Introduction

Cow’s milk protein allergy is an abnormal immune response to cow’s milk protein. It is one of the commonest food allergies in children less than 2 years. Current estimated prevalence is between 2-7.5% of infants affected, most present within the first 6 months of life but initial presentation is rare after 1 year. It affects both formula and breast fed infants. The increase in prevalence parallels the overall increase in allergic disease in the last 2-3 decades.

There are 2 main types of milk allergy; IgE mediated or immediate reactions usually within 2 hours of exposure and the non-IgE mediated or delayed reactions (2-72 hrs onset). In both forms there are multiple systemic involvement including 2 or more of the following:

- Skin: urticarial, angioedema, atopic dermatitis
- Gastrointestinal: diarrhoea, colic, food refusal and feeding aversion, reflux or GORD, bloody and or mucoid stools,
- Respiratory: persistent rhinitis, wheeze, difficulty in breathing.

Prognosis is generally good; average age of resolution is 5 years for IgE mediated and for non-IgE mediated allergy 50% will have resolved by 1 year and 80-90% at 3 years.

Diagnosis

A thorough clinical history is vital to accurate diagnosis, all IgE based tests should be interpreted in the context of the history. The NICE Guidance on Food Allergy in Children provides very detailed guidance on obtaining an allergy focused history to aid optimal care of all children with food allergies.

An Allergy Focused Clinical Assessment

1. An assessment of presenting symptoms and other symptoms that may be associated with food allergy including questions about:
   - The age of the child or young person when symptoms first started
   - Speed of onset of symptoms following food contact
   - Duration of symptoms and frequency of occurrence
   - Severity of reaction (mild involves one system, moderate >1 system no cardiorespiratory symptoms, anaphylaxis; one or more systems plus cardiorespiratory symptoms)
   - Setting of reaction (for example, at school or home)
   - Reproducibility of symptoms on repeated exposure
   - What food and how much exposure to it causes a reaction
   - Who has raised the concern and suspicion of food allergy
   - What the suspected food allergen is
   - Feeding history; if breast fed exclusively consider maternal diet
   - Details of any previous treatment and the response
   - Any response to the elimination and reintroduction of foods
Investigations

1. IgE based tests: skin prick tests and specific IgE to food allergens (previously RAST). IgE tests should be guided by clinical history of suspicion of specific allergens. They have limited use in differentiating sensitisation from allergy. Sensitisation is not always associated with clinical allergy i.e. symptoms on exposure. IgE tests cannot predict severity of reaction but only risk of reaction on exposure.

2. Dietary manipulation: exclusion of specific food allergens and re-challenge whilst monitoring symptoms. Dietetic supervision is mandatory to ensure nutritional adequacy of diet for optimal growth.

3. Oral food challenge: useful for confirming diagnosis in non-IgE mediated CMPA after a period of exclusion with resolution of symptoms. It can also be used to determine resolution of allergy. In children with immediate reactions it should be carried out more safely in hospital if required.

4. No current evidence to support use of IgG, Vega testing, hair analysis and kinesiology in the diagnosis of food allergy.

Managing CMPA

- **Most children with cow’s milk allergy can be managed in primary care with exclusion of cow’s milk, appropriate hydrolysed infant formulas and dietetic support**
- **The minority with severe symptoms such as anaphylaxis, growth faltering, multiple atopic comorbidities and multiple food allergies need referral to allergy specialists**
- Breast milk remains the ideal choice but in breast fed babies with CMPA, recommend maternal dairy free diet with calcium supplementation
- The MAP (Milk Allergy in Primary care) guideline provides practical flow diagrams for the management of CMPA. Venter C, Brown T, Shah N, Walsh J Fox AT Diagnosis and management of non-IgE-mediated cow's milk allergy in infancy - a UK primary care practical guide Clinical and Translational Allergy 2013, 3:23
- CMPA should be distinguished from lactose intolerance which is due to impaired lactase activity in the intestinal brush border. It is not immune mediated and not a feature of atopy. The secondary lactose intolerance in toddlers occurs post gastroenteritis and rarely following other gut insults such as prolonged courses of antibiotics. The main symptoms are bloating and diarrhoea. It is self-limiting but may require a lactose free formula **which can be purchased and should not be prescribed** for 4-6 weeks but not necessarily a hydrolysed formula
- Soya products are NOT recommended*
- In infants over 6 months if eHF not accepted due to issues with palatability try soya as first line
• Extensively hydrolysed protein formulae (eHF) should be first line for mild to moderate CMPA and can be used reflux symptoms combined with other atopic disorders and or family history of atopy.
  
