The Cow's Milk-related Symptom Score
CoMiSS®

A simple, fast and easy-to-use awareness tool for cow's milk-related symptoms in infants

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Background

SYMPTOMS RELATED TO COW'S MILK IN INFANCY AND COW'S MILK ALLERGY

Many infants present with symptoms that can possibly be related to cow's milk and suggestive of cow's milk allergy (CMA).

CMA is defined as a reproducible adverse reaction to one or more milk proteins mediated by IgE or non-IgE mechanisms. CMA is one of the most common food allergies in children under 3 years old.

CMA prevalence is reported to be up to 3% but is very variable depending on the country, region and the diagnostic method used.[1]

CMA is often not considered as a diagnosis, mainly due to the lack of specific diagnostic marker.

CMA can induce a diverse range of symptoms of variable intensity.[2,3,4] The majority of infants with CMA have ≥ 2 symptoms in ≥ 2 organ systems, including the respiratory and digestive systems and the skin.[3]

About 50%-70% have cutaneous symptoms, 50-60% gastrointestinal symptoms, and about 20-30% respiratory symptoms.[5]

There are two groups of patients that present with symptoms suggestive of CMA:

1. Those with immediate reactions (mostly IgE-mediated reactions), occuring within minutes to 1 to 2 hours after cow's milk ingestion. This group is usually easier to recognize. The immediate symptoms can affect the skin (pruritis, urticaria, acute angioedema), the respiratory tract (wheezing, difficulty breathing), the circulatory system (hypotension/tachycardia in cases of anaphylaxis) and less often the gastrointestinal tract (vomiting and potentially diarrhea).
2. Those with delayed symptoms occurring hours to weeks after cow's milk ingestion (mostly non IgE mediated). This group is usually more difficult to recognize, but does represent the majority of infants with suspected cow's milk related symptoms seen by primary healthcare providers. These delayed reactions can affect the gastrointestinal system (vomiting, diarrhea, constipation, blood in stools), the skin (atopic dermatitis, eczema) and general symptoms causing irritability such as pain/arching after eating, chronic irritability/crying. Circulatory symptoms are rare in this case.

WHY IS THE DIAGNOSIS OF CMA DIFFICULT?

Diagnosis of CMA can often be challenging because many of the symptoms are commonly occuring in healthy infants during their normal growth and development period.[6]

- **Infant crying, having 'colic'**
- **Difficult defecation or 2-3 loose stools per day**
- **Frequent regurgitation**
- **Atopic dermatitis or eczema**

In addition, non IgE mediated CMA has delayed symptoms so it is not always straight forward to associate the symptoms with ingestion of cow's milk.

Diagnosis needs to occur through a 2 to 4 week elimination diet and re-introduction of cow's milk (i.e. an oral food challenge, OFC) which is the gold standard,[7] however this is not always possible in clinical practice.

Other tests such as skin prick test and specific IgE can be conducted but are in many cases not sufficient alone to confirm diagnosis.[7]

WHAT IS CoMiSS®?

The Cow's Milk Related Symptom Score (CoMiSS®) was first developed by a group of internationally well-known experts in 2015 as an awareness tool for healthcare professionals to evaluate the presence of symptoms in infants related to cow's milk.[8] Since 2015 there have been 25 clinical studies conducted and published using CoMiSS®.[9] Based on this new clinical evidence and years of experience the group of international experts updated CoMiSS® in 2022.[10]

- CoMiSS® is a simple, fast and easy-to-use awareness tool for cow's milk-related symptoms, intended to be used by primary healthcare professionals.
- CoMiSS® increases awareness of the most common symptoms of CMA that can aid an earlier diagnosis.
- CoMiSS® can also be used to evaluate and quantify the evolution of symptoms during a therapeutic intervention.
- CoMiSS® is intended to be used in children under 1 year.
- The tool is not intended for infants with severe and life threatening symptoms clearly indicating CMA, including anaphylaxis, which requires urgent referral.

The CoMiSS® scoring form is not intended to be used as diagnostic tool and should not replace an oral food challenge (OFC). Diagnosis of CMA can only be confirmed by a 2 to 4 week elimination diet followed by an OFC.

