IMPORTANT INFORMATION

This medical guideline was developed for primary care providers to be able to discuss this information and support families. It is important to note that these resources are not recommended for broad public distribution (example: Please do not print and put copies on display for casual reading). One on one discussion between a primary care provider and family members in the sharing of this information is essential.

There are no print copies of these resources available for order. Please print from the PDF documents available online. Thank you

If you need information or advice on the management of an infant or child with CPT1a variant, please do not hesitate to call the Biochemical Disease physician on call through BC Children's Hospital paging service at (604) 875-2161.

Biochemical Disease Physician On Call:
604-875-2161

Electronic copies of this medical guideline and the affiliated family brochure can be found on Child Health BC's website at:

http://childhealthbc.ca/?drawer=Hypoglycemia in BC First Nations Infants and Young Children (CPT1a)

PREVENTION AND MANAGEMENT OF HYPOGLYCAEMIA IN BC FIRST NATIONS' INFANTS AND YOUNG CHILDREN INCLUDING SCREENING FOR CPT1A VARIANT IN INFANTS AND YOUNG CHILDREN WHO PRESENT WITH KETOTIC AND HYPOKETOTIC HYPOGLYCEMIA

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1.0 BACKGROUND

The development of this medical guideline was initiated in relation to the observation that some BC First Nations' infants and children may be susceptible to hypoglycaemia during prolonged fasting and/or illnesses that could interfere with feeding due to a common genetic variant and that awareness building about this topic amongst primary health professionals would be helpful.

This medical guideline was developed following several years of consultation with primary and acute health care providers and researchers in BC, with content expertise and leadership from BC Children's Hospital and support from health authority partners and the Tripartite Maternal, Child and Family Health Strategy Table members. An affiliated family brochure was developed in consultation with First Nations communities and families.

1.1 PURPOSE

This medical guideline provides evidence-based information on the prevention and management of hypoglycaemia in First Nations infants and young children. The guideline includes information about a common genetic variant (P479L) in carnitine palmitoyltransferase I (CPT1a) that may increase the risk of hypoglycaemia in infants and young children. The key message is that clinicians need to provide information to First Nations families about healthy feeding practices with an aim to prevent

hypoglycaemia, especially during intercurrent illness or during periods of prolonged fasting. This information should be integrated with other key prevention and health promotion messages, including breast feeding and safe sleep promotion messaging.

1.2 INTRODUCTION

Some BC First Nations' infants and children may be susceptible to hypoglycaemia during prolonged fasting and/or illnesses that interfere with feeding (such as fever, vomiting or diarrhea) due to a common genetic variant.

Carnitine palmitoyltransferase I (CPT1a) is the key regulatory enzyme for the oxidation of fatty acids. During the fasting state, the CPT1a enzyme is activated and fatty acids are broken down to produce energy and ketones.

Classic CPT1a Deficiency	CPT1a Variant
CPT1 Function	
Classic CPT1a deficiency is a rare autosomal recessive disorder (~1/100,000) associated with complete loss of enzyme activity.	The CPT1a variant is a common genetic variant that results in partial loss of enzyme activity.
Health Effects	
Classic CPT1a deficiency confers significant risk for hypoketotic hypoglycaemia, hepatic encephalopathy, seizures, and sudden unexpected death in infancy.	It is possible that the CPT1a variant may lead to low blood sugar in some children during long periods without eating and during sickness (fever, vomiting or diarrhea). Research is underway to further explore if there is a cause and effect relationship between the CPT1a variant and low blood sugar and other health risks.

Note: This guideline is an effort to find the balance between prevention of potential harm attributable to the CPT1a variant based on the evidence to date and avoidance of medicalization of a condition which might be more benign than currently known.

In BC First Nations, a common genetic variant in the CPT1a gene (p.P479L) results in a slower rate of fatty acid oxidation. The CPT1a variant, when homozygous (2 copies), results in partial loss of CPT1a activity. For these individuals, enzyme activity levels typically range between 15-25% of normal.

