

اپروچ بالینی به کبد چرب در کودکان

دکتر سارا صفری

فوق تخصص گوارش و کبد کودکان

POSITION STATEMENT

Hepatology

Paediatric steatotic liver disease has unique characteristics: A multisociety statement endorsing the new nomenclature

European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) | European Association for the Study of the Liver (EASL) | North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) | Latin-American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (LASPGHAN) | Asian Pan-Pacific Society for Pediatric Gastroenterology, Hepatology and Nutrition (APPSPGHAN) | Pan Arab Society for Pediatric Gastroenterology and Nutrition (PASPGHAN) | Commonwealth Association of Paediatric Gastroenterology & Nutrition (CAPGAN) | Federation of International Societies of Pediatric Hepatology, Gastroenterology and Nutrition (FISPGHAN)

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Abstract

Nonalcoholic fatty liver disease (NAFLD) has been a commonly used term

Metabolic dysfunction-associated steatotic liver disease in children and adolescents

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INTRODUCTION

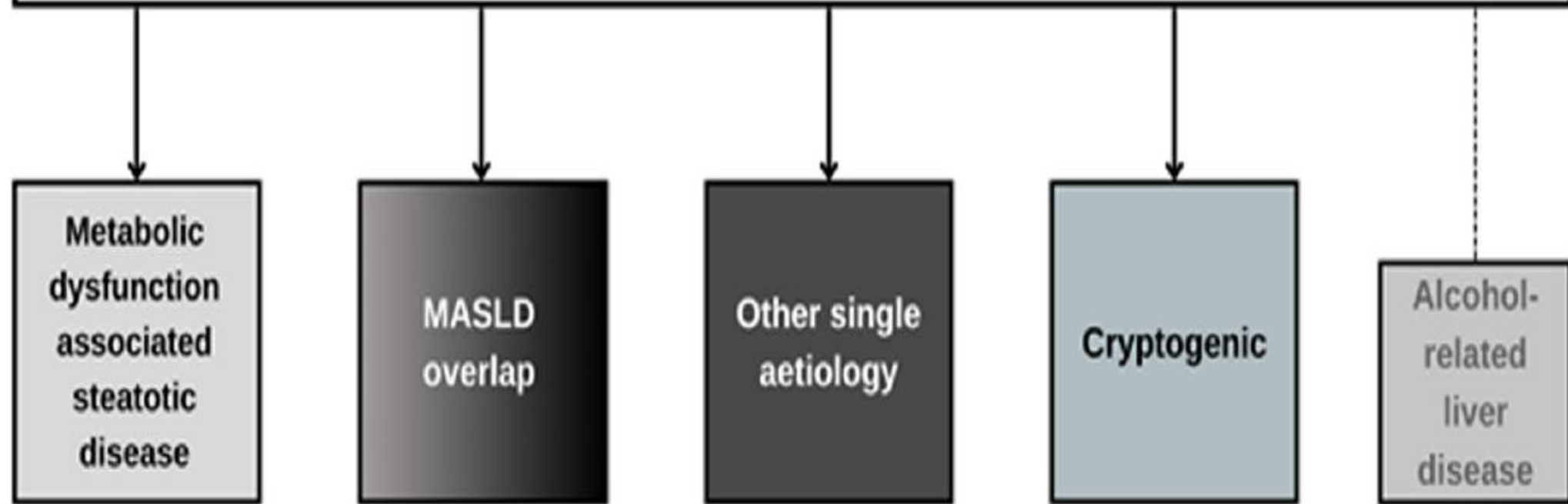
Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease (NAFLD) [1], is the most common cause of liver disease in children [2-4]. MASLD is a steatotic liver disease that occurs in

Zoom in



“Steatotic Liver Disease” (SLD):
as the overarching term for disorders associated with hepatic lipid accumulation.

