

Pediatric Oncology

Alfred Längler · Patrick J. Mansky  
Georg Seifert *Editors*

# Integrative Pediatric Oncology

 Springer

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## Preface

Scientific advancements over the past 30 years have resulted in a dramatic reduction in morbidity and mortality of pediatric oncologic therapy. However, over the last two decades the focus of the professional medical discourse has increasingly shifted from extending overall survival to enhancing quality of life. At the same time, individual needs of patients and their families have been more clearly delineated. In many instances, the improved prognosis of pediatric cancers has fostered the parallel development of a growing interest in complementary and alternative treatment approaches. Throughout the 1970s and 1980s the term “Alternative Medicine” was widely used. Over the last decade this term has been largely replaced by “Complementary Medicine,” which is considered a complement to conventional care. The scientific community subsequently adopted the term “Complementary and Alternative Medicine (CAM)”. As the scientific discourse of representatives of conventional medicine and CAM has gained momentum, the term “Integrative Medicine” has been favored.

The authors see this book as the first international scientific compendium dedicated to Integrative Pediatric Oncology. Integrative Medicine is meant to use the existing evidence to serve the individual patient’s needs while choosing the best available approaches. The editors have convened a panel of international authors to present and publish the evidence for complementary therapies most commonly used in pediatric oncology. Standards for conventional diagnosis and therapy in pediatric oncology are published in other volumes of this series. The individual chapters originated from internationally renowned groups of experts. During the author selection it became apparent that for certain areas of CAM the scientific underpinning has not been established. Therefore certain areas have not been addressed in this book, such as Ayurveda in pediatric oncology.

The authors hope that the publication of this book will stimulate an evidence-based discourse and further the development of Integrative Pediatric Oncology.

The authors are indebted to the staff of Springer Publishers, especially Frau Meike Stoeck and Wilma McHugh. This multinational project would not have been accomplished without the help of Frau Meike Stoeck and

Wilma McHugh, who stimulated the design and implementation of the project and maintained focus on the project goals and timelines.

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August 2012

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# Contents

<b>1 Introduction</b> . . . . .	1
Georg Seifert, Patrick J. Mansky, and Alfred Längler	
<b>2 CAM Use in Pediatric Oncology: What Do We Know in the Year 2012?</b> . . . . .	5
Alfred Längler and Tim Schütze	
<b>3 Attitudes, Beliefs, and Communication About Complementary and Alternative Medicine Among Oncologists, Pediatricians, and Pediatric Oncologists</b> . . . . .	19
Alfred Längler	
<b>4 Anthroposophic Medicine</b> . . . . .	29
Alfred Längler and Georg Seifert	
<b>5 Art Therapies Including Music Therapies</b> . . . . .	45
Clare O’Callaghan and Trygve Aasgaard	
<b>6 Homeopathy</b> . . . . .	59
Birthe Repenning, Tim Schütze, and Alfred Längler	
<b>7 Mind-Body Medicine</b> . . . . .	79
Janice Post-White and Deborah Hughes Ndao	
<b>8 Integrative Nutrition and Nutrition/Herbal Supplements</b> . . . . .	109
Elena J. Ladas	
<b>9 Traditional Chinese Medicine</b> . . . . .	125
Lixing Lao, Ling Xu, and Shifen Xu	
<b>10 Botanicals in Pediatric Oncology and the Issue of Botanical/Drug Interactions</b> . . . . .	137
Patrick J. Mansky	
<b>11 Potential Role of Complementary and Alternative Medicine in Pediatric Oncology: The Future of CAM Research – Addressing the “Effectiveness Gaps”</b> . . . . .	147
Sagar Chokshi and Kara Kelly	
<b>12 Medical Education in Complementary and Alternative Medicine (CAM): A European Perspective</b> . . . . .	157
Tim Schütze, Anne-Marie Schnell, Diethard Tauschel, Christian Scheffer, and Friedrich Edelhäuser	



**13 Communicating CAM: How to Talk to Children  
and Parents About CAM in Pediatric Oncology** ..... 169  
Tycho J. Zuzak and Genn Kameda

**14 Establishing a Comprehensive Pediatric  
Integrative Oncology Program** ..... 187  
Salima Punja, Mary Langevin, Susan Sencer, and Sunita Vohra

**Index**..... 201

Georg Seifert, Patrick J. Mansky, and Alfred Längler

## Contents

1.1 CAM and Salutogenesis.....	2
References .....	4

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The increased collaboration of international research networks has been credited with pushing overall survival for all pediatric cancers beyond 80 % (Pui et al. 2011). This success has shifted the focus of therapeutic gains from survival to parameters such as quality of life during cancer therapy and long-term effects in pediatric cancer survivors. Acute toxicities and long-term sequelae may affect the quality of life of cancer survivors for decades. Especially long-term effects can frequently only be addressed symptomatically (Oeffinger et al. 2006). Cancer patients and their families often reach for complementary treatment approaches out of concern for acute and chronic side effects of cancer therapy, pain relief, and occasionally the unfavorable prognosis of the disease, even though little data about the effectiveness of these interventions may be available (Längler et al. 2008). Children and their parents may also feel that they have little control over their conventional cancer treatment and outcome.

Complementary and alternative medicine often gains trust from children and their parents based on the notion that it represents a “gentler” and “more natural” medicine expected to show treatment benefits without side effects or interactions. Data suggest that patients place multiple and sometimes high expectations on CAM. In contrast, the evidence for the efficacy of many CAM approaches has been weak.

Two main reasons have been advocated for the promotion of science in CAM:

1. While CAM has been used for decades by cancer patients to a varying degree in many countries (see Chap. 02), pediatric oncologists have not been able to follow treatment effects and toxicities.
2. Clinical experience and a number of studies suggest that CAM approaches may be able to reduce acute and long-term toxicities of conventional cancer therapies.

Thus, there is an increasing demand for an expanded and intensified research effort on CAM approaches in pediatric oncology.

A number of CAM approaches have their roots in traditional medicine and have been practiced for many years, such as traditional Chinese medicine (TCM). However, there is a wide spectrum of CAM practices ranging from traditional and ethnomedicine to newer approaches such as anthroposophical medicine, homeopathy, and phytomedicine. In addition, there are concepts of vitamin, nutrition, and supplement use to support cancer patients.

Alternative medicine (Astin et al. 2003) represents an effort to replace conventional cancer therapies with alternative treatments, which is a questionable strategy in potentially life-threatening but also curable conditions like pediatric cancer.

Complementary medicine (<http://nccam.nih.gov/health/whatisacam/>) in contrast describes a number of therapies outside the realm of conventional medicine that are used on conjunction and to complement conventional care and are most often utilized to support conventional care and minimize side effects. The therapies can be divided into primarily medicinal therapies such as phytomedicine and homeopathy or combined efforts such as anthroposophical medicine, TCM, or naturopathy.

