# Micronutrient deficiencies and autism spectrum disorder

## CASE DEFINITION FOR MICRONUTRIENT DEFICIENCIES AND AUTISM SPECTRUM DISORDER

Report all children and youth less than 18 years of age (up to their 18th birthday) with autism spectrum disorder (ASD) **AND** a new diagnosis of one or more of the following micronutrient deficiencies:

- Vitamin A deficiency/xerophthalmia
- Scurvy
- Severe, symptomatic vitamin D deficiency
- Severe iron-deficiency anemia

The patient’s ASD must have been diagnosed by a general paediatrician, developmental paediatrician, psychiatrist, or psychologist.

Appendix 1 contains definitions for the micronutrient deficiencies and laboratory reference ranges for your information.

**Which of the following micronutrient deficiencies does the patient have? Select ALL that apply:**

- [ ] Vitamin A deficiency/xerophthalmia
- [ ] Scurvy
- [ ] Severe, symptomatic vitamin D deficiency
- [ ] Severe iron-deficiency anemia

## SECTION 1 – DEMOGRAPHIC INFORMATION

1. **Month and year of birth:** _______/_______  
   1.2 **Sex:**  
   - [ ] Male  
   - [ ] Female  
   - [ ] Intersex

1.3 **Province/territory of residence:** _______________  
   **Province/territory of diagnosis:** _______________

1.4 **Rural/remote residence?**  
   - [ ] Yes  
   - [ ] No  
   - [ ] Unknown

1.5 **Canadian-born?**  
   - [ ] Yes  
   - [ ] No  
   - [ ] Unknown  
   **If no, country of birth:** _______________________

1.6 **Population groups (select all that apply):**
   - [ ] Arab
   - [ ] Japanese
   - [ ] First Nations
   - [ ] Southeast Asian
     (e.g., Vietnamese, Cambodian, Laotian)
   - [ ] Black
   - [ ] Korean
   - [ ] South Asian
     (e.g., East Indian, Pakistani, Sri Lankan)
   - [ ] Chinese
   - [ ] Latin American
   - [ ] Métis
   - [ ] West Asian
     (e.g., Iranian, Afghan)
   - [ ] Filipino
   - [ ] White
   - [ ] Unknown
   - [ ] Other, specify: _______________________

## SECTION 2 – ASD INFORMATION

2.1 **Age at diagnosis of ASD:** _______ years or _______ months

2.2 **Who formally diagnosed the patient’s ASD?**
   - [ ] General paediatrician
   - [ ] Developmental paediatrician
   - [ ] Psychiatrist
   - [ ] Psychologist

2.3 **Estimate of ASD severity based on DSM-5 criteria:**
   - [ ] Level 1 “requiring support”
   - [ ] Level 2 “requiring substantial support”
   - [ ] Level 3 “requiring very substantial support”
   - [ ] Unknown
2.4 Is the patient non-verbal (i.e., uses no spoken language or only a few spoken words)?  ☑ Yes  ☐ No

2.5 With which of the following comorbidities has the patient been diagnosed? Select ALL that apply:
☐ Anxiety  ☐ Attention-deficit hyperactivity disorder (ADHD)
☐ Global developmental delay  ☐ Other mental health diagnosis, specify: _____________________________
☐ Intellectual disability  ☐ None of the above

2.6 Has the patient ever participated in ASD-specific therapy (e.g., ABA or IBI)?  ☑ Yes  ☐ No  ☐ Unknown
If yes, specify type, duration, and most recent year of therapy: _________________________________________
___________________________________________________________________________________________

SECTION 3 – MEDICAL HISTORY
3.1 Gestational age: Preterm (<37 weeks)_____ Term_____ Unknown_____

3.2 Does the patient have medical conditions other than ASD?  ☑ Yes  ☐ No  ☐ Unknown
If yes, specify: ____________________________________________

3.3 Has the patient been diagnosed with food allergies/intolerances by a medical professional?
☑ Yes  ☐ No  ☐ Unknown  If yes, specify: ____________________________________________

3.4 Was the patient on vitamins, herbal products and/or supplements at the time of diagnosis?
☑ Yes  ☐ No  ☐ Unknown
If yes, specify type, dose, and duration (if known): ____________________________________________

