

## Children and natural health products: What a clinician should know



Canadian  
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The use of complementary and alternative medicine (CAM) in Canada has grown exponentially in recent years (1-3). This patient-led trend creates new challenges for paediatricians because parents may integrate or consider the use of complementary and/or alternative therapies in the treatment of their children, without necessarily disclosing such use to their physician (3-7). It is vital that physicians are knowledgeable about the various and most commonly used types of CAM treatments to promote an open dialogue about CAM with their patients. This statement discusses the most common forms of CAM used by Canadians, with a focus on natural health products (NHPs). It also provides a practical approach for the physician whose paediatric patient is already using or is interested in using CAM.

### GENERAL BACKGROUND

#### CAM

While the definition of CAM is somewhat vague and ill-defined, it is commonly accepted as a "broad domain of healing resources that encompass all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period" (8). Of course, what is 'complementary' in North America is 'traditional' in many parts of the world; the World Health Organization estimates that most of the world's population regularly uses traditional medicine (as opposed to Western medicine) (9).

#### NHPs

Generally speaking, NHPs are manufactured, sold, or represented for use in the diagnosis, treatment or prevention of a disease or disorder, and for restoring or correcting organic functions or maintaining and/or promoting health. Canadians may receive NHPs from a care provider, seek NHPs on the recommendation of a care provider and/or opt for 'self care' by purchasing NHPs over the counter, either from a pharmacy or from other commercial establishments. According to the Natural Health Products Directorate of Health Canada (2), NHPs encompass:

- a homeopathic preparation;
- a substance or substances used as traditional medicine, including, but not limited to, a substance used as a

traditional Chinese medicine, a traditional Ayurvedic (East Indian) medicine or a North American Aboriginal medicine; and

- a mineral or a trace element, a vitamin, an amino acid, an essential fatty acid, or other botanical-, animal- or microorganism-derived substances.

#### Homeopathy

Homeopathy, a discipline developed by Samuel Hahnemann in 1790, has been gaining in popularity and is currently used by as many as 25% of children using CAM (10). The treatment is based on the 'principle of similitude' – treating like with like. High or pharmacological doses of an agent would cause symptoms similar to the disease state. The active preparation is made by diluting the agent and rapidly agitating the dilutions (succussion). Unlike classic pharmacology, the greater the dilution, the greater the potency of the product. Thus, homeopathy defies the normal rules of chemistry, relying instead on a concept of 'medicated energy'. The most commonly reported uses of homeopathy in paediatrics are ear, nose and throat, or respiratory problems. There are few double-blind, randomized clinical trials available; existing trials are all limited by small sample sizes, and their clinical significance is debatable. For more information, the Canadian Paediatric Society (CPS) has developed a statement on homeopathy in the paediatric population which can be accessed on the Web site <[www.cps.ca](http://www.cps.ca)> (11).

#### Traditional Chinese medicine

Traditional Chinese medicine (TCM) is a distinct system of health care with its own diagnostic and assessment methods, language and terminology, and unique treatment principles. Like Western medicine, the goal of TCM is the promotion, maintenance and restoration of health. TCM is rooted in Chinese culture and considers nature and the person as a whole to be interrelated. TCM theory emphasizes the importance of Qi, whose action manifests as all life phenomena, including the physical, mental and spiritual aspects. Disturbances in Qi manifest as disease. The main modalities used in TCM are traditional Chinese diagnosis, acupuncture/acupressure, traditional Chinese herbal remedies, traditional Chinese dietary therapy, traditional

**Table 1**  
**An abridged summary of identified randomized controlled trials (RCTs) involving natural health products and children**

Product	Sample indications	Number of RCTs
Vitamin A	Measles, respiratory and gastrointestinal (diarrhea) conditions, HIV and anemia	158
Vitamin B	Anemia, protein loss, anticonvulsants and muscular dystrophy	20
Vitamin C	Autism, attention deficit hyperactivity disorder, upper respiratory infections and oral health conditions	24
Vitamin E	Premature birth and low birth weight	34
Magnesium	Autism and asthma	12
Folic acid	Diarrhea, leukemia, rheumatoid arthritis and hemoglobinopathies	14
Zinc	Abnormal growth, diarrhea and recovery from malnutrition	45
Chinese herbal medicine	Liver and respiratory conditions, eczema, diarrhea and asthma	20
Homeopathy	Pain, warts, adenoids, diarrhea and respiratory conditions	9

Chinese exercise therapy, and tuina massage (data from the Health Professions Regulatory Advisory Council).