The National Center for Complementary and Alternative Medicine distinguishes four categories of CAM (<http://nccam.nih.gov/health/whatisacam/>): mind–body medicine such as Qigong, or Reiki, body-based approaches such as massage, alternative medical systems (homeopathy, TCM, anthroposophical medicine), and biologically based

therapies such as specialty diets, nutritional therapies, and hydrotherapy.

A growing area of practical use in cancer and research interest is mind–body medicine (MBM) (<http://nccam.nih.gov/health/whatisacam/>). Mind–body medicine understands the close interaction of mind, body, and spirit and seeks to employ this knowledge for improved cancer treatment. There has been an expanding body of scientific literature on the role of MBM in cancer, supported by interesting results from studies in physiology and neurobiology (Astin et al. 2003; Brewer et al. 2011; Musial et al. 2008; Shennan et al. 2011).

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## 1.1 CAM and Salutogenesis

Some CAM approaches may be better understood after considering the concepts of gaining health–retaining health.

Health and disease can be readily described on the physical plane using scientific concepts and the laws of nature. The concepts of physiology and pathology are more difficult to apply to phenomena observed in psychology and psychiatry. It is particularly difficult to scientifically describe aspects of an individual biography or personality characteristics and their relationship to cancer diagnosis.

The concept of *salutogenesis* (how to understand the development of health and well-being) has been developed to scientifically understand the phenomena of “health” and “healing” which may also be understood as “regaining health” (Antonovsky, 1997).

*Salutogenesis* is the science of identification, interpretation, and fostering of the capacity for healing in the physical, spiritual, and mental spheres. The term “salutogenesis” was coined and introduced into the scientific discourse by Aaron Antonovsky in the 1980s. The concept of *salutogenesis* represents the opposite to the concept of *pathogenesis* as introduced by conventional medicine. While pathology may be understood as the science of illness, *salutogenesis* represents the science of healing and maintaining health. Salutogenesis does not distinguish between health and illness but rather considers

a continuum between the two poles of health/bodily well-being and illness/bodily sickness. The individual's state of well-being moves between these 2 poles dynamically and gradually based on its ability to manage stressors and health compromise. The ability to show autonomy and express coherence allows individuals to relieve stressors. Autonomy and coherence are therefore also designated as salutogenetic resources (Antonovsky, 1979). Of central importance is the postulate that the individual inherits and acquires over the course of a lifetime the ability to successfully pathologic challenges in the physical and mental sphere. Antonovsky introduces the example of the "swimmer" to promote the understanding of his concept: "nobody was securely along the river. I am aware that a large part of the river is contaminated, both literally and figuratively. The river branches off into areas of gentle currents, cascades and vortices. I am challenged to answer the following question: How do I become a good swimmer in this river, whose nature is determined by historical, social-cultural and physical environmental factors?" (Raddatz et al. 2007). Extending the image to the different concept of medicine, conventional medicine may be pictured as throwing a life line to the person at risk of drowning, while salutogenesis offers swimming lessons to the nonswimmer. Both approaches deserve credit, especially in pediatric oncology, where the illness often presents with such physical and temporal urgency that a life line is needed. At the same time, however, swimming lessons should not be neglected.

According to Antonovsky, the *sense of coherence* (SOC) stands at the center of an individual's capacity for resistance and allows individuals to cope with pathologic stressors. It represents a sometimes unconscious optimism which promotes physical and spiritual well-being. There are three characteristics to that optimism: understandable, manageable, and significant. SOC as a concept has been applied in clinical questionnaires to measure individual coherence. In adult cancer patients, preliminary but somewhat controversial (Eriksson and Lindstrom 2005, 2006) data suggest an association of increased coherence and favorable prognosis.

Salutogenesis as a concept was developed in psychology. However, it may be applicable for physiologic processes as well where the organism may gain or loose strength. The human being has been equipped with the capacity of self-regeneration and defense against external health compromise. There may be physiologic mechanisms that resemble SOC in the mental sphere, which may be independent from neuropsychimmunologic links of SOC. These may be termed "physical SOC."

With all this said, it remains to be understood why certain individuals appear to have an extraordinary physical capacity for the recovery and maintenance of health in the face of extremely challenging and unhealthy living environments. This phenomenon awaits scientific explanation and has not been translated into clinical applications.

Almost all CAM approaches appear to be aiming at strengthening some sort of SOC. Therapeutic modalities such as homeopathy (constitution), TCM (qi), and Ayurveda (ojas) have an understanding of health-promoting approaches that are meant to establish physical or mental processes resembling salutogenesis.

These considerations can promote the understanding of many CAM therapies that appear more or less to strengthen SOC, such as a number of mind-body therapies like yoga, Qigong, therapeutic eurythmy, and Reiki. Several pharmacological approaches such as homeopathy and TCM also strive to stimulate health-promoting processes via stimulation of regulative capacities. Many CAM approaches are based on a different understanding of illness and healing than in conventional medicine. Conventional oncology focuses primarily on an understanding of deficits, while CAM more likely promotes resources facilitating self-healing.

Scientific publications focusing on salutogenesis concepts are primarily based on the experience with adults. However, fundamental traits that influence SOC are established during childhood and therefore are of essential interest to pediatrics.

The concept of salutogenesis promotes novel and resource-oriented perspectives about health

and illness that promise the development of novel therapeutic approaches in pediatrics and pediatric oncology more specifically.

Various CAM approaches described in this book are based on the salutogenetic concept. There is only little evidence about efficacy of these approaches based on controlled clinical trials. The individual provider has to decide based on his or her experience and professional training in discussion with patients and their families which CAM approaches to integrate into the care of the individual cancer patient. As promoted by the definition of integrative medicine by the Academic Health Centers for Integrative Medicine (“Integrative Medicine is the practice of medicine that affirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all the appropriate therapeutic approaches, health care professionals and disciplines to achieve optimal health and healing”)(<http://www.imconsortium.org/about/home.html>), one may envision a truly integrative medicine that is based on the doctor–patient relationship, considers the whole person and its physical, mental, and spiritual dimensions, and acts based on evidence.

A growing number of medical schools internationally have established scientifically and economically successful teaching and clinical programs in integrative medicine. In addition, a number of regions offer well-conceived training courses in CAM approaches (<http://www.imconsortium.org/about/home.html>).

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# CAM Use in Pediatric Oncology: What Do We Know in the Year 2012?

