Cow’s Milk Allergy and Intolerance

Information and Guidance

Includes interactive pathway, algorithms and resources for Primary Care

Compiled by Paediatric Dietitians
October 2014
IgE mediated Cow’s Milk Protein Allergy

This guidance will help us to address the following clinical questions:

1. How do we initially recognise possible food allergy in primary care and community settings? (including anaphylaxis overview)
2. What elements should be included in examination and allergy-focussed clinical history?
3. What information and support should be provided during the diagnostic process?
4. What tests should be used to diagnose IgE-mediated allergy?
5. What tests should be used to diagnose non-IgE mediated allergy?
6. When should referrals to secondary and/or specialist care be made?
7. When and where should food ‘challenge’ take place?
8. What are the possible prevention strategies?

**Food Hypersensitivity** is overall term used for food allergies and non-allergic food hypersensitivity (also referred to as food intolerances). Food allergy involves the immune system and is divided into IgE and Non-IgE –mediated food allergy.

**Nomenclature**¹

![Diagram of food hypersensitivity]

- **Adverse reactions to food**
- **Hypersensitivity**
  - Allergic Hypersensitivity
    - Food allergy
  - Non-Allergic Hypersensitivity
    - eg. Lactose intolerance
- **Toxic reactions**
- **Non-IgE mediated Cow’s Milk Protein Allergy**
- **IgE mediated Cow’s Milk Protein Allergy**
Cow’s milk hypersensitivity: allergy or intolerance?

Babies and young children can experience two types of reaction to milk: an allergy or intolerance.

**Allergy** to cow’s milk protein is the most common food allergy in childhood and affects 1.9-4.9% of infants and young children. It is more common in babies with atopic dermatitis/atopic eczema.

When might Cow’s milk allergy (CMA) first become apparent?

- when whole protein cow’s milk formula is given or
- when milk allergens are passed through the mother’s breast milk from her diet.
- when introducing cow’s milk products as part of the weaning diet

Lactose (the ‘sugar’ in mammalian milks) **intolerance** is a non-immunological reaction and can easily be mistaken for non-IgE mediated Cow’s milk allergy due to some symptoms in common eg. loose watery stools and abdominal bloating and pain. Symptoms of lactose intolerance occur due to insufficiency of the enzyme lactase in the small intestine leading to lack of or incomplete digestion of lactose i.e. the osmotic effects of lactose leading to diarrhoea and the gas production following its fermentation by intestinal bacteria.

- Primary lactase deficiency is rare, due to a congenital lack or in older children and adults when the ability to produce lactase is lost.
- Secondary lactase deficiency may occur-
  - following a Gastroenteritis infection and is usually transient –commonly 6-8 weeks,
  - or secondary to CMA before diagnosis and treatment.
Use this NICE online interactive PATHWAY for key information and guidance
‘click’ to open


Refer to full Document here

‘Click’ on file attachment below to open (may take a few seconds to open)

And: CYANS guidelines ‘click’ to open them
Diagnosis and management of non-IgE-mediated cow’s milk allergy in infancy - a UK primary care practical guide

Camila Veretta1,2, Nicola Brown2, Neto Shah3, Joanne Walsh1 and Adam Fox1,2

Abstract
The UK NICE guideline on the Diagnosis and Assessment of Food Allergy in Children and Young People was published in 2011. Highlighting the important role of primary care professionals, obstetrics nurses and other community-based health care professionals in the diagnosis and management of non-IgE and non-IgE-mediated food allergy in children, the guideline suggests that those with suspected non-IgE-mediated disease who are suspected to suffer from severe non-IgE-mediated disease are referred to secondary or tertiary-level care. What is evident from this guideline is that the responsibility for the diagnostic food challenges, empiric management and follow-up falls largely on the shoulders of the primary care practitioner. However, this can be challenging, as many of these children are outside the remit of the primary care team. The current UK NICE guideline provides detailed guidance on the role of the primary care team in the management of suspected cow’s milk allergy. This can be seen in the “Click here for background information and see abstracts included later in this guidance.” section.
Allergy-Focused Clinical History ‘checklist’/aide memoire
Do not offer allergy tests without first taking an allergy-focused clinical history.
A healthcare professional with the appropriate competencies (a GP or other healthcare professional) should take an allergy-focused clinical history tailored to the presenting symptoms and age of the child or young person using the questions below.