This differs from classic CPT1a deficiency which is a rare autosomal recessive disorder (~1/100,000) associated with complete loss of enzyme activity which confers significant risk for hypoketotic hypoglycaemia, hepatic encephalopathy, seizures, and sudden unexpected death in infancy.

Since 2004 in BC, CPT1a p.P479L genotyping has been performed on clinical request and for those First Nations children investigated at BC Children's Hospital (BCCH) for hypoglycaemia and seizures. Based on prevalence study data, it is estimated that between 2004 and 2011, approximately 1400 infants were born homozygous for the variant. During that time period, 80 children were referred to the Biochemical Diseases Clinical Service, BCCH, and followed thereafter (unpublished data, Sinclair, Stockler et al).

In this case series, 27 of the 80 cases referred had at least one documented episode of hypoglycaemia. Eighteen of these occurred before the age of one year and 9 after the age of one year. Most of the hypoglycaemia was reported in conjunction with serious chronic conditions (n=5) acute illness (n=11), prematurity (n=2), maternal gestational diabetes (n=2), or a combination of these (n=1). Three children, including two with chronic conditions, developed hypoglycaemia while fasting for medical procedures.

Five of the cases presented with hypoglycaemia without any obvious co-morbidity, risk factors or acute illness, representing 0.36% of the total expected CPT1a variant prevalence in the province. Therefore, it would appear that a First Nations infant who is homozygous for the CPT1a variant has minimal risk of developing hypoglycaemia when well, but this risk is higher than the expected risk in the general population [4].

In summary, infants and young children who are homozygous for the CPT1a variant may have an increased susceptibility for hypoglycaemia but this is uncommon in the absence of a significant trigger such as infection, prolonged fasting, co-morbidities or other acute illness.

However, even though the common CPT1a variant found in BC has some enzyme activity, hypoglycaemia in some children may occur during long periods of fasting and during sickness (fever, vomiting or diarrhea). This includes the possible consequences of seizures, coma, and in some circumstances unexpected death.

As a child grows older, this apparent susceptibility to hypoglycaemia appears to decrease. The CPT1a variant does not seem to cause other health or medical conditions.

For those with only one copy of the CPT1a variant (heterozygous), there is *no* clinically apparent decrease in activity levels; therefore, no clinical presentation is expected.

1.3 HOW COMMON IS THE CPT1A VARIANT?

Based on an anonymized research study [1], the CPT1a variant is more common in First Nations in certain regions of the province.

- Along the coast of B.C. and Vancouver Island, 1 in 5 First Nations babies are born homozygous for the variant.
- In the interior region of B.C., 1 in 25 First Nations babies are born homozygous for the variant.
- Outside of BC, the CPT1a variant has been identified in other Aboriginal populations (predominantly Inuit) in coastal Alaska, North West Territories and Nunavut, with homozygous rates between 25-80% [2,3].
- The CPT1a variant has not to date been found in non-Aboriginal populations.

1.4 DOES THE CPT1A VARIANT INCREASE THE RISK OF SUDDEN UNEXPECTED DEATH IN INFANCY (SUDI)?

An anonymized BC study found an increased odds ratio of 3.9 (95% CI 1.7-9.0) for the

association of SUDI and homozygosity for the CPT1a variant [1]. A similar trend suggesting an increased odds ratio for SUDI and the CPT1a variant was observed in Aboriginal populations in Nunavut and Alaska [2, 3, 5, 6].

Association studies in themselves do not prove causation since unmeasured confounding variables could be influencing the results. Further study is underway in Alaska, Nunavut and BC to determine whether there is evidence that the CPT1a variant itself confers risk either alone or in the presence of other known risk factors (such as non-optimum sleep position). Therefore, at this time, there is insufficient evidence to confirm that babies with the CPT1a variant are at higher risk of SUDI.

In FN communities, the risk of SUDI is higher than the general population [7]. Risk factors associated with SUDI are also higher in FN communities. As for all infants, parents should be advised to practice safe sleep practices.

See Appendix 1 for provincial safe sleep messages. Provincial, federal and First Nations partners have developed a set of discussion cards that can be used to facilitate discussions around safe sleep with First Nations and Aboriginal Families.