SECTION 4 – GROWTH & NUTRITION
4.1 Were height and weight measured at the time of micronutrient deficiency diagnosis?  ☑ Yes  ☐ No
If yes, height at time of micronutrient deficiency diagnosis: _____cm or ______ inches
weight at time of micronutrient deficiency diagnosis: _____kg or ______ lbs
If no, how would you classify the patient’s weight status?
☑ Underweight  ☑ Normal/healthy weight  ☑ Overweight  ☑ Obese  ☐ Unable to judge

4.2 Was the patient ever breastfed?  ☑ Yes  ☐ No  ☐ Unknown
If yes, duration of exclusive breastfeeding: ____ months  Total duration of breastfeeding: ___ months
If yes, vitamin D supplementation while breastfed?  ☑ Yes  ☐ No  ☐ Unknown
Dose of vitamin D (if known): ___________ IU

4.3 Prior to this micronutrient deficiency diagnosis, had the patient been assessed/treated by a dietitian?
☑ Yes  ☐ No  ☐ Unknown

4.4 Prior to this micronutrient deficiency diagnosis, had the patient ever received nutrition non-orally (e.g., TPN or G-tube)?  ☑ Yes (specify: _________________)  ☐ No  ☐ Unknown

4.5 In your judgement, was there restricted diet/limited food repertoire in this patient?
☑ Yes  ☐ No  ☐ Unable to judge
If yes, to what do you attribute the patient’s dietary restriction? Select ALL that apply:
☐ Imposed by patient himself/herself (e.g., “picky eater” unwilling to try new foods)
☐ Imposed by parent/caregiver in an effort to treat ASD (e.g., gluten-free, casein-free)
   Specify: ____________________________________________
☐ Imposed based on diagnosed food allergies or intolerances
☐ Food insecurity/lack of food availability
☐ Other, specify: ____________________________________________
☐ Unknown

4.6 Which of the following foods, if any, were consumed <5 times per week? Select ALL that apply:
☐ Meat  ☐ Fruits and vegetables  ☐ Milk and dairy products
☐ Grain products (e.g., cereal, bread)  ☐ Unknown

4.7 In a typical day, how many cups of cow’s milk were consumed? (1 cup = 8 ounces ≈ 250 ml)
☐ 0  ☐ 0.5  ☐ 1  ☐ 2  ☐ 3  ☐ 4  ☐ 5+  ☐ Unknown

4.8 Was the total number of different foods in the patient’s diet <10?  ☑ Yes  ☐ No  ☐ Unknown
SECTION 5 – CLINICAL PRESENTATION OF MICRONUTRIENT DEFICIENCY

5.1 Month and year of micronutrient deficiency diagnosis: ___ / _____ MM YYYY

5.2 Who first identified this patient’s micronutrient deficiency?

- Family physician
- General paediatrician
- Developmental paediatrician
- Ophthalmologist
- Orthopedic surgeon
- Infectious disease specialist
- Rheumatologist
- Endocrinologist
- Gastroenterologist
- Psychiatrist
- Hematologist
- Other, specify: ___________________________
- Optometrist

5.3 What were the presenting signs and symptoms of micronutrient deficiency? Select ALL that apply:

- Concern regarding visual acuity/vision loss
- Fever/infectious illness
- Night blindness
- Delayed closure of fontanelle
- Other visual concerns (e.g., tearing, squinting)
- Parietal or frontal bossing
- Headache
- Craniotabes (soft skull bones)
- Gingival swelling/changes
- "Rachitic rosary"
- Bruising/ecchymosis/petechiae
- Widening of wrist
- Rash or hyperkeratosis
- Bowing of femur & tibia or radius & ulna
- Arthralgia/limp/abnormal gait
- Short stature/failure to thrive
- Inability to bear weight/ambulate
- Abnormal dentition
- Corkscrew hairs
- Seizure
- Lethargy/fatigue
- Fracture
- Pallor
- Not applicable – incidental finding
- Concern regarding growth/weight gain
- Not applicable – routine screening
- Delayed development (not ASD-related)
- Other: ______________________________________

If you selected “not applicable,” please explain: ___________________________________________________