### Chiropractic treatment

According to the 1997 statement from the Association of Chiropractic Colleges, chiropractic treatment is concerned with subluxation, a complex of functional and/or pathological articular changes that compromise neural integrity and may influence organ system function and general health. While the practice of chiropractic treatment itself does not involve the use of NHPs, research suggests a substantial proportion of chiropractors recommend NHPs or dietary supplements to their paediatric patients (12). For more information, the CPS has issued a position statement regarding controversies and issues relevant to chiropractic care for children which can be accessed on the Web site <www.cps.ca> (13).

### USE OF NHPs IN CHILDREN

Until recently, the use of NHPs by Canadian children and youth has received little attention, and Canadian population-based data on the subject are lacking. However, population-based data on the use of vitamin/mineral supplements are available from the United States' National Health Interview Survey. This 1981 survey suggested that over 33% of American children and youth had taken some vitamin/mineral supplement in any given two-week period during that year (14). Other NHPs, particularly those derived from herbal medicine practice, have been used for generations (15-17). Whether these practices are derived from traditions from this continent, Europe, eastern Asia and/or the Indian sub-continent, each thrives within the multicultural milieu of

North America. Each cultural heritage is quite aware of which plants are poisonous and how to prepare them in a nontoxic manner. Moreover, these cultures have given us many drugs that are currently used (eg, reserpine, digoxin, vincristine) and there is no doubt that these practices will lead to continued discoveries.

It is suspected that the use of NHPs in paediatric populations is growing, but empirical data are sparse. In the limited studies that have been conducted, the use of NHPs seems to be less common in children than in adults. For example, in 1992, 11% of patients of a Montreal-based general paediatric outpatient clinic had used some form of CAM; of this 11%, 29% and 21% indicated that they had used naturopathy and homeopathy, respectively (5). More recent studies of the general paediatric population in the United States and the United Kingdom suggest that between 20% to 47% of patients have used homeopathic remedies for respiratory conditions, ear, nose and throat conditions, dermatological conditions and neurological conditions (10,18).

Rates of NHP use are much higher (up to 70%) within certain subgroups of the paediatric population (eg, children with arthritis, cancer, rheumatoid arthritis, cystic fibrosis), particularly for those who have suffered relapses or other setbacks (19-24). Parents of hospitalized children, particularly those in neonatal and paediatric intensive care units, report keen interest in providing homeopathy or naturopathy to their children during hospitalization (25,26). In a recent study conducted at The Hospital for Sick Children (27), more than 30% of adolescent girls who had been diagnosed with an eating disorder had used herbal supplements and other forms of alternative medicines to accelerate weight loss. Rates of NHP use are also high (70%) among homeless youth, many of whom suffer from chronic physical and mental health problems and who are disaffected by mainstream institutions (28). Additional information about CAM use in children with autism will be published in a future CPS statement. Despite these attempts to determine NHP use among various subgroups of the paediatric population, there is a paucity of systematically collected national data regarding NHP use in any paediatric population.

### Issues for the physician

It is a commonly held belief that the majority of randomized controlled trials (RCTs) examining the effectiveness of NHPs have concentrated on adult populations; however, recent work has identified hundreds of RCTs, published since 1965, that investigate NHPs in paediatric populations (18). An abridged summary of a select group of these RCTs is presented in Table 1.

Interestingly, the four journals that published the largest number of paediatric NHP RCTs were so-called 'mainstream' medical journals, including the *American Journal of Clinical Nutrition*, *Pediatrics*, *Journal of Pediatrics* and *The Lancet*. Moreover, MEDLINE indexed 93.2% of these RCTs, suggesting that the RCT-level evidence is easily accessed, if you look for it (29).

