

Differential Diagnosis in Pediatrics



R Arvind



Contents

SECTION 1

1. Abdominal Distention	1
2. Abdominal Movements.....	6
3. Abdominal Pain	8
4. Abdominal Paracentesis	13
5. Abdominal Pulsations	14
6. Abdominal Rigidity	15
7. Abdominal Tenderness.....	16
8. Abdominal Swellings.....	17
9. Acanthosis Nigricans	19
10. Accommodation Reflex	20
11. Achalasia	21
12. Achondroplasia.....	22
13. Acne Vulgaris	23
14. Acrocyanosis	24
15. Adie Tonic Pupil	25
16. Age-independent Growth Measurements.....	26
17. Albinism	27
18. Alopecia.....	28
19. Ambiguous Genitalia.....	31
20. Amblyopia	33
21. Amenorrhea	34
22. Amniocentesis.....	36
23. Amniotic Bands.....	37
24. Anaphylaxis.....	38

25. Anemia	39
26. Angioedema.....	43
27. Angiomata and Telangiectasia	44
28. Aniridia	45
29. Anisometropia	46
30. Antimongoloid Slant	47
31. Apex Beat, Displaced.....	48
32. Aphthous Ulcers.....	49
33. Aplasia Cutis Congenita	50
34. Apraxia	51
35. Arteriovenous Malformations	53
36. Arthrogyposis.....	54
37. Ash-leaf Spots	55
38. Asplenia.....	56
39. Astigmatism	57
40. Ataxia–Telangiectasia	58
41. Athetosis	59
42. Atopic Dermatitis.....	60
43. Atrial Fibrillation and Atrial Flutter.....	61
44. Auspitz Sign	62

SECTION 2

45. Back Pain	63
46. Bartholin Gland Abscess	65
47. Bleeding	66
48. Blood Pressure	68
49. Blood Samples	70
50. Blindness	73
51. Blue Dot Sign	74
52. Blue Sclera	75

53. Body Proportion	76
54. Borborygmi	78
55. Bossing: Frontal and Parietal.....	79
56. Brachial Plexus Injury.....	80
57. Breast Lumps.....	81
58. Breath Sounds.....	83
59. Bronchoscopy and Bronchoalveolar Lavage.....	85
60. Brown Syndrome	86
61. Brushfield Spots	87
62. Bulging Anterior Fontanel	88
63. Butterfly Rash	89

SECTION 3

64. Café-Au-Lait Macules	91
65. Camptodactyly.....	92
66. Candidiasis	93
67. Capillary Malformation	94
68. Caput Succedaneum.....	95
69. Cardiocentesis.....	96
70. Cataract	97
71. Cardiac Catheterization and Angiocardiology	98
72. Carditis	99
73. Central Venous Pressure Monitoring	100
74. Cephalhematoma	101
75. Cerebellar Signs	102
76. Cervical Spine Immobilization.....	103
77. Chest Circumference	104
78. Chest Deformity.....	105
79. Chest Pain.....	106
80. Cheyne–Stokes Respiration	109

81. Chordee	110
82. Chorea	111
83. Chorionic Villus Sampling	112
84. Choledochal Cyst	113
85. Chylothorax.....	114
86. Clinodactyly	115
87. Clonus	116
88. Cisternal Puncture	117
89. Clubbing of Fingers	118
90. Coin Test	120
91. Coloboma of Eyelid.....	121
92. Coloboma of Fundus	122
93. Coloboma of Retina	124
94. Collodion Body	125
95. Congenital Hemangioma	126
96. Congenital Hydronephrosis.....	128
97. Consciousness: Disorders	129
98. Constipation.....	130
99. Continuous Murmurs	132
100. Coombs Test	133
101. Contact Dermatitis.....	134
102. Coordination	135
103. Corneal Reflex	136
104. Cortical Sensory Function.....	137
105. Cough	138
106. Costochondral Beading.....	142
107. Craniosynostosis.....	143
108. Craniotabes	144
109. Crepitus (Subcutaneous Emphysema)	145
110. Cryptorchidism	146

111. Cutis Marmorata	147
112. Cyanosis.....	148
113. Cystic Hygroma	149

SECTION 4

114. Dandy–Walker Malformation	151
115. Deafness	152
116. Decerebrate Rigidity	154
117. Decorticate Rigidity.....	155
118. Defibrillation.....	156
119. Delayed Puberty	157
120. Dennie Sign	160
121. Depressed Nasal Bridge	161
122. Dermatomyositis	162
123. Diaper Dermatitis	164
124. Diarrhea.....	165
125. Diastasis Recti	167
126. Diastrophic Dysplasia.....	168
127. Diplopia	169
128. Dysmorphology	170
129. Dysphagia	171
130. Dysuria.....	172
131. Dystonia	174