“click” to open checklist and save or print

Allergy Focused Clinical History for Inc

Having taken an Allergy-focussed Clinical history (see above),
click on the MAP Guideline below for both algorithms

Milk Allergy in Primary Care, Suspected Cow’s Milk Allergy (CMA) in the first year of Life

Figure 1:
Suspected Cow’s Milk Allergy (CMA) in the first year of life – having taken an Allergy-focussed Clinical History.

Exclusively Breast-Fed

**Strict Exclusion of cow’s milk containing foods from Maternal Diet**

- Maternal supplements of Calcium (1000mg) and Vitamin D (10mcg) daily
- Refer to dietitian

**If CMA - most symptoms will settle well within the agreed 2-4 week Elimination Diet**

**No Improvement**

- Need to confirm Diagnosis

**CMA still suspected:**

- Referral to paediatrician with an interest in allergy

**CMA no longer suspected:**

- Return to usual maternal diet

*Consider referral to general paediatricians if symptoms persist*

**Formula-Fed or ‘Mixed Feeding’ (Breast and Formula)**

**Strict Cow’s Milk Protein free Diet**

- Formula-fed: Trial of an Extensively Hydrolysed Formula (eHF) in infant
- Mixed feeding: Trial of a cow’s milk free Maternal Diet
- With eHF top-ups for infant if needed
- Refer to dietitian

**If CMA - most symptoms will settle well within the agreed 2-4 week Elimination Diet**

**Improvement - need to confirm Diagnosis**

**No Improvement**

- CMA still suspected:
  - Refer to a paediatrician with an interest in allergy
  - Consider a trial of eHF

- CMA no longer suspected:
  - Unrestricted diet again
  - Consider referral to general paediatricians if symptoms persist

**Home Challenge:**

- Mum to revert to normal diet containing cow’s milk containing foods over period of one week in to be done between 2-4 weeks of starting Elimination Diet
- If symptoms settle: CMA NOW CONFIRMED
- If symptoms return: Perform Home Challenge using cow’s milk formula
  - (to be done between 2-4 weeks of starting Elimination Diet)
- If symptoms return: No return of Symptoms: NOT CMA
- CMA still suspected:
  - Refer to a paediatrician with an interest in allergy
  - Consider a trial of eHF

- CMA no longer suspected:
  - Return to the eHF again.
  - Consider referral to general paediatricians if symptoms persist

**Primary Care Management of Mild to Moderate Non-IgE CMA**

- (No initial IgE Skin Prick Tests or Serum Specific IgE Assays necessary)
- TB/TB/AF/
- NS/CV/JW
- Oct 2013

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**A planned Reintroduction or Supervised Challenge is then needed to determine if tolerance has been achieved.**

- Performing a Reintroduction vs. a Supervised Challenge is dependant on the answer to the question:
  - Does the child have Current Eczema or ANY history at ANY time of acute onset symptoms?

**No Current Eczema**

- And no history at any stage of acute onset symptoms
  - Reintroduction at Home using a MILK LADDER
    - Check Serum Specific IgE or Skin Prick Test needed
    - Retest with local Allergy Service 6-8 weeks later
    - Reactivated Symptoms: Refer to a paediatrician with an interest in allergy
    - (A Supervised Challenge may be needed)

**Current Eczema**

- Check Serum Specific IgE or Skin Prick Test needed
  - Positive
    - Refer to a paediatrician with an interest in allergy
    - (A Supervised Challenge may be needed)
  - Negative

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**CMA still suspected**:

- Refer to dietitian

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**History of acute onset symptoms at any time**

- Serum Specific IgE or Skin Prick Test needed
  - Negative
    - Referral to general practitioner
    - Reintroduction at Home using a MILK LADDER
    - (Recommended 2-4 weeks after starting Elimination Diet)
  - Positive
    - Referral to paediatrician
    - (A Supervised Challenge may be needed)

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**CMA no longer suspected**: Unrestricted diet again

- Consider referral to general paediatricians if symptoms persist

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**Performing a Reintroduction vs. a Supervised Challenge is dependant on the answer to the question:**

- Does the child have Current Eczema or ANY history at ANY time of acute onset symptoms?

