

## Early diagnosis of neonatal cholestatic jaundice

### Test at 2 weeks

Eric I. Benchimol MD FRCPC Catharine M. Walsh MD MEd FRCPC FAAP Simon C. Ling MBChB

**F**riends, family, and health care workers often reassure parents that their infants' jaundice is normal, requires neither investigation nor treatment, and will resolve without adverse consequences. Unfortunately, misdiagnosis of cholestasis (**Box 1**<sup>1</sup>) as physiologic jaundice delays the identification of important liver disease and substantially impairs long-term health. We have conducted a review of the literature to summarize the evidence for early identification and intervention in biliary atresia and other forms of cholestatic jaundice. In response to an observed pattern of late referral of infants with cholestasis, we aim to provide primary care physicians with evidence of the benefits of early identification, reinforcing the need to test for the condition at 2 to 3 weeks of age in jaundiced infants, and to provide an approach to investigation.

Up to 15% of breastfed infants experience jaundice lasting more than 3 weeks<sup>2</sup>; meanwhile, neonatal cholestasis occurs in 0.04% to 0.2% of live births.<sup>1,3</sup> Cholestasis and direct reacting hyperbilirubinemia arise from abnormalities in the uptake, handling, transport, and excretion of bile salts and bilirubin by hepatocytes or in the flow of bile through the bile canaliculi and ducts.<sup>4</sup> A detailed description of the molecular mechanisms of cholestasis is beyond the scope of this review, but is available in a recent article by Trauner et al.<sup>4</sup> Of the many conditions that can present with neonatal cholestasis (**Table 1**<sup>5</sup>), biliary atresia and idiopathic

#### Box 1. Indicators of cholestasis

- Direct reacting serum bilirubin levels > 17 µmol/L (1.0 mg/dL)
- Direct reacting bilirubin > 20% of the total serum bilirubin concentration, if total bilirubin is > 85 µmol/L (5.0 mg/dL)

Data from the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition.<sup>1</sup>

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#### Abstract

**OBJECTIVE** To review best practices for early recognition and treatment of conditions resulting in neonatal cholestasis, in order to improve long-term outcomes for affected infants.

**QUALITY OF EVIDENCE** Studies, review articles, and meta-analyses pertaining to neonatal-onset cholestasis were sought via electronic databases. Reference lists of studies and review articles supplemented the electronic search. Studies were included if they examined the importance of early diagnosis and intervention for cholestatic jaundice of any cause, and mainly comprised Level II and Level III evidence.

**MAIN MESSAGE** Review of the relevant literature supports the recommendation that infants with jaundice at 2 weeks of age should be tested for cholestasis by quantifying the direct reacting bilirubin levels in their blood. Subsequent rapid investigation using a diagnostic algorithm enables early diagnosis of the specific cause and facilitates timely intervention for conditions whose outcomes are improved by early treatment.

**CONCLUSION** Universal screening for neonatal cholestasis might help with early identification of cases and improve outcomes, although further study is required in the North American setting.

#### Résumé

**OBJECTIF** Revoir les meilleures méthodes pour détecter et traiter précocement les conditions résultant de la cholestase néonatale afin d'améliorer les issues à long terme chez les nourrissons affectés.

**QUALITÉ DES PREUVES** On a utilisé des bases de données pour répertorier les études, articles de revue et méta-analyses traitant de la cholestase néonatale. On a complété cette recherche électronique par des bibliographies d'études et d'articles de revue. On n'a retenu que les études traitant de l'importance de diagnostiquer et de traiter précocement toutes les formes d'ictère cholestatique et fondées sur des preuves de niveaux II et III.

**PRINCIPAL MESSAGE** Cette revue de la littérature pertinente appuie la recommandation voulant qu'on recherche la cholestase chez les nourrissons qui présentent un ictère 2 semaines après la naissance par le dosage des niveaux de bilirubine conjuguée dans le sang. Une brève investigation subséquente à l'aide d'un algorithme de diagnostic permettra alors de préciser rapidement la cause et facilitera l'intervention appropriée dans les cas où une issue favorable dépend d'un traitement précoce.

