitinib Peficitinib Filgotinib



Algorithm Therapy



Rise your hand!

any question?

Studi kasus

DM, Tiroid, dan Osteoporosis

SOAP

- Subjective
- Objective
- Assessment (DRP)
- Plan/ Suggestion (asuhan kefarmasian)

Poin DRP – berdasarkan PCNE

- Adverse drugs reaction (efek samping, alergi, toksisitas)
- Drugs choice problem (ketepatan pemilihan terapi, duplikasi, kontraindikasi, obat tanpa indikasi, indikasi tanpa terapi)

Indikasi medis:

Terapi:

Analisa:

- Dosing problem (dosis terlalu tinggi, dosis terlalu rendah, frekuensi dosis tidak tepat)
- Drug use problem (ketidak patuhan, salah penggunaan co/ rute, frekuensi, jumlah obat)
- Interaction (interaksi potensial, interaksi actual)

Contoh soal dan cara menjawab

- Tn. M.B mengeluhkan akhir-akhir ini badan selalu lemas, frekuensi urin yang meningkat, cepat lapar, dan cepat haus. Diketahui hasil GDP bulan ini adalah 135 mg/dl, dengan riwayat bulan lalu 145 mg/dl dan sebelumnya 130 mg/dl. Tn. M.B didiagnosa DM tipe II oleh dokter di puskesmas setelah sebelumnya melakukan pemeriksaan pertama GDP didapatkan hasil 120 mg/dl. Pasien juga memiliki riwayat penyakit hipertensi stabil di 130/80mmHg. Obat yang diberikan dan rutin dikonsumsi oleh pasien adalah metformin 3x500mg dan amlodipine 1x5mg.
  Analisa DRP kasus ini, dan berikan saran.

Jawaban contoh soal DM (1):

- **Subjektif:** badan selalu lemas, frekuensi urin yang meningkat, cepat lapar, dan cepat haus.
- **Objektif:**

GDP bulan 1: 110 mg/dl.

GPD bulan 2: 130 mg/dl

GPD bulan 3: 145 mg/dl

GPD bulan 4: 135 mg/dl

BP: 130/80mmHg

- **Assessment**

1. Adverse effect: tidak ada
2. Drugs choice problem:

Indikasi: DM tidak terkontrol, lemas, poliuri, polifagi (gejala DM), hipertensi terkontrol

Terapi: metformin 3x500mg dan amlodipine 1x5mg

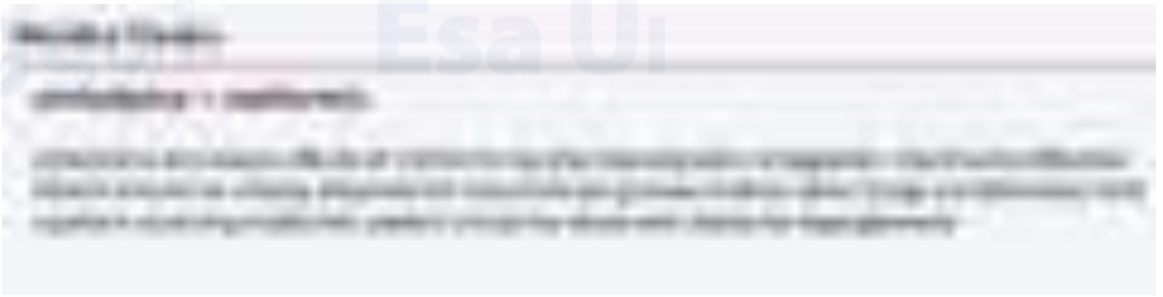
Analisa: terapi kurang tepat, GPD tidak sesuai target.

3. Dosing problem: tidak ada

4. Drug Use problem: tidak diketahui

5. interaction: amlodipine menurunkan efek metformin

- **Plan:** kombinasi terapi dengan SU/ GLN untuk mencapai target GDP. Evaluasi dilakukan $\leq 3bulan$



Soal DM

- Ny. M.M sudah terdiagnosa DM tipe II selama 3 tahun, beliau juga memiliki riwayat infark miokard sehingga terapi yang rutin dikonsumsi adalah metformin 3x500 mg, glimepiride 1x2mg, aspilet 1x80mg, dan bisoprolol 1x2,5mg. Pemeriksaan terakhir HbA1C pasien adalah 6,5 dan tekanan darah 135/70mmHg. Pasien mengeluhkan sering pusing dan limbung setelah konsumsi obat gula.
  Analisa DRP kasus ini, dan berikan saran.