SECTION 5

132. Earache	175
133. Ear Discharge	177
134. Ectopia Lentis.....	180
135. Edema, Dependent.....	181
136. Edema, Generalized.....	182

137. Electrocardiogram	183
138. Electroencephalogram	186
139. Encephalocele	187
140. Encopresis	188
141. Enophthalmos (Retraction of the Eyeball).....	189
142. Entropion and Ectropion.....	190
143. Enuresis	191
144. Epicanthic Fold	192
145. Epidermolysis Bullae	193
146. Epididymis.....	194
147. Epigastric Hernia	195
148. Epispadias	196
149. Epistaxis	197
150. Epulis	198
151. Erb's Palsy	199
152. Erysipelas	200
153. Erythema Toxicum	201
154. Exophthalmos	202
155. Eye Inflammation (Red Eye)	203

SECTION 6

156. Face, Abnormalities of Appearance and Movements	205
157. Face Paralysis	206
158. Failure to Thrive	208
159. Faints or Syncope.....	211
160. Fasciculation (Muscle Twitching).....	213
161. Fetal Alcohol Syndrome	214
162. Fetal Scalp Blood Sampling	215
163. Fever	216
164. Fibroadenoma of Breast.....	220

165. Fits and Convulsions.....	221
166. Fixed Drug Eruption	223
167. Flaring of Alae Nasi.....	224
168. Flat Nasal Bridge.....	225
169. Flow Murmurs	226
170. Fluid Thrill	227
171. Folliculitis	228
172. Fontanel.....	229
173. Friction Rub	231
174. Frequency of Micturition	232
175. Furuncle.....	233

SECTION 7

176. Gag Reflex	235
177. Gait, Abnormalities	236
178. Gallbladder, Palpable	239
179. Gallop Rhythm	240
180. Gastroesophageal Reflux.....	241
181. Gastrointestinal Bleeding	242
182. Genu Valgum.....	245
183. Genu Varus	246
184. Geographic Tongue (Benign Migratory Glossitis).....	247
185. Glasgow Coma Scale.....	248
186. Glaucoma	249
187. Graves Disease	251
188. Gums, Hypertrophy	252
189. Gynecomastia	253

SECTION 8

190. Halitosis.....	255
191. Hamman Sign.....	256

192. Harlequin Color Change	257
193. Harrison's Sulcus	258
194. Head Bobbing	259
195. Headache.....	260
196. Head Circumference	264
197. Head Variants	266
198. Heart Murmurs.....	268
199. Heart Sounds	271
200. Hematemesis.....	274
201. Hematuria	275
202. Hemiballismus	276
203. Hemihypertrophy	277
204. Hemiparesis	278
205. Hemiplegia	279
206. Hemoptysis	280
207. Hepatomegaly	281
208. Herpangina	283
209. Hiccup	284
210. High-arched Palate	285
211. Hoarseness of Voice	286
212. Hoffmann Reflex	287
213. Horner's Syndrome	288
214. Hordeolum	289
215. Horseshoe Kidney.....	290
216. Hydranencephaly	291
217. Hydrocephalus	292
218. Hypertelorism	294
219. Hypertrichosis.....	295
220. Hydrocele	296
221. Hypercyanotic Spells	297
222. Hyperopia.....	298

223. Hyperthyroidism	299
224. Hyphema	300
225. Hypospadias	301
226. Hypotonia.....	302

SECTION 9

227. Immotile Cilia Syndrome.....	307
228. Imperforate Anus.....	308
229. Impetigo	309
230. Infantile Hemangioma	311
231. Innocent Murmurs	312
232. Insect Bite.....	313
233. Intraosseous Transfusion	314
234. Intrauterine Transfusion	315
235. Involuntary Movements.....	316

SECTION 10

236. Jaundice	319
237. Jugular Venous Pressure	326
238. Jugular Venous Pulsations.....	327

SECTION 11

239. Keloid.....	329
240. Kidney: Palpable	330
241. Knock Knees.....	331

SECTION 12

242. Laryngomalacia	333
243. Length and Height.....	334
244. Leukemoid Reaction.....	336
245. Leukocoria (White Pupillary Reflex).....	337

246. Lips: Affections	338
247. Light Reflex	339
248. Lisch Nodules	340
249. Lordosis	341
250. Low-set Ears	342
251. Lumbar Puncture	343
252. Lymphadenopathy	345