Honouring Our Babies: Safe Sleep Cards are available at http://fnha.ca/what-we-do/children-youth-and-maternal-health. It is a commitment of the *Transformative Change Accord: First Nations Health Plan* to address the higher rates of infant death among Aboriginal populations.

1.5 IS THERE NEWBORN SCREENING FOR THE CPT1A VARIANT?

There is currently no newborn screening in BC for either classical CPT1a deficiency or the CPT1a variant as it is not clear at this time if the health benefits of screening outweigh potential harms.

1.6 HAVE BC FIRST NATIONS COMMUNITIES BEEN INFORMED ABOUT THE CPT1A VARIANT?

Yes, messaging has been shared with health providers working in BC First Nation communities. A First Nations Parent Resource brochure is available at the:

- Child Health BC website: http://childhealthbc.ca/?drawer=Hypoglycemia in BC First Nations Infants and Young Children (CPT1a)

Parents are advised:

- To provide age-appropriate regular meals and avoid long periods between feedings.
- To feed their infants more often when sick with fever, vomiting or diarrhea.
- To seek medical attention when their infant:
    - Has a fever, vomiting or diarrhea;
    - Refuses feeds; or
    - Is excessively sleepy and hard to wake up.

If you need information or advice on the management of an infant or child with CPT1a variant, please do not hesitate to call the Biochemical Disease physician on call through BC Children's Hospital paging service at (604) 875-2161.

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2.1 INITIAL CLINICAL EVALUATION

The CPT1a variant should be considered in a First Nations or Inuit child with hypoglycaemia in the case of prolonged fasting and/or fever, vomiting or diarrhea, known past episode of hypoglycaemia or in a case of family history of sudden unexpected death. There is some evidence from case study that children with the CPT1a variant can mount a ketotic response during hypoglycemia. Therefore, children with both ketotic and hypoketoic hypoglycemia should be investigated.
The appropriate investigations are as follows:

- Check blood sugar. If low, treat as per standard hypoglycaemia protocols.
- Document presence or absence of ketones in urine.
- Bloodspot ACYLCARNITINE PROFILE.

If the acylcarnitine profile is suggestive of the CPT1a variant, the Biochemical Genetics Lab will reflex to molecular confirmation of the CPT1a variant from the bloodspot sample submitted for acylcarnitines.* A sample can be collected using the standard newborn screening bloodspot card available at any birthing hospital. The bottom of the card has a tick box for ACYLCARNITINE PROFILING. The genotyping results will be reported with an interpretive comment outlining the uncertain clinical significance of the CPT1a variant and will be updated as further knowledge is gained from ongoing research.

Of note: Neonatal hypoglycaemia is a common problem and usually due to other causes (IUGR, prematurity, maternal diabetes, etc.). In the context of neonatal hypoglycaemia without risk factors, or any presentation of hypoketotic hypoglycaemia, the CPT1a variant should be considered therefore acylcarnitine profiling should be carried out. If you would like prompt review of the newborn screening acylcarnitine profile, contact the newborn screening lab at (604) 875-2148.

*Acylcarnitine profiles in the newborn period are highly sensitive for the CPT1a variant (~ 95%) with some decrease in test sensitivity with age. When an acylcarnitine profile is ordered, the newborn screening program will also review the original newborn screening acylcarnitine profile and reflex to molecular testing for the CPT1a variant if one or both profiles are suggestive.

2.2 ACUTE CARE MANAGEMENT

Since there is a potential for brain injury with severe hypoglycaemia in infants and children of any age, children with the CPT1a variant who present to the ER and have an intercurrent illness where oral carbohydrate intake has been limited should be assessed and treated as follows:

- If blood glucose low, treat as per standard hypoglycaemia measures. Assess hydration and rehydrate as condition dictates. If child is only mildly dehydrated and normoglycemic, consider the following:

  - Has parent tried Oral Rehydration Solution (ORS) at home?
  - How did they do it?
- If the trial of ORS sounded adequate but the child failed, consider IV dextrose solutions and retry ORS.
- If there was no trial, consider a trial of ORS and monitor blood glucose.
- If child is unable to tolerate ORS after 2 hours, or if there is evidence of hypoglycaemia, consider IV dextrose solutions to provide maintenance fluids until child is able to tolerate fluids.

