UK NATIONAL SCREENING COMMITTEE

Newborn Screening for Biliary Atresia

20 March 2013

Aim

1. To agree the UK National Screening Committee's (UK NSC) formal policy position on newborn screening for biliary atresia

Background

2. The current policy is that newborn screening for biliary atresia should not be offered.

3. The last document produced on this subject was published in the BMJ in 1999 (Mushtaq I,Logan S, Morris M, Johnson AW, Wade AM, Kelly D, Clayton PT *et al*. Screening of newborn infants for cholestatic hepatobiliary disease with tandem mass spectrometry. *British Medical Journal* 1999; 319 (7208):471-7).

UK National Screening Committee review of screening

4. Bazian were asked to assess the literature published since the previous review.

5. The following were identified as key areas for this review:

Test – the lack of an acceptable test was a key issue in the review at the end of the 1990's. Measurement of bile acid concentration in the blood was suggested as a potential screening marker which could be detected by TMS. This was explored in the 1999 BMJ article with reference to four metabolites (glycodihydroxycholanoates, glycotrihydroxycholanoates, taurodihydroxycholanoates and taurotrihydroxycholanoates). However, it was not possible to establish an acceptable cut off for risk. Since then programmes using stool colour as an alternative screening test have been implemented in some countries.
Treatment – surgery, the Kasai procedure aims to reconstruct the bile duct, can restore bile flow and slow progression but the majority of cases eventually undergo liver transplantation. The timing of surgery is important with higher rates of success reported where the procedure is undertaken earlier, less than 60 days is often cited.
Natural history – the cause or causes of biliary atresia are not well understood. The condition has been associated with congenital anomalies of the heart, abdomen and genitourinary tract in approximately 20% of cases.

Consultation

6. A consultation on the screening review opened in August 2012 and closed on 2nd November 2012. Two responses were received to the consultation. A copy of the responses are attached at Annex A.

Recommendation

7. The UK NSC is asked to agree the policy position on newborn biliary atresia screening as follows:-

Newborn screening for biliary atresia is not recommended.

The natural history of the condition remains poorly understood and the continuing lack of a viable screening test is a significant obstacle to the development of a screening strategy.

8. The UK NSC is asked to agree that the policy should be reviewed in three years time unless there is significant new peer reviewed evidence in the meantime.

Annex A

Consultation Responses

Organisation:	**Birmingham Children's Hospital**		
Name:	Prof Deirdre Kelly	**Email address:**	[redacted]
Section and / or page number	**Text or issue to which comments relate**	**Comment**	
	Agree – no good evidence provided to screen for biliary atresia at present.		

Organisation:	**Children's Liver Disease Foundation (CLDF)**		
Name:	Catherine Arkley	**Email address:**	[redacted]
Section and / or page number	**Text or issue to which comments relate**	**Comment**	
Introduction – Pg 2	General	CLDF welcomes the opportunity of a review of screening for biliary atresia	
Page 17	Nice Guidelines	There is no mention of CLDF's Yellow Alert campaign which is referred to in the NICE neonatal jaundice guidelines. This campaign highlights prolonged jaundice and checking stool colour against a stool chart. The stool chart is made available to healthcare professionals on a laminated bookmark and to parents in a CLDF mails an average of 20 packs per week to community healthcare professionals throughout the UK. It has a dedicated website -	

<table>
<tr><td></td><td></td><td>(www.yellowalert.org) which has 9,500 site visitors per annum. 847 download the files on the site including a stool colour chart and parents leaflet.</td></tr>
<tr><td>Page 18</td><td>Stool colour screening – Taiwan (para 2)</td><td>Data from the Taiwan study indicates a small reduction in the age of referral and treatment within the country and is comparable with UK data but where there has been a difference has been in reducing the number of late referrals (defined as greater than 90 days). Despite centralisation of services and a significant campaign in the UK, run by CLDF, Yellow Alert, the UK does experience late diagnosis. Data submitted to CLDF from King's College Hospital reveals:

KCH manages approximately about half of all UK BA cases

2006 - present - median age at KASAI = 56 days at KCH. At Birmingham and Leeds the median age is less than this.