**CONCLUSION** Un dépistage systématique de la cholestase néonatale pourrait aider à détecter précocement les cas et en améliorer les issues; des études additionnelles seront toutefois nécessaires dans le contexte nord-américain.

neonatal hepatitis are the most common; in a study of affected infants presenting to King's College Hospital in London, England, these conditions accounted for 35% and 30% of cases, respectively.<sup>6</sup> Other common causes included  $\alpha_1$ -antitrypsin deficiency (17%), Alagille syndrome (6%), and choledochal cysts (3%).<sup>6</sup> New diagnostic techniques have decreased the number of infants diagnosed with idiopathic hepatitis in favour of previously under-reported conditions, such as progressive familial intrahepatic cholestasis, storage disorders, mitochondrial disorders, and bile acid synthetic defects.<sup>7</sup>

A recent retrospective cohort study from the Canadian Pediatric Hepatology Research Group (CPHRG) estimated the incidence of biliary atresia in Canada to be 1 in 19065 (5.25 per 100 000 live births).<sup>8</sup> Approximately 60% to 70% of patients with biliary atresia will develop cirrhosis and require liver transplantation in childhood,<sup>8,9</sup> half within the first 2 years of life.<sup>10</sup> Biliary atresia is the most common single indication for liver transplantation in children.<sup>11,12</sup>

The CPHRG reported that 14% of Canadian infants with jaundice caused by biliary atresia presented to tertiary referral centres after the age of 3 months. However, multiple cohort studies have reported that infants surgically treated for biliary atresia before 3 months of age had improved overall survival at up to 15 years of age.<sup>8,13,14</sup> In 2 studies that examined the reasons for late referral of infants with cholestatic jaundice,<sup>6,15</sup> most involved either inadequate follow-up of neonatal jaundice or reassurances by primary health care providers that the jaundice was physiologic; however, both are preventable causes of delay.

## Quality of evidence

All studies, review articles, and meta-analyses pertaining to neonatal-onset cholestasis were identified by a search of electronic databases, including MEDLINE (from January 1950 to October 2008); EMBASE (January 1980 to October 2008); OVID Evidence-Based Medicine Reviews databases (eg, the Cochrane Database of Systematic Reviews, the ACP Journal Club, the Database of Abstracts of Reviews of Effectiveness, the Cochrane Central Register of Controlled Trials, the Cochrane Methodology Register, Health Technology Assessment, and the National Health Service Economic Evaluation Database, from January 1991 to July 2008); and the

Cochrane Methodology Register (until July 2008). Search terms included *cholestasis, jaundice and conjugated, mass screening, biliary atresia, galactosemia, tyrosinemia, congenital hypothyroidism, cystic fibrosis, Kasai, and hepatoportoenterostomy, with randomized controlled trial, controlled clinical trial, systematic review, cohort study, guideline, diagnosis, and early diagnosis*. These terms were searched by subject heading and key word. Search terms were combined using Boolean logic, while studies, publications, and guidelines included in this review were limited to the neonatal population (<60 days old) and were directed toward ascertaining the importance of early diagnosis and mass screening for neonatal cholestatic conditions.

Reference lists of studies and review articles supplemented the electronic search. Studies were included if they examined the importance of early diagnosis and intervention for cholestatic jaundice, of any cause.

## Evaluation of neonatal cholestasis

Total and direct reacting serum bilirubin levels must be measured in any infant who is still jaundiced at 2 to 3 weeks of age, according to recommendations from the Canadian Paediatric Society,<sup>16</sup> the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition,<sup>1</sup> and the American Academy of Pediatrics.<sup>17</sup> Early detection is essential to facilitate timely intervention and minimize adverse outcomes in several conditions, including biliary atresia, hypothyroidism, and galactosemia. It is important to note that infants with biliary atresia might not necessarily present with typical symptoms of failure to thrive or ascites,<sup>15</sup> and the primary care physician must be suspicious of cholestasis in all cases of prolonged jaundice.