2.3 WHAT IF AN INFANT/CHILD IS FASTING FOR A DENTAL OR MEDICAL PROCEDURE OR FOR SURGERY?

- Avoid fluid fasting > 4 hours for all children. Give PO clear fluids (clear juice, or other clear glucose containing beverage) for expected delay of > 2 hours.
  Note: A 4 hour fast is required after feeding with breast milk.
- Dextrose containing isotonic IV solutions such as D5NS should be strongly considered for fasts of greater than 4 hours duration whether due to delayed procedure start, procedure duration or delayed post-procedure resumption of PO intake.
- Blood glucose should be monitored for all fasts of greater than 4 hours duration to monitor for both hypoglycaemia and iatrogenic hyperglycemia.
- As for any child on IV therapy, fluid rates need to be monitored to prevent risk of fluid overload.

3.1 LONG TERM FOLLOW UP OF INDIVIDUALS WITH THE CPT1A VARIANT

Children identified as homozygous for the CPT1a P479L variant should be followed by a paediatrician. If there are persistent problems with hypoglycaemia, a referral to Biochemical Diseases Clinical service at BCCH, may be warranted to rule out other diagnoses.

Our case review suggests that the first year of life is the riskiest time for adverse events that may be associated with CPT1a variant; therefore, a minimum of biannual follow-up is recommended in the first year of life. The following should be reviewed: parent's infant/child feeding practices; management of any concurrent illnesses that occurred between the visits; any symptoms of hypoglycaemia (and consequences such as seizures); and parent knowledge of managing CPT1a variant. Annual review after age 1 to the age of 4 years of age is recommended.

Medical Alert Bracelet
For children with a history of ongoing hypoglycaemia, a medical alert bracelet may be advisable. The bracelet could have a focus on hypoglycaemia and its treatment.

<u>Management:</u>
Management is based on the assumption that individuals with the CPT1a variant carry a risk to develop clinical manifestations such as hypoglycaemia and encephalopathy once they are in a situation of catabolic stress occurring during illness, surgery and prolonged fasting for various other reasons. Because there is no certainty about this assumption, our management plan is an attempt to find the balance between prevention of potential harm attributable from the metabolic condition and avoidance of medicalization of a condition which might be more benign than currently known.

Initial evaluation:

- History and physical exam
- LFTs (AST, ALT, GGT, Alkaline Phosphatase, LDH, conjugated and unconjugated bilirubin) to rule out cholestasis* in infants under 3 months. At the doctor's discretion in older infants and children.

* There is some case evidence of mild cholestasis during the first few months of life that appears to resolve. There is no evidence to date of liver injury associated with the CPT1a variant.

Treatment:

Infants with CPT1a variant may be at risk for hypoglycaemia. Although further research is necessary to define the full natural history of this variant, there are currently sufficient case examples to warrant a preventative approach that would potentially prevent brain injury, or even death, associated with hypoglycaemia.

- The treatment goal is to provide age appropriate regular feedings and avoidance of fasting.
- Fasting times are based on age.
- Parents need to understand the increased risk for hypoglycaemia during illness such as fever, vomiting, or poor oral intake.
- Patients should be given an emergency letter to present to emergency personnel (see Appendix 2 for template).
- In cases of cholestatic liver disease, monitor LFTs which should return to normal range by the age of 2-3 months.

Possible consequences of hypoglycaemia include seizures, coma, and even death in cases where a child goes without eating or drinking for prolonged periods of time (see Table 1, below).

Infants and children with CPT1a variant, who cannot or will not eat, may need intravenous dextrose solution to prevent hypoglycaemia.
*See table 1 below for age appropriate feeding guidelines when well and during intercurrent illness.

For Medical and Dental Procedures requiring prolonged fasting:

See section 2.3 above for recommendations for fasting for a procedure which applies to all First Nations children including those homozygous for CPT1a.

