Interpreting Abnormal LFTs in Kids: When, Why & What Next?

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Disclosures

- None

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Objectives

- When to check ”LFTs” in an outpatient
- What to do when these numbers come back abnormal
  - Etiologies
  - Next steps
  - Follow-up
- When to refer – electively and urgently

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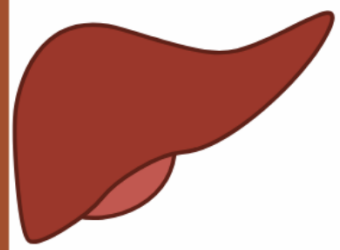
THE CURB SIDERS INTERNAL MEDICINE

BEST OF LIVER TEST

with Dr. Elliot Tapper @ebtapper



Definitions

Liver Chemistries:AST/ALT & Alkalin
phosphatase (ALP)

ALP: family of enzymes in liver. bone
placenta, intestine & kidn

Tests of Function: INR,
platelets

Acute Liver Injury

In
•

Make sure you talk about elevated Alk phos

R= (ALT / ULN ALT)
(ALP / ULN ALP)
>5: Hepatocellualr
2-5: Mixed
<2: Cholestatic

s/ingestions

C/B/A screening, ANA, Anti-smooth
ibody, serum IgG, ultrasound
tic: consider MRCP, AMA (PBC)

AST & A
Most co
1. Ische
2. Pancr
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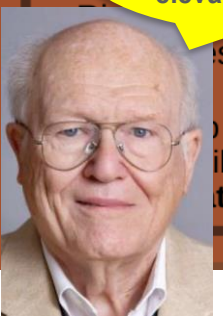
aceta
4. Viral



NASPGHAN Clinical
and Treatment of
in Children: Recc
Committee on NAFL
Society of Pediatri
and Nu

Liver enzymes: 1. If the AST or ALT is elevated mildly, when do these labs need to be repeated and do

PRACTICE GUIDELINE Guidance for the Clinician in Rendering Pediatric Care

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Sensible Medicine

MASLD: Another Disease Label for that Leads to Overtesting

JULIE LAURENCE AND EMMA GLASER
NOV 11, 2025

91 17 1

AGA Technical Review on the Evaluation of Liver Chemistry Tests

This literature review and the recommendations therein were prepared for the American Gastroenterological Association Clin Practice Committee. The paper was approved by the Committee on March 3, 2002 and the AGA Governing Board on May 2002.

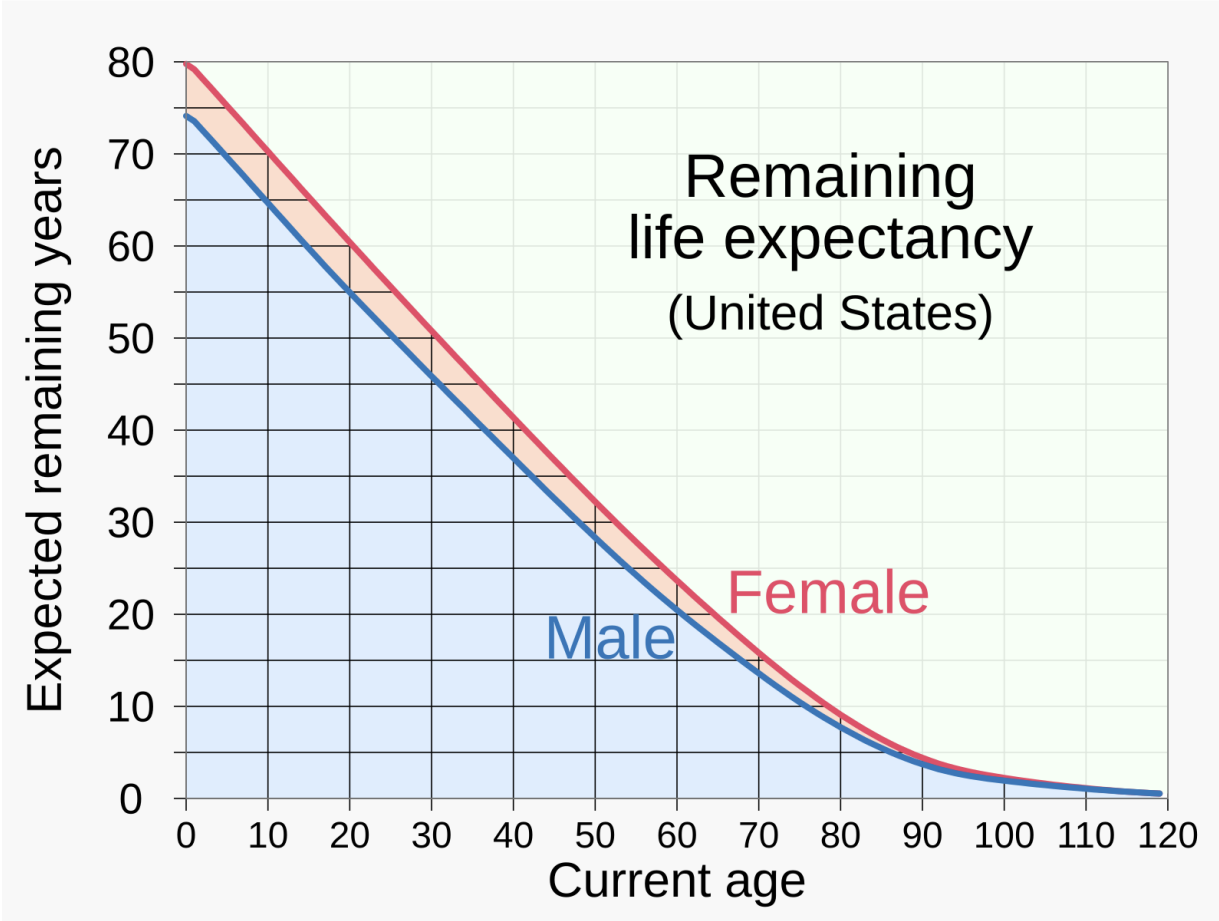
Over what time frame would you see a patient progress from fatty liver disease (NAFLD)to non-alcoholic steatohepatitis

What Lab values for AST/ALT/GGT that are concerning as I am just using the reference ranges in epic


Why do we even measure LFTs?? What does it all really mean?

Why do we send a liver panel?

- Decrease morbidity and mortality of children by:
  - Identifying liver diseases with targeted therapy, predictable outcomes
    - Autoimmune hepatitis, chronic viral hepatitis, PSC, genetic liver disease
  - Preventing progression to serious liver-related outcomes (cirrhosis, variceal hemorrhage, ascites, cancer)



US Social Security Admin, 2023

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When to send a liver panel

- Purpose:
  - Evaluating for potential acute or chronic liver disease in a child with signs/symptoms
    - Jaundice
    - Hepatomegaly (>2 yo ➡ up to 2 cm ⬇ RCM)
    - Obesity
    - Easy bruising/bleeding
  - Evaluating for potential systemic disease in a child with
    - Weight loss/poor weight gain
    - Recurrent fever
    - Chronic abdominal pain
- A liver panel is not an appropriate screening test in healthy children

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What are LFTs?
And do they really measure ***liver function***?