Any infant with cholestatic jaundice or liver disease should be immediately referred to a pediatric gastroenterologist. The differential diagnosis of cholestatic jaundice is extensive and its evaluation demands a systematic approach. A clinical practice guideline for the investigation of cholestatic jaundice has recently been composed by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition,<sup>1</sup> with an algorithm to guide the investigation of infants with cholestatic jaundice **Figure 1**<sup>1,17</sup>). A detailed history and physical examination can provide clues to diagnosis. Pale, acholic stools suggest an obstructive process such as biliary atresia; deeply pigmented stools usually rule this out. Medical practitioners should directly observe the stool, as parental reports might overestimate the degree of pigmentation.<sup>18</sup> Urine colour is less useful as a sign of neonatal cholestasis. The urine of a normal newborn is usually colourless; however, although yellow urine should raise suspicion in a jaundiced infant, the absence of dark urine does not rule out disease and further testing is warranted.<sup>1</sup> Liver function should be established by determining albumin levels,

### Levels of evidence

**Level I:** At least one properly conducted randomized controlled trial, systematic review, or meta-analysis

**Level II:** Other comparison trials, non-randomized, cohort, case-control, or epidemiologic studies, and preferably more than one study

**Level III:** Expert opinion or consensus statements

**Table 1. Differential diagnoses and diagnostic approaches for infants with cholestasis**

DISEASE	DIAGNOSTIC APPROACH
<b>Obstructive cholestasis</b>	
<b>Structural</b>	
• Biliary atresia	Ultrasound (presence, size, and appearance of gallbladder; evidence of cirrhosis and portal hypertension, polysplenia, or asplenia) Hepatobiliary scintigraphy (delayed or absent excretion) Liver biopsy Intraoperative cholangiogram
• Choledochal cyst, or other congenital bile duct anomaly	Ultrasound Cholangiogram (percutaneous and scintigraphic, to show communication with biliary tree and to rule out associated atresia)
• Caroli disease and congenital hepatic fibrosis	Ultrasound (liver and kidneys) Liver biopsy (rarely required)
• Gallstones or biliary sludge	Ultrasound
• Neonatal sclerosing cholangitis	Cholangiogram (endoscopic retrograde, percutaneous or intraoperative)
<b>Duct paucity syndrome</b>	
• Alagille syndrome	Physical examination for typical facial features, which might not be obvious during newborn period (broad forehead, pointed chin, elongated nose with bulbous tip) Chest x-ray scan (butterfly vertebrae) Ophthalmologic examination (posterior embryotoxon) Echocardiogram (peripheral pulmonic stenosis) Liver biopsy (paucity of small ducts) Genetic analysis (mutations in JAG1 gene)
<b>Hepatocellular cholestasis</b>	
• Idiopathic neonatal hepatitis	Diagnosed by exclusion of other causes of neonatal liver disease Liver biopsy (often not required)
<b>Genetic and metabolic disorders</b>	
• $\alpha_1$ -Antitrypsin deficiency	$\alpha_1$ -Antitrypsin levels (reduced) Protein or genetic analysis (homozygous Pi type ZZ, SZ, or other rare deficiency variant)
• Galactosemia	Results of newborn screening Non-glucose reducing substances (positive) Galactose-1-phosphate uridyl transferase in red blood cells (low activity) Blood cultures (association with <i>Escherichia coli</i> sepsis)
• Tyrosinemia	Results of newborn screening Serum tyrosine and methionine levels (high) Serum $\alpha$ -fetoprotein levels (high) Succinylacetone detection in urine
• Hereditary fructosemia	Fructose-1-phosphate aldolase B activity low or absent in liver tissue Liver biopsy with EM Genetic analysis
• Neonatal hemochromatosis	Ferritin (high, usually > 1000 $\mu$ g/L) Total iron binding capacity (low) Liver biopsy with iron stain, or buccal mucosal biopsy MRI (abdomen, for typical pattern of iron deposition)
• Cystic fibrosis	Results of newborn screening Sweat chloride test Genetic analysis
• Inborn errors of bile acid synthesis	Urinary bile acid analysis