SECTION 6 – INVESTIGATIONS PRIOR TO TREATMENT

6.1 Please complete with as much information as was available (including units):

<table>
<thead>
<tr>
<th>Blood work (serum)</th>
<th>Units</th>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td></td>
<td>X-rays:   ☐ Yes ☐ No</td>
</tr>
<tr>
<td>Vitamin C (ascorbic acid)</td>
<td></td>
<td>If yes, radiographic signs of rickets?</td>
</tr>
<tr>
<td>25-hydroxyvitamin D</td>
<td></td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>Total calcium</td>
<td></td>
<td>MRI: ☐ Yes ☐ No</td>
</tr>
<tr>
<td>Ionized calcium</td>
<td></td>
<td>If yes, describe findings:</td>
</tr>
<tr>
<td>Phosphate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parathyroid hormone</td>
<td></td>
<td>Eye exam: ☐ Yes ☐ No</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td></td>
<td>If yes, signs of xerophthalmia?</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td></td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>Mean corpuscular volume</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferritin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron</td>
<td></td>
<td></td>
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<tr>
<td>Soluble transferrin receptor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transferrin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reticulocyte count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B1 (thiamine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SECTION 7 – USE OF HEALTHCARE RESOURCES

7.1 Was the patient admitted to hospital due to their micronutrient deficiency, either for investigations leading to diagnosis or for management?  ○ Yes  ○ No  ○ Unknown
If yes, duration of hospitalization: _______days  Service under which patient was admitted: _________________

7.2 Did the patient have an invasive procedure as part of their diagnostic work-up?
○ Yes  ○ No  ○ Unknown
If yes, which of the following did the patient have? Select ALL that apply:
- Bone marrow aspirate/biopsy
- Bone biopsy
- General anaesthetic for imaging
- Other, specify: _______________________________________________

SECTION 8 – MANAGEMENT AND OUTCOMES

8.1 How was the patient’s micronutrient deficiency treated? Select ALL that apply:
- Enteral vitamin administration
- Parenteral vitamin administration, specify: _________________
- Nutritional support – TPN
- Nutritional support – enterostomy tube
- Blood transfusion
- Other, specify: _________________

8.2 Has the patient had blood work following treatment for his/her micronutrient deficiency?
○ Yes  ○ No  ○ Unknown
If yes, please indicate the relevant result and date/timing from initiation of treatment: ____________________
________________________________________________________________________________________

8.3 Which of the following has the patient experienced as a result of his/her micronutrient deficiency?
Select ALL that apply:
- Permanent vision loss
- Permanent musculoskeletal deformity
- Prolonged immobilization
- Short stature
- Fracture
- Stroke
- Gross motor delay (not pre-existing)
- Congestive heart failure
- Cardiomyopathy
- Death
- Other, specify: _______________________________________________

○ I agree to be contacted by the CPSP for further information on this questionnaire.
○ I do not wish to be contacted by the CPSP for further information on this questionnaire.

SECTION 9 – REPORTING PHYSICIAN

9.1 Which of the following best describes your practice?
○ General paediatrician
○ Paediatric subspecialist, specify: _________________________________
○ Other, specify: _________________________________

First name ___________________________ Surname ___________________________
Address ______________________________________________________________
City ___________________________ Province ___________________________ Postal code ___________________________
Telephone number ___________________________ Fax number ___________________________
E-mail ___________________________ Date completed ___________________________

Thank you for completing this form.  
(MASD 2019/12)
### Vitamin A deficiency/xerophthalmia

Vitamin A level below normal for age AND one or more of the following:
- Visual symptoms including a sensation of dryness and night blindness
- Diagnosis of xerophthalmia by an ophthalmologist or optometrist
- Correction/resolution of vision symptoms with vitamin A supplementation

<table>
<thead>
<tr>
<th>References ranges for serum vitamin A level&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Age</th>
<th>Range (µmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1 year</td>
<td>0.3 – 1.9</td>
</tr>
<tr>
<td></td>
<td>1–10 years</td>
<td>1.0 – 1.6</td>
</tr>
<tr>
<td></td>
<td>11–15 years</td>
<td>0.9 – 1.9</td>
</tr>
<tr>
<td></td>
<td>16–19 years</td>
<td>1.0 – 2.6</td>
</tr>
</tbody>
</table>

<sup>1</sup> Based on reference ranges of the Department of Paediatric Laboratory Medicine at The Hospital for Sick Children