# 2

Alfred Längler and Tim Schütze

## Contents

<b>2.1</b>	<b>Introduction</b> .....	5	<b>2.7</b>	<b>Parental Expectations of CAM Treatments</b> .....	15
<b>2.2</b>	<b>Frequency of CAM Use in Pediatric Oncology</b> .....	6	<b>2.8</b>	<b>Perceived Benefits of CAM Treatments</b> ...	15
2.2.1	Europe.....	6	<b>2.9</b>	<b>Communication Between Parents/Patients and Physicians About CAM</b> .....	16
2.2.2	Middle East.....	6	<b>References</b> .....		16
2.2.3	Canada.....	6			
2.2.4	USA.....	7			
2.2.5	Mexico.....	7			
2.2.6	Asia.....	7			
<b>2.3</b>	<b>Specific CAM Treatments</b> .....	8			
2.3.1	Natural Products.....	8			
2.3.2	Mind-Body Medicine.....	10			
2.3.3	Manipulative and Body-Based Practices.....	11			
2.3.4	Other CAM Practices.....	12			
<b>2.4</b>	<b>Factors Associated with CAM Use</b> .....	13			
<b>2.5</b>	<b>Side Effects of CAM Treatments</b> .....	14			
<b>2.6</b>	<b>Source of Information Concerning CAM Treatments</b> .....	14			

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## 2.1 Introduction

Complementary and alternative therapies are often used in pediatric oncology to complement children's conventional cancer treatments. In rare cases, they may also be used as an alternative to conventional therapy. There are published studies from several parts of the world analysing different aspects of CAM use in pediatric cancer patients. The main issues examined are:

- Frequency of CAM use in pediatric oncology
- Specific CAM treatment options
- Factors associated with CAM use
- Reported side effects and safety issues of CAM use in pediatric oncology
- Source of information concerning CAM treatments
- Parental expectations of CAM treatment
- Perceived benefits of CAM use in pediatric oncology
- Communication between parents/patients and physicians about CAM

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For a number of reasons, it is often difficult to compare these surveys. Study designs frequently differ, and there is no validated and internationally accepted questionnaire. Individual studies often reflect a specific population and culture. The definitions of CAM being used may also differ from study to study. The participating groups often differ in size, and the childhood malignancies included in the individual studies vary and are hardly comparable. Geographic disparities and cultural differences in the investigated populations can make it difficult to match various findings with each other.

Bearing in mind these disparities, the following synopsis should nevertheless give a rough idea of what we know about use of complementary and alternative therapies in pediatric oncology in the second decade of the twenty-first century.

## 2.2 Frequency of CAM Use in Pediatric Oncology

The reported overall percentages of pediatric cancer patients treated with complementary and alternative therapies vary widely from 12 to 85% (Clerici et al. 2009; Hamidah et al. 2009).

### 2.2.1 Europe

Figures for CAM use in pediatric oncology patients in Europe vary from 12 to 35% (Clerici et al. 2009; Längler et al. 2008).

In 1998 a small cohort of 84 families was investigated in the Netherlands. Among these families with children diagnosed with cancer, 31% were using CAM methods (Grootenhuis et al. 1998).

Two German surveys conducted in 2003 and 2008 showed rates of CAM treatment use of 34 and 35%, respectively. The respondents comprised a small non-representative group of 64 families of pediatric cancer patients and a representative nationwide cohort of 1063 families attending one of all German pediatric oncology care units (Längler et al. 2003, 2008).

In Italy the CAM-use rate in a small non-representative group of 97 pediatric oncology patients in 2009 was 12% (Clerici et al. 2009).

### 2.2.2 Middle East

A cross-sectional descriptive study from Haifa, Israel, investigated all parents of children or adolescents who attended a pediatric haematology/oncology department for oncology treatments, hospitalisation or follow-up during the last half of 2003. One hundred pediatric oncology patients were examined. Of these 61% had used complementary and alternative treatments (Weyl Ben Arush et al. 2006).

At five conventional primary care clinics and 21 CAM-specialised clinics, parents of Israeli children suffering from cancer completed a questionnaire asking if they were using CAM treatments during 2007. Of 280 patients attending CAM clinics, 74% were using complementary and alternative therapies. Of 319 patients attending conventional primary care clinics, 35% of the parents of pediatric cancer patients reported the use of CAM (Ben-Arye et al. 2010).

During a cross-sectional investigation in Jordan between August 2007 and April 2008, a small cohort of 69 pediatric cancer patients answered a questionnaire on the use of CAM in pediatric oncology. Sixty-five percent of the children suffering from cancer used at least one type of complementary and alternative treatment (Al-Qudimat et al. 2011).

### 2.2.3 Canada

A large-scale, population-based study in the only tertiary care pediatric oncology department in British Columbia investigated the usage rates of complementary and alternative treatments by pediatric cancer patients. The retrospective study looked at 366 children with cancer diagnosed between June 30, 1989 and July 1, 1995. The CAM usage rate for this cohort of children was 42% (Fernandez et al. 1998).

Another survey of a group of 92 pediatric cancer patients who attended the haemato-oncological outpatient clinic or were hospitalised in haemato-oncological wards of the Sainte-Justine Hospital in Montreal between the end of November 2001 and the end of January 2002 showed a frequency of CAM use of 49% (Martel et al. 2005).



### 2.2.4 USA

In the USA, the reported frequency of complementary and alternative medicine use among pediatric cancer patients varies from 25 to 84% (Kelly et al. 2000; Nathanson et al. 2007).

In 1997 a frequency of CAM usage of 65% was found in a small cohort of 81 pediatric oncology patients in the USA. A control group of 80 patients attending the continuity care clinic for routine checkups or acute care had a CAM usage rate of 51%. However, the cancer group and the control group can hardly be regarded as comparable because the control patients did not have serious illnesses (Friedman et al. 1997).

Patients or parents of patients treated for cancer at the Babies and Children's Hospital of New York in the period May 1997 to November 1998 were asked in an interview whether they were using complementary and alternative medical treatments. In a non-representative group of 75 pediatric oncology patients, 84% reported use of CAM methods on one or more occasions (Kelly et al. 2000).

In an area covering 13 counties in western Washington State, the parents of a non-representative cohort of 75 patients with pediatric malignancies first diagnosed between February 1997 and December 1998 were asked in a population-based telephone survey whether they were using CAM methods to treat their child. The CAM usage rate found in this survey was 73% (Neuhouser et al. 2001).

The usage rate of complementary and alternative medicine among 195 children suffering from cancer investigated in a pediatric oncology clinic in a relatively small geographic area in central/northwestern North Carolina was 47%. The parents or guardians of these children were asked to complete a self-administered questionnaire during a 12-month period from August 1999 to August 2000 (McCurdy et al. 2003).

In a cross-sectional exploration of 274 pediatric cancer patients of two different regions of the United States, 25% were using CAM methods. The parents of these 274 children suffering from cancer had responded to a questionnaire administered while attending the haematology/oncology division of the Nemours Children's Clinic of

Jacksonville, FL; Orlando, FL; Pensacola, FL and Wilmington, DE, between January 1, 1999 and June 30, 2002 (Nathanson et al. 2007).

Another investigation among a group of 118 pediatric cancer patients in the United States in 2003 demonstrated a frequency of complementary and alternative treatment use of 46% (Gagnon and Recklitis 2003).

Forty-four children suffering from cancer were investigated at the oncology department of the Children's Hospital of Philadelphia in 2011. For these patients the frontline chemotherapy had failed. Eighty-two percent of these pediatric cancer patients reported the use of CAM treatments (Paisley et al. 2011).