SECTION 13

253. Macewen's Sign	347
254. Macrocephaly.....	348
255. Macroglossia	350
256. Marasmus	351
257. Marcus Gunn Pupil	352
258. Mastitis	353
259. Melena	354
260. Menorrhagia	355
261. Memory	357
262. Meningococcal Exanthem.....	358
263. Microcephaly.....	360
264. Microcornea	362
265. Microphallus	363
266. Midarm Circumference.....	364
267. Milia	365
268. Mongoloid Slant	366
269. Mongoloid Spots	367
270. Motor Reflexes	368
271. Mouth Pigmentation	369
272. Mucocele and Ranula	370
273. Murphy's Sign	371
274. Muscular Hypertrophy	372

275. Muscle Power	373
276. Myalgia	374

SECTION 14

277. Nails Abnormalities	375
278. Nasal Deformity	377
279. Nasal Discharge	378
280. Nasal Obstruction	379
281. Nasal Polyps	381
282. Nasolacrimal Duct	382
283. Natal Teeth	384
284. Nausea	385
285. Neck Webbing	386
286. Neurocysticercosis.....	387
287. Neurofibroma	388
288. Nummular Eczema.....	389
289. Nystagmus	390

SECTION 15

290. Obesity	393
291. Obturator Test	396
292. Obstructive Murmurs	397
293. Oliguria.....	398
294. Optic Disk Atrophy	399
295. Optic Fundus Abnormalities	400
296. Orotracheal Intubation	402
297. Otorrhea	403

SECTION 16

298. Paronychia.....	405
299. Parotid Gland Swelling.....	406

300. Pectus Carinatum.....	407
301. Pectus Excavatum.....	408
302. Percussion Notes	409
303. Pericardial Bulge.....	411
304. Precordial Pulsations.....	412
305. Pericardial Puncture	413
306. Pericardial Rub.....	414
307. Peristalsis, Visible	415
308. Peritonsillar Abscess	417
309. Pes Planus (Flat Foot)	418
310. Pigmentary Mosaicism.....	419
311. Pinpoint Pupils.....	420
312. Pityriasis Alba	421
313. Pleural Rub	422
314. Polyarteritis Nodosa.....	423
315. Polydactyly.....	424
316. Polydipsia.....	425
317. Polyuria	426
318. Popliteal (Baker) Cyst	429
319. Posterior Urethral Valve	430
320. Post-tussive Crepitus	431
321. Precocious Puberty.....	432
322. Prehn Sign	438
323. Premature Pubarche.....	439
324. Premature Thelarche	440
325. Premenstrual Syndrome	441
326. Priapism.....	442
327. Primitive Reflexes	444
328. Proteinuria	446
329. Prune-Belly Syndrome.....	448

330. Pruritus Ani	449
331. Pseudohypertrophy	450
332. Pseudotumor Cerebri	451
333. Ptosis	452
334. Puddle Sign	453
335. Pulse	454
336. Pulse Character	456
337. Pulse Rate	458
338. Pulse, Rhythm	459
339. Pulse, Unequal	462
340. Pupils, Abnormalities	463
341. Purpura.....	465
342. Pyrexia of Unknown Origin.....	466

SECTION 17

343. Rebound Tenderness	469
344. Rectal Prolapse	470
345. Reflexes, Abnormalities	471
346. Renal Ectopia	473
347. Respiratory Distress	474
348. Respiratory Rate	477
349. Retinoblastoma	479
350. Retinal Detachment.....	480
351. Retinitis Pigmentosa	481
352. Retinopathy of Prematurity	482
353. Rumination.....	483

SECTION 18

354. Salivary Glands Pain.....	485
355. Salivary Gland Swelling	486
356. Scabies.....	487

357. Scleroderma	488
358. Scrofuloderma	490
359. Scrotal Swelling	491
360. Seborrhea: Cradle Cap.....	492
361. Sensation Abnormalities.....	493
362. Shifting Dullness	497
363. Short Neck.....	498
364. Short Stature	499
365. Signs of Meningeal Irritation.....	507
366. Simian Crease.....	508
367. Sjögren Syndrome	509
368. Skinfold Thickness	510
369. Skin Pigmentation	511
370. Sneezing	514
371. Soft Neurologic Signs.....	515
372. Speech	516
373. Spermatocoele	518
374. Spine	519
375. Spina Bifida	520
376. Splenomegaly	522
377. Staphylococcal Scalded Skin Syndrome	523
378. Startle Response	524
379. Stiff Neck	525
380. Straight Leg Test	526
381. Strabismus	527
382. Stridor.....	528
383. Sturge–Weber Syndrome	529
384. Subcutaneous Nodules	530
385. Subdural Tap	531
386. Succession Sounds/Succession Splash	532

