NHS
Wiltshire
Clinical Commissioning Group

Cow's Milk Protein Allergy (CMPA) Diagnosis and Management in Infants

This guidance has been developed by Paediatricians from GWH, RUH and SFT, and Paediatric Dietitians from GWH in conjunction with the NHS Wiltshire CCG Medicines Management Team.

The guidance is designed to be used by all health care professionals involved in the care of infants and young children with suspected Cow's Milk Protein Allergy.

It includes further information on:

- Differentiation between IgE and non-IgE allergy
- Distinction between lactose intolerance and CMPA
- Assessment and diagnosis of CMPA
- Ongoing management of CMPA
- Different types of formula milk
- Prescribing guide for quantities of formula
- Patient information leaflets (Appendicies)
    - Milk free diet
    - Milk challenge to confirm diagnosis
    - Milk Ladder

Please refer patients to the Paediatric Dietitians (non-urgent) for any further advice.

Salisbury (SFT) : 01722 429333

Swindon (GWH) : 01793 605149

Bath (RUH) : 01225 824398

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Background Information

- Milk allergy is common in infants although in the majority it will resolve with age.
- The symptoms of milk allergy can be non-specific.
- Accurate assessment is important to allow prompt relief of symptoms for those affected but also to avoid over-diagnosis leading to unnecessary exclusion diets.

Non-IgE mediated allergy (delayed):

- The majority of infants with milk allergy have 'non-IgE' milk allergy.
- Non-IgE milk allergy is also termed 'delayed onset' or type 2 allergy.
- Sometimes referred to as milk intolerance although this term can include other non-allergic symptoms from milk.
- Syptoms occur between 2 - 48 hours or longer
- Symptoms are thought to occur due to T-cell activation and localised antibodies in the gut or other tissues. There are no accurate laboratory tests available for clinical use to diagnose non-IgE allergy.

IgE mediated allergy (immediate):

- A smaller group of infants have IgE-mediated ('acute onset'/type 1 allergy).
- Symptoms within minutes to 2 hours

Differentiation

- There is overlap between the symptoms of non-IgE and IgE related milk allergy but an 'allergy focused history' can help to distinguish the two groups (see NICE guidance CG116 for further information)
- **Differentiation of the two groups is important as management is different**

Other Information

- Goat's milk, sheep's milk etc have similar proteins to cow's milk so all need to be excluded at least initially. Some infants will be sensitised to the small quantities of cow's milk proteins which get into breast milk from maternal diets
- **Milk allergy is due to an immune reaction to milk protein, not a reaction to lactose which is the main sugar in milk**

Lactose Intolerance

- Relatively uncommon in infants except as a temporary problem after gastroenteritis; it does not cause rashes, eczema etc.
- Caused by a deficiency of the enzyme 'lactase' which digests the milk sugar element of milk, and is NOT an allergy
- Lactose free formulae therefore do **not** have a role in the management of children requiring a cow's milk protein free diet
- Lactose free formula products can be bought at a similar cost to standard infant formula and should NOT be supplied on FP10 prescription. Most pharmacies can order supplies for next day delivery
- There is separate guidance available (can be used throughout Wiltshire)
- http://nww.ruh-bath.nhs.uk/For_Clinicians/clinical_guidelines/documents/paediatrics/Lactose_intolerance_in_children.pdf

Principles of Assessment and Management

- History and examination to assess severity and determine if any features of acute Type 1 (IgE mediated allergy)
- Commence a milk free diet
- Skin prick tests or serum specific IgE are important in the assessment of possible IgE mediated symptoms
- For those with delayed non-IgE mediated symptoms without acute IgE mediated symptoms reintroduce milk into diet after a short (2-4 week) exclusion trial
- **There is no validated test for non-IgE mediated milk allergy except exclusion diet followed by a reintroduction challenge.**
- Those with severe symptoms and those with possible IgE mediated allergy require referral to paediatrics and dietetics for further assessment.