Continued on page 1187

continued from page 1186

• Progressive familial intrahepatic cholestasis	GGT (low to normal in types 1 and 2, high in type 3) Liver biopsy Genetic analysis
<b>Endocrine disorders</b>	
• Hypothyroidism	Results of newborn screening TSH (high), free T4 (usually low)
• Panhypopituitarism	Glucose (hypoglycemia common) Cortisol (low) TSH (low), T4 (low)
<b>Toxic or secondary disorders</b>	
• Parenteral nutrition–associated cholestasis	Correlation with clinical history Exclusion of other causes of cholestasis
• Drugs (acetaminophen, anticonvulsants, etc)	Correlation with clinical history Urine and serum toxicology screen
<b>Infectious disorders</b>	
• Toxoplasmosis	IgM-specific antibodies (detectable 2 weeks after infection, peak approximately 4 weeks after infection) Isolation of organism from blood, CSF, or liver Ophthalmologic examination (chorioretinitis) CT (head, intracranial calcifications)
• Rubella	IgM-specific antibodies (detectable 2 weeks after infection) Viral isolation (CSF, liver, urine, pharyngeal secretions) Ophthalmologic examination (cataracts)
• Cytomegalovirus	IgM-specific antibodies Viral isolation from blood, urine, CSF Ophthalmologic examination (for chorioretinitis) CT (head, intracranial calcifications)
• Herpes simplex virus	EM or viral culture of vesicle scrapings PCR of blood and CSF
• Human immunodeficiency virus	HIV DNA PCR Immunoglobulin levels CD4 count
• Syphilis	VDRL test Syphilis indirect hemagglutination test (TPHA) Fluorescent treponemal antibody levels Long-bone x-ray scans (osteochondritis, periostitis)
• Urinary tract infection	Urine culture, full septic workup where indicated
• Sepsis	Blood culture, full septic workup where indicated