### 2.2.5 Mexico

In Mexico the frequency of CAM use among pediatric cancer patients treated at the UMAE Hospital de Pediatria from Centro Medico Nacional de Occidente located in the city of Guadalajara was 70%. The hospital receives patients from eleven states. During a 6-month period from April through September 2005, 110 parents of pediatric cancer patients were asked to answer a questionnaire concerning CAM use (Gomez-Martinez et al. 2007).

### 2.2.6 Asia

In a non-representative group of 63 pediatric cancer patients attending a pediatric oncology department at the Chang Gung Children's Hospital at Linko in Taiwan, 73% of the primary caregivers reported usage of complementary and alternative medical treatments. The parents of these children suffering from cancer had taken part in a semi-structured interview in May, June and July 1998 (Yeh et al. 2000).

The first published exploration on CAM use among children suffering from cancer in Turkey was conducted at the outpatient clinic of the Pediatric Oncology Department of the Yakutiye Hospital in Erzurum between November 2004 and June 2005. The examination revealed a frequency of CAM use of 49% within a small



**Table 2.1** Synopsis of the described studies

Author	Year	Country	Participants	Response rate (%)	CAM frequency (%)
Längler et al. (2003)	2003	Germany	64	76	34
Längler et al. (2008)	2008	Germany	1063	66	35
Grootenhuis et al. (1998)	1998	Netherlands	84	74	31
Clerici et al. (2009)	2009	Italy	97	67	12
Weyl Ben Arush et al. (2006)	2006	Israel	100	100	61
Ben-Arye et al. (2010)	2010	Israel	319	84	35
Al-Qudimat (2011)	2011	Jordan	69	82	65
Fernandez et al. (1998)	1998	Canada	366	76	42
Martel et al. (2005)	2005	Canada	92	80	49
Neuhouser et al. (2001)	2001	USA	75	74	73
Kelly et al. (2000)	2000	USA	75	96	84
Gagnon and Recklitis (2003)	2003	USA	118	83	46
McCurdy et al. (2003)	2003	USA	195	83	47
Friedman et al. (1997)	1997	USA	81	100	65
Nathanson et al. (2007)	2007	USA	274	45	25
Paisley et al. (2011)	2011	USA	44	81	82
Gomez-Martinez et al. (2007)	2007	Mexico	110	100	70
Yeh et al. (2000)	2000	Taiwan	63	100	73
Hamidah et al. (2009)	2009	Malaysia	97	95	85
Gözüm et al. (2007)	2007	Turkey	88	100	49

non-representative group of 88 pediatric oncology patients (Gözüm et al. 2007).

The CAM usage rate in pediatric oncology patients documented for Kuala Lumpur in Malaysia in 2009 was 85%. This figure was obtained in a survey in which parents of 97 children with cancer attending the pediatric oncology centre at the Hospital Universiti Kebangsaan Malaysia in Kuala Lumpur were asked to answer a questionnaire concerning CAM treatment usage in their diseased child (Hamidah et al. 2009).

Table 2.1 gives a summary of the described studies worldwide examining the frequency of CAM use in pediatric oncology patients.

## 2.3 Specific CAM Treatments

The National Center for Complementary and Alternative Medicine subdivides the manifold CAM treatments into four groups (<http://nccam.nih.gov/health/whatisacam/>):

1. Natural products
2. Mind-body medicine
3. Manipulative and body-based practices
4. Other CAM practices

### 2.3.1 Natural Products

This subgroup of complementary and alternative treatments comprises the whole multitude of herbal remedies or botanicals, vitamin and mineral supplements and other ‘natural products’. The latter group includes probiotics – live microorganisms, normally bacteria that are similar to microorganisms naturally found in the human digestive tract. Probiotics can be found in foods like yogurts or in dietary supplements (<http://nccam.nih.gov/health/whatisacam/>). Another group in this subcategory are dietary changes such as specific diets. Changes in the diet often go hand in hand with general changes in lifestyle.

Looking at the situation worldwide, natural products are used in North America as well as in Asia, the Middle East and Europe. Nevertheless, the frequency of their use is inhomogeneous.

#### 2.3.1.1 Herbal Supplements

An exploration of this question looking specifically at the use of herbal supplements among 43 Turkish children with cancer showed a high usage rate of 91% (Gözüm et al. 2007). In this synopsis, this is the highest usage rate of

herbal supplements in this subcategory of CAM. Another study from Asia revealed that among 46 Malaysian pediatric cancer patients using CAM supportively for their cancer therapy, 28% were using so-called folk medicine including secret recipes and herbs (Yeh et al. 2000).

In the Middle East herbal preparations are common. Among 61 Israeli children suffering from cancer, 57% were using traditional Arab treatments such as Arab herbal remedies. Twenty-one percent of them were using botanicals (Weyl Ben Arush et al. 2006).

In Europe usage of herbal supplements in pediatric oncology patients is not reported that frequently. In a study in Germany, it was found that only 9% of a representative group of 367 pediatric CAM users took herbal supplements for the concomitant therapy of cancer (Längler et al. 2008).

The studies in the United States, Canada and Mexico show more frequent use of herbal preparations in children suffering from cancer, with prevalences ranging between 9 and 70% (Friedman et al. 1997; Gomez-Martinez et al. 2007). A representative exploration among Canadian pediatric cancer patients revealed a usage rate of 61% for herbal teas and 56% for plant extracts (Fernandez et al. 1998).

### 2.3.1.2 Vitamin/Mineral Supplements

In North America usage of vitamins and mineral supplements is less common than that of herbal remedies. Vitamin and mineral supplements include high doses of vitamin C, E, B complex, antioxidant mixtures, calcium, selenium, folic acid and niacin. Figures vary from 7 to 56% for additional vitamin and mineral intake (Martel et al. 2005; Friedman et al. 1997).

An Asian study found that among 82 pediatric cancer patients already using CAM methods, 27% were taking additional vitamin C and 23% reported the use of multivitamin supplements (Hamidah et al. 2009).

Chemical and biological preparations such as various vitamins, for example, high doses of vitamin C, food additives, minerals, selenium, fish oil and omega-three fatty acids were used by 34% of a small group of 61 pediatric CAM users in the Middle East (Weyl Ben Arush et al. 2006).

In Europe a German investigation found that 35% of 367 pediatric CAM users were taking additional dietary supplements including vitamins and trace elements. Nine percent of these German pediatric oncology patients were using megavitamins to complement their conventional cancer treatment (Längler et al. 2008).

### 2.3.1.3 Other Natural Products

Use of other natural products or other herbal supplements is found primarily in North America. For example, among 156 Canadian children who developed cancer, 46% were drinking essiac tea, 19% were taking shark cartilage and 15% were using *Lactobacillus* to support their conventional cancer therapy (Fernandez et al. 1998). Other natural products that were used were aloe vera, *Astragalus*, garlic, goldenseal, shiitake mushrooms, ginkgo biloba, hoxy tonic, yew needle, blue-green algae, Chem X and various herbal mixtures (Kelly et al. 2000; Neuhouser et al. 2001).