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Initial Assessment of Suspected Cow's Milk Allergy in Infants

- From the history put into one of the three groups below

Severe Symptoms
Either IgE or non-IgE

Anaphylaxis
Severe persisting gastrointestinal symptoms
Faltering growth with associated symptoms of possible milk allergy
Severe difficult to control eczema with faltering growth

Mild to Moderate Symptoms
Possible IgE mediated symptoms/'Acute' onset

Symptoms usually within minutes of ingestion
Most often formula feed or at onset of mixed feeding
One or more of:

Skin:
Acute pruritus, erythema, urticaria, angioedema
Acute eczema flares

Gastrointestinal:
Vomiting, diarrhoea, abdo pain

Respiratory:
Acute wheeze
Acute rhinitis/conjunctivitis

Mild to Moderate Symptoms
Non-IgE mediated symptoms/'Delayed' onset

Symptoms usually 2-72 hours after ingestion
Breast fed, formula fed or mixed feeding

Gastrointestinal
Colic
Reflux/ GORD
Loose or frequent stools
Perianal redness
Constipation
Abdominal discomfort
PR blood/mucus in an otherwise well child

Skin
Pruritus, erythema
Atopic eczema

Respiratory
'Catarrhal' airway symptoms (usually in association with other symptoms above)

Urgent referral to paediatrics -discuss with local Paediatric Registrar:

RUH bleep 2701 or fax 01225 824212 for Consultant triage

GWH contact on-call Paediatrics via switchboard on 01793 604020

SFT bleep 1165 of fax 01722 425284 for Consultant triage

Start milk free diet (consider the use of amino acid based formula eg Neocate LCP®)

Start milk free diet (exclude cow's, sheep and goat milk)
Parent leaflet: https://prescribing.wiltshireccg.nhs.uk/?wpdmdl=642
Milk-free diet for mother if breast fed (maternal supplements: Calcium 1000mg and Vitamin D 10mcg) - Available as Healthy Start (91p for 56 tablets) or free to eligible women under the Healthy Start scheme - www.healthystart.nhs.uk. A suitable alternative to buy over the counter (OTC) is Pregnacare (£13.23 for 90 tablets)

Hypoallergenic (extensively hydrolysed) milk to replace formula feeds: Nutramigen LIPIL® 1 (from birth) or Nutramigen 2® (from 6 months)
Milk-free solid foods - If milk allergy symptoms will settle within 1-4 weeks

Possible IgE group

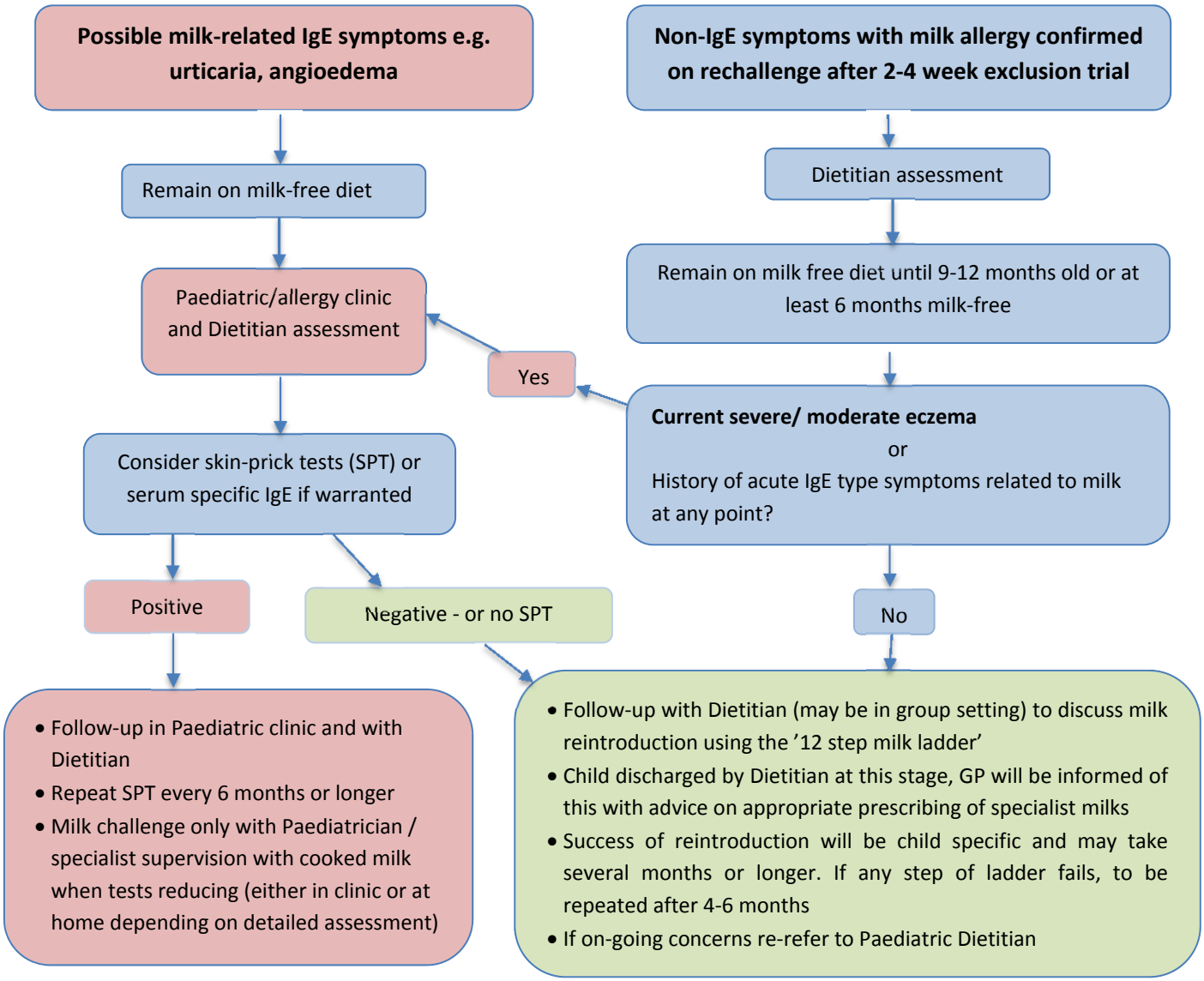
Refer to Paediatric clinic and Dietitian. Continue milk-free diet until further assessment. Mother **MAY** be able to gradually reintroduce some milk into her diet if breastfeeding