387. Sunsetting Sign.....	533
388. Superficial Reflexes	534
389. Suprapubic Aspiration	536
390. Sydenham's Chorea	537
391. Syndactyly.....	538
392. Sweat Chloride Test	539

SECTION 19

393. Tachycardia	541
394. Tachypnea	542
395. Tactile Vocal Fremitus.....	543
396. Tall Stature	544
397. Telescopic Test.....	545
398. Tinea Cruris	546
399. Tinea Versicolor	547
400. Testes	548
401. Tetany	550
402. Thoracocentesis	552
403. Thyroglossal Duct Cyst	553
404. Thyroid Gland	554
405. Tics	556
406. Tinnitus.....	557
407. Toe Walking	558
408. Tongue.....	559
409. Torticollis	562
410. Tracheal Deviation.....	563
411. Tracheal Position	564
412. Trendelenburg Test.....	565
413. Tremor	566
414. Tuberous Sclerosis	568

SECTION 20

415. Umbilicus.....	569
416. Umbilical Artery Catheterization	571
417. Umbilical Hernia	572
418. Umbilical Vein Catheterization	574
419. Undescended Testes	576
420. Upper Limb.....	577
421. Urticaria.....	580
422. Uveitis.....	582

SECTION 21

423. Vaginal Bleeding.....	583
424. Varicocele	584
425. Venous Hum	585
426. Ventricular Puncture	586
427. Vernix Caseosa	587
428. Vertigo	588
429. Visual Acuity.....	590
430. Visual Field	591
431. Vitiligo	592
432. Vocal Fremitus	594
433. Vocal Resonance	595
434. Vomiting	596

SECTION 22

435. Warts.....	605
436. Weight	606
437. Wheezing.....	608
<i>Bibliography</i>	<i>611</i>
<i>Index</i>	<i>613</i>

Jaundice

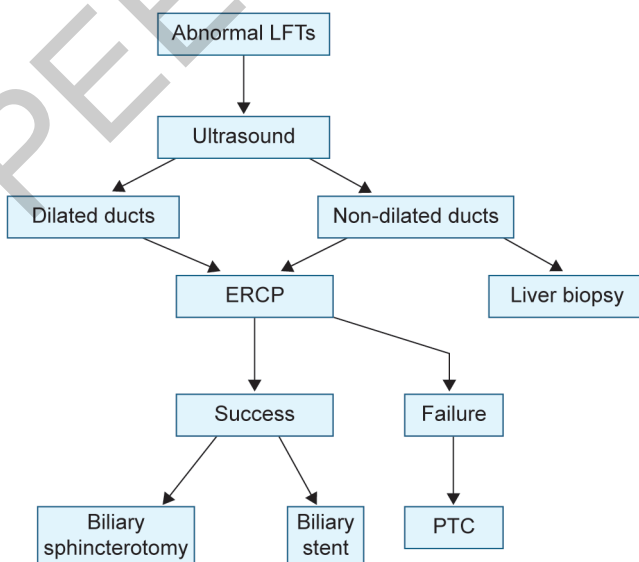
Jaundice may be caused by a raised conjugated or unconjugated bilirubin. Unconjugated hyperbilirubinemia may be due to excessive production of bilirubin (hemolysis), reduced uptake of bilirubin, or a failure of conjugation by the liver. Conjugated hyperbilirubinemia results from hepatocellular damage or obstruction of the bile ducts, either within the liver (intrahepatic cholestasis) or of a major bile duct (extrahepatic obstruction jaundice). Jaundice is also often classified into pre-hepatic (hemolysis), hepatic, and extrahepatic types.

■ HISTORY

Chronic fatigue, though nonspecific, is a common symptom of liver disease and should trigger at least a basic evaluation including aminotransferases even in the absence of overt jaundice (**Flowchart 1**). Myalgias, nausea, vomiting, and fever are often seen in patients with viral hepatitis or autoimmune hepatitis.

Acute biliary obstruction is signaled by right upper quadrant pain, vomiting, fever, and acholic stools in addition to jaundice.

Flowchart 1: Evaluation of cholestatic jaundice.