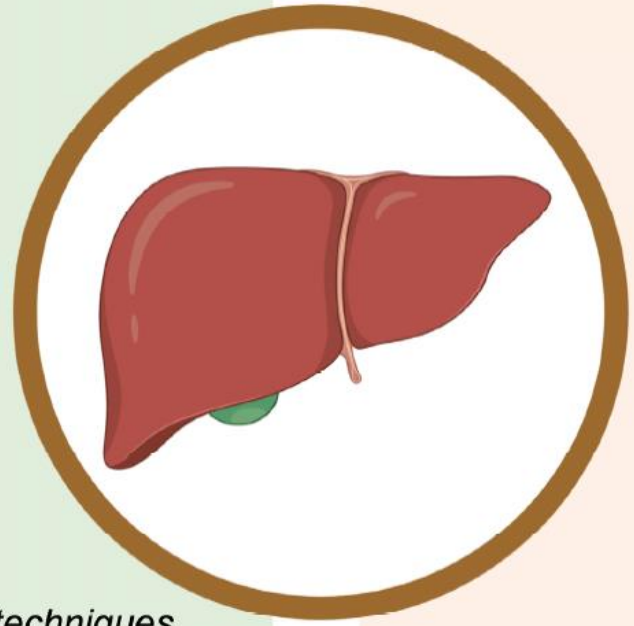
Dynamic tests

Clearance half - life
-> ICG
-> Caffeine
-> Bromosulfophthalien

Elimination capacity
-> Galactose

Metabolic formation
-> $^{14}CO_2$ exhalation
-> $^{13}CO_2$ exhalation
(Aminopyrine, methacetin)
-> Lidocaine (MEGX)

Molecular nuclear imaging techniques
-> ^{99m}Tc-galactosyl serum albumin scintigraphy
->^{99m}Tc-mebrofenin hepatobiliary scintigraphy



Static tests

Excretion
-> Bilirubin

Cholestasis
-> AP
-> yGT

Hepatic integrity
-> ASAT
-> ALAT
-> GLDH

Synthetic processes
-> Albumin
-> Coagulation

Haertel, J Clin Med, 2024

Bilirubin
- Hemolysis

Alk Phosphatase
- Bone
- Intestine & Kidney

AST
- Muscle, Heart
- Kidney
- Mitochondria

ALT
- Liver

GGT
- Liver
- EtOH

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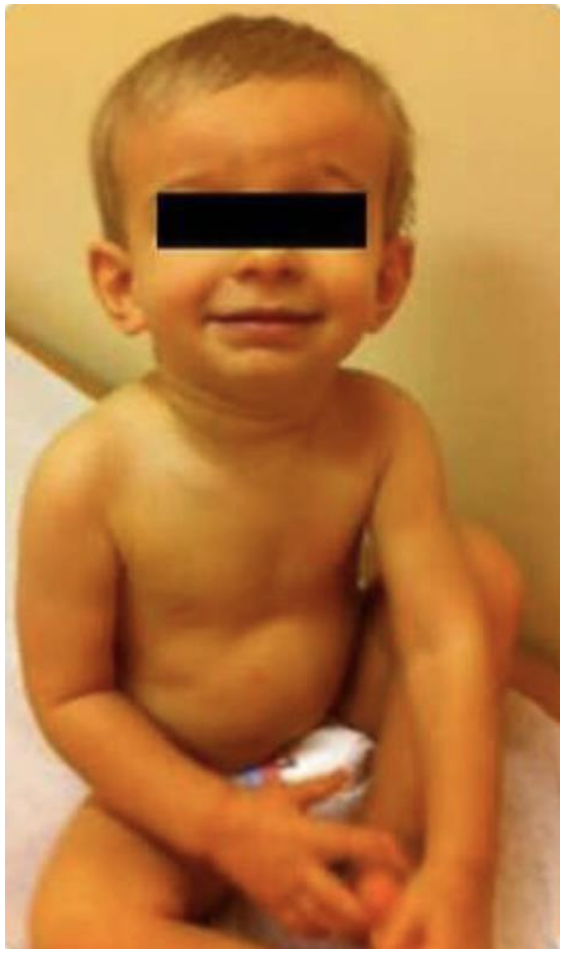
Differential Diagnosis of Abnormal LFTs

- By age of patient
- By pattern of elevation
- By associated signs/symptoms



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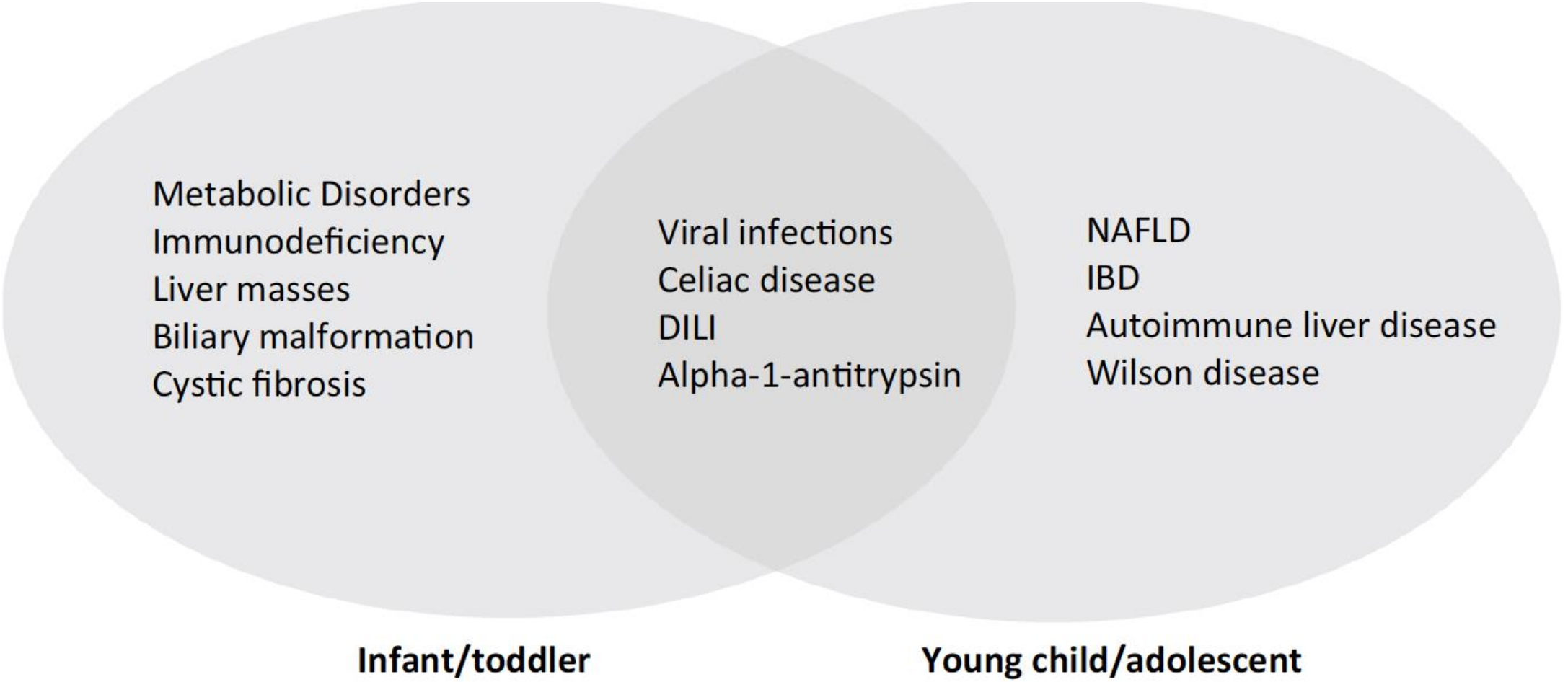
Differential Diagnosis by Age