  **Similac Alimentum £9.10/400g**
  **Nutramigen Lipil 1 and 2 £10.38/400g**
  **Aptamil Pepti 1 £9.54/400g**
  **Aptamil Pepti 2 £9.10/400g (£20.48/900g)**
  **Althera £10.68/450g (=£9.43/400g)**

• Amino Acid Formulas) are recommended only for treatment for severe CMPA including anaphylaxis and growth faltering. Paediatric referral recommended. These are significantly more expensive
  
  **Neocate LCP £27.40/400g**
  **Nutramigen AA £25.58/400g**

• Reintroduction of milk after at least 6 months of dairy exclusion or from 1 year of age is recommended. A graded reintroduction is usually better tolerated. The milk ladder guideline for reintroduction can be found [here](#).

  - The quantity required is dependent upon age and size with highest requirements at 4-6 months prior to weaning, normally between 4-12 tins per month. Over the age of one up to 6 tins per month should be sufficient unless specific guidance is given by a Dietitian.

1. [NICE Guidance on Food Allergy in Children](#)
2. MAP guidelines Venter C, Brown T, Shah N, Walsh J Fox AT Diagnosis and management of non-IgE-mediated cow's milk allergy in infancy - a UK primary care practical guide Clinical and Translational Allergy 2013, 3:23
6. Consortium of Food Allergy Group online milk allergy calculator (www.cofargroup.org)—Tool to help predict likely age of milk tolerance development in IgE mediated allergy based on clinical features and allergy test results
7. Managing cows’ milk allergy in children

* In 2004 The Chief Medical Officer issued a statement advising against the use of soya –based formula in infants if they have cows milk allergy or lactose intolerance. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) recommends that due to phytoestrogen content there is a potential risk to health in infants before 6 months, Soya products can be used as part of the weaning diet from 6 months of age and for mild to moderate persistent CMPA as a main drink from 12 months of age if tolerated. Soya formula should be purchased OTC.

**Contact details**

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Suspected Cow’s Milk Allergy (CMA) in the 1st Year of Life
- having taken an Allergy-focused Clinical History

Mild to Moderate
Non-IgE-mediated CMA
‘Delayed’ Onset Symptoms
Mostly 2-72 hrs. after ingestion of cow’s milk protein
Formula fed, exclusively breast fed or with onset of mixed feeding
One or more of these symptoms:
Gastrointestinal
‘Colic’
‘Reflux’ - GORD
Food refusal or aversion
Loose or frequent stools
Perianal redness
Constipation
Abdominal discomfort, blood and/or mucus in stools in an otherwise well infant

Skin
Pruritus, erythema
Significant atopic eczema

Respiratory
‘Catastral’ airways symptoms
(usually in combination with one or more of the above symptoms)

Can be managed in
Primary Care
See Management Algorithm

Severe
Non-IgE-mediated CMA
‘Delayed’ Onset Symptoms
Mostly 2-72 hrs. after ingestion of cow’s milk protein
Formula fed, exclusively breast fed or at onset of mixed feeding
Severe persisting symptoms of one or more of:
Gastrointestinal
Diarrhoea, vomiting, abdominal pain, food refusal or aversion, significant blood and/or mucus in stools, irregular or uncomfortable stools +/- Fasting growth
Skin
Severe atopic eczema +/- Fasting Growth

Cow’s Milk Free Diet
Amino Acid Formula
AAF
Advise breast feeding mother to exclude all cow’s milk containing foods from her own diet and to take daily Calcium (1000mg) and Vitamin D (10mcg) supplements
Issue:
Urgent referral to a paediatrician with an interest in allergy
Urgent dietetic referral

Amino Acid Formulas:
Neocate
Nutramigen AA

Severe
IgE CMA
ANAPHYLAXIS
Immediate reaction with severe respiratory and/or CVS symptoms
(Rarely a severe gastrointestinal presentation)
Emergency Treatment and Admission