In Asia, more precisely in Malaysia, the use of other natural products included the drinking of spring water. Seventy-eight percent of 82 pediatric cancer patients were drinking water from wells to support their cancer therapy (Hamidah et al. 2009).

Middle-Eastern or European investigations did not reveal the usage of other natural products.

### 2.3.1.4 Dietary Changes

Changes in the child's diet are found in pediatric cancer patients in North America as well as in children suffering from cancer in Asia, the Middle East and Europe. They are less commonly reported than the use of herbal and vitamin/mineral supplements and other natural products.

The findings in a Canadian study in 156 pediatric cancer patients were similar to those obtained in 63 American children suffering from cancer. Forty-nine percent and 47% of the children, respectively, had changed their nutritional habits. This consisted in an increased intake of fruit and vegetables, a switch to organic food or a reduced fat intake (Fernandez et al. 1998; Kelly et al. 2000). Other studies examining this question for the United States, Canada and Mexico showed frequencies of dietary changes varying between 3 and 31% (Friedman et al. 1997; Neuhouser et al. 2001).

Apart from the previously mentioned changes, 3% of a group of 81 pediatric oncology patients were using a macrobiotic diet (Friedman et al. 1997). Macrobiotics is a dietary regimen that consists of grains as basic foodstuffs complemented with beans, vegetables and natural animal foods.

Use of a macrobiotic diet was also found among a group of 26 Dutch pediatric cancer patients. More than half of the study group, that is, 58%, were on a diet containing grains as staple food (Grootenhuis et al. 1998). A German investigation showed a lower frequency of dietary changes. Only 12% of 367 children suffering from cancer had made dietary changes (Längler et al. 2008).

Similar figures were found among a cohort of 43 Turkish children with cancer. Only 8% had changed their diet as a complementary treatment to support their regular conventional cancer treatment (Gözüm et al. 2007).

### 2.3.2 Mind-Body Medicine

The treatments included in the category of mind-body practices concentrate on the interaction between the brain, mind, body and behaviour. The intention is to use the mind to affect physical functioning and to promote health.

Treatments that involve this kind of mind-body interaction include meditation techniques. Meditation is focused attention in a specific posture that can interrupt the stream of thoughts or lead to deep relaxation of the body and mind. It increases tranquillity and relaxation, improves the psychological balance, helps in coping with the illness or enhances overall health and physical comfort.

The different types of yoga are also included in this subcategory. Yoga usually combines physical exercise with proper breathing and meditation or relaxation techniques.

Acupuncture is listed within this area of complementary and alternative medicines since it is also a component of energy medicine, manipulative and body-based practices and traditional Chinese medicine. Acupuncture is one of the key elements of traditional Chinese medicine and is based on the concept of qi. The aim is to resolve an imbalance of qi by penetrating the skin with

needles in order to stimulate the stream of qi (for more details see chapter 9).

The subgroup of mind-body medicine also includes practices such as deep-breathing exercises, guided imagery, hypnotherapy, progressive muscle relaxation, qigong, tai chi and eurhythmy therapy (<http://nccam.nih.gov/health/whatisacam/>).

Examination of the situation worldwide concerning the usage of mind-body medicine to complement conventional treatment in children with cancer shows a geographical disparity between North America, the Middle East, Europe and Asia.

In Asia mind-body interventions are rare compared with other complementary and alternative treatments.

We find a similar situation when we look at the Middle East and Europe. In a very small non-representative cohort of 12 Italian pediatric cancer patients using CAM, only one patient was using mind-body medicine in the form of yoga (Clerici et al. 2009). Another European study from Germany revealed the use of eurhythmy therapy as mind-body intervention in the field of CAM – therapy in children suffering from cancer (Längler et al. 2010).

In a group of 61 Middle-Eastern pediatric cancer patients, 18% reported the use of meditation, yoga, guided imagery, horseback riding, tai chi and/or crystals. Twelve percent of these children were treated with acupuncture in addition to their conventional medical therapy (Weyl Ben Arush et al. 2006).

Studies from North America, meaning the United States and Canada without Mexico, reveal frequent usage of mind-body medicine. In a cohort of 67 American children treated for cancer and supportively using CAM treatments, more than half were using mind-body interventions (Nathanson et al. 2007).

The treatment most often reported among American and Canadian pediatric CAM users was visual imagery including guided imagery and visualisation. These treatments are a group of various techniques practised under the direction of a therapist or alone involving imagining sensations, often by visualising an image in the mind or by verbal suggestion, in order to achieve a response

of the body such as stress reduction (<http://nccam.nih.gov/health/whatisacam/>). In a large group of 156 Canadian children using CAM therapies additionally while treated for cancer, 75% were using imagery in combination with relaxation techniques (Fernandez et al. 1998). Further studies from the United States and from Canada underline the frequent use of imagery and visualisation as a complementary and alternative medical treatment in children with cancer (Martel et al. 2005; Friedman et al. 1997; Kelly et al. 2000; McCurdy et al. 2003). The corresponding data show usage rates of between 5 and 27% for visual imagery (Friedman et al. 1997; Kelly et al. 2000).

The practice of relaxation techniques is another very common therapy in the United States and Canada after imagery and visualisation practices. The most frequent usage of relaxation techniques was found in the Canadian group of pediatric cancer patients mentioned above (75% in combination with imagery) (Fernandez et al. 1998). Apart from that, relaxation techniques were used by 11–28% of the children suffering from cancer (Martel et al. 2005; Friedman et al. 1997).

Less popular CAM treatments in the subgroup of mind-body techniques used for supportive treatment of cancer by American and Canadian pediatric cancer patients were hypnosis, acupuncture, psychotherapy and music therapy (Fernandez et al. 1998; Kelly et al. 2000; McCurdy et al. 2003; Gagnon and Recklitis 2003).

### 2.3.3 Manipulative and Body-Based Practices

These kinds of treatment focus mainly on the structures and systems of the body. This includes techniques to affect the bones, joints, soft tissues, circulatory system and lymphatic system.

Spinal manipulation is one of the therapies that falls within this area of complementary and alternative medicine. It consists of the application of controlled force to a joint of the spine and moving it beyond its passive range of motion. Spinal manipulation is performed by chiropractors, physical therapists, osteopaths and other health-care professionals.

Massage therapy is the second item within this subcategory. Massage therapists manipulate the muscles and soft tissues by rubbing and pressing in order to provide a variety of health benefits (<http://nccam.nih.gov/health/whatisacam/>).

An American study revealed that 34% of a cohort of 67 pediatric cancer patients were using manipulative and body-based methods as a form of CAM treatment (Nathanson et al. 2007). Treatments used by pediatric cancer patients in America to complement conventional cancer therapy include chiropractic. Treatment by a chiropractor is found mainly in the United States and Canada. For Asia, the Middle East and Europe, chiropractic use is not documented in survey results, and osteopathic treatment is also only reported for North America. Twenty-one percent of 55 children with cancer saw chiropractors and/or osteopaths (Neuhausser et al. 2001). A Canadian study among 30 pediatric cancer patients using manipulative and body-based medicine revealed that 7%, respectively, were seeing a chiropractor or an osteopath (Martel et al. 2005).