Costa et al, European J Pediatrics, 2023

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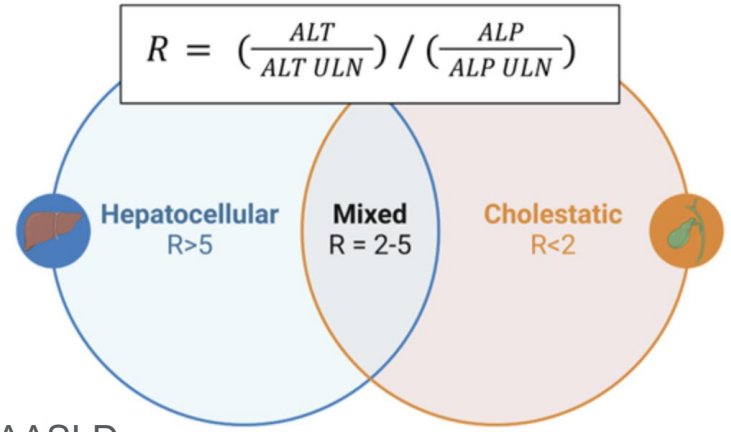
Differential Diagnosis by pattern

- Hepatocellular vs. Cholestatic vs. Mixed

Hepatocellular	Cholestatic	Mixed
Drugs/Toxins	Drugs/Toxins	Drugs/Toxins
MASLD	Primary Sclerosing Cholangitis	MASLD
Viral Hepatitis	Viral Hepatitis	Viral Hepatitis
Autoimmune Hepatitis	Choledocholithiasis	
Shock Liver	Sepsis/UTI	
Wilson's disease	Biliary Atresia	
Alpha-1-AT def	Genetic Cholestasis	

Any elevation of bilirubin should prompt call to GI-Liver



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Differential Diagnosis by pattern

- Degree of AST/ALT elevation

Borderline (< 2 ULN)	Mild (2-5 x ULN)	Moderate (5-15 x ULN)	Severe (> 15 X ULN)
Drugs/Toxins	Drugs/Toxins	Drugs/Toxins	Drugs/Toxins
MASL-D	MASL-D	Viral Hepatitis	Viral Hepatitis
Viral Hepatitis	Viral Hepatitis	AIH	Ischemic Hepatitis
AIH	AIH	Wilson's disease	Rhabdomyolysis
Wilson's disease	Wilson's disease		
Alpha-1-AT def	Alpha-1-AT def		
Celiac disease	Celiac disease		
Thyroid disease	Thyroid disease		
Muscle disease	Muscle disease		
Other systemic disorder	Other systemic disorder		

ALT >1000 should prompt consideration of acute liver failure and/or call to GI-Liver

ACG Clinical Guideline 2017

Differential Diagnosis by pattern

- Isolated bilirubin elevation in INFANT
  - **First Step – Fractionate bilirubin**
    - If direct bilirubin is normal – likely breast milk jaundice
    - Hemolysis
    - Crigler-Najjar
- Isolated bilirubin elevation in ADOLESCENT
  - **First Step – Fractionate bilirubin**
    - If direct bilirubin is normal – likely Gilbert's Syndrome

Differential Diagnosis by pattern

- Isolated elevated Alkaline Phosphatase (found in bile ducts)
  - Alk Phos also found in bone, intestine, kidneys
  - Confirm Alk phos is from liver by measuring GGT
  - ↑ Alk Phos with normal GGT = no liver disease
- Non-hepatic causes
  - Benign transient hyperphosphatasia/semia (Alk Phos > 1000, most < 2 yo, normalize within 1 year)
  - Biomarker of metabolic syndrome?

Zemer et al, European J Peds, 2023

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Differential Diagnosis by clinical presentation – Case 1

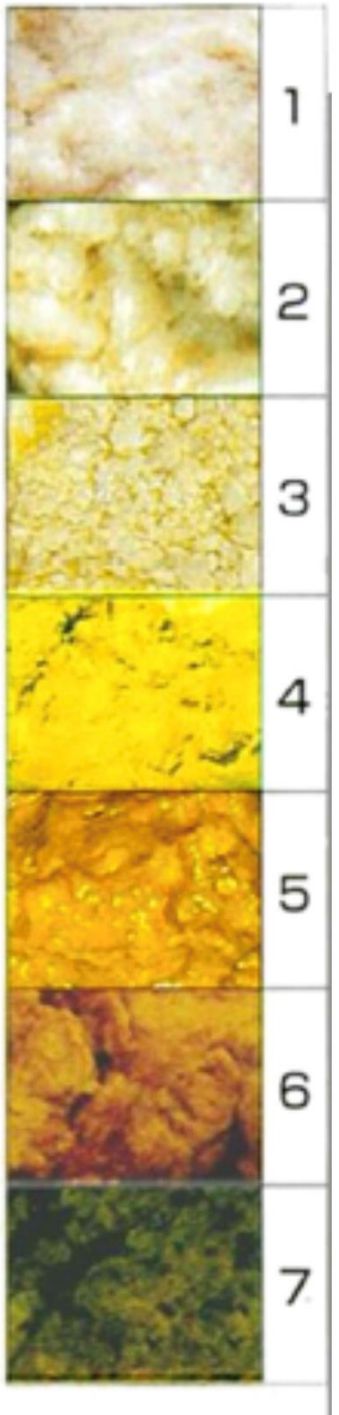
- 5-week-old well baby exam
- Feeding well (exclusively BM), good growth
- No fevers, sick contacts, skin lesions
- Unremarkable perinatal history
- No family history of jaundice, liver disease, hemolytic dz
- Jaundiced since leaving hospital
- Exam – liver 2.5 cm ↓ RCM