Adapted from Walsh et al.<sup>5</sup>

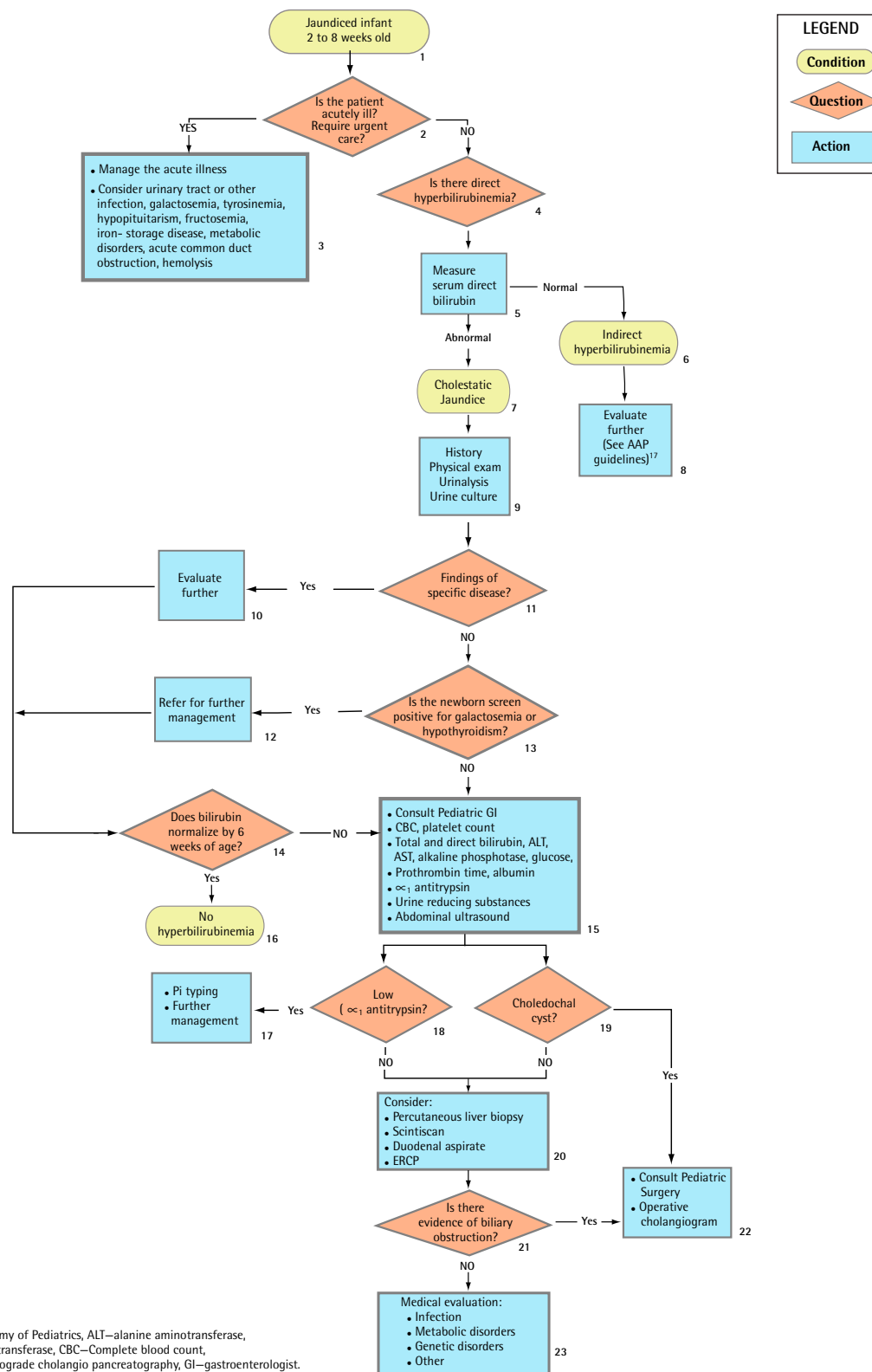
CSF—cerebrospinal fluid, CT—computed tomography, DNA—deoxyribonucleic acid, EM—electron microscopy, GGT— $\gamma$ -glutamyltransferase, HIV—human immunodeficiency virus, IgM—immunoglobulin M, MRI—magnetic resonance imaging, PCR—polymerase chain reaction, T4—thyroxine, TPHA—treponema pallidum hemagglutination, TSH—thyroid stimulating hormone, VDRL—venereal disease research laboratory.

the international normalized ratio (for anticoagulant monitoring), serum ammonia, and blood glucose levels. Concentrations of alanine aminotransferase and aspartate aminotransferase further evaluate the extent of hepatocellular injury, and elevated  $\gamma$ -glutamyltransferase and alkaline phosphatase levels indicate possible obstructive causes of cholestasis. Liver enzyme concentrations are poor predictors of etiology (sensitivity 68%, specificity 43% for the diagnosis of biliary atresia),<sup>19</sup> but

might provide useful information in combination with clinical evaluation to guide further investigation.

Imaging via abdominal ultrasound can help diagnose biliary sludging, inspissated bile, or gallstones and discern structural abnormalities, such as choledochal cysts. A small or absent gallbladder on hepatic ultrasound suggests biliary atresia, but a sensitivity as low as 23% in a recent prospective study indicates that ultrasound cannot be used to rule out this diagnosis.<sup>20</sup>

Figure 1. Algorithm for investigation of the neonate with cholestatic jaundice



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Studies found that the “triangular cord” sign, identified at the porta hepatis during ultrasound and probably representing fibrosis at the portal plate, was 73% to 100% sensitive and 98% to 100% specific for the diagnosis of biliary atresia. The range of sensitivities might have been due to study design or operator experience.<sup>19,21,22</sup> Additionally, polysplenia and situs inversus are associated with biliary atresia.<sup>1</sup> Hepatic ultrasound is best performed at a centre with pediatric radiologic expertise, as its accuracy is operator-dependent.