Non IgE group

Rechallenge with milk at home after 2 to 4 week exclusion trial. Give family written information about doing this – "Milk Challenge to Diagnose Milk Allergy". **May be managed in primary care.** Refer to Dietitian if milk allergy confirmed by return of symptoms on reintroduction

If no improvement in symptoms when milk excluded consider other diagnoses. If milk allergy still highly suspected consider a trial of amino acid formula eg Neocate LCP®

On-going Management of Milk Allergy



Note on Soya Products:

- Can usually try soya, for example as margarine or small amount of soya dessert, from about 9 months.
- If tolerated, change to soya milk from approx. 12 months of age (as infant formula or Alpro Junior 1+®).
- 'Adult' soy milks can be used in small amounts for cooking etc.
- If also soya allergic will need to continue hypoallergenic milk (eHF or AAF) **until 2 years old**.

Patient Leaflets

For more information about milk free diets, re-challenge procedures for those with non-IgE symptoms, and reintroduction of milk as tolerance develops please see the allergy information patient leaflets:

- **Milk Free Diet - Parent Information** https://prescribing.wiltshireccg.nhs.uk/?wpdmdl=642
- **Milk Challenge to Diagnose Milk Allergy** https://prescribing.wiltshireccg.nhs.uk/?wpdmdl=643
- **Milk Ladder** https://prescribing.wiltshireccg.nhs.uk/?wpdmdl=644
- **FAISG Cow's Milk Free Diet for Infants and Children** https://prescribing.wiltshireccg.nhs.uk/?wpdmdl=645

Types of Infant Formula and Milks

Hypoallergenic Infant Milks

- An extensively hydrolysed formula (eHF) will be appropriate for the majority of cow's milk allergic infants. In eHF the cow's milk protein has been broken down into small peptides
- Inform the family that these milks have an unusual smell and taste but that most babies will tolerate them. There is no significant difference in taste tolerance between the various brands
- If there is any difficulty getting the baby to take the eHF try the following
  - 1) breast fed infants requiring top-ups eHF can be initially mixed with expressed breast milk
  - 2) For those with non-IgE symptoms the eHF can be mixed with the infant's normal formula until the baby is used to it
- If the first eHF prescribed is refused ask for dietitian advice or try an alternative eHF

First-line hypoallergenic milk = Nutramigen LIPIL® 1 (from birth) or 2 (from 6 months)

- Alternative brands available:
  - **Aptamil Pepti®** (Milupa) '1' from birth onwards, '2' from 6 months*
  - **Similac Alimentum®** (Abbott Nutrition) from birth onwards
  - **Althera** (Vitaflo) from birth onwards
- (* All the whey based extensively hydrolysed formulas on UK market contain lactose; this is not clinically important for most infants unless have significant enteropathy)
- Hypoallergenic milks where the fats are also altered eg. Cow & Gate Pepti-Junior® and Mead Johnson Pregestimil® are aimed at gastrointestinal disorders such as short gut where there is also fat malabsorption so are not usually first line for cow's milk allergy where fat absorption is not a problem