---

**CMA still suspected**:

- Refer to a paediatrician with an interest in allergy

---

**CMA no longer suspected**:

- Unrestricted diet again

- Consider referral to general paediatricians if symptoms persist

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**Symptoms do not settle**:

- Exclude cow’s milk containing foods from maternal diet again
  - If symptoms settle: CMA NOW CONFIRMED
  - If symptoms return: Perform Home Challenge using cow’s milk formula
    - (to be done between 2-4 weeks of starting Elimination Diet)
  - If symptoms return: No return of Symptoms: NOT CMA

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**Can’t take the risk with first few months of age and so to avoid a challenge with support in decision:**

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**A planned Reintroduction or Supervised Challenge is then needed to determine if tolerance has been achieved.**

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**Perform Home Challenge using cow’s milk formula**

- (to be done between 2-4 weeks of starting Elimination Diet)
### Infant Formulas for Cow’s Milk Protein allergy

**eHF-Extensively Hydrolysed Formula**  
**AAF-Amino Acid Formula**  
**MCT-Medium Chain Triglycerides**

<table>
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<tr>
<th>Formula Type</th>
<th>Name</th>
<th>Properties</th>
<th>Manufacturer</th>
<th>Presentation</th>
<th>PIP code</th>
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<tr>
<td>eHF</td>
<td>Nutramigen Lipil 1</td>
<td>Casein hydrolysate and supplementary amino acids. Lactose free. Age under 6 months</td>
<td>Mead Johnson</td>
<td>400g</td>
<td>019-8861</td>
</tr>
<tr>
<td>eHF</td>
<td>Nutramigen Lipil 2</td>
<td>Casein hydrolysate. Lactose free. Age over 6 months</td>
<td>Mead Johnson</td>
<td>400g</td>
<td>298-7766</td>
</tr>
<tr>
<td>eHF</td>
<td>Aptamil Pepti 1</td>
<td>Whey hydrolysate. Under 6 months. Contains lactose (lactose reduced)</td>
<td>Milupa</td>
<td>400g 900g</td>
<td>346-5689 346-5671</td>
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<tr>
<td>eHF</td>
<td>Aptamil Pepti 2</td>
<td>Whey hydrolysate. Over 6 months. Contains lactose</td>
<td>Milupa</td>
<td>900g</td>
<td>359-7002</td>
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<tr>
<td>eHF</td>
<td>Althera</td>
<td>Whey hydrolysate</td>
<td>SMA</td>
<td>450g</td>
<td>378-7413</td>
</tr>
<tr>
<td>eHF</td>
<td>Similac Alimentum</td>
<td>Casein hydrolysate</td>
<td>Abbott</td>
<td>400g</td>
<td>379-8584</td>
</tr>
<tr>
<td>eHF semi-elemental formula with MCT</td>
<td>Pepti junior</td>
<td>Whey hydrolysate with 50 % Fats as MCT Nutricia</td>
<td>Cow + Gate Nutricia</td>
<td>450g</td>
<td>049-0714</td>
</tr>
<tr>
<td>eHF with MCT</td>
<td>Pregestimil</td>
<td>Casein hydrolysate and Supplementary amino acids 55% Fats as MCT</td>
<td>Mead Johnson</td>
<td>400g</td>
<td>043-4050</td>
</tr>
<tr>
<td>AAF</td>
<td>Nutramigen AA</td>
<td>Free amino acids</td>
<td>Mead Johnson</td>
<td>400g</td>
<td>338-3394</td>
</tr>
<tr>
<td>AAF</td>
<td>Neocate LCP</td>
<td>Free amino acids</td>
<td>Nutricia</td>
<td>400g</td>
<td>329-0301</td>
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<tr>
<td>AAF</td>
<td>Alfamino</td>
<td>Free amino acids 25% of fat as MCT</td>
<td>SMA</td>
<td>400g</td>
<td>385-6416</td>
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<tr>
<td>Soya Formula*</td>
<td>Infasoy</td>
<td>Both products-Soya protein hydrolysate. Not recommended for under 6 months. After 6 months, can be used if taste of eHF not tolerated</td>
<td>Cow + Gate Nutricia</td>
<td>900g</td>
<td>057-6058</td>
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<tr>
<td></td>
<td>Wysoy</td>
<td></td>
<td>SMA</td>
<td>860g</td>
<td>030-2570</td>
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</tbody>
</table>