Although some RCTs demonstrated the effectiveness of certain aspects of NHPs in the paediatric population, the interpretation of the results is clouded by less-than-optimal methodological rigour (30). Although some of these methodological issues are shared with RCTs involving conventional medicine, their persistence facilitates ongoing skepticism of NHPs by mainstream science.

### STANDARDIZATION

There are many elements that contribute to the heterogeneity of NHPs. For example, product standards are affected by species (mis)identification, what part of the plant is collected (aerial versus root), extraction technique (aqueous versus alcoholic), adulteration, etc. There is considerable variation in the purity and potency of products, and contamination is a major concern (eg, heavy metal poisoning from traditional Chinese medicines has been reported several times) (31-33). Other studies examining the quantity of active ingredient across brands found the range to be from 0% to 200% of the label claim (34). In the United States, with the passage of the Dietary Supplement Health and Education Act of 1994, this heterogeneity is condoned if manufacturers choose to call their product a 'dietary supplement' and thereby avoid the required premarket testing of efficacy and safety required of pharmaceuticals. In Canada, the Natural Health Products Directorate has new regulations regarding good manufacturing practices and is working to develop standards of evidence for labeling claims. The burden to regulate is not eased by the exponential growth in the number of CAM products or practices available.

### DOSAGE

Physicians are well aware of Paracelsus' notion that the "dose makes the poison". There is much evidence to suggest that this is particularly true for paediatric patients, with discussions involving dosing having obvious parallels between traditional pharmacotherapies and NHPs.

At present, only 20% to 30% of drugs approved by the United States Food and Drug Administration are labelled for paediatric use (35). Because the majority of drugs prescribed for children have not been tested in children, physicians routinely prescribe pharmaceuticals to children 'off label' and rely on their medical judgment to determine the most appropriate dose for children. Although the reliance on adult-based data for interpolations according to a child's weight is frequent and has met with much success, there is evidence to suggest that adult experiences do not necessarily predict those of children. In fact, a flurry of paediatric studies seen in the late 1990s (encouraged by the United States Food and Drug Administration) revealed many instances of underdosing, overdosing, ineffectiveness and safety problems for pharmaceuticals that had, until that point, been used 'off label' in the paediatric population (35).

These findings confirm what paediatricians have always known: children are not small adults. Children are a special population by virtue of their small size, immature physiology and ongoing growth and development. In children and

youth, the volumes of distribution of products (whether pharmaceutical or an NHP) may differ from those in older patients because of the paediatric patient's high body surface area-to-weight ratio and different body composition vis-à-vis water and fat. Extra care must be taken with very young paediatric patients because the blood-brain barrier may not be fully mature, allowing active products and endogenous substances (eg, bilirubin) to gain access to the central nervous system with resultant toxicity. Among paediatric patients, oral absorption of products may be less predictable than in older patients because the hepatic and renal clearance mechanisms of paediatric patients are immature and changing rapidly. This, along with rapid weight changes in this population, may necessitate frequent dosage adjustments.

Products, whether they be pharmaceuticals or NHPs, may affect physical and cognitive growth and development and, because children's developing systems may respond differently from mature adult organs, some adverse events that could occur in paediatric patients may not be identified in adult studies. In addition, the dynamic processes of growth and development may not manifest an adverse event acutely but rather, at a later stage of growth and maturation. While paediatric patients pose a unique challenge, the issues regarding the determination of optimal dosing for NHPs (even if standardized) for children and youth are, for the most part, very similar to the issues still facing pharmaceuticals.

### DRUG-HERB INTERACTIONS

Three factors combine to increase the likelihood of drug-herb interactions. First, patients with serious, chronic or recurrent illness are the most likely to use CAM (36,37); these patients are also most likely to be on prescription medications. Second, most patients using CAM use it to complement their health care, not replace it (36,37). Third, research confirms that a substantial proportion of Canadians who use NHPs use more than one simultaneously (3,38). Lessons learned from experience with drug interactions, whereby the likelihood of an adverse event increases exponentially as the number of medications increases (39), would predict that this scenario makes such patients likely to experience an adverse event (40,41).