Amino acid-based Formula (AAF)

- A small number of infants will need an amino acid based formula (elemental formula) but this should usually be prescribed on the advice of a Paediatric Dietitian or Consultant Paediatrician
- A very small proportion of those who are milk allergic will still have significant symptoms on extensively hydrolysed formula (eHF) and so a trial of an amino acid based formula may be advised. AAF are more expensive than eHF
- AAF can be considered first line for those who have had anaphylaxis to milk or who have significant enteropathy eg. persistent watery diarrhoea and faltering growth. They are sometimes recommended if top-up feeds are needed if the baby was getting significant symptoms related to maternal milk intake when breast fed
- Current brands available in the UK
  - **Neocate LCP** (Nutricia) from birth to one year or **Neocate active®** (Nutricia) for over one year (can continue with LCP in most cases)
  - (Neocate advance® is for children over one year who are not having significant amounts of solid foods)
  - **Nutramigen AA®** (Mead Johnson) from birth onwards

Other milks:

- **Soya based infant formulae**
  - not used first line for babies under 6 months as there is a high chance of cross reactivity in that age group
  - theoretical concerns about phytate levels which may reduce nutrient absorption in very young babies and about phytoestrogen levels in the soya milk
  - can be used in babies over 6 months if extensively hydrolysed milk (eHF) is refused by the baby
- **Sheep and goat's milk**, including infant formula based on these milks contain similar proteins to cow's milk and should also be excluded. They are sometimes tolerated relatively early during the reintroduction phase when the allergy is improving or by some children with mild symptoms eg. eczema
- **Lactose free formula** (eg SMA lactose free®, Enfamil LF®) is not suitable for treatment of symptoms of milk allergy as the protein is unaltered (see separate guideline on lactose intolerance in childhood)
- **Oat milk, nut milks, coconut based milks** etc should not be used as a main milk drink for under 2 year olds as their protein and vitamin content is not high enough. They can be be used in small amounts in cooking etc.
- **Rice milk** is not advised until over 4½ years old (due to arsenic levels which may theoretically increase future cancer risk)

Guidelines for quantity of infant formula required on prescription

Age	Fluid intake ml/kg	Average infant formula intake /24 hours	Total average amount per 24 hr	Cans per month required
0-2 weeks	150	90ml x 6-8 feeds	630ml (21oz)	7 x 400g tins
2-4 weeks	150	120ml x 6-7 feeds	780ml (26oz)	8 x 400g tins
2 months	150	150ml x 5-6 feeds	825ml (28oz)	9 x 400g tins
4-6 month	130	210ml x 5-6 feeds	1155ml (39oz)	13 x 400g tins
7-9 months	120	240ml x 4-5 feeds	1080ml (36oz)	12 x 400g tins 5 x 900g tins
10-12 months	110	120ml x 3-4 feeds	420ml (14oz)	5 x 400g tins 2 x 900g tins
>12 months up to 2 years*			300ml (10oz)	4 x 400g tins 2 x 900g tins

*Only prescribe for those on cow's milk and soya free diets.

Prescriptions should not be issued for children over the age of 2 years.

Parents should be informed their prescription will be discontinued and it can be explained that there are now a wide range of milk and soya free milk alternatives available, such as: oat, nut, and coconut based milks. In most case they are highly fortified with calcium (120mg per 100ml) apart from the "organic" products. Rice milk should NOT be used in children under 5.

Requirement for 2-3 year old – 300ml (10floz) Requirement for 4-6 year old – 400ml (13floz) this can be as a drink, on cereal or in recipes.

If taste is a problem, then parents can add small amount to the prescribed formula and introduce the taste slowly or make use of milk shake powders provided dental hygiene advice is followed. If a child takes their prescribed milk from a bottle then this is the perfect opportunity to stop this habit.

Nationally it is advised that all children under five are given a vitamin supplement to provide vitamins A, C and D if they are breast fed or drinking less than 500ml formula per day. These can be purchased by the parent unless they are entitled to Healthy Start vitamins (http://www.healthystart.nhs.uk).

For further advice contact your local Paediatric Dietitian (non-urgent).

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