Hepatobiliary scintigraphy is helpful in distinguishing obstructive from nonobstructive cases of cholestasis. Uptake of the tracer by hepatocytes should be followed by its excretion in bile into the intestine within 24 hours; absence of this excretion is an abnormal result that indicates biliary obstruction or severe hepatocellular dysfunction.<sup>23</sup> The sensitivity of scintigraphy for the diagnosis of biliary atresia was demonstrated to be high in 2 retrospective studies (83% to 100%, respectively), with virtually all affected patients showing no excretion, but specificity was considerably lower, ranging from 33% to 80%.<sup>24,25</sup> Rarely, bile drainage is initially present in infants with cholestatic disease but is subsequently lost after 2 to 3 weeks of age; therefore, early scintigraphy might be misleading. Pretreatment with phenobarbital (5 mg/kg/d) for 5 days before the study was shown to enhance test precision in one study,<sup>26</sup> while another found improved specificity with ursodeoxycholic acid (5 mg/kg twice daily).<sup>27</sup>

Recent expansion of newborn screening programs in certain jurisdictions has improved the amount of information available to primary care providers investigating neonatal jaundice. Results of newborn screening tests should be verified by further testing of all infants with cholestatic jaundice. Although review of the diagnostic accuracy of all investigations for neonatal cholestasis is beyond the scope of this article, an extensive list of investigations is provided in **Table 1**.<sup>5</sup>

### Management and outcome of biliary atresia

Biliary atresia is uniformly fatal within 1 to 2 years if left untreated. Initial management is surgical (portoenterostomy, or Kasai operation), entailing excision of the atretic biliary tree and fibrous plate and Roux-en-Y anastomosis of jejunum to the remaining ducts to allow for biliary drainage.<sup>28</sup> European and North American studies have revealed medium-term survival rates (2 to 10 years' follow-up) without liver transplantation in 25% to 60% of patients who underwent portoenterostomy.<sup>13,23,29,30</sup> The Canadian experience with biliary atresia shows a 10-year overall survival rate of 77% after portoenterostomy and native liver survival rates of 46% at 2 years, 36% at 4 years, and 26% at 10 years.<sup>8</sup> Any intervention that improves native liver and overall survival rates could affect the quality of life of these children as well as the availability of transplant organs.

### Importance of early diagnosis

The outcome of patients with biliary atresia is directly affected by the speed with which health care providers arrive at the diagnosis. The CPHRG recently discovered that 10-year native liver survival rates declined with increasing age at the time of portoenterostomy; 49% of infants who underwent surgery in Canada at 30 days of age were living with their own liver 10 years later, compared with 25% of those whose operations occurred at 31 to 90 days of age and 15% of those treated after 90 days of age.<sup>8</sup> This finding is consistent with other studies,<sup>9</sup> although an American retrospective cohort study was unable to demonstrate whether age at the time of portoenterostomy affected native liver survival, likely owing to small numbers of study subjects and a short (2 year) follow-up.<sup>10</sup> A recent study from France demonstrated the benefit of earlier intervention—15-year survival with native liver.<sup>14</sup> The consensus that younger age at the time of portoenterostomy leads to improved outcomes has led professional organizations to recommend measurement of direct reacting bilirubin levels in infants with persisting jaundice at 2 to 3 weeks of age.<sup>2,16</sup>

One barrier to early identification of cholestatic jaundice might be the schedules for newborn infant assessment commonly followed by health care providers. According to the Rourke Baby Record,<sup>31</sup> endorsed by the Canadian Paediatric Society and the College of Family Physicians of Canada, visits at 2 weeks and 1 month of age are considered “optional”; measurement of direct reacting bilirubin serum levels is not mentioned. The American Academy of Pediatrics' Recommendations for Preventive Pediatric Health Care<sup>32</sup> contain no mention of assessment for cholestasis at the 1-month visit.