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*Not recommended for under 6 months. After 6 months, can be used if taste of eHF not tolerated.
Soya-based infant formula\textsuperscript{7,17}

The Department of Health advises that soya-based infant formulas should not be used as the first choice for the management of infants with proven cow’s milk sensitivity, lactose intolerance, galactokinase deficiency and galactosaemia. Soya-based formulas have a high phytoestrogen content, which could pose a risk to the long-term reproductive health of infants, according to a 2003 report from the Committee on Toxicity of Chemicals in food, consumer products and the environment (COT), an independent scientific committee that advises the Department of Health and other government agencies. Furthermore, the Scientific Advisory Committee on Nutrition (SACN), another independent advisory body, has advised that there is no particular health benefit associated with the consumption of soya-based formula by infants who are healthy (no clinically diagnosed conditions). SACN also advised there is no unique clinical condition that particularly requires the use of soya-based infant formulas. However a recent systematic review with meta analysis concludes that the patterns of growth, bone health and metabolic, reproductive, endocrine, immune and neurological functions are similar to those observed in children fed cows’ milk formula or human milk. Some infants with cows’ milk allergy may also be sensitised to soya protein, particularly below the age of 6 months so use of soya formulas is not recommended under 6 months. Soya formulas are not recommended for premature infants.

Lactose Intolerance

Infants may have primary lactose (milk sugar) intolerance as a result of inherited deficiency of lactase, the enzyme needed to digest lactose. Others may be intolerant to lactose secondary to an untreated cow’s milk protein allergy or following gastroenteritis and this will gradually resolve as the gut recovers. As the sugar replacing the lactose is likely to be glucose and more cariogenic than lactose, parents should avoid prolonged contact of lactose free milk feeds with their baby’s teeth and to clean their baby’s teeth after the last feed at night. Referral should be made to a paediatrician and Dietitian for suspected primary lactose intolerance where there is significant weight loss or no improvement after withdrawal of lactose.

<table>
<thead>
<tr>
<th>Formula Type</th>
<th>Name</th>
<th>Properties</th>
<th>Manufacturer</th>
<th>Presentation</th>
<th>PIP order code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactose free only</td>
<td>Enfamil O-lac</td>
<td>Contains whole milk protein. (Casein and Whey) Prescription or to buy</td>
<td>Mead Johnson</td>
<td>400g</td>
<td>241-4605</td>
</tr>
<tr>
<td></td>
<td>SMA LF</td>
<td>Contains whole milk protein (Whey). Prescription or to buy</td>
<td>Nestle</td>
<td>430g</td>
<td>240-4127</td>
</tr>
<tr>
<td></td>
<td>Aptamil Lactose free</td>
<td>Contains whole milk protein. To buy only.</td>
<td>Milupa</td>
<td>400g</td>
<td>-pip</td>
</tr>
</tbody>
</table>
Other mammal milks\textsuperscript{8,18}

Infants with CMA should also avoid milk (including formula milk) from other mammals eg goats, due to the high risk of cross-reactivity between proteins in cows' milk and in other mammalian milk, including goats' milk which could lead to life-threatening reactions in cows’ milk allergic infants if goats’ milk is consumed. The Government will be advising the following: Goats’ milk infant formulas and follow-on formula is not suitable for infants with a cows’ milk protein allergy unless directed by a healthcare professional.

Non-Formula milk substitutes based on soya, oat, coconut, almond, pea should not be used as a main milk drink till child is over 1 year, provided there is no concomitant allergy to these foodstuffs. Care is needed in case of growth faltering as these can be lower in energy than formula or full cream cow’s milk. They also need to be fortified with calcium to 120mg/100ml to provide the level comparable to cow’s milk. Rice milk is not suitable for the under 5s due to its potentially toxic levels of arsenic.