Paediatric steatotic liver disease (SLD)



MASLD:

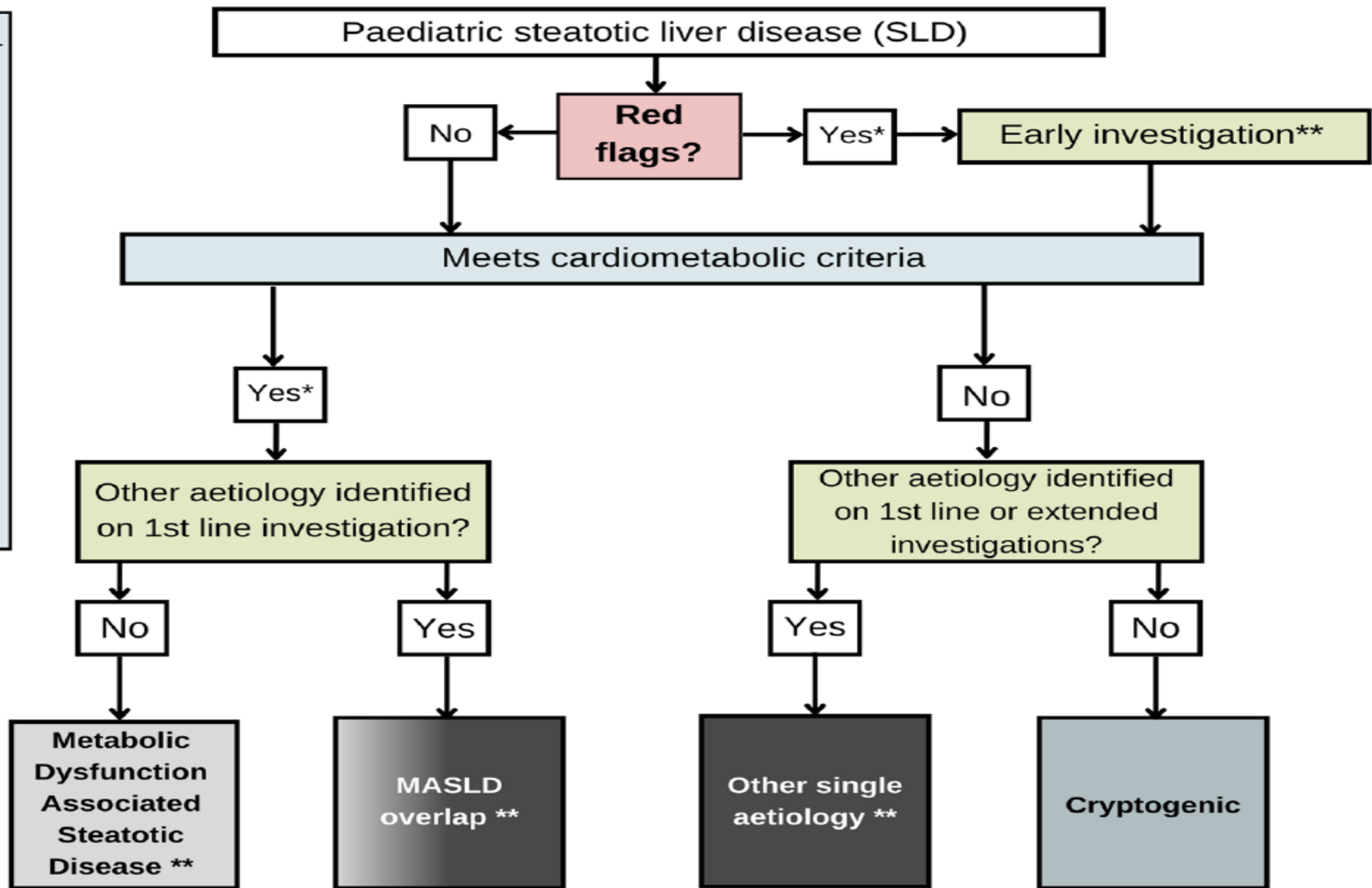
- may be made when the child has signs of **steatosis** and meets **at least one cardiometabolic** criterion and no evidence of other disease is found on investigation.
- Steatosis may be suspected on the basis of **elevated alanine aminotransferase** or of **abnormal imaging**(sono can detect moderate to severe steatosis (>33%) but increased hepatic echogenicity may also occur in the setting of inflammation and infiltration of other substances (such as glycogen), not just fat. MRI is a more sensitive imaging technique(>5%).elastography is being increasingly used and studied in children)
- Elevated ALT is obviously nonspecific and may indeed be normal in the context of even severe Steatosis.