Differential Diagnosis by clinical presentatio
Case 1

- Labs

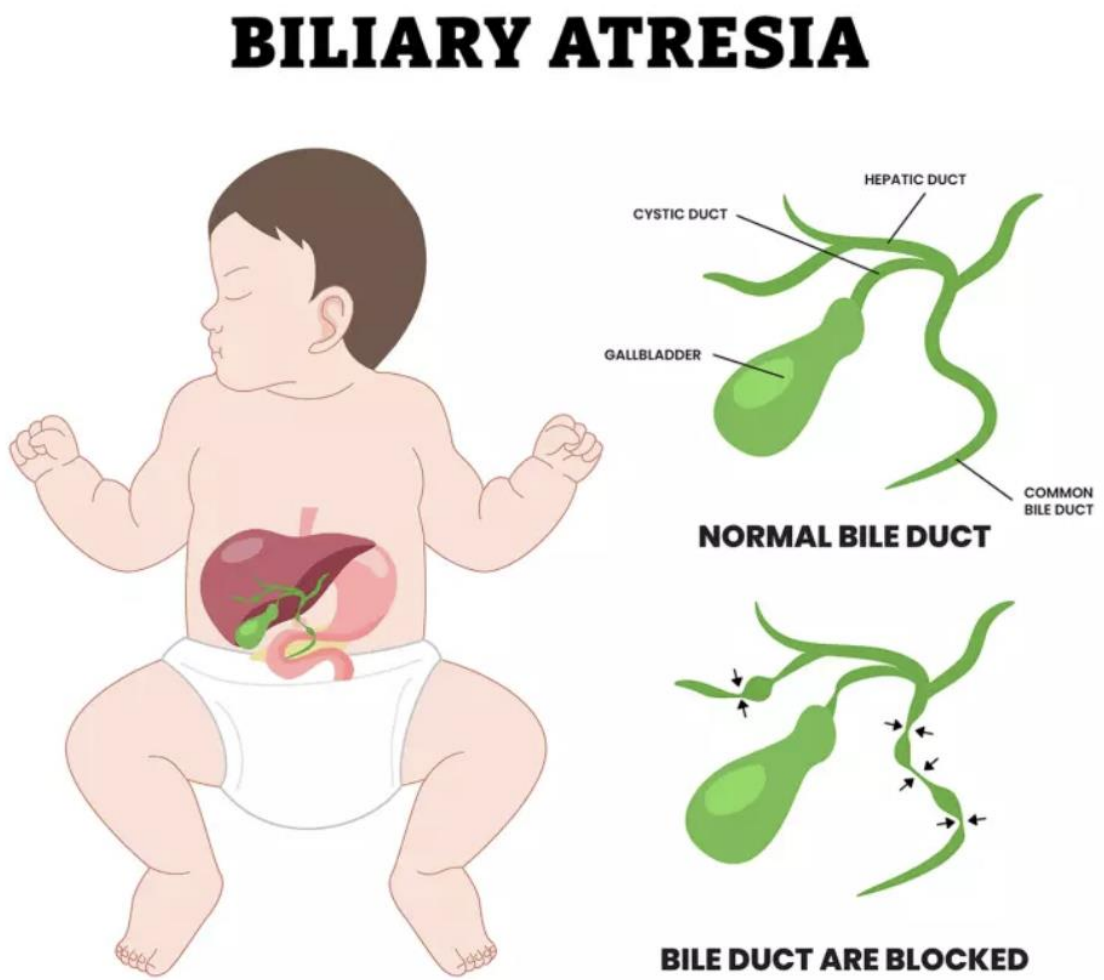
CBC – WBC 9.32, Hgb 11.9
Hct 34.2, Platelets 663
Liver – ALT 152, AST 130,
T bili 5.1, D bili 4.0,
Alk Phos 489, Alb 4.0
Electrolytes –
Normal, Glu 93

Acholic stool with jaundice is a sign of biliary obstruction and should prompt urgent call to GI-Liver, especially in infant



Biliary Atresia

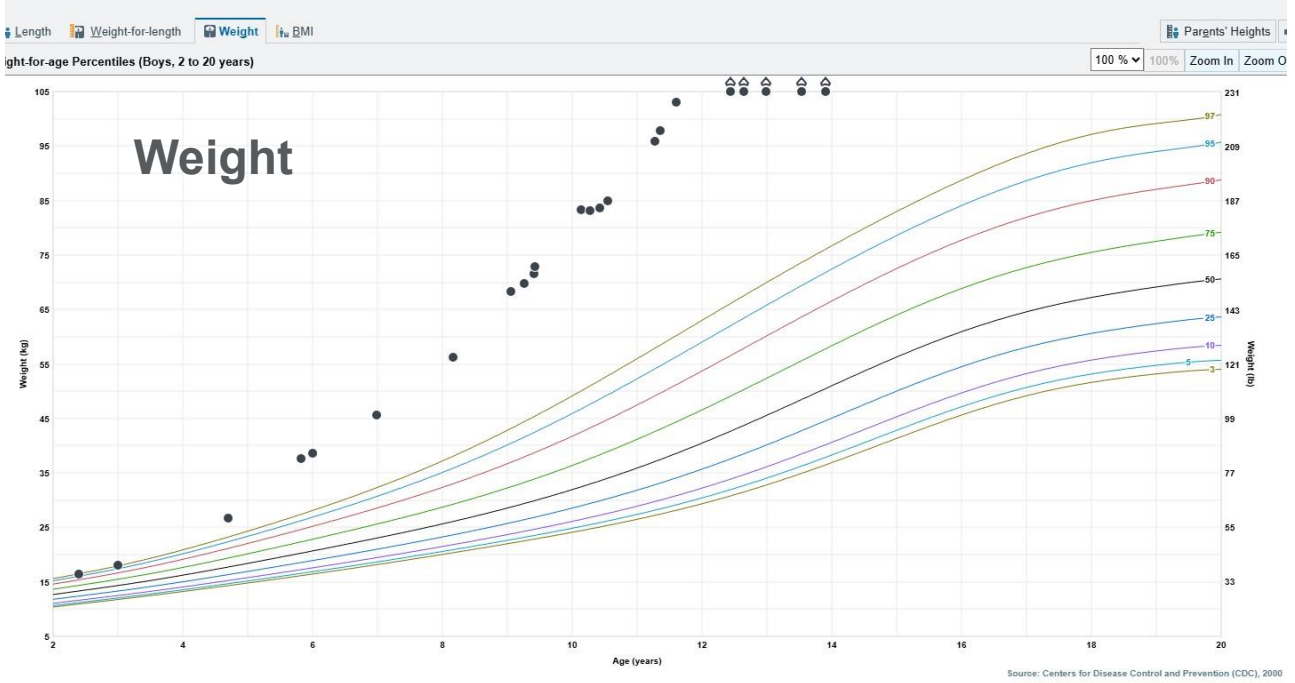
- 1 in 15,000 babies
- Progressive, fibrosing disease of extrahepatic bile ducts
- Early diagnosis and timely intervention are critical for best outcomes
- Presents in otherwise well-appearing infant with jaundice at > 2 weeks of age