### Scurvy

Classic signs and symptoms of scurvy including any of petechiae, ecchymosis, hyperkeratosis, corkscrew hairs, gingival disease, and joint pain AND one or more of the following:
- Vitamin C (ascorbic acid) level below normal for age
- Improvement/resolution in signs and symptoms of scurvy with vitamin C (ascorbic acid) supplementation

<table>
<thead>
<tr>
<th>References range for serum vitamin C (ascorbic acid) level&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Age</th>
<th>Range (µmol/L)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>≥25</td>
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</table>

<sup>2</sup> Based on reference ranges of the Department of Paediatric Laboratory Medicine at The Hospital for Sick Children

### Severe, symptomatic vitamin D deficiency

Serum 25-hydroxyvitamin D <25 nmol/L AND one or more of the following:
- Radiographic signs of rickets
- Symptoms consistent with vitamin D deficiency (seizures, hypocalcemia, inability to ambulate) without another identified cause<sup>3</sup>

<sup>3</sup> Based on definition used in previous CPSP study (https://www.cpsp.cps.ca/uploads/surveys/vitamin-d-deficiency-rickets-survey-results.pdf)
Severe iron-deficiency anemia

Hemoglobin <80 g/L AND low mean corpuscular volume AND one or more of the following:

- Ferritin <12 µg/L
- Iron below normal for age
- Soluble transferrin receptor above normal for age
- Transferrin above normal for age
- Correction of anemia with iron therapy

<table>
<thead>
<tr>
<th>References ranges for mean corpuscular volume (MCV)</th>
<th>Age</th>
<th>Range (fL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–14 days</td>
<td>Male (M): 91.3–103.1</td>
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<tr>
<td></td>
<td></td>
<td>Female (F): 92.7–106.4</td>
</tr>
<tr>
<td></td>
<td>15–30 days</td>
<td>M: 89.4–99.7</td>
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<tr>
<td></td>
<td></td>
<td>F: 90.1–103.0</td>
</tr>
<tr>
<td></td>
<td>31–60 days</td>
<td>M: 84.3–94.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F: 83.4–96.4</td>
</tr>
<tr>
<td></td>
<td>61–180 days</td>
<td>M: 74.1–87.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F: 74.8–88.3</td>
</tr>
<tr>
<td></td>
<td>6 months – &lt;2 years</td>
<td>M: 69.5–81.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F: 71.3–82.6</td>
</tr>
<tr>
<td></td>
<td>2 – &lt;6 years</td>
<td>M: 71.3–84.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F: 72.3–85.0</td>
</tr>
<tr>
<td></td>
<td>&gt;6 – &lt;12 years</td>
<td>M: 74.4–86.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F: 75.9–87.6</td>
</tr>
<tr>
<td></td>
<td>&gt;12 – &lt;18 years</td>
<td>M: 76.7–89.2</td>
</tr>
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<td></td>
<td></td>
<td>F: 76.9–90.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>References ranges for iron</th>
<th>Age</th>
<th>Range (µmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–14 years</td>
<td>M: 4.8–25.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F: 4.8–25.3</td>
</tr>
<tr>
<td></td>
<td>14 – &lt;19 years</td>
<td>M: 7.5–32.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F: 5.5–31.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>References ranges for soluble transferrin receptor</th>
<th>Age</th>
<th>Range (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1–11 years</td>
<td>0.8–1.6</td>
</tr>
<tr>
<td></td>
<td>12–19 years</td>
<td>0.7–1.5</td>
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<thead>
<tr>
<th>References ranges for transferrin</th>
<th>Age</th>
<th>Range (µmol/L)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>0–&lt;2 months</td>
<td>12.8–27.6</td>
</tr>
<tr>
<td></td>
<td>2 months–&lt;1 year</td>
<td>13.2–39.9</td>
</tr>
<tr>
<td></td>
<td>1–&lt;19 years</td>
<td>27.1–41.5</td>
</tr>
</tbody>
</table>

4 Adapted from definition used in previous CPSP study (https://www.cpsp.cps.ca/uploads/studies/iron-deficiency-anemia-protocol.pdf)
5 Based on recent consensus in the iron-deficiency literature
6 Based on reference ranges of the Department of Paediatric Laboratory Medicine at The Hospital for Sick Children