Reliable data on NHP-drug interactions are often difficult to find. Depending on the resources consulted, the quality of information regarding drug interactions for a particular NHP can vary significantly. Some texts do not report any interactions between St John's wort and conventional drugs, or else report that there are "no known interactions" (42). In contrast, other references state that St John's wort can induce cytochrome P450, thereby reducing plasma levels of various drugs (eg, oral contraceptives, chemotherapy, anesthetics, etc) (43-46). Even in those references with extensive drug-herb interaction tables, it may not be apparent that very little of the information is based on rigorous scientific evaluation of actual interactions (42). Many entries are based on case reports of 'possible', often unconfirmed, interactions and others are noted as 'theoretical'. Another important issue limiting the value of case

**Table 2**  
**Counselling families who choose complementary and alternative medicine (CAM)**

Paediatricians should consider the following when discussing CAM with their patients:

1. Ask about use; inquiring does not equal endorsing use
2. Try to have a nonjudgmental attitude
3. Seek information for yourself and be prepared to share it with families
4. Evaluate scientific merits of specific therapeutic approaches
5. Identify risks or potential harmful effects (including opportunity costs, whereby known effective therapies are not pursued, and possible financial burden)
6. Provide families with information on a range of therapeutic options (avoid therapeutic nihilism)
7. Educate families to evaluate information about all treatment approaches
8. Avoid dismissal of alternative therapies in a way that communicates a lack of sensitivity or concern for the family's perspective
9. Recognize feeling threatened and guard against becoming defensive
10. Offer to assist in monitoring and evaluating the patients in ongoing follow-up

*Data from reference 66*

reports of drug-herb interactions is that the herb may have been adulterated or even substituted; the identity and quality of the product should first be verified by appropriate testing to attribute the adverse reaction to the herb (47).

To improve our knowledge of drug-herb interactions, physicians need to be proactive in asking their patients about CAM use and report suspected interactions to regulatory authorities for further investigation. In January 2004, the Canadian Paediatric Surveillance Program began monitoring for serious adverse drug reactions. This study includes adverse events related to NHPs and herbal remedies (48).

### NEXT STEPS

With gaps identified in almost every aspect of paediatric CAM use, there is a pressing need to collect effectiveness and safety data in children. The obstacles to CAM research that are frequently quoted include: limited clinical data, lack of standardized products, complex interventions that are highly dependent on the individual, and concerns about the applicability of traditional research methodology (46,49-53). Proponents of NHPs tout their 'wide margin of safety' in the absence of evidence to the contrary. This is less reassuring because there are several factors that may have contributed to the historical lack of reported adverse events with NHPs. Patients have been shown to be less likely to report adverse events (including drug interactions) with NHPs to health care providers than they are to report similar events associated with conventional medications (54). Again, this issue is not unique to NHPs. Inadequate reporting of adverse events with conventional pharmaceuticals is a well-recognized phenomenon (55,56).

Another key issue is to address educational gaps. CAM providers, especially those still in training, need formal education about key issues in paediatrics. When surveying acupuncturists and chiropractors in the Boston area, Lee et al (12,57) found critical gaps in their knowledge (eg, whether to refer a febrile neonate for a septic workup). Another critical area for paediatricians is the knowledge, attitudes, and beliefs held by some CAM providers with respect to childhood immunization (37).

The current cohort of paediatricians may not necessarily have had exposure to issues related to CAM products and practices (58-60). Teaching about CAM is being incorporated into medical curriculum across North America. Initiatives are underway to develop a 'core' CAM curriculum for undergraduate medical education (61).

### PUBLIC EDUCATION

There is a widespread perception among the public that because NHPs are 'natural', they are completely safe and thus have no interactions with drugs (or with each other) (62-65). It should not be a surprise to physicians that NHPs can have an effect (and side effect); more than one-quarter of modern day pharmaceuticals are plant-based. The Marketed Health Products Directorate, in conjunction with the Natural Health Products Directorate, monitors the safety of NHPs. All health care professionals and consumers are encouraged to report suspected adverse events, including exact product name and list of ingredients if possible.