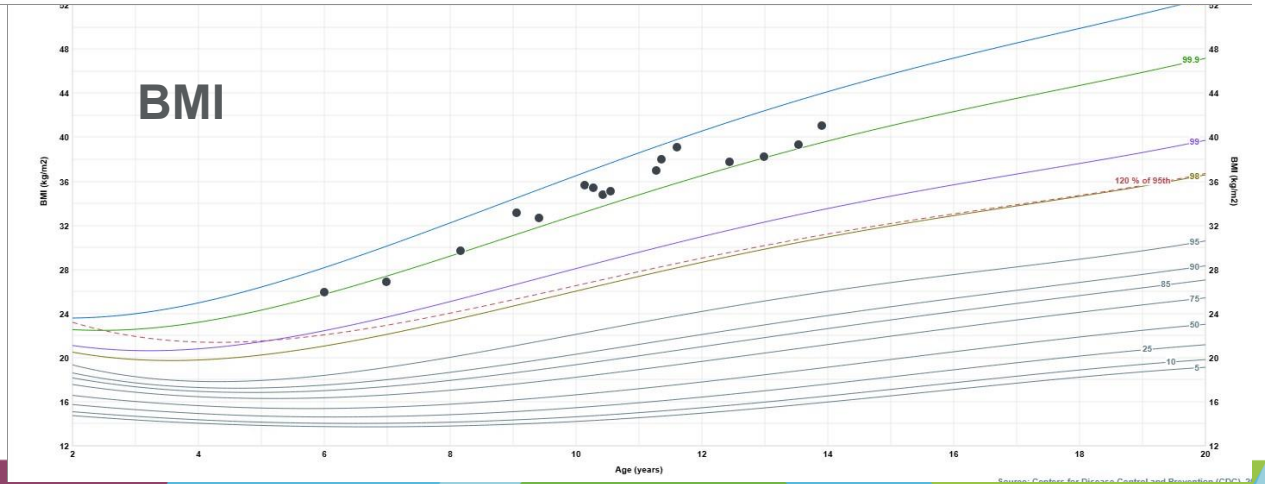


LA Times

Differential Diagnosis by clinical presentation – Case 2

- 14 yo new patient to your practice
- H/o food allergies, headaches
- Family history – Mom with overweight, “fatty liver”, thyroid disease; Dad with diabetes, older sister has high cholesterol
- Meds – Epi pen, Zyrtec





Should you check LFTs?

Who	What	How Often	Endorsed By
>/= 10 years, BMI >/= 95%	ALT, fasting glucose, fasting lipid panel	If ALT is normal – rescreen yearly if risk factors are unchanged, sooner if additional risk factors develop AASLD, 2025	AAP CPG Obesity, 2023 NASPGHAN NAFLD Guidelines, 2017 AASLD, 2025
>/= 10 years, BMI 85 – 95% + risk factors for T2DM or MASLD (sleep apnea, fm hx, known dyslipidemia, insulin resistance)	ALT, fasting glucose		AAP CPG Obesity, 2023 NASPGHAN NAFLD Guidelines, 2017 AASLD, 2025
Consider in < 10 years, severe obesity, + family history of MASLD, or hypopituitarism	ALT		NASPGHAN NAFLD Guidelines, 2017 AASLD, 2025
Consider in siblings of children with MASLD + risk factors (obesity, Hispanic ethnicity, T2DM, insulin resistance, dyslipidemia)	ALT		NASPGHAN NAFLD Guidelines, 2017 AASLD, 2025

Differential Diagnosis by clinical presentation – Case 2

- Labs
- Liver – ALT **51**, AST 32,
  T bili 0.3, D bili <0.1,
  Alk Phos 287, Alb 4.0

Abnormal ALT that persists for more than 3 months, OR any s/s of advanced liver disease (hepatomegaly, splenomegaly, thrombocytopenia, RUQ pain, chronic fatigue) – refer to GI/Liver

- How abnormal is this?
- Validated cut offs for ALT (NHANES data)
  - > 22 U/L in Females
  - > 26 U/L in Males
- These thresholds have high sensitivity (85% in boys and 92% in girls) and specificity (80%) **for detecting NAFLD** in US children with obesity

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Steatotic Liver Disease is the most common form of liver disease in children

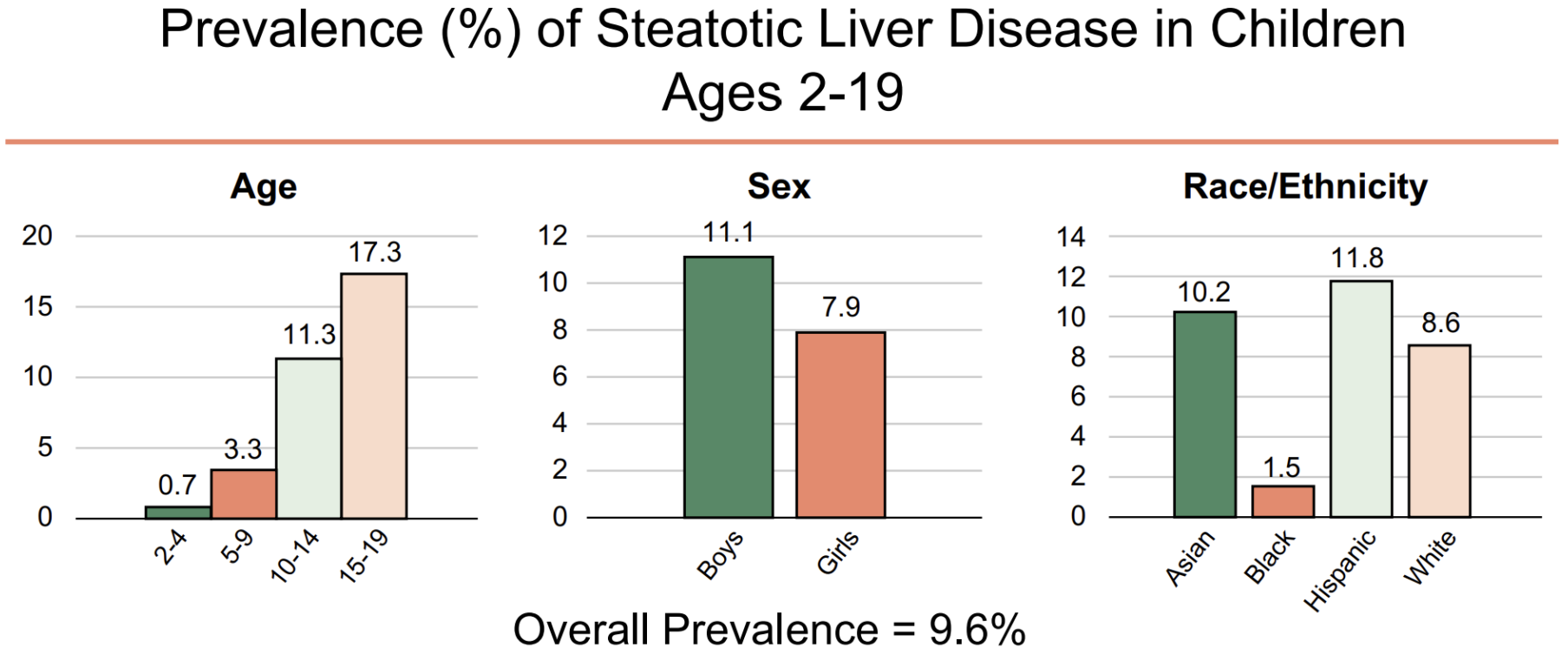

FIGURE 2 Distribution of age, sex, race/ethnicity among children with steatotic liver disease. The prevalence of steatotic liver disease by age, sex, race, and ethnicity was determined in a population-based autopsy analysis of 742 children in San Diego county, who died from traumatic or accidental causes.[5]