Massage therapy is the third most frequent treatment reported in this subgroup of complementary and alternative medicine after chiropractic and osteopathy. It is reported for North America as well as for Asia, the Middle East and Europe. In Europe the frequency of massage use ranges from one patient in a group of 12 other Italian pediatric cancer patients to 9% of a group of 367 German pediatric cancer patients using CAM to 35% of a cohort of 26 Dutch children (Clerici et al. 2009; Grootenhuis et al. 1998; Längler et al. 2008). With the following two exceptions, these data are comparable with the situation in the United States and Canada. A Canadian group of 30 children with cancer showed the highest rate of massage usage of 67%, followed by massage use by 66% of another group of 156 Canadian children suffering from cancer (Fernandez et al. 1998; Martel et al. 2005). Other findings from the United States vary from 7% of 81 children to 28% of 54 pediatric cancer patients (Friedman et al. 1997; Gagnon and Recklitis 2003).

According to survey results, rarely used treatments in this subcategory of manipulative and body-based therapies are acupressure, reflexology,

passive mobilisation, shiatsu, biofeedback and touch for health (Grootenhuis et al. 1998; Weyl Ben Arush et al. 2006; Martel et al. 2005; Friedman et al. 1997; Gagnon and Recklitis 2003).

### 2.3.4 Other CAM Practices

The fourth area of CAM treatments defined by The National Center for Complementary and Alternative Medicine contains movement therapies such as the Feldenkrais method, Alexander technique, Pilates, Rolfing structural integration and Trager psychophysical integration. These therapies are designed to promote physical, mental, emotional and spiritual well-being.

The practices of traditional healers also fall within this area of CAM. Traditional healers use various methods based on specific theories, beliefs and experiences drawn from a deep-rooted tradition handed down from generation to generation.

Other CAM practices involve manipulation of various energy fields, for example, electromagnetic fields, such as magnet therapy and light therapy.

There are other treatments based on the concept of a more subtle energy that flows within the human body. These practices include qigong, Reiki and healing touch, for example.

Finally, whole medical systems containing a complete system of theory and practice originating under different cultural circumstances from those of western, conventional medicine fall within this fourth group of CAM treatments. Examples are ayurvedic medicine, traditional Chinese medicine, homoeopathy, anthroposophic medicine and naturopathy (<http://nccam.nih.gov/health/whatiscam/>).

#### 2.3.4.1 Movement Therapies

These kinds of CAM treatment are used by children with cancer as a therapy to integrate the body and the mind and to promote general well-being. The figures range from 16% of a cohort of 81 American children using physical exercises to 37% of 55 American children suffering from cancer who used physical exercises in a not otherwise specified form (Friedman et al. 1997;

Neuhouser et al. 2001). Swimming, as another movement therapy, was reported by one of 30 pediatric cancer patients from Canada (Martel et al. 2005). Movement therapies were not used by Asian, Middle-Eastern or European children suffering from cancer.

#### 2.3.4.2 Traditional Healer

Reported visits to a traditional healer are not so common among pediatric oncology patients. However, 41% of a group of 91 American children were seeing a faith healer in addition to their conventional cancer therapy (McCurdy et al. 2003). In Asia the reported rate was lower than in the United States, with 22% of a group of 82 Malaysian children making use of a traditional healer (Hamidah et al. 2009). For Europe the only report of a visit to a faith healer to complement cancer therapy in children comes from the Netherlands. Twenty-three percent of 26 children suffering from cancer were seeing a faith healer (Grootenhuis et al. 1998). Finally, a visit to a clairvoyant was reported in a single case in Canada (Martel et al. 2005).

#### 2.3.4.3 Measurable Energy Fields

The highest use of energy fields was reported among a group of 26 Dutch pediatric cancer patients of whom 35% were using light therapy (Grootenhuis et al. 1998). Other treatments in this area of complementary and alternative medicine found in American and Canadian children with cancer are, in descending order of frequency, bioenergies, ozone therapy and magnets (Fernandez et al. 1998; Gagnon and Recklitis 2003; Gomez-Martinez et al. 2007).

#### 2.3.4.4 Subtle Forms of Energy

Most of these treatments dealing with a non-measurable form of energy are found to be used by children with cancer in the United States and Canada. In a representative group of 156 pediatric oncology patients, 42% were employing therapeutic touch therapies (Fernandez et al. 1998). Reiki was the technique used second most frequently among children suffering from cancer in North America (Martel et al. 2005; Kelly et al. 2000; Gagnon and Recklitis 2003). A German



investigation showed that 10% of a group of 367 children were using Reiki treatments (Längler et al. 2008). The use of pranotherapy was mentioned only once in an Italian child with cancer (Clerici et al. 2009).

### 2.3.4.5 Whole Medical Systems

The self-contained systems used to complement conventional cancer treatments are primarily homoeopathy, anthroposophic medicine and traditional Chinese medicine. Especially in Europe, treatment with homeopathy and anthroposophic medicine is widespread. More than half of a group of 26 Dutch children with cancer, that is, 58%, were using homoeopathic and/or anthroposophic medicine (Grootenhuis et al. 1998). Among a cohort of 367 pediatric cancer patients in Germany, 45% were utilising homoeopathy (Längler et al. 2011) and 27% used anthroposophic medicine (Längler et al. 2010). Among a very small group of 12 Italian children, seven reported the use of homoeopathy (Clerici et al. 2009).

Mexico shows the highest usage rate of homoeopathy in North America. Twenty-five percent of a group of 77 children investigated were using this kind of complementary and alternative medical treatment (Gomez-Martinez et al. 2007). Compared with Europe, the frequency of homoeopathic treatments in the United States and Canada is low. One percent to 17% of pediatric cancer patients were using homoeopathy to complement their conventional treatment (Fernandez et al. 1998; Friedman et al. 1997). Usage of anthroposophic medicine is not well documented for North America.

In 20% of a group of 46 pediatric oncology patients in Taiwan, the complementary and alternative treatment used in addition to the conventional treatment was traditional Chinese medicine (Yeh et al. 2000). In Canada, 15% of a group of 156 children suffering from cancer were using traditional Chinese medicine as well (Fernandez et al. 1998).

Rarely listed treatments based on a coherent medical system are naturopathy, Bach flower therapy and the Hamer method (Clerici et al. 2009; Längler et al. 2008; McCurdy et al. 2003).

## 2.4 Factors Associated with CAM Use

In the literature some parameters are described that tend to correlate with the usage of CAM treatments. These include:

- The age of the pediatric cancer patient
- The level of parental education
- The income of the parents
- Prior CAM experience of the family

Many studies (if they looked at these aspects at all) were not able to show with statistical relevance that these four specific factors play a role for parents of children with cancer in choosing a complementary and alternative therapy (Hamidah et al. 2009; Kelly et al. 2000; McCurdy et al. 2003; Gagnon and Recklitis 2003; Gomez-Martinez et al. 2007). Nevertheless a Canadian exploration of parameters associated with the usage of complementary and alternative medical treatments did show with statistical relevance that CAM use is associated with the father's educational level and prior CAM use in the family (Martel et al. 2005).