3.2 SHOULD SIBLINGS BE TESTED FOR CPT1A?

For those infants/children presenting with hypoglycaemia and subsequently found to be homozygous for the CPT1a variant, please refer to Medical Genetics (VIHA: 250-727-4461, BCCH: 604-875-2157) for Genetic Counselling and consideration of testing young siblings.

<u>Table 1:</u> Key Points for Diet and Emergency Care Counselling for Families for all First Nations Infants and Children*

AGE	When Well	With Fever (38C or greater) and/or Poor Feeding and/ or Vomiting	
0-3 months	Provide breast milk (preferable) or formula on demand. Babies typically feed every 2 to 4 hours. Call a health care provider if your baby goes longer than 4 hours between feeds in the first few weeks.	Provide breast milk (preferable) or formula on demand but no longer than 3 hours between feeds both day and night. Take baby to hospital or medical clinic if baby has a fever, vomiting (2 times in a row 30 minutes apart), feeding less than usual, or excessively sleepy. Infants that become very sleepy, do not want to feed even though it is time to feed, and cannot be stimulated awake with undressing and handling, should be taken to the local ER urgently.	
3-6 months	Provide breast milk (preferable) or formula on demand. Babies typically feed every 4-6 hours.	Provide breast milk (preferable) or formula on demand but no longer than 4 hours between feeds day and night. Take baby to hospital or medical clinic if baby has a fever, vomiting (2 times in a row 30 minutes apart), feeding less than usual, or excessively sleepy. Infants that become very sleepy do not want to feed even though it is time to feed, and cannot be stimulated awake with undressing and handling, should be taken to the local ER urgently.	
AGE	When Well	With Fever (38C or greater) and/or Poor Feeding	Vomiting (Oral Rehydration)
6-12 months	Offer breast milk, formula, or food every 3-4 hours during the day. Baby can sleep 8-10 hours at night.	Provide breast milk (preferable) or formula on demand but no longer than 4 hours between feeds day and night. Take baby to hospital or	Oral rehydration solution (ORS) if child is vomiting and does not tolerate usual drinks and food. Give 5 mls of ORS every 5 minutes.

AGE	When Well	With Fever (38C or greater) and/or Poor Feeding and/ or Vomiting	
		medical clinic with emergency letter if vomiting, feeding less than usual or excessively sleepy.	If your child continues vomiting after 2 hours of attempting ORS, go to the nearest emergency.
1-4 years	Offer regular meals and snacks throughout the day. All children should have breakfast. Child can sleep 10-12 hours. Children should not go without food or drink longer that a 12 hour period. For children ages 2 and older, refer to Eating Well with Canada's Food Guide - First Nations, Inuit and Métis.	Offer food and fluids such as breast milk or juice every 4 hours, both day and night. If the child is refusing both food and fluids, or is unable to keep fluids down using the Oral Rehydration Solution (ORS) protocol, take child to the nearest hospital or medical clinic with an emergency letter.	Provide an oral rehydration solution (ORS) if child is vomiting and does not tolerate usual drinks and food. For children 1-5 yrs: give 10 mls every 5 minutes. If your child continues vomiting after 2 hours of attempting ORS, go to the nearest emergency.
>4 years	Offer regular meals and snacks throughout the day. All children should have breakfast. Child can sleep 10-12 hours. Children should not go without food or drink longer that a 12 hour period. Refer to Eating Well with Canada's Food Guide - First Nations, Inuit and Métis.	Seek medical care for children who have been vomiting or who have very poor oral intake that has persisted 8 hours.	Provide an oral rehydration solution (ORS) For children 1-5 yrs: give 10 mls every 5 minutes For children greater than 5 years old: give 15 mls every 5 minutes. If your child continues vomiting after 2 hours of attempting ORS, go to the nearest emergency.

*Guidelines in this table apply to all First Nations infants and children, regardless of known CPT1a status. Children with CPT1a variant do not need additional calories compared to other children on a daily basis. Excessive caloric intake may lead to obesity.

