Micronutrient deficiencies and autism spectrum disorder

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REPORTING INFORMATION
(To be completed by the CPSP)

Report number:	
Month of reporting:	
Province:	
Today's date:	

Please complete the following sections for the case identified above. If the information asked below is not readily available, please leave it blank. Strict confidentiality of information will be assured.

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

1.1 Month and year of birth: _____ /_____ (MM / YYYY) 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	❑ Black	❑ Chinese	❑ Filipino
❑ Japanese	❑ Korean	❑ Latin American	❑ White
❑ First Nations	❑ Inuit	❑ Métis	❑ Unknown
❑ Southeast Asian (e.g., Vietnamese, Cambodian, Laotian)	❑ South Asian (e.g., East Indian, Pakistani, Sri Lankan)	❑ West Asian (e.g., Iranian, Afghan)	❑ 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
- ❑ Night blindness
- ❑ Other visual concerns (e.g., tearing, squinting)
- ❑ Headache
- ❑ Gingival swelling/changes
- ❑ Bruising/ecchymosis/petechiae
- ❑ Rash or hyperkeratosis
- ❑ Arthralgia/limp/abnormal gait
- ❑ Inability to bear weight/ambulate
- ❑ Corkscrew hairs
- ❑ Lethargy/fatigue
- ❑ Pallor
- ❑ Concern regarding growth/weight gain
- ❑ Delayed development (not ASD-related)
- ❑ Fever/infectious illness
- ❑ Delayed closure of fontanelle
- ❑ Parietal or frontal bossing
- ❑ Craniotabes (soft skull bones)
- ❑ "Rachitic rosary"
- ❑ Widening of wrist
- ❑ Bowing of femur & tibia or radius & ulna
- ❑ Short stature/failure to thrive
- ❑ Abnormal dentition
- ❑ Seizure
- ❑ Fracture
- ❑ Not applicable – incidental finding
- ❑ Not applicable – routine screening
- ❑ 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):

Blood work (serum)	**Units**
Vitamin A	
Vitamin C (ascorbic acid)	
25-hydroxyvitamin D	
Total calcium	
Ionized calcium	
Phosphate	
Parathyroid hormone	
Alkaline phosphatase	
Hemoglobin	
Mean corpuscular volume	
Ferritin	
Iron	
Soluble transferrin receptor	
Transferrin	
Reticulocyte count	
Zinc	
Vitamin B1 (thiamine)	
Other:	

Imaging

X-rays: ❍ Yes ❍ No

If yes, radiographic signs of rickets?
❍ Yes ❍ No

MRI: ❍ Yes ❍ No

If yes, describe findings:

Eye exam: ❍ Yes ❍ No

If yes, signs of xerophthalmia? ❍ Yes ❍ No

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
- ❑ Endoscopy (upper and/or lower)
- ❑ 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)

Appendix 1 — Micronutrient deficiency definitions with laboratory reference values

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

References ranges for serum vitamin A level[1]	**Age**	**Range (µmol/L)**
	<1 year	0.3 – 1.9
	1–10 years	1.0 –1.6
	11–15 years	0.9 –1.9
	16–19 years	1.0 – 2.6

[1] 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

References range for serum vitamin C (ascorbic acid) level[2]	**Age**	**Range (µmol/L)**
	All	≥25

[2] 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[3]

[3] 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[4]:

- Ferritin <12 µg/L[5]
- Iron below normal for age[6]
- Soluble transferrin receptor above normal for age[6]
- Transferrin above normal for age
- Correction of anemia with iron therapy

References ranges for mean corpuscular volume (MCV)[5]	**Age**	**Range (fL)**
	0–14 days	Male (M): 91.3–103.1 Female (F): 92.7–106.4
	15–30 days	M: 89.4–99.7 F: 90.1–103.0
	31–60 days	M: 84.3–94.2 F: 83.4–96.4
	61–180 days	M: 74.1–87.5 F: 74.8–88.3
	6 months – <2 years	M: 69.5–81.7 F: 71.3–82.6
	2 – <6 years	M: 71.3–84.0 F: 72.3–85.0
	>6 – <12 years	M: 74.4–86.1 F: 75.9–87.6
	>12 – <18 years	M: 76.7–89.2 F: 76.9–90.6
References ranges for iron	**Age**	**Range (µmol/L)**
	0–14 years	M: 4.8–25.3 F: 4.8–25.3
	14 – <19 years	M: 7.5–32.6 F: 5.5–31.5
References ranges for soluble transferrin receptor	**Age**	**Range (mg/L)**
	1–11 years	0.8–1.6
	12–19 years	0.7–1.5
References ranges for transferrin	**Age**	**Range (µmol/L)**
	0– <2 months	12.8–27.6
	2 months– <1 year	13.2–39.9
	1– <19 years	27.1–41.5

[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