An investigation among children suffering from cancer in the United States reveals that parents who themselves used six or more CAM therapies were 33 times more likely to use CAM for their children compared to those who did not use CAM (Nathanson et al. 2007). Findings from Canada, Israel and Germany also indicate that prior CAM use in the family or a prior positive attitude towards CAM might be a factor associated with the usage of CAM (Längler et al. 2008; Weyl Ben Arush et al. 2006; Fernandez et al. 1998).

A higher level of parental education might also be associated with more frequent use of CAM (Clerici et al. 2009; Fernandez et al. 1998). An Asian study from Malaysia and Israeli findings substantiate the finding that the higher educational level is based on the higher education of the mother rather than the father (Weyl Ben Arush et al. 2006; Yeh et al. 2000).

An American research group also discovered a trend towards a higher rate of CAM use in children over the age of five compared to pediatric cancer patients aged four or younger. Furthermore, they reported a higher rate of use of CAM

therapies in white patients compared to minorities. A third finding of this group was a trend towards more frequent use by families in the middle income bracket than by those with incomes in the lower and upper ranges (Neuhouser et al. 2001). The role of age in the usage of CAM methods was also seen in a group of Turkish children. The CAM usage rate was higher in a group of children who were on average 3 years older than non-users of CAM (Gözüm et al. 2007). This third finding of the American research group was also supported by the finding of a higher socioeconomic status among CAM users in Israeli and German investigations (Längler et al. 2008; Weyl Ben Arush et al. 2006).

Besides age, parental education, prior usage of CAM and income or general social status, other findings that might influence the usage of CAM are a high risk of death at the time of diagnosis, a lower survival perspective and a diagnosis with poor prognosis (Grootenhuis et al. 1998; Längler et al. 2008; Fernandez et al. 1998).

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## 2.5 Side Effects of CAM Treatments

Like every medical treatment, CAM treatments may carry a risk of undesired side effects. Nevertheless, reports of adverse reactions are rare (Zuzak et al. 2009). Evidence is anecdotal since only single reports of adverse reactions exist, and therefore the evidence is not representative due to the small number of cases (Lim et al. 2011; Seifert et al. 2011). Side effects of CAM treatments are often explored by means of retrospective non-controlled interviews rather than prospective, controlled study designs. This complicates the assessment and controversy of side effects and safety issues in the field of complementary and alternative medicine.

Most reported side effects were associated with the use of herbal supplements taken orally as complementary or alternative medical treatment for a pediatric cancer patient. They included nausea, vomiting, skin irritation, sleep disturbances, pain, diarrhoea or unpleasant taste (Fernandez et al. 1998; Neuhouser et al. 2001; Yeh et al. 2000). Laboratory investigations have

frequently shown toxicity of some herbs, contamination with heavy metals such as lead or adulteration of the herbal medicine with undeclared synthetic drugs (Ernst 2003). Herbal toxicity may lead to bradycardia, respiratory depression and central nervous system depression. Contamination of the remedy especially with lead was found in supplements produced in India or China (Ernst 2003).

Side effects were also reported by parents of pediatric cancer patients after topical application of herbal supplements, inhalation of herbal remedies, for example, eucalyptus oil, and use of herbal enemas. In single non-representative cases, homoeopathy also caused illness in pediatric cancer patients (Montoya-Cabrera et al. 1991).

Other adverse reactions that were not due to herbal remedies were reported after the use of acupuncture, spinal manipulation and massage therapy. Acupuncture poses the risk of infection when not applied properly. There are anecdotal reports of ruptured ventricles due to wrongly placed acupuncture needles (Ye 1956). Chiropractic manipulation of the spine may lead to adverse events such as cerebrovascular accidents (di Fabio 1999).

As mentioned above, the reported occurrences of adverse reactions are rare, single and non-representative cases. Conventional medicine poses a risk of serious adverse reactions as well. Anecdotal reports of side effects on complementary and alternative medical treatments often result in excessive controversy about the safety of complementary and alternative medicine (Lim et al. 2011; Seifert et al. 2011; Ernst 2003).

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## 2.6 Source of Information Concerning CAM Treatments

Information about complementary and alternative medical treatments is rarely provided by primary pediatric care physicians. On a worldwide scale findings of research groups looking at this question show that the primary sources of information about complementary and alternative therapies are the families, friends or relatives of the pediatric cancer patients. Parents also learned

about CAM methods from parents of other diseased children (Clerici et al. 2009; Grootenhuis et al. 1998; Längler et al. 2008; Fernandez et al. 1998; Friedman et al. 1997; Kelly et al. 2000; Gomez-Martinez et al. 2007; Gözüim et al. 2007). The media also played a relevant role in providing information (Längler et al. 2008; Fernandez et al. 1998; Gomez-Martinez et al. 2007). The parents' or patients' knowledge about CAM also led them to avail themselves of complementary and alternative treatments on their own initiative (Kelly et al. 2000; Gomez-Martinez et al. 2007). Alternative care providers, physician experts in natural medicine, health-care professionals or hospital staff were only reported as secondary sources of information about CAM by parents of pediatric cancer patients (Clerici et al. 2009; Längler et al. 2008; Fernandez et al. 1998; Kelly et al. 2000).

The primary sources of information are non-medical sources from the families' environment. Parents less frequently mentioned that they received information from medical staff.

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## 2.7 Parental Expectations of CAM Treatments

Parental expectations and reasons for using CAM therapies in a child suffering from cancer are manifold. Nevertheless reasons such as strengthening and reinforcing the child's immune system, physical and mental stabilisation in the sense of improving the patient's inner strength and ability to cope with the disease are common (Clerici et al. 2009; Hamidah et al. 2009; Längler et al. 2003, 2008; Weyl Ben Arush et al. 2006; Kelly et al. 2000; Yeh et al. 2000). Furthermore, many parents expect CAM methods to improve the compatibility of conventional treatments and especially to help the patients to cope with side effects and symptoms resulting from the conventional medical therapy. This includes reduction of pain and improvement of relaxation (Martel et al. 2005; Neuhouser et al. 2001; McCurdy et al. 2003; Gagnon and Recklitis 2003; Yeh et al. 2000). The belief in the healing power of a specific complementary and alternative treatment played a role in parental expectations of CAM as

well (Friedman et al. 1997). Expectations such as curing the cancer, fighting and stopping the cancer, reducing the tumour size or prevention of recurrence are less common among parents of pediatric cancer patients (Martel et al. 2005; Kelly et al. 2000; Gomez-Martinez et al. 2007). Some parents also use complementary and alternative treatments for their child in order to make sure they are doing everything possible (Clerici et al. 2009; Fernandez et al. 1998). Only few parents mentioned dissatisfaction with conventional treatment and therefore the expectation that CAM treatment would be a better therapy (Längler et al. 2008; Friedman et al. 1997).