How to use

THE CoMiSS® AWARENESS TOOL IN CLINICAL PRACTICE

CoMiSS® quantifies the number and severity of symptoms.

It evaluates the suspicion of 'cow's milk-related symptoms' based on the presence of a combination of the following signs and symptoms for a duration of ≥ to 1 week and in the absence of infectious disease:

GENERAL DISCOMFORT

Persistent distress or infantile colic, measured by crying in a clinical situation.

GASTROINTESTINAL SYMPTOMS

Frequent regurgitation, vomiting, diarrhea and constipation.

RESPIRATORY SYMPTOMS

Runny nose, chronic cough and wheezing.

DERMATOLOGICAL SYMPTOMS

Atopic dermatitis (eczema), angioedema and urticaria.

CoMiSS®: Cow's Milk-related Symptom Score

Last name: ..... First name: ..... Age: ..... Date: .....

PURPOSE

CoMiSS® is a simple, fast and easy-to-use awareness tool for cow's milk-related symptoms. It increases awareness of the most common symptoms of cow's milk allergy (CMA). CoMiSS® can also be used to evaluate and quantify the evolution of symptoms during a therapeutic intervention. CoMiSS® is intended to be used in children under 1 year.

The tool is not intended for infants with severe and life threatening symptoms clearly indicating CMA, including anaphylaxis, which requires urgent referral.

Infants presenting with failure to thrive and sick infants with hematochezia, require urgent referral and full diagnostic work up.

INSTRUCTIONS

If the infant presents with symptoms possibly related to cow's milk, rate the observed/reported symptoms by choosing the most appropriate score for each type of symptom. Once completed, add the individual symptom scores together to obtain a total score. For more detailed information refer to the CoMiSS® User Guide *(www.nestlehealthscience.com/health-management/food-allergy/milk-allergy-hcp/diagnosing-cmpa/comiss)*.

SYMPTOM	SCORE		
Crying* assessed by parents without any obvious cause ≥ 1 week duration	0 1 2 3 4 5 6	≤ 1 hour/day 1 to 1.5 hours/day 1.5 to 2 hours/day 2 to 3 hours/day 3 to 4 hours/day 4 to 5 hours/day ≥ 5 hours/day	SCORE
Regurgitation* ≥ 1 week duration	0 1 2 3 4 5 6	0 to 2 episodes/day ≥ 3 to ≤ 5 episodes of volume < 5ml > 5 episodes of > 5ml > 5 episodes of ± half of the feeds in < half of the feeds Continuous regurgitations of small volumes > 30 min after each feed Regurgitation of half to complete volume of a feed in at least half of the feeds Regurgitation of the complete feed after each feeding	SCORE
Stools* Brussels Infant and Toddlers Stool Scale (BITSS) ≥ 1 week duration	4 0 4 6	Hard stools Formed stools Loose stools Watery stools	SCORE
Skin	0 to 6	Atopic eczema ≥ 1 week duration Absent Mild Moderate Severe	HEAD-NECK-TRUNK 0 1 2 3 ARMS-HANDS-LEGS-FEET 0 1 2 3
	0 to 6	(Acute) Urticaria* and/or angioedema* (**no** 0 / **yes** 6)	
Respiratory* ≥ 1 week duration	0 1 2 3	No respiratory symptoms Slight symptoms Mild symptoms Severe symptoms	SCORE

* In the absence of infectious disease.

TOTAL SCORE

INTERPRETATION OF THE TOTAL SCORE

Total score ≥ 10: May be suggestive of cows milk-related symptoms and could potentially be CMA.

Total score < 6: Symptoms are not likely to be related to CMA. Look for other causes.

The CoMiSS® scoring form is not intended to be used as a diagnostic tool and should not replace an oral food challenge.
CMA diagnosis should be confirmed by a 2 to 4 week elimination diet followed by an oral food challenge.

ADDITIONAL INFORMATION TO CONSIDER

Worsening of eczema might be indicative of CMA. If urticaria/angioedema can be directly related to cow's milk (e.g. drinking milk in the absence of other food) this is strongly suggestive of CMA.