Paediatric cardiometabolic criteria

BMI $\geq$ 85th percentile for age/sex (BMI z score $\geq +1$) OR waist circumference $>$ 95th percentile OR ethnicity adjusted

+/-

- Fasting serum glucose $\geq$ 5.6mmol/l ($\geq$ 100mg / dl) OR serum glucose $\geq$ 11.1 mmol. l ($\geq$ 200mg/dl) OR 2-hour post-load glucose levels $\geq$ 7.8mmol/l (140mg/dl) OR HbA1c $\geq$ 5.7% (39 mmol/L) OR already diagnosed / treated type 2 diabetes OR treatment for type 2 diabetes**
- Blood pressure age $<$ 13years, BP $\geq$ 95th percentile OR $\geq$ 130/80 mmHg (whichever is lower); age $\geq$ 13y, 130/85mm/Hg OR specific antihypertensive drug treatment**
- Plasma triglycerides $<$ 10 y, $\geq$ 1.15mmol/L ($\geq$ 100mg/dl); age $\geq$ 10 y, $\geq$ 1.7mmol/L ($\geq$ 150mg/dL) OR lipid lowering treatment**
- Plasma HDL-cholesterol $\leq$ 1.0mmol/L ($\leq$ 40mg/dL) or lipid lowering treatment**



1st line investigation

- Autoimmune liver disease
- Wilson's disease
- Alpha 1 anti-trypsin deficiency
- Thyroid function tests
- Coeliac disease
- Hepatitis B and C
- Consider Drug Induced Liver Injury (DILI) / alcohol