Kasus Tiroid

- Pasien wanita 50 tahun, dengan berat badan 72kg mengeluhkan peningkatan berat badan secara massif selama satu tahun terakhir. Pasien juga mengeluhkan kelelahan, pusing, mudah lupa/ gangguan ingatan, serta gangguan pencernaan konstipasi. Didapatkan kadar serum TSH= 6,5 uIU/ml dengan serum T4= 4 pmol/L. Pasien didiagnosa gangguan tiroid. Diberikan terapi inisial LT4 200ug.
  Kategori gangguan tiroid apa yang dialami pasien? Analisa DRP dan berikan saran.
- Pasien 35 tahun mengeluhkan tremor dan cemas yang akhir-akhir ini sering muncul. Tidak terdapat perubahan BB akan tetapi nafsu makan pasien dirasa sangat meningkat. Tekanan darah pasien 130/70mmHg, dengan kadar TSH TSH= 0,5 uIU/ml dengan serum T4= 30 pmol/L. Akhir-akhir ini dirasa sering palpitasi dan HR menunjukkan 120/menit. Pasien konsultasi ke puskesmas dan diberikan terapi captopril 1x25mg dan PTU 3x150mg.

Analisa DRP dan berikan saran

Kasus Osteoporosis

- Seorang wanita berusia 62 tahun mengalami nyeri pinggang, dan penurunan tinggi badan dalam satu tahun terakhir. Pasien diketahui sudah menopause. Melakukan pemeriksaan di Rumah Sakit dan didapatkan Tscore= 2,5 maka pasien didiagnosa mengalami osteoporosis. Pasien diberikan terapi ibuprofen 3x400mg, suplemen kalsium dan vitamin D, alendronat 1x10mg, dan risendronat 1x5mg.

Analisis DRP dan berikan saran.

Studi kasus

Epilepsi, RA dan SLE

Kasus Epilepsi

- Pasien anak berusia 14 tahun dengan berat badan 35kg terdiagnosa kejang tonic-clonic sejak 2 bulan lalu, pasien diberikan asam valproate 2x3,5ml (175mg). Namun Ibu pasien melaporkan kejadian kejang masih sering terjadi. Pasien juga terlihat seringkali tremor. Analisis DRP dan berikan saran

Kasus autoimun

- Wanita berusia 32 tahun mengeluhkan ruam ringan berbentuk kupu dimuka, dengan nyeri berat pada sendi-sendi dan adanya sariawan pada mulut. Selama ini pasien rutin mengonsumsi piroxicam sebagai terapi nyeri sendinya, namun pasien sering mengeluh nyeri perut. Pasien mendapatkan pemeriksaan autoimun dan dikatakan positif SLE. Dokter memberikan terapi hidroksiklorokuin dan glucocorticoid dosis menengah, dan memperbolehkan piroxicam dilanjutkan.
  Analisis DRP dan berikan saran.
- Wanita berusia 58 tahun mengeluhkan persendian di tangannya nyeri hebat dan nampak bengkak ruam, hangat, dan terasa mulai kaku dan bengkok. Pasien selama ini hanya mengonsumsi ibuprofen untuk mengatasi nyeri. Pemeriksaan di puskesmas direkomendasikan rujukan ke RS karena diagnose RA. Kemudian diberikan terapi tambahan oleh dokter puskesmas metilprednisolon, dan Ibuprofen disarankan untuk dilanjutkan.

Analisis DRP dan berikan saran

DRP (drugs related problems)

- Unnecessary drug therapy.
- Wrong drug. ...
- Dose too low. ...
- Dose too high. ...
- Adverse drug reaction. ...
- Inappropriate adherence. ...
- Needs additional drug therapy.

Studi Kasus

Farmakoterapi Kardiovaskuler

Farmakoterapi Stroke

- Seorang pasien wanita 47 tahun memiliki pola hidup yang cenderung sehat dalam nutrisi, namun kurang aktivitas olahraga. Diketahui tidak memiliki riwayat penyakit. Beberapa waktu belakangan mengeluhkan sering pusing dan tidak hilang dengan obat Pereda nyeri, kondisi kantor sedang bermasalah dan pasien mengalami stress berlebih. Pasien ditemukan pingsan di meja kantor dengan kepala telungkup berada di meja kantor. Pasien dilarikan ke UGD dan segera masuk ke ICU karena hasil CT scan otak menunjukkan tidak menunjukkan adanya perdarahan. Pasien diberikan terapi oksigen, dan fibrinolitik intravena. Jelaskan mengenai terapi tersebut, apakah ada DRP, dan bagaimana terapi selanjutnya sebagai pemeliharaan?

Farmakoterapi Gagal Jantung

- Pasien 46 tahun mengalami gagal jantung. Dengan gejala nyeri dada dan sesak yang muncul intens terlebih ketika beraktivitas, namun Ketika beristirahat seringkali juga muncul. Lemas tidak berkesudahan dan palpitasi, dan adanya bengkak pada tungkai. Terapi yang diberikan adalah digoksin yang diketahui memiliki indeks terapi yang sempit. Selain itu, pemberian captopril dan spironolactone juga direkomendasikan oleh dokter untuk pasien tersebut. Apa yang dapat kamu jelaskan mengenai indeks terapi sempit? Jelaskan mengenai terapi tersebut, apakah ada DRP?