‘Primary Care Management’\textsuperscript{9}

For babies whose ‘delayed’ onset symptoms are assessed as
‘Mild to Moderate Non-IgE mediated Cow’s Milk Allergy’,

**click the MAP guideline below-**

**page 2**
To CONFIRM THE DIAGNOSIS of Mild to Moderate Non-IgE Cow's Milk Allergy (After an agreed period of milk exclusion, usually 2 to 4 weeks)

Click file to open, save or print

MAP Home Challenge for initial diagnosis
In babies with mild-moderate Non-IgE Cow’s Milk Allergy, following at least 6 months of exclusion of Cow’s milk, reintroduce Milk at home to test for tolerance\textsuperscript{11}

See the stages of gradual reintroduction to tolerance, outlined in the ‘Milk Ladder’ below. ‘click’ picture to open file, save or print

Practical Pointers on using the MAP ‘MILK LADDER’ for Parents
The following ‘Pointers’ should make it easier for you to understand how best to use this Ladder.

We advise that you are supported by a Health Care Professional (HCP) until the Ladder has been successfully climbed. This may be your doctor, nurse or ideally your dietitian.

- Before starting the Ladder and progressing to each further Step, please ensure that your child is well at the time and also that any gastrointestinal symptoms or eczema are settled.

- Most children will start on Step 1. Some may already eat one or more of the foods on the Ladder. If that is the case, you need to be advised which Step of the Ladder you should start on.

- The Ladder has 12 Steps, but your HCP may adjust the number of Steps to suit your child best.

- The time spent on each Step will vary from one child to another (e.g. one day or 1 week) and this should also be discussed and agreed with you.

- The amounts in the Ladder are given as a guide - occasionally smaller or larger amounts maybe recommended.

- The Ladder includes commercially available and home-made options. Recipe ideas are available at http://www.ctajournal.com/content/3/1/23

- Each of the recipes has an egg and wheat free option (they are all soya free) to make the Ladder suitable for those children who may have other co-existing allergies.

- If the food on any Step of the Ladder is tolerated, your child should continue to consume this (as well as all the foods in the previous Steps) and then try the food suggested on the next agreed Step.

- If your child does not tolerate the food in a particular Step, simply go back to the previous one.

- You should then be advised when that next Step can be tried again.

In a few of the more severe cases of CMA a more cautious start to the Milk Ladder may be recommended, beginning with smaller amounts in Step 1, e.g. a ¼ or ½ of a malted milk biscuit.

Carina Venter, Trevor Brown, Neil Shah, Joanne Walsh, Adam T. Fox
Clin Transl Allergy DOI 10.1186/2045-7022-3-23 Nov 2013

Also\textsuperscript{12} — CYANS ‘Information on home introduction of cow’s milk.

Appendix 3 of main document or click here to save or print
The Main CYANS document also offers information re: **egg avoidance and vaccines.**

NICE Guideline 116\(^3\) agreed that ‘for non-IgE mediated hypersensitivity, ‘although a referral would not always be necessary, advice should be sought from a dietitian and this should include follow up and nutritional issues’ (page 55). Health Professionals should ‘seek advice from a dietitian with appropriate competencies, about nutritional adequacies, timings of elimination and reintroduction and follow up’ (Page 56)

NICE Guideline 116\(^2\) states that ‘the standard method of written referral is not timely, yet there is no evidence whether providing indirect dietary advice via a healthcare professional is acceptable to the family. This system however, could result in reduced attendances at GP surgeries and health clinics, reduced need for unnecessary medication s and treatment, improved health for the whole family and improved skills for the healthcare professionals being supported in the diagnosis. However, it would need increased dietetic support and skills. A community –based randomised controlled trial is needed to compare …’
Prevention of Food Allergy \textsuperscript{13,14,15,16}

Based on evidence, The European Academy of Allergy and Clinical Immunology (EAACI) Taskforce on Prevention (EAACI) Draft guideline \textsuperscript{13} suggests that families can be provided with some advice about preventing food allergy particularly amongst infants at high-risk for development of allergic disease:

- All mothers include a normal healthy diet without restrictions during pregnancy and lactation.
- For all infants exclusive breastfeeding is recommended for the first 4-6 months of life.
- If breastfeeding is insufficient or not possible for the first four months, infants at high-risk can be recommended a hypoallergenic formula with a documented preventive effect for the first 4 months.\textsuperscript{ref 14 GINI study **. (see below-extensively hydrolysed casein cow's milk based formulas –Nutramigen Lipil and partially hydrolysed whey-SMA HA). Difficulties may arise when introducing complimentary feeding at the same time as switching to a 'regular' cow's milk formula around the same time due to 2 interventions at the same time.
- There is no need to avoid introducing complementary foods beyond four months, and the present evidence does not justify recommendations about either withholding or encouraging exposure to potentially allergenic foods after four months of age once weaning has commenced, irrespective of atopic heredity.
- There is no evidence for the use of supplements such as prebiotics or probiotics for food allergy prevention.