3.3 ARE THERE HEALTH IMPLICATIONS FOR THE CPT1A VARIANT IN YOUTH AND ADULTS?

Interestingly, some studies have shown a potential health advantage of the CPT1a variant with decreased body mass index and favorable lipid profiles in Inuit adults who follow a traditional marine diet [8,9]. However, we do not have data on the effects of the CPT1a variant on lipids or body mass index in FN adults. We also do not know if the effects of the CPT1a variant on lipids and body mass index vary in people on more "North American diets" rather than traditional aboriginal diets. We do not yet know if youth and adults with the CPT1a variant are at risk of health problems. Table 2 outlines key points counselling youth adults around diet and emergency care.

Table 2: Key Points for Diet and Emergency Care Counselling for Youth and Adults

Youth and adults	Dieting	During weight loss the body uses up stored fats. Children and youth need regular meals and snacks to provide a constant supply of energy to the body. Avoid fasting during dieting. Decrease total number of calories but not the frequency of eating.
	Drugs/alcohol	Alcohol/drug abuse can lead to periods of prolonged fasting. Vomiting and periods of intoxication may also place the youth at increased risk for potentially serious consequences of CPT1a variant. Seek emergency medical care if a youth has abused alcohol or drugs and cannot or will not eat. An IV with glucose may need to be provided.
	Exercise	As for all children, youth, and adults exercise is encouraged.
General	Medical Fast (NPO) for Surgery or Medical/Dental Procedures	If a patient requires a total NPO time that is longer than 10-12 hours, IV dextrose should be given to support carbohydrate requirements until able to eat and drink again. It is the parent's/ patient's responsibility to tell their doctor, dentist or other health professional of the CPT1a status and therefore possible need for intravenous glucose fluid for the time the patient cannot eat or drink.

REFERENCES

1. Sinclair GB, Collins S, Popescu O, McFadden D, Arbour L, Vallance HD. Carnitine palmitoyltransferase 1 and sudden unexpected infant death in British Columbia First Nations. Pediatrics 2012;130(5):1162-9.

2. Collins SA, Sinclair G, McIntosh S, Bamforth F, Thompson R, Sobol I, Osborne G, Corriveau A, Santos M, Hanley B, Greenberg CR, Vallance HD, Arbour L. Carnitine palmitoyltransferase 1A (CPT1A) P479L prevalence in live newborns in Yukon, Northwest Territories and Nunavut. Mol Genet Metab 2010;101(2-3):200-204.

3. Gessner BD, Gillingham MB, Johnson MA, Richards CS, Lambert WE, Sesser D, Rien LC, Hermerath CA, Skeels MR, Birch S, Harding CO, Wood T, Koeller DM. Prevalence and distribution of the c. 1436C→T sequence variant of carnitine palmitoyltransferase 1A among Alaska Native Infants. J Pediatr 2011;158(1):46-51.

4. Daly LP, Osterhoudt KC, Weinzimer SA. Presenting features of idiopathic ketotic hypoglycemia. J Emerg Med. Jul 2003;25(1):39-43.

5. Gessner, BD., Gillingham, M.B., Birch, S., Wood, T., Koeller, D. Evidence for an association between infant mortality and a carnitine palmitoyltransferase 1A genetic variant. Pediatrics 2010 126(5):945-51.

6. Collins SA, Surmala P, Osborne G, Greenberg C, Bathory LW, Edmunds-Potvin S, Arbour L. Causes and risk factors for infant mortality in Nunavut, Canada 1999-2011. BMC Pediatr. 2012 Dec 12; 12:190.

7. Child Death Review Unit. BC Coroners Service. Ministry of Public Safety and Solicitor General. Safe and Sound: A Five Year Retrospective. Report on Sudden Infant Death in Sleep-Related Circumstances. 2009. Retrieved from http://www.pssg.gov.bc.ca/coroners/child-death-review/docs/sudden-infant-death-cdru-report.pdf

8. Lemas DJ, Wiener HW, O'Brien DM, Hopkins S, Stanhope KL, Havel PJ, Allison DB, Fernandez JR, Tiwari HK, Boyer BB. Genetic polymorphisms in *carnitine palmitoyltransferase 1A* gene are associated with variation in body composition and fasting lipid traits in Yup'ik Eskimos. J of Lipid Res 2012 Jan;53(1):175-84.

