

# *Drug Induced Liver injury*

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Bagian Penyakit Dalam Unissula-RSISA

# *DILI*

- 3-8 % pasien datang ke rumah sakit karena efek samping obat
- Hepar menjadi salah satu organ yang paling riskan terkena efek?
- Hepatotoksisitas karena obat :
  1. Hepatotoksisitas intrinsik (direct/predictable)
  2. Hepatotoksisitas idiosinkrasi (indirect/unpredictable)

# *DILI*

- Biasanya mulai terlihat 1 minggu sampai beberapa bulan setelah pertama kali terapi
- Gejala mereda setelah obat dihentikan, memburuk jika diteruskan
- Rechallenged → recur lebih berat
- Merupakan alasan obat gagal edar atau ditarik dari peredaran

# Macam Obat

Withdrawals or not approved in the USA	Warnings
Iproniazid	Paracetamol (acetaminophen)
Ticrynafen	Leflunomide
Benoxaprofen	Nefazodone*
Nefazodone*	Isoniazid
Ibufenac	Labetolol
Perhexiline	Nevirapine
Dilevalol	Pyrazinimide/ rifampicin
Fipexide	Terbinafine
Benzarone	Valproic acid
Alpidem	Zifurlukast
Bendazac	Atomexitine
Chlormezanone	Saquinavir/ rifampicin
Pemoline	Interferon- $\alpha$ -1
Felbamate	Infliximab
Bromfenac	Telithromycin
Tolcapone	(Kava)
Trovafloxacin	(Lipokinex)
Troglitazone	
Ximelagatran	
Nimeluside (Hydroxycut)	

- Jika menemukan peningkatan transaminase yang belum jelas sebabnya → anamnesis penggunaan obat sebelumnya

# Jenis kerusakan

Type of Injury	Representative responsible drug(s)
<b><i>Acute liver diseases</i></b>	
Acute hepatocellular injury	Numerous drugs such as Isoniazid, rifampicin, methyl dopa, telithromycin, ketoconazole, diclofenac
Mononucleosis-like	Sulfonamides, phenytoin, dapsone
Fulminant hepatitis	Paracetamol (acetaminophen)
Bland cholestasis	Anabolic/ androgenic steroids, ciclosporin
Cholestatic hepatitis	Chlorpromazine, erythromycin, amoxicillin-clavulanate, clarithromycin
<b><i>Chronic liver diseases</i></b>	
Chronic hepatitis	Methotrexate, lisinopril, trazodone, uracil
Autoimmune hepatitis	Nitrofurantoin, minocycline, methyldopa, oxyphenisatin
Macrovesicular hepatitis	Corticosteroids, methotrexate, asparaginase, alcohol, halothane
Microvesicular hepatitis	Valproic acid, tetracyclines, cocaine, amiodarone
Steatohepatitis	Amiodarone, griseofulvin, perhexiline maleate
Cirrhosis	Methotrexate, amiodarone
Granulomatous hepatitis	Allopurinol, rosiglitazone, sulfonamide, phenylbutazone, quinidine
Primary biliary cirrhosis-like	Chlorpromazine, erythromycin, amoxicillin-clavulanate, haloperidol
Peliosis hepatic	Anabolic steroids, oral contraceptives
Portal vein thrombosis	Oral contraceptives
Sinusoidal obstructive syndrome	Pyrolozidine alkaloids, adriamycin, floxuridine, oncotherapy
Nodular transformation	Anabolic and contraceptive steroids
Adenoma	Anabolic and contraceptive steroids
Hepatocellular carcinoma	Thorotrast, anabolic and contraceptive steroids
Cholangiocarcinoma	Thorotrast
Angiosarcoma	Vinyl chloride, Inorganic arsenicals

# Faktor Predisposisi DILI dan Outcome

- Jenis Kerusakan
- Wanita
- Usia
- Hep B / C kronis
- Alkohol

# Pendekatan Diagnosis

- Merupakan diagnosis eksklusi
- Anamnesis cermat
- klinis dan lab lengkap
- Kondisi medis kenapa obat diberikan
- Interaksi sinergistik dari beberapa obat

# Metode Assessment

- RUCAM score
- M and V system

# Tampilan Klinis

- Asimtomatis – fulminan
- Fatigue, myalgia, nausea, vomit, abdominal discomfort, demam, artralgia, ikterus, pruritus
- AST ALT ↑ (tipe hepatoseluler)
- ALP ↑(tipe kolestatik)
- Bilirubin total ↑ !!
- PT,INR
- Eosinofil

# Pengelolaan

- Stop obat segera