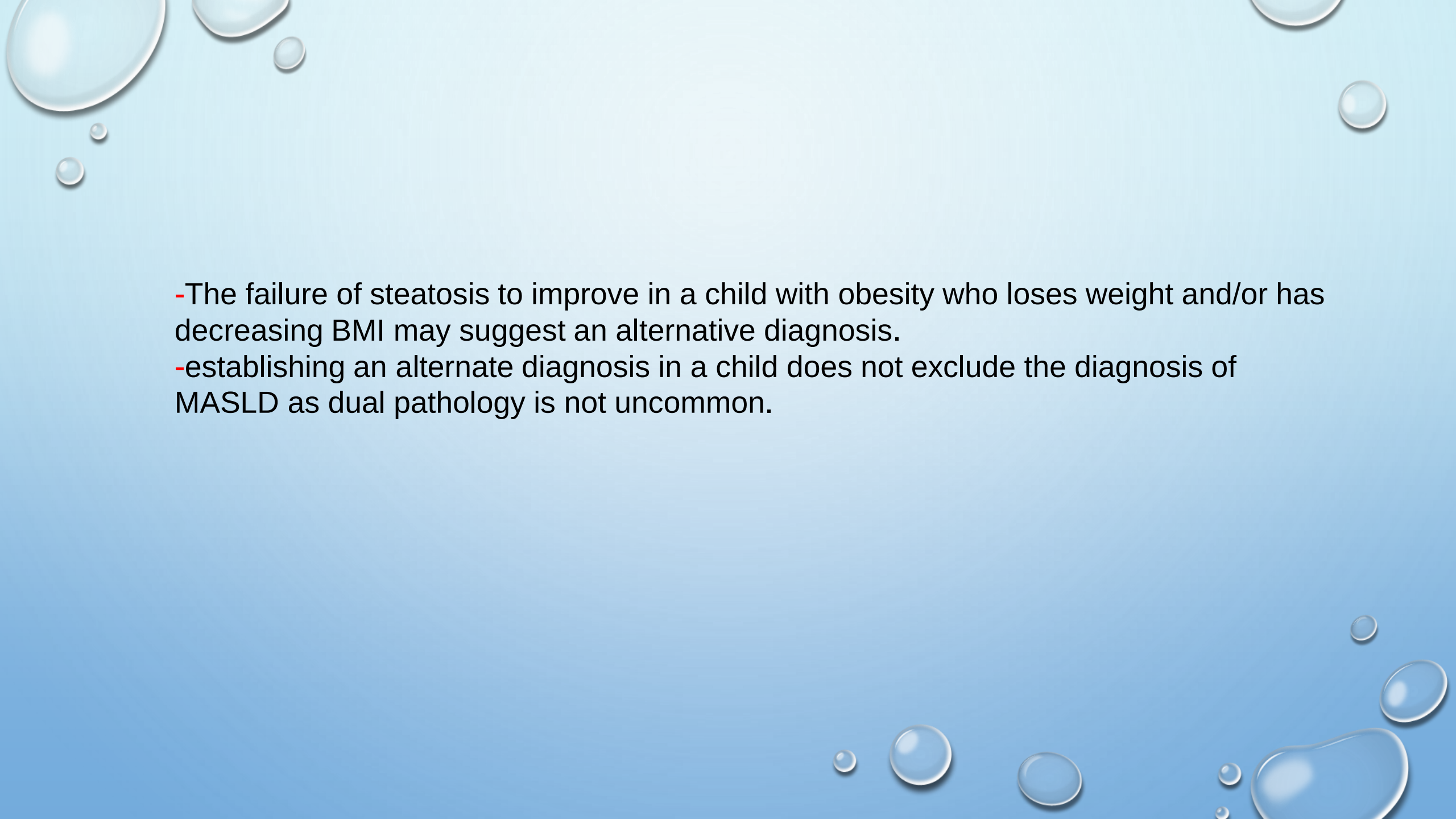
Red flags

- Under 8yrs old
- Developmental delay
- Synthetic dysfunction
- BMI z score <1
- Splenomegaly
- History suspicious of other aetiology

Extended investigation

To include:

- Inborn errors of metabolism
- Genetics
- Liver biopsy

- 
- The failure of steatosis to improve in a child with obesity who loses weight and/or has decreasing BMI may suggest an alternative diagnosis.
 - establishing an alternate diagnosis in a child does not exclude the diagnosis of MASLD as dual pathology is not uncommon.

SCREENING:

Under the new MASLD criterion, imaging or biopsy evidence of steatosis is the key definition, but updated guidance for screening is not yet available. Until new screening guidelines are developed, we continue to suggest screening with ALT because this strategy will help to identify the subset of children with MASLD who are at increased risk for more severe disease (eg, metabolic dysfunction-associated steatohepatitis/nonalcoholic steatohepatitis [MASH/NASH]), even if it fails to identify the subset of children with hepatic steatosis who have normal liver enzymes.