Reference: Vandenplas Y, Bajerova K, Dupont C, Eigenmann P, Kuitunen M, Meyer R, Ribes-Koninckx C, Salvatore S, Shamir R, Szajewska H. The Cow's Milk Related Symptom Score: The 2022 Update. Nutrients 2022, 14, 2682. https://doi.org/10.3390/nu14132682

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HOW TO SCORE SYMPTOMS IN CoMiSS®

If there is a suspicion of cow's milk-related symptoms, rate the observed/reported symptoms by choosing the most appropriate score for each type of symptom.

CRYING

- Crying relates to colic. Colic is defined as > 3 hours crying/day for at least 3 days during 1 week for at least 1 week.
- The duration of crying is evaluated. The longer the crying-time, the higher the score.
- Crying should be present at least > 3 days/week for 1 week or more, assessed by parents, without any other obvious cause.
- The score is related to the number of hours the infant cries on a daily basis e.g. up to 3 hours of crying/day will equal a score of 3.
- The age range during which crying (colic) should be considered is between > 2 weeks and < 4 months.

Crying*

SCORE	
0	≤ 1 hour/day
1	1 to 1.5 hours/day
2	1.5 to 2 hours/day
3	2 to 3 hours/day
4	3 to 4 hours/day
5	4 to 5 hours/day
6	≥ 5 hours/day

*In the absence of infectious disease.

REGURGITATION

- The grading of regurgitation defines the score.[11]
- Each score applies to a specific volume regurgitated and the severity of the regurgitation.
- Regurgitation also includes vomiting.
- Regurgitation should only be considered if it is ≥ to 1 week duration and in the absence of infectious disease.
- The age range during which regurgitation should be considered is between > 2 weeks and < 6 months.

Regurgitation*

SCORE	
0	0 to 2 episodes/day
1	≥ 3 to ≤ 5 episodes of volume < 5ml
2	> 5 episodes of > 5ml
3	> 5 episodes of ± half of the feeds in < half of the feeds
4	Continuous regurgitations of small volumes > 30 min after each feed
5	Regurgitation of half to complete volume of a feed in at least half of the feeds
6	Regurgitation of the complete feed after each feeding

*In the absence of infectious disease.

STOOLS

The Brussels Infants and Toddlers Stool Scale (BITSS) is used to evaluate the consistency of stools for Infants less than 1 year.[12]

- **Type 1, 2 and 3** indicate hard stools
- **Type 4** are formed stools
- **Type 5 and 6** indicate loose stools
- **Type 7** indicates watery stools

Gastrointestinal symptoms and stool changes should only be considered if they are ≥ to 1 week duration and in the absence of infectious disease.

Stools (BITSS scale)*

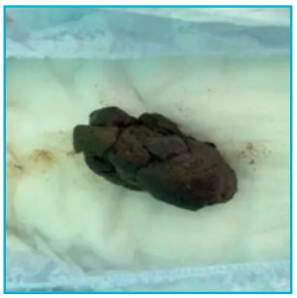
SCORE	
4	Type 1, 2 and 3 (hard stools)
0	Type 4 (formed stools)
4	Type 5 and 6 (loose stools)
6	Type 7 (watery stools)

*In the absence of infectious disease.

- **Type 1**

- **Type 2**

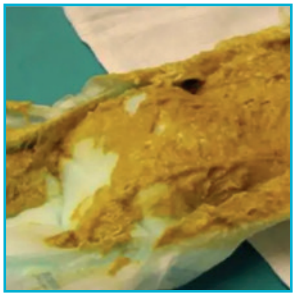
- **Type 3**



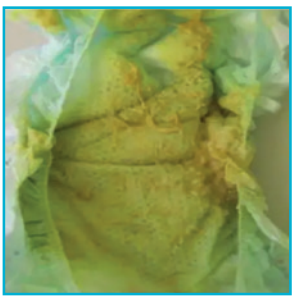
- **Type 4**

- **Type 5**

- **Type 6**



- **Type 7**



Reproduced with permission from: Huysentruyt K , Koppen I, Benninga M, et al; BITSS working group. The Brussels Infant and Toddler Stool Scale: A Study on Interobserver Reliability J Pediatr Gastroenterol Nutr. 2019 Feb;68(2):207-213. (https://journals.lww.com/jpgn/Fulltext/2019/02000/The_Brussels_Infant_and_Toddler_Stool_Scale__A.9.aspx)