- 26% of children with obesity
- Incidence rate appears to be increasing (NHANES data)
- Children with NAFLD have ↑ liver-related mortality long-term

Xanthakos, AASLD, 2025

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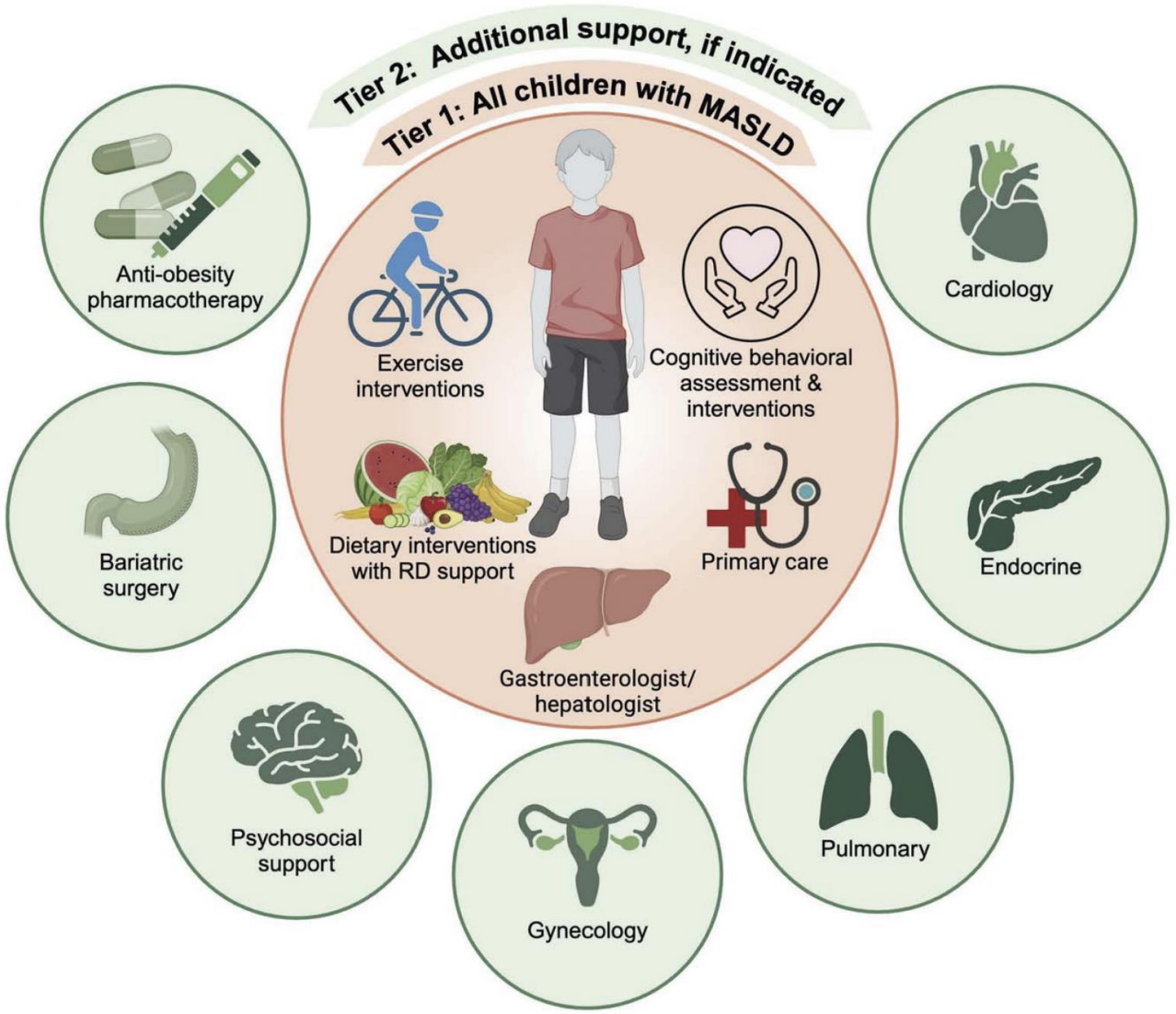
Multidisciplinary Care Model



Xanthakos, AASLD, 2025

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Differential Diagnosis by clinical presentation – Case 3

- 14 yo F being seen for ill visit
- Genetic syndrome associated with intellectual disability, autism spectrum disorder and drug-resistant epilepsy
- CC: rhinorrhea and cough x 1 month, excessive fatigue and “just not acting like self”
- Normal PE, extremely friendly and happy
- Meds: Diazepam, Seroquel, Sertraline, Trazodone, Zonisamide, Clonazepam, Phenobarbital, Guanfacine, Aygestin

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Differential Diagnosis by clinical presentation – Case 3

- Labs done yesterday
- Liver – **ALT 473, AST 258**,
  T bili 0.2, D bili --,
  Alk Phos 218, Alb 3.8

ALT in 400's consider calling GI-Liver (or re-check in 48 hours)

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Drug-Induced Liver Injury

- All Patients (n=1257); Hoofnagle, NEJM, 2019

Rank	Agent	Year of FDA Approval	No. (%)†
1	Amoxicillin–clavulanate	1984	91 (10.1)
2	Isoniazid	1952	48 (5.3)
3	Nitrofurantoin	1953	42 (4.7)
4	TMP-SMZ	1973	31 (3.4)
5	Minocycline	1971	28 (3.1)
6	Cefazolin	1973	20 (2.2)
7	Azithromycin	1991	18 (2.0)
8	Ciprofloxacin	1987	16 (1.8)
9	Levofloxacin	1996	13 (1.4)
10	Diclofenac	1988	12 (1.3)
11	Phenytoin	1946	12 (1.3)
12	Methyldopa	1962	11 (1.2)
13	Azathioprine	1968	10 (1.1)

- Pediatric Patients Only (n=57); DiPaola, JPGN, 2020

Antimicrobial (29)	**Antiepileptic**(12)	**Antineoplastic** (5)	**Psychotropic** (5)
Minocycline (11)	Valproate (6)	Mercaptopurine (2)	Atomoxetine (3)
Azithromycin (4)	Lamotrigine (2)	Thioguanine (1)	Methylphenidate (1)
Isoniazid (4)	Carbamazepine (1)	Asparaginase (1)	Fluoxetine (1)
Trimethoprim/sulfa (4)	Ethosuximide (1)	Pegaspargase (1)	
Oxacillin (2)	Phenobarbital (1)		
Amoxicillin/clavulanate (1)	Phenytoin (1)		**Other** (7)
Cefdinir (1)			Ethinyl estradiol (2)
Cefepime (1)			Hydroxycut (1)
Erythromycin (1)			Methyldopa (1)
			Nicotinic acid (1)
			Sulfasalazine (1)
			* Multiple drugs (1)

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Differential Diagnosis by case presentation – Case 4

- 16 yo F being seen for ill visit
- No significant PMHx or FmHx, no meds
- Fever x 4 days, mild throat pain, no cough, rhinorrhea, N/V, diarrhea
- Ill appearing, AC and PC LAD, pharyngitis and tonsillitis, palpable spleen tip, hint of scleral icterus