(ERCP: endoscopic retrograde cholangiopancreatography; LFTs: liver function tests; PTC: percutaneous transhepatic cholangiography)

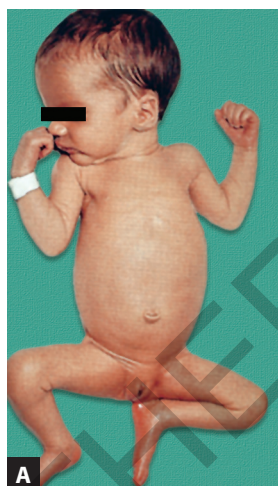
Neurologic and psychiatric symptoms may be among the manifestations of Wilson disease. Autoimmune hepatitis may be accompanied by manifestations of other autoimmune disorders.

The child's age at the onset of symptoms may be helpful. Wilson disease commonly manifests in school-aged children and adolescents. Similarly, autoimmune hepatitis is most prevalent in school-aged children and adolescents with female predominance. A thorough history should include past and present use of prescription, over-the-counter (e.g., acetaminophen), and street drugs.

Symptoms of cholestasis such as jaundice, dark urine, steatorrhea, symptoms of fat-soluble vitamin deficiency, failure to thrive, and pruritus should be explored in detail.

CLINICAL FEATURES

The clinician should focus on signs of portal hypertension—spider angiomas, palmar erythema, dilated abdominal veins, ascites, and splenomegaly with a small liver (**Figs. 1A and B**). Cutaneous excoriation as evidence of pruritus, xanthomas, and jaundice support cholestasis. Clubbing of digits may suggest hepatopulmonary syndrome. A large, tender liver is suggestive of acute viral hepatitis or congestive heart failure. A small liver may be found in patients with severe hepatitis or cirrhosis. A tender gallbladder is indicative of choledocholithiasis or cholecystitis. Abnormal neurologic findings, including tremor, fine motor incoordination, clumsy gait, and choreiform movements, suggest Wilson disease. A slit-lamp examination should be included to look for the Kayser-Fleischer rings (a brownish discoloration at the periphery of the cornea) of Wilson disease.



Figs. 1A and B: Jaundice.

CAUSES

- *Hemolytic (pre-hepatic):*
 - Red blood cell (RBC) membrane defects
 - ♦ Spherocytosis
 - ♦ Elliptocytosis
 - RBC enzyme defects
 - ♦ Glucose-6-phosphate dehydrogenase (G6PD) deficiency
 - Globin chain synthesis defect—thalassemic
 - Acquired hemolysis
 - ♦ Drug—surfs
 - ♦ Penicillin
 - ♦ Anti malaria
- *Liver cell disease:*
 - Neonatal jaundice

- Viral hepatitis
- Crigler-Najjar syndrome
- Gilbert's disease
- Galactosemia
- Hypothyroidism
- Intrauterine infection
- *Obstructive (posthepatic):*
 - Biliary atresia
 - Choledochal cyst
 - Instigated bile
 - Stricture and calculus in biliary tree
 - Alpha-1 antitrypsin deficiency
 - Dubin-Johnson syndrome
 - Rotor syndrome

UNCONJUGATED HYPERBILIRUBINEMIA

A complete blood count with evaluation of the smear, reticulocyte count, and Coombs test can differentiate hemolytic from non-hemolytic disorders.

Erythrocyte membrane defects (spherocytosis) and enzyme defects (pyruvate kinase deficiency, G6PD) may not be apparent until childhood or adolescence. Acquired autoimmune hemolytic anemia is characterized by pallor, abdominal pain, fever, and dark urine in addition to jaundice. Laboratory studies document anemia and reticulocytosis. The direct Coombs test result is positive. Hemolytic anemia can be associated with infection, immunodeficiency, malignancy, hemolytic uremic syndrome, or other autoimmune disorders, such as systemic lupus erythematosus, rheumatoid arthritis, thyroid disorders, and autoimmune hepatitis.

Unconjugated hyperbilirubinemia can be caused by congestive heart failure and infection should in such circumstances extrahepatic symptoms, cardiac failure, or sepsis dominate the picture. If no other explanation is found, Gilbert syndrome or Crigler-Najjar syndrome type II should be considered.

This condition is due to:

- *An increased production of bilirubin:*
 - Inefficient marrow production
 - Increased breakdown (hemolysis)
 - ♦ Hemoglobinopathies
 - ♦ Antibody-mediated
 - ♦ Drug-induced
- Decreased uptake of bilirubin into the liver; Gilbert's disease
- *Decreased conjugation of bilirubin in the liver:*
 - Crigler-Najjar syndrome
 - Neonatal jaundice
 - Drugs
 - Lucey-Driscoll syndrome

Viral Hepatitis

Infection

Infections are a common cause of jaundice in the child and adolescent. The most important step is to evaluate patients for synthetic liver failure and for signs of chronicity (portal hypertension, growth failure, risk factors for blood-borne, or sexually transmitted disorders). Patients with synthetic liver failure should be referred for urgent evaluation by the liver transplant center.