9. Rajakumar C, Ban MR, Cao H, YoungTK, Bjerregaard P, Hegele RA. Carnitine Palmitoyltransferase 1a polymorphism P479L is common in Greenland Inuit and is associated with elevated plasma apolipoprotein A-I. J of Lipid Res 2009;(50(6):1223-8.

APPENDIX 1: KEY MESSAGES FOR INFANT SAFE SLEEP

The following key messages are reprinted from *Honouring Our Babies: Safe Sleep Cards*, available at http://fnha.ca/what-we-do/children-youth-and-maternal-health. These key messages are based on *Perinatal Services BC Health Promotion Guideline 1: Safe Sleep Guideline for Infants 0 to 12 Months of Age* (February 2011).

The most important ways to create a safe place for your baby are to:

1. Place your baby on his or her back to sleep every time (at night and for naps).
2. Ensure a tobacco free environment while pregnant and after your baby is born.
3. Place your baby to sleep in the same room as you for the first six months (on a separate safe sleep surface). Adult mattresses are too soft for babies to sleep safely on.
4. Breastfeed your baby. It helps protect against SIDS.
5. Ensure you baby does not overheat while sleeping (do not use toques or hats indoors, heavy blankets, or swaddling).
6. Place your baby on a firm surface that is free of hazards. Waterbeds, adult mattresses, couches, recliners and sheepskins are not firm enough for baby to sleep safely. Loose blankets, pillows and toys should not be in your baby's sleep area.
7. Ensure the crib, cradle, bassinet, or other sleep equipment meets the safety standards in the Crib and Cradle Regulations. Cribs made before September 1986 do not meet the standards and should not be used.

When you baby is sleeping outside the home, take extra care to plan ahead to make sure your baby's sleep area is safe.

APPENDIX 2: EMERGENCY LETTER

Medical management of the child/youth with the Carnitine Palmitoyl Transferase 1a (CPT1a) – P479L Variant

Name:
DOB:

What is the CPT1a P479L variant?

The CPT1a P479L variant is a mild condition affecting fatty acid oxidation. Children with this variant have about 25% of normal CPT1a enzyme function of children without the condition. The function of the CPT1a enzyme is important during fasting or when children require additional energy during illness or prolonged exercise. CPT1a aids in the conversion of fat stores to energy in the liver thus producing ketones and energy in the process. There is a risk, during fasting stress that some children with the CPT1a variant will develop hypoglycaemia in infancy. This risk gradually decreases with age. The greatest risk for hypoglycaemia is during periods of intercurrent illness such as vomiting or poor oral intake.

The CPT1a variant is prevalent in coastal First Nations populations of BC, Alaska, Northwest Territories, Nunavut and Greenland. In BC, 1 in 5 coastal First Nations' babies, including Vancouver Island, are homozygous for the CPT1a variant. In the interior of BC, 1 in 25 First Nations' babies are homozygous for the CPT1a variant. Most are asymptomatic and do not have any disease symptoms.

How do I treat such a patient?

Since there is a potential for brain injury with severe hypoglycaemia in the absence of ketones, First Nations children who present to the ER, are known to have the CPT1a variant and an intercurrent illness where oral carbohydrate intake has been limited, should be assessed and treated as follows:

- Check blood sugar and urine for ketones.
- Assess if parent tried Oral Rehydration Solution (ORS) at home. How did they do it?
- If the trial of ORS sounded adequate but the child failed, consider IV dextrose solutions and retry ORS.
- If there was no trial, consider a trial of ORS and monitor blood glucose.
- If child unable to tolerate ORS after 2 hours, consider IV dextrose solutions to provide maintenance fluids.
- If the child is dehydrated, then hydrate as condition dictates.

Remember: It is poor carbohydrate intake that can be an indication for IV glucose fluid therapy.

If you wish information or advice on the management of a child with CPT1a P479L variant, please do not hesitate to call the Biochemical Disease physician on call through BC Children's Hospital paging service.

Biochemical Disease physician on call: 604-875-2161