Differential Diagnosis by case presentation – Case 4

- Liver – **ALT 854, AST 650**,
  T bili 3.9, D bili 2.5,
  Alk Phos 347, Alb 2.7
- INR 1.0, PT 12.4
- Mono Spot positive
- EBV qPCR 534,200
- EBV IgM +, IgG -, EBNA +

- **Acute EBV Infection**
  - ↑ LFTs in 80-90% of patients
  - Jaundice in 5%
  - Hepatitis resolves over 5-6 weeks in **immunocompetent** patients

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Natural history of EBV hepatitis

- 36 children from Korea (hospitalized)

Symptoms and signs	No. of patients (%)
Fever	30 (83.3)
High fever (>39.5°C)	19 (52.8)
Abdominal pain	8 (22.2)
Vomiting	4 (11.1)
Rash	3 (8.3)
Icteric sclera	2 (5.6)
Cervical Lymphadenopathy	28 (77.8)
Tonsillar exudate	16 (44.4)
Nasal stuffness	13 (36.1)
Hepatomegaly	11 (30.6)
Splenomegaly	10 (27.8)
Eyelid swelling	10 (27.8)

27.8% ALT > 10X ULN
11.1% ALT >1000

- 166 children from Poland (hospitalized)

Signs and Symptoms	No. of Patients (%)
Lymphadenopathy	154 (92.8)
Pharyngitis with tonsillar exudate	150 (90.3)
Fever	143 (86.1)
Hepatomegaly	134 (80.7)
Splenomegaly	111 (66.9)
Rash	55 (33.1)
Abdominal pain	52 (31.3)
Eyelid swelling	49 (27.7)
Nausea or vomiting	45 (27.1)
Rash after amoxicillin administration	28 (16.9)
Jaundice/icteric sclera	19 (11.4)
Pruritus	19 (11.4)
Abdominal tenderness	18 (10.8)
Dark urine	8 (4.8)
Acholic stools	2 (1.2)

Differential Diagnosis by case presentation – Case 4 – EBV hepatitis

- 16 yo F being seen for ill visit
- No significant PMHx or FmHx, no meds
- Fever x 4 days, mild throat pain, no cough, rhinorrhea, N/V, dyspnea
- Ill
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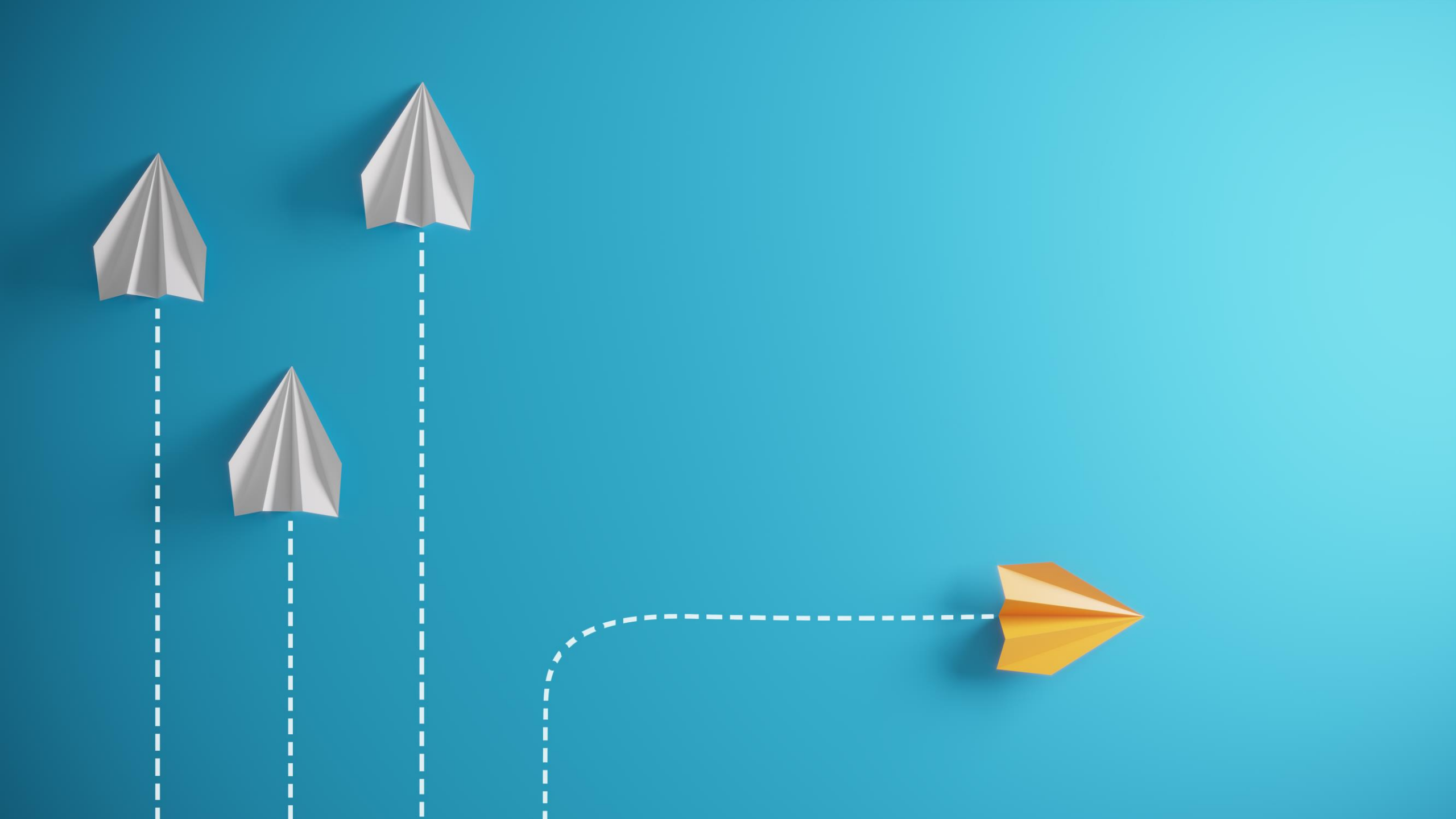
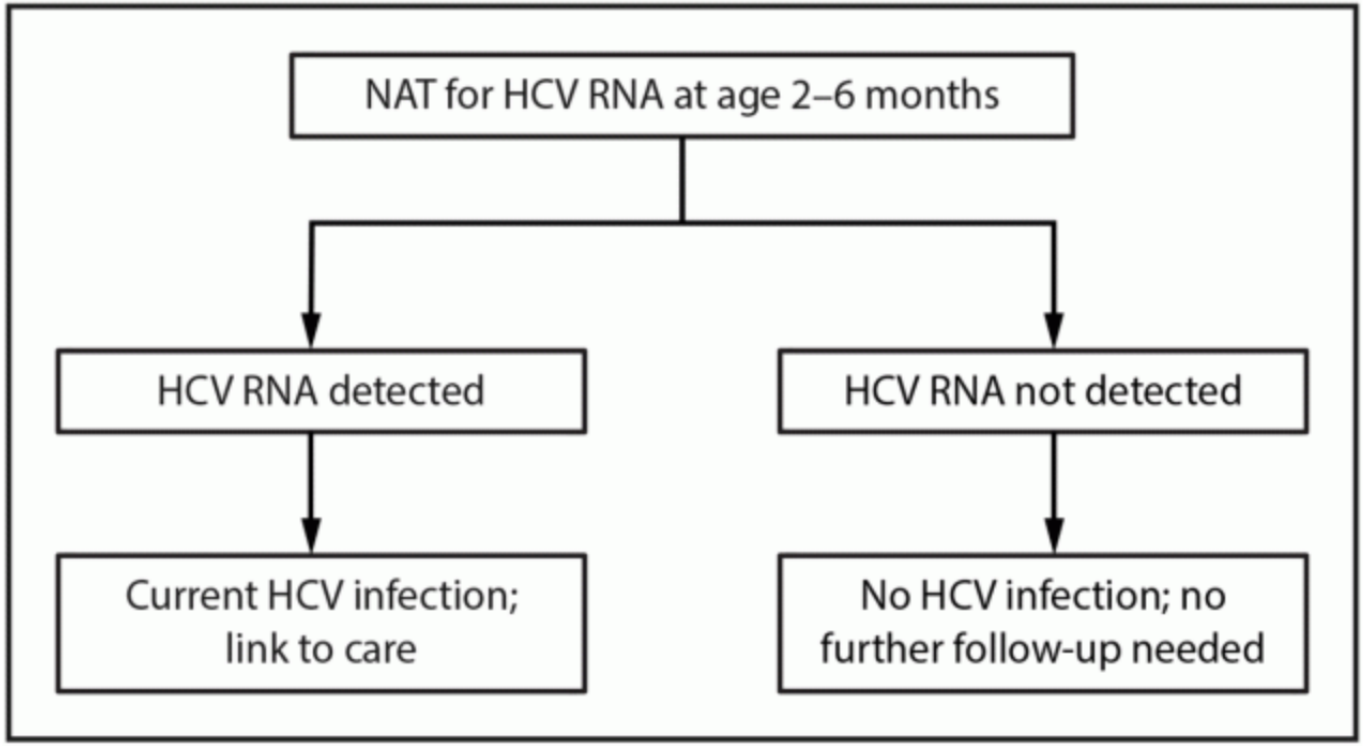
  sp