Hepatitis A virus (HAV) infection is usually anicteric or asymptomatic in children <5 years of age. About 2–7 days before the onset of jaundice, there is a flulike illness with symptoms that can include malaise, headache, myalgias, anorexia, vomiting, diarrhea, right upper quadrant pain, and fever. Some children present with cough and coryza. The urine becomes dark, and jaundice and pale or acholic stools develop. Aminotransferase levels are 10–100 times normal. The diagnosis is confirmed by an HAV IgM study. Children generally recover within 2 weeks.

Acute hepatitis C virus (HCV) infection is often mild and usually subclinical. Jaundice

is unusual. Screening for hepatitis uses anti-HCV antibodies, and infection is confirmed via polymerase chain reaction (PCR) for HCV RNA. Transmission may be parenteral due to IV drug use or exposure to blood, or sexual or vertical transmission is also possible.

Wilson's Disease

Wilson disease is an autosomal recessive disorder of copper metabolism. As a result of ATP7B mutation, copper cannot be excreted and it accumulates in the liver, which causes hepatic steatosis and necrosis. Copper is then released into the circulation and is ultimately deposited in the central nervous system, kidneys, and cornea. The hepatic manifestation predominates in childhood; a neuropsychiatric manifestation becomes more common later, in adolescence and adulthood. The liver involvement may manifest as acute hepatitis, fulminant hepatic failure, chronic hepatitis, cirrhosis, or asymptomatic elevation of serum aminotransferases. Neurologic symptoms such as dysarthria, clumsiness, tremor, and mood disorders may or may not be present. In the kidney, the result is tubular dysfunction; in the cornea, the result is Kayser–Fleischer rings. Hemolysis can be present as a result of copper toxicity. The diagnosis is supported by documenting a low serum ceruloplasmin level, high urinary copper excretion, and increased hepatic copper concentrations on liver biopsy.

Autoimmune Hepatitis

Autoimmune hepatitis (AIH) is a common cause of chronic liver injury. The most frequent course is insidious with fatigue as a dominant symptom. Autoimmune hepatitis can present acutely with malaise, anorexia, nausea, vomiting, and jaundice. Autoimmune disorders such as arthritis, thyroiditis, vasculitis, nephritis, hemolytic anemia, or

diabetes mellitus are often associated with AIH.

Biliary Disease

Primary Sclerosing Cholangitis

Primary sclerosing cholangitis (PSC) is characterized by focal dilatation and stenosis of the intrahepatic or extrahepatic bile ducts with surrounding fibrosis resulting from an inflammatory process. It can manifest from early childhood through adulthood.

Extrahepatic Biliary Obstruction

Gallstones

Gallstones are particularly common in children with hemolytic disorders, such as sickle cell disease, thalassemia, erythrocyte membrane defects, erythrocyte enzyme defects, and autoimmune hemolytic anemia. The mean age at presentation is 12 years. Gallstones are also associated with anatomic abnormalities of the biliary tract, cystic fibrosis, ileal dysfunction, obesity, parenteral nutrition, sepsis, prematurity, and pregnancy.

JAUNDICE IN THE NEONATE AND INFANT

Physiologic and Breast Milk Jaundice

In neonates, increased bilirubin production is caused by the normally increased neonatal red blood cell mass and the decreased life span of the red blood cells (80 vs. 120 days). Albumin binding is decreased because of lower albumin concentrations and diminished binding capacity, which results in decreased transport of unconjugated bilirubin (UCB) to the liver with increased deposition in tissues. Uptake of bilirubin by the hepatocytes during the 1st weeks of life is defective. Low levels of glutathione S-transferase B decrease intracellular binding,

which may impede the transport of UCB to the endoplasmic reticulum. Conjugation is impaired by decreased activity of uridine diphosphate glucuronosyltransferase (UDPGT). Secretion into the canaliculi is impaired. There is increased enterohepatic circulation of unconjugated bilirubin as a result of increased concentrations of β -glucuronidase in the intestinal lumen and as a result of decreased intestinal bacterial flora, leading to diminished urobilinogen formation.

These features contribute in varying degrees to physiologic jaundice, characterized by a peak bilirubin level of <13 mg/dL on postnatal days 3–5, a decrease to normal by 2 weeks of age, and a conjugated fraction of $<20\%$. In premature, breastfed infants of diabetic mother, the peak is higher and lasts longer. Conjugated bilirubin should be checked if there is any question of the nature of jaundice.