Mild to Moderate
IgE-mediated CMA
‘Acute’ Onset Symptoms
Mostly within minutes of ingestion of cow’s milk protein
Mostly formula fed or at onset of mixed feeding
One or more of these symptoms:
Skin
Acute pruritus, erythema, urticaria,
Angioedema
Acute ‘flaring’ of atopic eczema
Gastrointestinal
Vomiting, diarrhoea, abdominal pain/colic
Respiratory
Acute rhinitis and/or conjunctivitis

Cow’s Milk Free Diet
Extensively Hydrolysed Formula - eHF
(Initial choice, but some infants may then need an
Amino Acid Formula - AAF trial if not settling)
Advise breast feeding mother to exclude all cow’s milk containing foods from her own diet and to take daily Calcium (1000mg) and Vitamin D (10mcg) supplements
IgG testing needed.
If diagnosis confirmed (which may require a
Supervised Challenge) - Follow-up with serial IgG testing and later planned and supervised challenge to test for acquired tolerance
Dietetic referral required
If competencies to arrange and interpret testing are not in place - early referral to a paediatrician
with an interest in allergy - advised

eHF formula
- First Line
Aptamil Pepti
Nutramigen Lipil 1 and 2
Althera,
Similac Alimentum
Formulae use – first line: Aptamil, Nutramigen Lipil 1 and 2, Similac Alimentum, Althera
**Management Algorithm**

**Primary Care**
- Can be managed in:
  - Referral to Paediatrician
  - Specialist Paediatric Dietitian
  - Specialist Paediatric Allergy Care

**Admission and Treatment**
- Referral to Paediatrician for further investigation
- Initial investigation and treatment
- Review and management in collaboration with Paediatric Dietitian
- Referral to Paediatric Allergy Specialist

**Anaphylaxis**
- Anaphylaxis is a medical emergency
- Immediate treatment is essential
- Call 999 for an ambulance
- Use adrenaline auto-injector
- Call 111 or visit A&E

**Severe**
- Anaphylaxis is a medical emergency
- Immediate treatment is essential
- Call 999 for an ambulance
- Use adrenaline auto-injector
- Call 111 or visit A&E

**Reactions to Elemental Formulae**
- Anaphylaxis is a medical emergency
- Immediate treatment is essential
- Call 999 for an ambulance
- Use adrenaline auto-injector
- Call 111 or visit A&E

**Severe**
- Anaphylaxis is a medical emergency
- Immediate treatment is essential
- Call 999 for an ambulance
- Use adrenaline auto-injector
- Call 111 or visit A&E

**Non-severe**
- Anaphylaxis is a medical emergency
- Immediate treatment is essential
- Call 999 for an ambulance
- Use adrenaline auto-injector
- Call 111 or visit A&E

**Common Reactions to Elemental Formulae**
- Anaphylaxis is a medical emergency
- Immediate treatment is essential
- Call 999 for an ambulance
- Use adrenaline auto-injector
- Call 111 or visit A&E

**Severe**
- Anaphylaxis is a medical emergency
- Immediate treatment is essential
- Call 999 for an ambulance
- Use adrenaline auto-injector
- Call 111 or visit A&E

**Non-severe**
- Anaphylaxis is a medical emergency
- Immediate treatment is essential
- Call 999 for an ambulance
- Use adrenaline auto-injector
- Call 111 or visit A&E

**The Map Guideline**

**Suspected Cow's Milk Allergy (CMA)** in the 1st Year of Life
- Having taken an allergy-focused clinical history
- Undertaken Cow's Milk Allergy (CMA) in the 1st Year of Life
Jane Lynch, Medicines Management Team OCCG
Felicitas Obetoh, Paediatrician with interest in allergy
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**Primary Care Management of Milk to Moderate Non-IgE CMA**

- **No Improvement** - need to consider other causes
  - CMA - most symptoms will settle within the age of 2-4 weeks Emphasize Diet
  - avoids CMA - lactose-free diet
  - CMA milk formula

- **Improvement** - need to consider allergies
  - Protein: Milk formula
  - No protein: Exclusive breast feeding, (breast and formula)

- **No History of severe reactions to cow's milk at age 2-4 months** or any time

- **Current Exema**

  - History of severe symptoms at any time

  - Negative Positive

  - Skin prick test to cow's milk

  - CMA skin scratch test

  - CMA skin prick test

  - Current Exema

- **Exclusively Breast Fed**

  - ruins feeding on cow's milk

  - CMA skin prick test

  - Current Exema

- **Any history of severe reaction to cow's milk at any time**

  - No Current Exema