KCH data:

<table>
<tr><td></td><td>>100 days</td><td>>90 days</td><td>total</td></tr>
<tr><td>2006</td><td>3</td><td>+ 4</td><td>25</td></tr>
<tr><td>2007</td><td>4</td><td>+1</td><td>24</td></tr>
<tr><td>2008</td><td>3</td><td>+2</td><td>28</td></tr>
<tr><td>2009</td><td>0</td><td>0</td><td>23</td></tr>
<tr><td>2010</td><td>3</td><td>+1</td><td>19</td></tr>
<tr><td>2011</td><td>1</td><td>+2</td><td>28</td></tr>
</table>

It this data is extrapolated to annual data, there can be up to 8 late diagnoses per annum. Most will move directly to transplantation being denied the chance of</td></tr>
</table>

		corrective surgery – see criterion 1. The committee are asked to consider the following two papers: ***Dis Child Fetal Neonatal Ed* 2012;**97**:F385-F387 doi:10.1136/fetalneonatal-2010-209700** How reliably can paediatric professionals identify pale stool from cholestatic newborns? B Bakshi[1], A Sutcliffe[2], M Akindolie[1], B Vadamalayan[1], S John[3], C Arkley[4], L D Griffin[5], A Baker[1] This paper concluded that experienced professionals often do not recognise stool colour associated with biliary obstruction. The authors propose that stool colour cards similar to those used in Japan and Taiwan may improve early detection of hepatobiliary disease at a minimal cost. And *Arch Dis Child* doi:10.1136/archdischild-2012-302058 **Skin colour: a barrier to early referral of infants with biliary atresia in the UK - Lily Rose Martin, Mark Davenport, Anil Dhawan**
Page 19	Test acceptable to the public	CLDF has a dedicated website for its Yellow Alert campaign and records any concerns from parents and members of the public relating to the messages contained therein. This campaign has run since 1993 and is now in phase 2.

		Since 1993 only one concern has ever been raised by the public and that was from a grandparent. More concern is raised from parents with infants with a late diagnosis (over 90 days) about the lack of information to support parents to be empowered to ask for referral. Parents require information so they can seek advice from primary care teams and appropriate and prompt referral. CLDF believes that a page in the Parent Held Child Record on prolonged jaundice and stool colour information would be the most effective method to empower parents/carers to seek further investigations. CLDF understands that there is not a strong case for a screening programme per se but there is important information to be given to parents to help them recognise that prolonged jaundice is not normal especially if accompanied by pale stools. The Parent Held Child Record book would be a highly effective medium to do so.
Page 20	Further evaluation of biliary atresia	The British Society of Paediatric Gastroenterology, Hepatology & Nutrition (BSPGHAN), Liver Committee has developed and published diagnostic tests for those infants requiring further diagnostic investigation. - www.bspghan.org.uk/Word%20docs%20and%20PDFs/Investigation%20of%20Conjugated%20hyperbilirubinaemia%202012.doc This information is available to professionals and the public on the BSPGHAN website.

Page 32	Biliary atresia & liver transplantation	All infants undergoing kasai-porto-enterostomy are referred to a national supra-regional service for surgical treatment. If this proves unsuccessful which occurs in up to 60% of patients during infancy/childhood and adolescence then the only chance of survival is by liver transplantation. Biliary atresia is the main indication for liver transplantation in childhood. There is a limiting factor is donor shortage but it is inaccurate to state that timely access to transplantation remains an obstacle to improving surgical outcomes. It is because of the donor organ shortage that parents are undertaking live related transplantation in order to improve survival outcomes. CLDF believes that criterion 12 is fully met
Page 33	Criterion 15	CLDF refers the commentary re page 19 and the lack of parental concern received. Screening backed up by accurate and appropriate information on a website – www.yellowalert.org will ensure that parents are reassured, seek advice continue to breast feed.
Page 34	Criterion 17	There is only one option for the management of biliary atresia; kasai porto-enterostomy. The other studies identified are all concerned with post surgery drug therapy. The conclusions to date are that the drug regimens are unproven but work continues. CLDF does not agree with the summary of this criterion.
Page 35	Criterion 18	There is no data on this because a screening programme has not been considered. If it was considered then a plan would be developed which would have professional and parental input. The latter provided via Children's Liver Disease Foundation
Page 35	Criterion 19	There is no data on this because a screening programme has not been considered. If it was considered then a staffing and facilities would be developed which would have professional and parental input. The latter provided via Children's Liver Disease Foundation

Page 36	Criterion 20	There is already information in the public domain provide by CLDF's Yellow Alert campaign. This has extensive professional and parent's literature and a website with information for download. . Families faced with late diagnosis are denied the chance of effective treatment under the current proposal. As a result, the only chance of survival is without their native liver. This is unacceptable given the level of information and data already available.