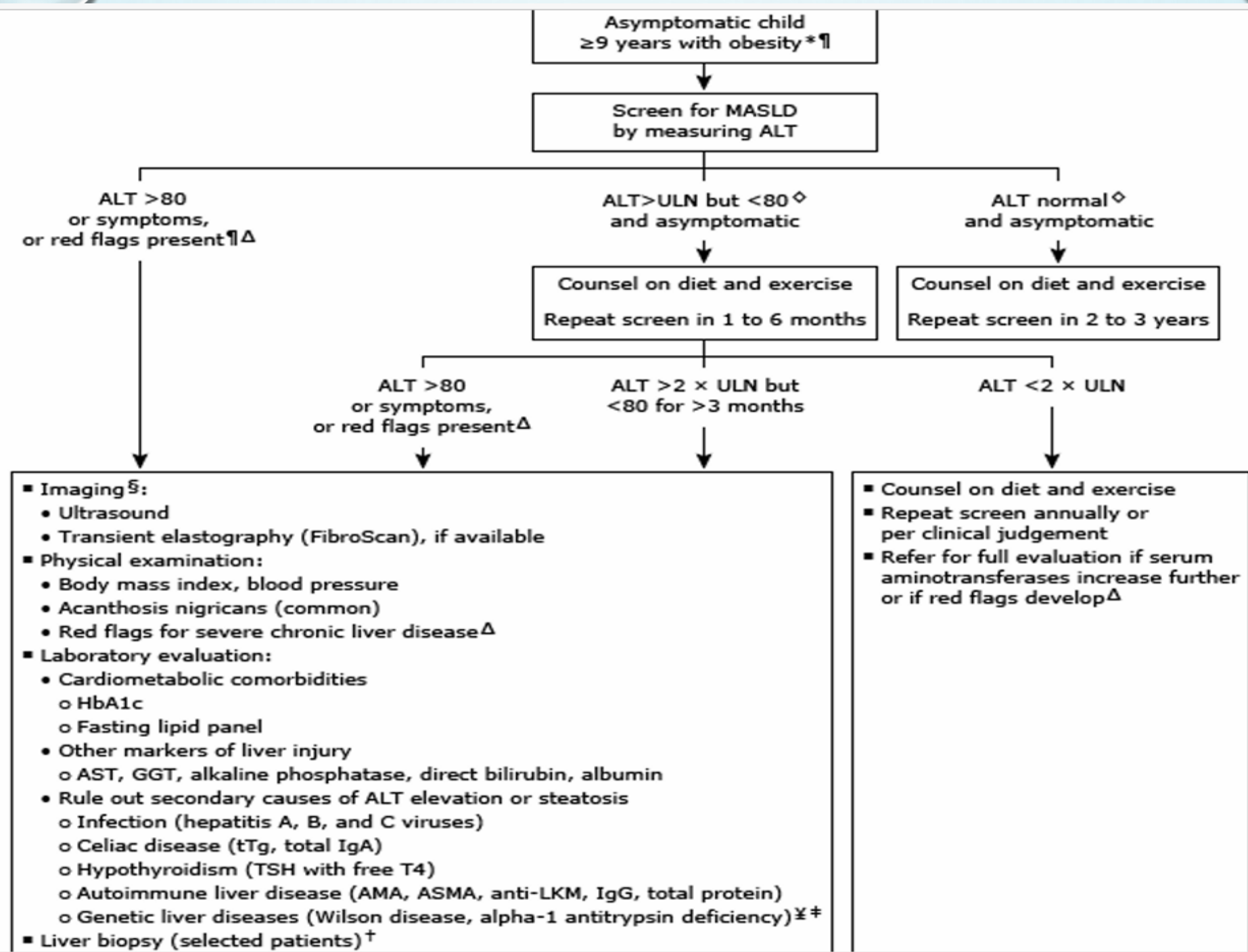
Indications:

- 1.all children with obesity (body mass index $\geq$ 95th percentile)
- 2.overweight children (body mass index $\geq$ 85th percentile) if other risk factors are present (eg, signs of insulin resistance or a family history of NAFLD or MASLD).

Begin screening:

between 9 and 11 years of age or
younger age if there are strong risk factors for MASLD:

1. metabolic syndrome (abdominal fat distribution, insulin resistance, diabetes, dyslipidemia, and hypertension)
2. polycystic ovary syndrome
3. obstructive sleep apnea (OSA)
3. maternal obesity during gestation
4. Panhypopituitarism
5. Sarcopenia
6. Lower muscle mass
7. Hispanic ethnicity



ALT interpretation:

- Adolescents 12 to 17 years:
 - Girls – 22 units/L
 - Boys – 26 units/L
- Children 1 to <12 years – 30 units/L

For patients with elevated ALT and symptoms of an acute infection (fever, vomiting, diarrhea, pharyngitis, etc), measure ALT again 2-4 weeks after resolution of the illness to verify if the ALT elevation persists, before initiating further evaluation.

for asymptomatic patients with more marked acute liver enzyme elevations ($>10 \times \text{ULN}$), repeat the test 2 weeks later rather than initiating a more extensive evaluation.

Many viral illnesses, including influenza, Epstein-Barr virus, cytomegalovirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and others, can be associated with mild to marked liver enzyme elevations, and some of these infections can be asymptomatic.