Breastfeeding has been associated with an increased incidence of unconjugated hyperbilirubinemia outside the expected range (>13 mg/dL). Jaundice of this level may occur in 10–25% of breastfed infants, in contrast to 4–7% of formula-fed infants. It can occur within the 1st 5 days of life and is referred to as “early” or “breastfeeding” jaundice. Breastfeeding jaundice is seen in infants who are not feeding adequately and may be dehydrated or malnourished. In a second group of breastfed infants, the jaundice develops slowly, occurring after the first week of life, and peaks between the 2nd and 3rd weeks of life at 10–20 mg/dL. This is referred to as “late” or “breast milk” jaundice. The precise cause of increased bilirubin levels in this latter setting has not been established; alternative theories include inhibition of glucuronosyltransferase activity and increased enterohepatic circulation of UCB. Kernicterus appears to be very rare

but has been reported in association with breastfeeding. No treatment is necessary for physiologic jaundice (**Fig. 2**).

Polycythemia: Neonatal polycythemia, defined as a hematocrit $>65\%$ by venipuncture, can be caused by maternal diabetes, maternal-fetal, or twin-twin transfusion, intrauterine hypoxemia, endocrine disorders, and delayed cord clamping. Polycythemia results in increased bilirubin production because of the increased red blood cell mass.

Hemolytic disorders: Reticulocytosis, unconjugated hyperbilirubinemia, and an increased nucleated red blood cell count, with either a low or normal hematocrit, suggest hemolysis. This can result from isoimmunization; erythrocyte membrane, hemoglobin, or enzyme defects; or sepsis with disseminated intravascular coagulation.

Isoimmune hemolytic disease: In this group of disorders, maternal antibodies



Fig. 2: Kernicterus.

(immunoglobulin G) to the infant's erythrocytes cross the placenta, resulting in red blood cell destruction. The administration of anti-D gamma globulin [RhO(D) immune globulin (RhoGAM)] after delivery to women who are Rh-negative has reduced the incidence of Rh sensitization and erythroblastosis fetalis.

The diagnosis is confirmed by demonstrating that the infant is Rh-positive, that the direct Coombs test result is positive, and that maternal antibody is coating the infant's red blood cells.

ABO blood type incompatibility causes a less severe form of isoimmune hemolytic disease with a less rapid development of jaundice. It is more common in infants with blood type A or B who are born to mothers with blood type O.

Erythrocyte enzyme defects: G6PD deficiency is common. Jaundice is seen more frequently in persons with a Mediterranean or Far Eastern ancestry who have a complete absence of the enzyme. In these individuals, hemolysis can occur without a precipitant. In African-American patients, the disease is generally less severe, and hemolysis is rare without exposure to a drug, toxin, or infection that causes an oxidant stress. G6PD deficiency can manifest as neonatal jaundice on day 2 or 3 after birth; alternatively, it may not manifest until later in childhood, when jaundice is associated with an acute hemolytic crisis. The diagnosis of G6PD deficiency is confirmed by documenting deficiency of the enzyme in red blood cells.

Familial Disorders of Bilirubin Metabolism

Gilbert syndrome is a heterogeneous group of disorders that have in common at least a 50% decrease in UDPGT activity as a result

of a defect in the gene responsible for this enzyme. In 20–30% of individuals with Gilbert syndrome, there is also a decrease in hepatocyte bilirubin uptake. Affected individuals are generally asymptomatic and may not present with jaundice until the 2nd or 3rd decade of life. Gilbert syndrome may be responsible for some cases of neonatal jaundice. Mild jaundice with a bilirubin level up to 7 mg/dL can occur transiently with fatigue, exercise, fasting, febrile illness, and alcohol ingestion in older patients.

Crigler-Najjar syndrome: Crigler-Najjar syndrome types I and II (also known as Arias syndrome) are rare autosomal recessive conditions caused by mutations (different alleles from those of Gilbert syndrome) in the gene coding for UDPGT.

The onset of Crigler-Najjar syndrome type II is usually at birth, although it can be in late childhood. There is <5% of the normal UDPGT activity. Bile contains bilirubin monoglucuronides. Bilirubin levels, generally 8–25 mg/dL, respond to phenobarbital administration with a significant decrease. Neurologic disease is rare.

Lucey-Driscoll syndrome: Lucey-Driscoll syndrome is a transient familial neonatal hyperbilirubinemia that appears in the 1st few days of life and resolves by 2–3 weeks of age. This results from the inhibition of UDPGT by a substance that has been found in both maternal and infant serum.