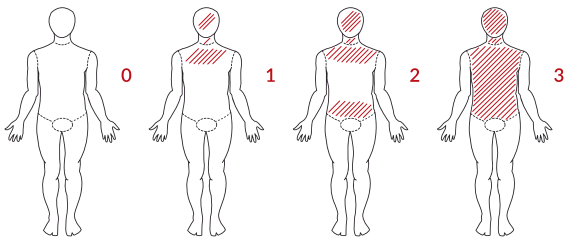
Skin symptoms

SCORE 0 to 6	ATOPIC ECZEMA ≥ 1 WEEK DURATION	HEAD-NECK TRUNK	ARMS-HANDS LEGS-FEET
	Absent	0	0
	Mild	1	1
	Moderate	2	2
	Severe	3	3

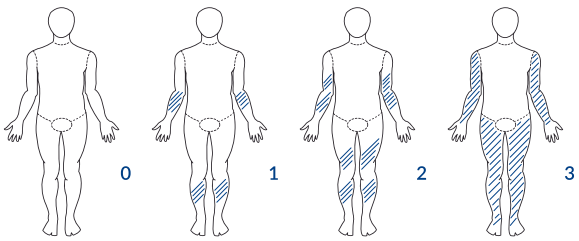
SKIN

- An easy to apply score based on an estimation of the surface covered by the dermatitis, using the surface estimation drawings from burns.
- Atopic eczema should only be considered if it is ≥ to 1 week duration.

HEAD-NECK-TRUNK



ARMS-HANDS-LEGS-FEET



Estimated surface:

0 = **0** | < 1/3rd = **1** | 1/3-2/3rd = **2** | > 2/3rd = **3**

Skin symptoms

SCORE 0 to 6	(ACUTE) URTICARIA* AND/OR ANGIOEDEMA*	NO	YES
		0	6

- If urticaria/angioedema can be directly related to cow's milk (e.g. drinking milk in the absence of other food) this is strongly suggestive of CMA.
- Worsening of eczema might be indicative of CMA.

RESPIRATORY

- Respiratory symptoms are considered in CoMiSS® but do not carry the same weight as other symptoms. This is because respiratory symptoms can be caused by cow's milk, but most of the time chronic cough, runny nose and even wheezing are caused by viral infections.

Symptoms to be considered are*:

- ▶ Chronic cough
- ▶ Runny nose
- ▶ Wheezing

For a duration of ≥ to 1 week.

Respiratory symptoms*

SCORE	
0	No respiratory symptoms
1	Slight symptoms
2	Mild symptoms
3	Severe symptoms

*In the absence of infectious disease.

CoMiSS®

Interpretation of the total score

CoMiSS® ranges from 0 to 33.

Each symptom has a maximum score of six, with the exception of respiratory symptoms (maximum score of three).

- **Total ≥ 10:** If the total CoMiSS® score is ≥ 10, this may be suggestive of cow's milk-related symptoms. This could potentially be CMA.
- **Total < 6:** If the total CoMiSS® score is < 6, the symptoms are not likely to be related to CMA. Look for other causes.

A score of 10 requires the presence of at least two severe symptoms and a score higher than 10 requires the presence of at least three symptoms and the involvement of two organ systems.

WHAT IS DIFFERENT ABOUT THE NEW UPDATED CoMiSS®?

The key updates to CoMiSS are:[10]

- **The overall cut off score has been reduced to ≥10 (from ≥12) which is suggestive of CMA.**
- **The Bristol Stool Scale has been replaced by the Brussels Infant and Toddlers Stool Scale which better reflects the stool consistency of non toilet trained infants.**
- **Clearer guidance is provided for healthcare professionals to indicate those infants for whom the tool is not intended and those infants that require immediate referral e.g. with anaphylaxis, failure to thrive and sick infants with hematochezia.**

References:

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