Short interval follow-up with serial exam and labs until clinically back to baseline and LFTs normalize



Hep C screening in perinatally exposed infants



- Refer as soon as diagnosed
- Treatment available at age 3 years
- Cure Hepatitis C Act of 2025 (S. 1941) currently being reviewed in Congress
  - Fund screening, treatment, public health infrastructure

Abbreviations: FDA = Food and Drug Administration; HCV = hepatitis C virus; NAT = nucleic acid test.

MMWR, 11/2023

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Management of Hep B exposed infants

with Birth Weights ≥2,000 grams (≥4.4 lbs)

Administer hepatitis B immune globulin (HBIG) and single-antigen vaccine in separate limbs at birth (≤12 hours).
Complete vaccine series with 2 additional doses of single-antigen vaccine (3 total doses) OR with 3 additional doses of combination vaccine (4 total doses).

	≤12 hours of birth	1 mo	2 mos	4 mos	6 mos
Single-Antigen Vaccine Series*	1st dose	2nd dose			3rd dose
Single-Antigen and Combination Vaccine Series*	1st dose (*single-antigen vaccine*)		2nd dose	3rd dose	4th dose

At 9-12 months of test for ONLY HBsAg and anti-HBs.

Interpreting Post Vaccination Serologic Test (PVST) Results

Immune	Still Susceptible	Infected
HBsAg-Negative Anti-HBs-Positive Antibody Level ≥10mIU/mL **No further follow up necessary** Report results to your Perinatal Hepatitis B Prevention Program (PHBPP) coordinator. https://www.cdc.gov/vaccines/vpd/hepb/hcp/perinatal-contacts.html	HBsAg-Negative Anti-HBs-Negative Antibody Level <10mIU/mL **Needs additional follow up and vaccines** Contact your PHBPP coordinator for assistance https://www.cdc.gov/vaccines/vpd/hepb/hcp/perinatal-contacts.html	HBsAg-Positive Anti-HBs-Negative Antibody Level <10mIU/mL **Needs additional follow up** Contact your PHBPP coordinator for assistance https://www.cdc.gov/vaccines/vpd/hepb/hcp/perinatal-contacts.html

If you identify a perinatally HBV exposed infant who did not receive HBIG before hospital discharge

- The infant should receive an urgent referral to receive HBIG, up to 7 days after birth.
- If > 7 days have passed, HBIG is unlikely to be effective.
- It is still important for the infant to complete the Hep B vaccine series, and providers should adhere to the minimum intervals between doses.

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Summary and Take Aways

- Elevated liver numbers can be categorized based on patient age, pattern of elevation, and associated clinical scenario
- Next steps in work-up, and urgency of subspeciality evaluation, depend on differential diagnosis and severity of liver injury
- Many chronic (and acute) liver disorders are best managed when the primary care practitioner and liver specialist work together!

Random Rules (Kathy's version)

- The higher the ALT – the quicker you should repeat it (triple digits – repeat in 3 days, double digits – repeat in 2 weeks)
- Persistently (or intermittently) elevated AST/ALT are never normal, even if the elevation is minimal/mild. Those patients should be referred after 3-5 abnormal values
- An isolated direct bilirubin of 0.4-0.5 is unlikely to be clinically significant
- Pale stools in the absence of jaundice is not liver disease (rapid transit, dietary – high milk intake, low-fat diet, iron deficiency, malabsorption)

To Learn More

- **Algorithm for management of elevated LFTs**
  - Costa JM, Pinto SM, Santos-Silva E, Moreira-Silva H. Incidental hypertransaminasemia in children-a stepwise approach in primary care. Eur J Pediatr. 2023 Apr;182(4):1601-1609. doi: 10.1007/s00431-023-04825-4. Epub 2023 Jan 26. PMID: 36697884; PMCID: PMC9877494.
- **Obesity and MASLD Management**
  - Hampl SE, et al. Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity. Pediatrics. 2023 Feb 1;151(2):e2022060640. doi: 10.1542/peds.2022-060640. PMID: 36622115.
  - Vos MB, Xanthakos SA, et al. NASPGHAN Clinical Practice Guideline for the Diagnosis and Treatment of Nonalcoholic Fatty Liver Disease in Children: Recommendations from the Expert Committee on NAFLD (ECON) and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). J Pediatr Gastroenterol Nutr. 2017 Feb;64(2):319-334. PMID: 28107283; PMCID: PMC5413933.
  - Xanthakos SA, et al. AASLD Practice Statement on the evaluation and management of metabolic dysfunction-associated steatotic liver disease in children. Hepatology. 2025 Nov 1;82(5):1352-1394. PMID: 40300071.
- **Questions about Drug-Induced-Liver-Injury**
  - LiverTox - NCBI Bookshelf – NIH
- **Hepatitis C**
  - https://www.cdc.gov/mmwr/volumes/72/rr/rr7204a1.htm

Dr. Mike Farrell'ism

- "Don't pick your nose if you don't know what you're going to do with it"

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