### DISCUSSING CAM WITH YOUR PATIENTS

In addition to those whose children have a chronic illness, it was found that even in general paediatric practice (community practice), a significant number of parents are interested in discussing CAM therapies with their paediatrician (4). The American Academy of Pediatrics' Committee on Children with Disabilities has developed a document entitled "Counseling families who choose complementary and alternative medicine for their child with chronic illness or disability" (66). Their recommendations are listed in Table 2.

### CONCLUSIONS

With the challenges faced by the ever increasing number of therapeutic options available, it is useful to review 'first principles' with regard to CAM in children:

- 1) First, do no harm;
- 2) Ensure no opportunity cost (ie, do not delay treating a serious illness for which there is known effective therapy);
- 3) If the CAM therapy carries little risk of harm, then consider its use and follow the patient closely;
- 4) If the CAM therapy carries serious risk of harm, advise the patient accordingly and follow the patient closely;
- 5) Where possible, it is recommended to try to follow an evidence-based rationale for therapy; and
- 6) Where the evidence is lacking, try to maintain an open mind and a balanced approach. The use of CAM is a



patient-led phenomenon. If we are to counsel patients about the potential risks and benefits of CAM, we have to engage them in meaningful discussion that is based on reason and evidence, not prejudice or emotion.

## Appendix

### Reliable sources of information about complementary and alternative medicine (CAM)

Web sites	<ul style="list-style-type: none"> <li>• &lt;<a href="http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn/index_e.html">www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn/index_e.html</a>&gt; (Natural Health Products Directorate)</li> <li>• &lt;<a href="http://nccam.nih.gov">http://nccam.nih.gov</a>&gt; (National Center for Complementary and Alternative Medicine [NCCAM])</li> <li>• &lt;<a href="http://www.nlm.nih.gov/nccam/camonpubmed.html">www.nlm.nih.gov/nccam/camonpubmed.html</a>&gt; (CAM on PubMed through National Institutes of Health)</li> <li>• &lt;<a href="http://www.herbalgram.org">www.herbalgram.org</a>&gt; (nonprofit American Botanical Council)</li> <li>• &lt;<a href="http://www.ncahf.org">www.ncahf.org</a>&gt; (National Council for Reliable Health Information)</li> <li>• &lt;<a href="http://health.nih.gov/search.asp/24">http://health.nih.gov/search.asp/24</a>&gt; (Combined health information database)</li> <li>• &lt;<a href="http://www.reseauproteus.net/fr/Accueil/Accueil/Accueil.aspx">www.reseauproteus.net/fr/Accueil/Accueil/Accueil.aspx</a>&gt; (Reseau Proteus)</li> </ul>
Databases	<ul style="list-style-type: none"> <li>• &lt;<a href="http://www.cochrane.org/reviews/clibintro.htm">www.cochrane.org/reviews/clibintro.htm</a>&gt; (The Cochrane Collaboration and The Cochrane Database of Systematic Reviews)</li> <li>• &lt;<a href="http://www.naturalstandard.com">www.naturalstandard.com</a>&gt; (Natural Standard)</li> <li>• &lt;<a href="http://www.naturaldatabase.com/(e0glkvadbaqm fuec0iqwtl45)/home.aspx?li=0&amp;st=0&amp;cs=&amp;s=ND">www.naturaldatabase.com/(e0glkvadbaqm fuec0iqwtl45)/home.aspx?li=0&amp;st=0&amp;cs=&amp;s=ND</a>&gt; (Natural Medicines Comprehensive Database)</li> </ul>
Textbooks	<ul style="list-style-type: none"> <li>• Chandler F, ed. <i>Herbs: Everyday Reference for Health Professionals</i>. Nepean: Canadian Pharmacists Association and the Canadian Medical Association, 2000</li> <li>• Ernst E, ed. <i>The Desktop guide to Complementary and Alternative Medicine</i>. St Louis: Mosby, 2001.</li> </ul>
Information services	<ul style="list-style-type: none"> <li>• For information related to pregnancy and breastfeeding, consider phoning Motherisk</li> </ul>

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The recommendations in this statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances, may be appropriate. Internet addresses are current at time of publication.