Farmakoterapi obat Acute Coronary Syndrome

- Seorang pasien mengeluhkan nyeri dada yang tidak tentu waktunya, saat istirahat nyeri tetap dirasakan. Mual muntah dan sesak seringkali dirasakan. Pasien diketahui memiliki riwayat aterosklerosis dengan LDL 220mg/dL dan hipertensi dengan 143/92 mmHg. Saat ini pasien datang ke dokter dalam kondisi stabil tidak nyeri dada. Pasien didiagnosa unstable angina oleh dokter dengan terapi atorvastatin, ISDN, clopidogrel, aspirin, bisoprolol, amlodipine, captopril. Jelaskan mengenai terapi tersebut, apakah ada DRP, dan bagaimana terapi selanjutnya sebagai pemeliharaan?

Farmakoterapi Aritmia

- Pasien berusia 46 tahun mengalami aritmia ventricular extra systole. Diketahui bahwa aritmi tersebut terdapat gangguan pada AV node. Terapi yang diberikan adalah bisoprolol dan juga diltiazem. Jelaskan mengenai terapi tersebut, apakah ada DRP?

Farmakoterapi Gagal Ginjal

- Seorang pria 55 tahun datang ke IGD dengan gejala mual, muntah, dan kelelahan yang parah selama beberapa hari terakhir. Dengan berat badan 70kg, dan didiagnosa hipertensi sejak 5 tahun yang lalu dengan tekanan sehari-hari stabil di 147/85 mmHg, terapi yang digunakan rutin adalah amlodipin. Riwayat Diabetes Mellitus tipe II terkontrol sejak 3 tahun yang lalu. Saat ini pasien datang ke RS dengan kondisi shock karena asidosis. Diketahui mengalami penurunan fungsi ginjal yang akut selama beberapa hari terakhir. Pemeriksaan laboratorium menunjukkan peningkatan kadar kreatinin serum (1.9 mg/dL) dengan pH darah 7.25 dan bikarbonat serum rendah. Bagaimana rekomendasi terapi pasien tersebut, dan monitoring apa yang perlu dilakukan.

Jawaban Kasus 1

- Assessment farmasi:
  - Indikasi: stroke iskemik akut, hipertensi, stress
  - Terapi yang dibutuhkan stroke iskemik akut: fibrinolitik, suplementasi oksigen
  - Terapi yang dibutuhkan maintenance: antihipertensi – ACE inhibitor/ Beta blocker, atau CCB, antiplatelet terapi (kombinasi: untuk short term) – aspirin, CPG, lalu aspirin monoterapi untuk long term, antihiperlipidemia – atorvastatin

DRP:

Needs additional drug therapy – Riwayat sering pusing belakangan yang tidak tertangani dengan obat Pereda nyeri : kemungkinan hipertensi yang tidak tertangani.

Jawaban Kasus 2

- Assessment farmasi:
  - Indikasi: Gagal Jantung Kelas IV
  - Terapi yang dibutuhkan HF stage IV: ACE/ARB – captopril kombinasi valsartan, Diuretik (edema paru – sesak, edema tungkai)- spironolactone, beta blocker – bisoprolol, digoksin.

DRP:

Needs additional drug therapy – ARB, beta blocker – bisoprolol

Jawaban Kasus 5

- Assessment farmasi:
  - Indikasi: Gagal Ginjal Akut, Hipertensi, Diabetes Mellitus, Asidosis
  - Data Objektif: 55 tahun, 70 kg, 147/85 mmHg, kreatinin serum (1.9 mg/dL) dengan pH darah 7.25 dan bikarbonat serum rendah.
  - Terapi yang dibutuhkan:
    - Insulin intravena: Untuk mengatasi hiperglikemia dan menyeimbangkan metabolisme asam basa.
    - Bikarbonat sodium: Diberikan secara hati-hati untuk mengkoreksi asidosis metabolik.
    - Diuretik loop (misalnya, furosemid): Untuk mengurangi beban cairan dan edema, serta membantu mengurangi kadar kalium serum yang tinggi.
    - Obat antihipertensi (misalnya, ACE inhibitor atau ARB): Jika tekanan darah meningkat, tetapi harus digunakan dengan hati-hati karena risiko penurunan fungsi ginjal.
    - Suplemen kalsium: Jika terjadi hiperkalemia yang signifikan, suplemen kalsium dapat membantu melawan efek toksisitas kalium pada jantung.

  DRP:

  Needs additional drug therapy – Riwayat sering pusing belakangan yang tidak tertangani dengan obat Pereda nyeri : kemungkinan hipertensi yang tidak tertangani.

- **Stadium 1 AKI:** CrCl > 90 mL/min
- **Stadium 2 AKI:** CrCl 60-89 mL/min
- **Stadium 3 AKI:** CrCl < 60 mL/min