**Hypoallergenic Formulas for the possible prevention of Allergic Disease (mainly atopic dermatitis) in high risk infants.**

<table>
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<tr>
<th>Formula properties</th>
<th>Name</th>
<th>Age</th>
<th>Manufacturer</th>
<th>Presentation</th>
<th>PIP code</th>
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<tr>
<td>Extensively Hydrolysed –eHF-c. Casein-based properties</td>
<td>Nutramigen Lipil 1</td>
<td>Birth onwards</td>
<td>Mead Johnson</td>
<td>400g tin</td>
<td>019-8861</td>
</tr>
<tr>
<td></td>
<td>Nutramigen Lipil 2</td>
<td>From 6 months</td>
<td>Mead Johnson</td>
<td>400g tin</td>
<td>298-7766</td>
</tr>
<tr>
<td>Partially Hydrolysed-pHF-w Whey –based properties</td>
<td>SMA HA not suitable for the diagnosis and management of CMA</td>
<td>Birth onwards</td>
<td>SMA (Nestle Nutrition)</td>
<td>800g tin</td>
<td>OTC only 378-5912</td>
</tr>
</tbody>
</table>

**New born infants with parents or siblings who have/have suffered from asthma, eczema or hayfever. **

SMA HA formula (Hypoallergenic Formula) has recently become available, aimed at the above infants, if formula feeding from birth or from their first formula feed following breastfeeding or as complimentary feeds. Research has been cited \textsuperscript{14,15} to suggest that use of this or (Nutramigen Lipil) reduces the risk of these infants developing allergic disease(mainly atopic dermatitis) , with risk reduction continuing till 10 years .

Discussion may arise with pregnant women who already have a child with the above allergic symptoms and/or one of the parents had/has, and parents may consider purchasing this formula. (Their decision is likely to be influenced by the severity and length of time their previous child was affected).
This product is not available on prescription but can be bought from pharmacies. It is not available in Cresswell or Clenoch but parents may bring it in if they choose not to breastfeed. (Nutramigen Lipil eHF is available on prescription.) ** further guidance is awaited from NICE and the Scottish Infant Feeding Network before consideration of our specifically recommending this practice locally. **

References


4. CYANS. Children and Young People’s Allergy Network Scotland. (2013) Recommendations for the diagnosis and Management of Food Allergy in Children and Young People. (September 2013)


6. NHS Dumfries and Galloway Formulary for infant formulas suitable for Cow’s Milk Allergy/Intolerance.


10. To Confirm the diagnosis of Mild to Moderate Non-IgE Cow’s Milk Allergy- MAP Guideline from Venter C et al (2013): Diagnosis and Management of Non-IgE-mediated Cow’s Milk Allergy in infancy – a UK primary care practical guide. Clinical and Translational Allergy 3:(23).Review

12. CYANS ‘Information on home introduction of cow’s milk. Appendix 3 from: Children and Young People’s Allergy Network Scotland. (2013) Recommendations for the diagnosis and Management of Food Allergy in Children and Young People. (September 2013)


Useful resources for the general public.

British Dietetic Association – Food Facts – [www.bda.uk.com](http://www.bda.uk.com) /food facts

click to open, save or print

Food Allergy and intolerances

Food allergy and intolerance Testing

Milk allergy

AllergyUK [www.allergyuk.org](http://www.allergyuk.org)

Allergy action [www.allergyaction.org](http://www.allergyaction.org)

Cow’s Milk Allergy Awareness Campaign [www.cowsmilkallergy.co.uk](http://www.cowsmilkallergy.co.uk)

The Food Standards Agency [http://food.gov.uk/policy-advice/allergyintol](http://food.gov.uk/policy-advice/allergyintol)

Compiled by Paediatric Dietitians, NHS Dumfries and Galloway, October 2014.

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