Neonatal Conjugated Hyperbilirubinemia

Common to all of these conditions is the potential for hypoprothrombinemia. If the PT is prolonged, the infant should be treated with intravenous vitamin K to avoid spontaneous hemorrhage, particularly intracranial. Depending on the degree of

hepatocellular damage, vitamin K may not correct the PT.

Hypoglycemia is another danger that is associated with diseases that cause severe hepatic dysfunction, metabolic disorders as well as with hypopituitarism. The infant may be relatively asymptomatic despite significant hypoglycemia. The serum glucose level can be measured before a feeding. If hypoglycemia is present, the infant should receive frequent feedings, continuous feedings, or intravenous dextrose infusions. Glucose level should always be the part of the evaluation of conjugated hyperbilirubinemia.

Obstructive/Anatomic Abnormalities, Idiopathic Cholestasis, and Idiopathic Neonatal Hepatitis

Biliary atresia: Untreated biliary atresia is lethal, and only prompt diagnosis and surgical treatment can prevent mortality. Biliary atresia accounts for approximately 30% of cases of neonatal cholestasis seen at major referral centers. It occurs in one in 8,000–15,000 live births. It is the result of a progressive inflammatory process leading to obliteration of the lumen of the extrahepatic duct. It is the leading indication for liver transplantation in the pediatric population. Infants are less often icteric from birth and more often develop jaundice at 2–6 weeks of age. Infants are usually full term and initially appear healthy except for jaundice, dark urine, and acholic stools. The family history usually is negative for liver disease. There appear to be two forms of biliary atresia:

BOX 1: Conditions not to miss in infants with conjugated hyperbilirubinemia.

- *Priorities:*
 - Hypoprote thrombinemia
 - Hypoglycemia
 - Extrahepatic biliary atresia
- *Infections:*
 - Sepsis
 - Urinary tract infection
 - Syphilis
 - Toxoplasmosis
 - Herpes simplex virus
- *Endocrine disorders:*
 - Hypopituitarism
 - Hypothyroidism
- *Metabolic disorders:*
 - Galactosemia
 - Hereditary fructose intolerance (fructosemia)
 - Tyrosinemia
- *Other:*
 - Neonatal hemochromatosis
 - Bile acid abnormalities
 - Choledochal cyst
 - Intestinal obstruction
 - Familial hemophagocytic syndromes
 - Heart disease
 - Toxins

1. In the “embryonic” or “fetal form,” which occurs in 15–30% of cases, there is no jaundice-free period. There are often associated defects, including cardiac defects, polysplenia, malrotation, and situs inversus.
2. In the “perinatal form,” there may be a jaundice-free interval after resolution of the normal physiologic jaundice, and there are no associated anomalies.

There are a few conditions “Not to Miss in Infants with Conjugated Hyperbilirubinemia” given in **Box 1**.

Differential Diagnosis in Pediatrics

Salient Features

- All the symptoms and signs related to pediatrics have been listed in alphabetical order
- Symptoms and signs have been discussed completely up to the possible clinical diagnosis level. This includes definition, pathophysiology, causes, techniques to elicit, and impression of the respective symptoms and signs
- Clinical approaches, such as general examination, systemic examination, investigations, and relevant procedures, to reach a diagnosis have been discussed
- Wherever possible, these have been illustrated with photographs
- This book acts as a ready reckoner for the reader to search for any symptoms and signs in an indexing format and go through them completely in a single place
- The reader need not go to different pages or books for material, as all the possible information have been compiled at one place
- This is useful to undergraduates and postgraduates for reading text as well as preparing for competitive examinations
- This is useful to academic pediatricians and practicing pediatricians to brush up their clinical skill as well as clinical knowledge to help themselves reach a clinical diagnosis
- This is a clinical pediatric book presented in a unique way.

R Arvind MBBS DCH DNB is one of the well-known Pediatricians in Bengaluru, Karnataka, India. He is Consultant Pediatrician and Neonatologist. He is Proprietor and Medical Director of Vathsalya Speciality Clinic, Bengaluru. He received his medical degree from Bangalore Medical College and Research Institute, Bengaluru, in 1988 and postgraduate degree from Bellary Medical College, Bellary, Karnataka, in 1992. He had worked in the Department of Nephrology, St John's Medical College Hospital, Bengaluru. He has authored many reference books in pediatrics for medical students, being published by international publishers. Many of his papers and articles have been published in leading international journals and magazines.



Buy from ejaypee



**JAYPEE
BROTHERS**

Shelving Recommendation
PEDIATRICS