The natural history of many other conditions that present with neonatal cholestasis can also be altered by early medical intervention. In patients with congenital hypothyroidism, 2 retrospective cohort studies demonstrated the importance of early (<2 weeks of age) intervention with high-dose (10 to 15 µg/kg/d) levothyroxine in improving neurodevelopmental outcomes.<sup>33,34</sup> In symptomatic patients with congenital cytomegalovirus infection and multiorgan involvement, timely introduction of ganciclovir reduces the prevalence of congenital hearing loss,<sup>35</sup> although criteria for selection of candidates for treatment are controversial, and consultation with an infectious disease specialist is necessary. Dietary treatment of galactosemia improves outcomes of affected infants, although mental retardation and other neurologic abnormalities are still occasionally seen in patients adherent to treatment.<sup>36</sup> Treatment of tyrosinemia with nitisinone and a diet low in tyrosine, phenylalanine, and methionine reduces the risk of developmental delay, cardiomyopathy, hepatic failure, and hepatocellular carcinoma; however, patients should still be screened regularly for the development of liver masses.<sup>37,38</sup>

## Screening for cholestatic jaundice

Screening tests represent a unique opportunity to detect neonatal cholestasis at an early age. Biliary atresia fulfils criteria of a condition considered appropriate for universal newborn screening; it is an important health problem with a latent or early symptomatic period during which timely intervention will improve outcomes.<sup>39</sup> Therefore, investigators have studied the feasibility and efficacy of various screening methods.

Persistently pale stools are found in up to 95% of infants with biliary atresia.<sup>40</sup> Screening of newborns for biliary atresia using stool colour cards was initiated in Japan in the early 1990s.<sup>18,41</sup> Parents compared their infants' stool colours with 7 shades printed on a "stool colour card" and notified their doctors of the results at the routine 1-month health visit. The sensitivity and specificity of the screening program in Japan were 67% and 99.9%, respectively.<sup>42</sup> The average age at the time of portoenterostomy was reduced to 53 days (range 40 to 109 days) in the screened group, compared with an average age of 84 days (range 25 to 138 days) for children not screened. Introduction of a similar nationwide screening program in Taiwan<sup>43</sup> coincided with an increased proportion of infants undergoing portoenterostomy before 60 days of age (74.3% in 2005, compared with historical rates of 23% from 1976 to 1989 and 36% from 1976 to 2000).<sup>43-45</sup> The sensitivity and specificity of stool colour card screening tests in Taiwan were 72% to 97% and 99.9%, respectively.<sup>45</sup>

Several studies have been carried out to investigate the utility of serum and urine bile acid measurements as screening modalities for cholestasis and biliary atresia; however, pathological elevations might not be present until 2 to 4 weeks of age, and the pattern of bile acid elevations in biliary atresia is indistinguishable from other causes of cholestatic liver disease.<sup>46-49</sup> New

technologies (eg, genomics, proteomics) might have the potential to identify novel serum and urine biomarkers of biliary atresia, which would be useful in future screening initiatives.

## Conclusion

**Table 2** summarizes the strategies to improve outcomes of infants with cholestatic jaundice. Early identification of cholestatic jaundice to enable optimal timing of medical and surgical management can be achieved through universal assessment of infants at 2 weeks of age, measurement of direct reacting bilirubin in any that appear jaundiced, and immediate referral to pediatric liver services if cholestasis is identified. Biliary atresia fulfils the criteria for a condition considered to be appropriate for a universal screening program, the implementation of which would have the potential to improve outcomes through enhanced early detection. The availability of a reliable and convenient screening test remains a challenge, although the use of stool colour cards seems promising and should be investigated further. In the meantime, health care workers, including family practitioners and pediatricians, should adopt a "test at 2 weeks" strategy to ensure that we are doing everything possible to positively affect the outcomes of infants with cholestatic jaundice.