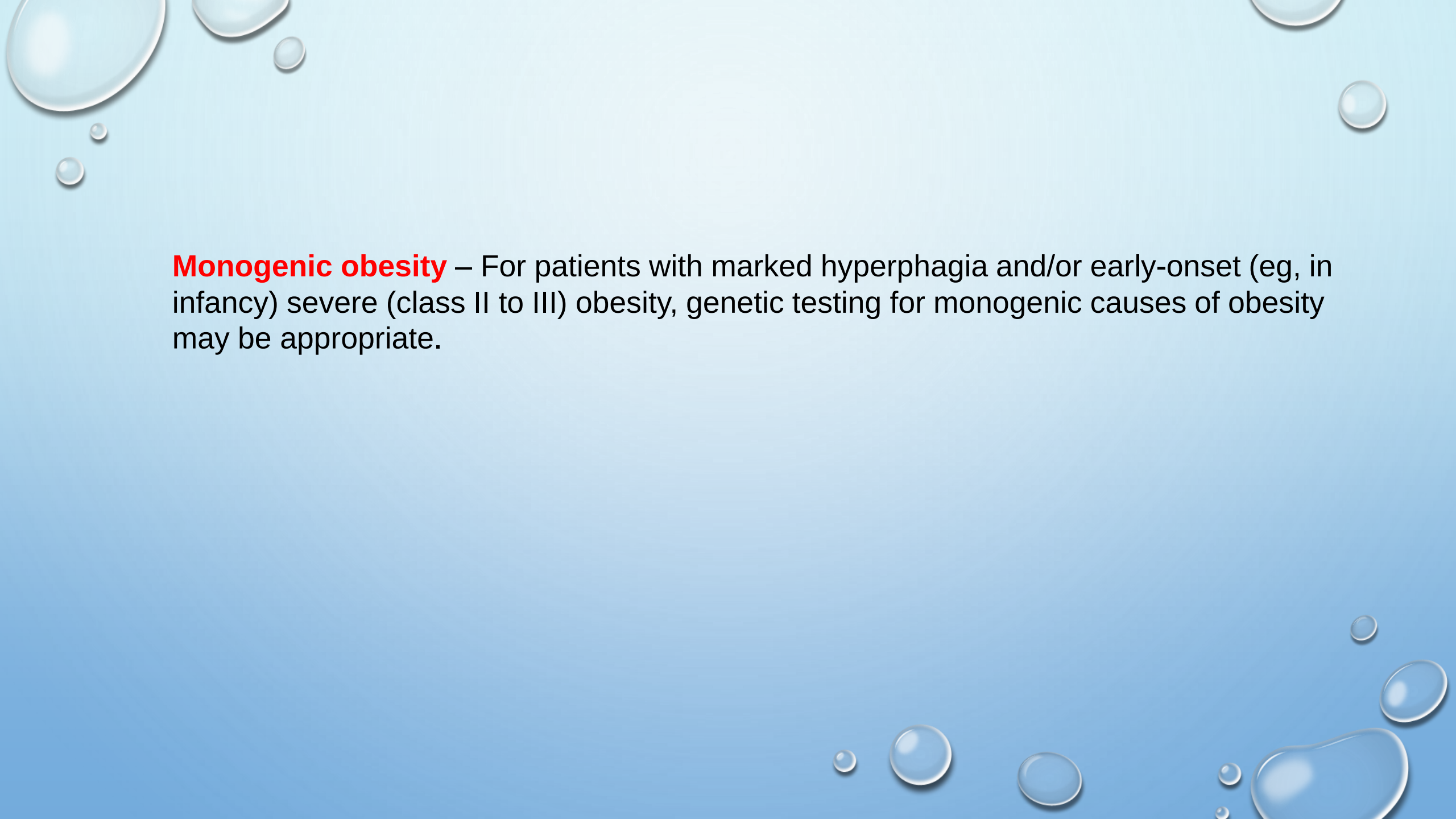
Red flags for advanced liver disease:

- 1-chronic fatigue
- 2-gastrointestinal bleeding
- 3-jaundice
- 4-splenomegaly
- 5-firm liver edge
- 6-enlarged left lobe
- 7-low Platelets
- 8-low white blood cells
- 9-elevated direct bilirubin
- 10-elevated INR

Liver biopsy:

the gold standard for diagnosis of MASH.

we suggest liver biopsy for patients who have had ALT elevations $>2 \times \text{ULN}$ for 6 or more months or for those with ALT >80 unit/L, red flags for advanced liver disease , or features that suggest an alternate cause of the liver disease that requires biopsy for diagnosis.



Monogenic obesity – For patients with marked hyperphagia and/or early-onset (eg, in infancy) severe (class II to III) obesity, genetic testing for monogenic causes of obesity may be appropriate.