**Dr Benchimol** is a research fellow in the Division of Gastroenterology, Hepatology and Nutrition at the Hospital for Sick Children in Toronto, Ont, and a doctoral candidate in clinical epidemiology at the University of Toronto. **Dr Walsh** is a research fellow in the Division of Gastroenterology, Hepatology and Nutrition at the Hospital for Sick Children and a doctoral candidate in medical education at the University of Toronto. **Dr Ling** is a staff hepatologist in the Division of Gastroenterology, Hepatology and Nutrition at the Hospital for Sick Children and Assistant Professor in the Department of Paediatrics at the University of Toronto.

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**Table 2. Summary of recommendations and evidence base for strategies to improve outcome of patients with neonatal cholestasis**

RECOMMENDATION	STRATEGY	EVIDENCE
Test at 2 weeks (fractionated bilirubin levels at 2-3 weeks of age)	Early identification of neonatal cholestasis	Level III: Guidelines from professional organizations (NASPGHAN, CPS, AAP)
Application of diagnostic algorithm and early referral to pediatric gastroenterologist	Accurate diagnosis of cause of cholestasis enables early initiation of treatment	Level III: Case series, guidelines from professional organizations (NASPGHAN, CPS, AAP)
Immediate intervention to address the underlying condition if cholestasis is identified	Early intervention improves outcomes of biliary atresia, congenital hypothyroidism, galactosemia, tyrosinemia, congenital CMV infection	Level II and III: Retrospective cohort studies, guidelines from professional organizations (NASPGHAN)
Further investigation of efficacy and feasibility of screening for neonatal cholestasis	Early identification of neonatal cholestasis results in early intervention	Level II: Prospective cohort studies

AAP—American Academy of Pediatrics, CMV—cytomegalovirus, CPS—Canadian Paediatric Society, NASPGHAN—North American Society for Pediatric Gastroenterology, Hepatology and Nutrition.

## EDITOR'S KEY POINTS

- Many societies recommend measuring total and direct reacting serum bilirubin levels in any infant who is still jaundiced at 2 to 3 weeks of age; however, 14% of Canadian infants with biliary atresia were referred for portoenterostomy only after 3 months of age.
- The main reason for late referral of infants with cholestatic jaundice is either inadequate follow-up of neonatal jaundice or reassurances by primary health care providers that the jaundice is physiologic; further, the schedules for newborn infant assessment commonly followed by health care providers might be a contributing factor.
- Early identification of cholestatic jaundice to enable optimal timing of medical and surgical management can be achieved through universal assessment of infants at 2 weeks of age, measurement of direct reacting bilirubin levels in any who appear jaundiced, and immediate referral to pediatric liver services if cholestasia is identified.

## POINTS DE REPÈRE DU RÉDACTEUR

- De nombreuses sociétés recommandent de mesurer les niveaux de bilirubine totale et conjuguée chez tout nourrisson qui est encore ictérique 2 à 3 semaines après la naissance; pourtant, 14% des nourrissons nés avec une atresie biliaire étaient âgés d'au moins 3 mois lorsqu'ils ont été dirigés pour une portoentérostomie.
- La principale raison pour retarder le transfert des nourrissons qui ont un ictère cholestatique est le suivi inadéquat d'un ictère néonatal ou l'assurance donnée par les soignants de première ligne que l'ictère est «physiologique»; ajoutons que le calendrier généralement utilisé par les soignants de première ligne pour l'évaluation des nouveau-nés pourrait aussi être en cause.
- On peut faire la détection précoce de l'ictère cholestatique et permettre une chronologie optimale pour le traitement médical et chirurgical en pratiquant une évaluation systématique des nourrissons à 2 semaines, un dosage de la bilirubine conjuguée chez tous ceux qui semblent ictériques et un transfert immédiat vers un département d'hépatologie pédiatrique dès qu'une cholestase est confirmée.

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## Contributors

Drs Benchimol, Walsh, and Ling contributed to the literature search and the preparation of the article for submission.

## Competing interests

None declared

## Correspondence

Dr Simon C. Ling, Hospital for Sick Children, 555 University Ave, Toronto, ON M4S 1C5; telephone 416 813-8757; fax: 416 813-6531; e-mail [simon.ling@sickkids.ca](mailto:simon.ling@sickkids.ca)

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