Parental expectations of CAM usage in a child diagnosed with cancer vary from supporting the conventional treatment to using CAM as an alternative treatment due to dissatisfaction with orthodox medicine. Many frequently mentioned parental issues lie between these two poles.

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## 2.8 Perceived Benefits of CAM Treatments

Perceived benefits from complementary and alternative therapies in children suffering from cancer are hard to evaluate because they are subjective. However, parents report benefits that are in line with their reported expectations of the CAM treatment. These include an improvement in the child's general well-being, relief of pain, enhanced immune defences and improved blood values (Clerici et al. 2009; Längler et al. 2008; Weyl Ben Arush et al. 2006). On the psychological side, the parents of these children suffering from cancer report that complementary and alternative medical treatments lead to stabilisation of the child's psyche (Längler et al. 2008). CAM may support relaxation and help the child to manage and cope with the disease and the overall situation (Clerici et al. 2009; Weyl Ben Arush et al. 2006). In an American study, 50% of a small cohort of 63 pediatric cancer patients who had been using at least one CAM therapy described CAM as 'very effective' (Kelly et al. 2000). An investigation of 77 children suffering from cancer in Mexico showed that 53% of the parents judged CAM as



‘very useful’ (Gomez-Martinez et al. 2007). A Canadian study found that in a group of 156 pediatric cancer patients, 20% of the parents rated CAM therapies as ‘very beneficial’, while 49% classed them as ‘beneficial’ (Fernandez et al. 1998). In a survey from Germany, at least 50% of 367 parents whose child suffered from cancer and used CAM reported an ‘improvement’ or even a ‘marked improvement’ due to the usage of complementary and alternative therapies (Längler et al. 2008). An American investigation supports these findings and ascertains that about 60–90% of their 55 surveyed pediatric cancer patients using CAM noted improvements owing to various CAM treatments (Neuhouser et al. 2001).

## 2.9 Communication Between Parents/Patients and Physicians About CAM

Children suffering from cancer or their parents often do not inform their physicians, pediatric oncologists or nurses that they are using CAM treatments to support their conventional cancer therapy (Clerici et al. 2009; Martel et al. 2005). Except in an investigation among German pediatric cancer patients, the willingness of pediatric oncology patients, or rather their parents, to discuss CAM treatments with the pediatric oncologist or physician is low all over the world. The study from Germany constitutes an exception, the parents of 71% of the 367 children with cancer reporting that they had informed their treating physician, most often the treating pediatric oncologist, about their CAM usage (Längler et al. 2008).

Apart from this, the communication situation is bad. Sixty-four percent of 61 CAM users among pediatric cancer patients in Israel did not inform their physician about the use of CAM. If the conversation did take place 79% of the Israeli parents stated that they were the ones who brought up the topic of CAM treatments (Weyl Ben Arush et al. 2006). Among Malaysian children suffering from cancer only 15% of the parents informed their treating physician (Hamidah et al. 2009). Other findings from various geographical regions around the world show figures between 9 and

28% of patients/parents informing their treating physicians about CAM usage (Gomez-Martinez et al. 2007; Gözüüm et al. 2007). An American study analysed reasons for this low rate of communication among patients and physicians about CAM and found that only 43% of the pediatric oncologists occasionally ask their patients about the use of complementary and alternative medicine (Roth et al. 2009). This figure is in line with German data showing that 41% of German pediatric oncologists often or always ask their patients or their parents about CAM use (Längler et al. 2012). The American study mentioned above also revealed that 7% of 101 pediatric oncologists surveyed never asked their patients about CAM usage at all. Lack of time during the normal routine was given by 49% of the US pediatric oncologists as the reason for their low level of communication with pediatric cancer patients and their parents about CAM. Forty-seven percent reported a lack of knowledge about CAM (Roth et al. 2009) and therefore felt that they were not capable of counselling their patients about the use of complementary and alternative medical treatments in addition to their conventional cancer therapy (for more details see chapter 3).

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# Attitudes, Beliefs, and Communication About Complementary and Alternative Medicine Among Oncologists, Pediatricians, and Pediatric Oncologists

## 3

Alfred Längler

### Contents

3.1	Introduction.....	19
3.2	Communication About CAM.....	20
3.3	Doctors' Estimations of the Frequency of CAM Use by Their Patients.....	21
3.4	Personal Experience of CAM.....	22
3.5	CAM Treatments Recommended by Doctors for Their Patients.....	22
3.6	Referral of Patients to CAM Specialists.....	23
3.7	Concerns About CAM Use by Patients.....	24
3.8	Effects and Side Effects of CAM Use Observed by Doctors.....	24
3.9	Doctors' Qualification and Training.....	25
3.10	Summary.....	25
	References.....	26

### 3.1 Introduction

The diagnosis and treatment of cancer in children and adolescents have improved considerably in the last decades. Increasingly sophisticated diagnostics, with improved staging and more differentiated treatment, have led to better chances of cure, reduced recurrence rates, and in individual cases also to a reduction of the treatment-associated toxicity and sequelae. These improvements have been made possible by national and international collaboration in the context of specialist societies and research groups. In addition to the optimization of treatment on the clinical level, research in pediatric oncology is looking increasingly at molecular and genetic issues, with increasing focus on individual patterns of tumor-inhibiting and tumor-promoting factors. However, this trend toward individualized diagnosis and treatment is paralleled by another development which is driven mainly by the patients themselves and/or their parents. The frequency with which complementary and alternative medicine (CAM) is used in the context of treatment of a child or adolescent with cancer varies from country to country but is almost always relevant in relation to the overall population. However, this development has so far played practically no part in scientific discourse in pediatric oncology. Except in the USA, where there is systematic publicly funded research on the topic of CAM and cancer (<http://nccam.nih.gov/research>), research on CAM in pediatric oncology, whether epidemiological, basic, or applied

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research, plays little more than a marginal role in the overall context of research in pediatric oncology. The large research institutions which have contributed substantially to the successes in pediatric oncology have so far given practically no attention to the topic of CAM in pediatric oncology. Where this topic has been scientifically addressed in institutions practicing conventional pediatric oncology, the relevant working groups are usually not more than a marginal phenomenon in the overall scientific context of the research institution concerned. Nevertheless, various scientific working groups do exist which have addressed the topic of CAM in pediatric oncology. Their activities have so far focused mainly on the question of the frequency with which CAM is used in children with cancer, the expected effects of this treatment, and the specific CAM practices used. Studies conducted on this are almost without exception retrospective surveys using either written questionnaires or interviews, or in some cases a combination of the two (see chapter 2). Thus, numerous details regarding the CAM treatment methods used, the motivation of the parents, the general frequency of use, and the factors influencing the likelihood of using CAM have now been described for various populations. On the other hand, practically no data have been systematically collected on side effects, interactions, and adverse effects of CAM practices. Data available in the scientific literature on individual CAM medications or nonmedication interventions from some CAM sectors with a specifically pediatric oncological focus are described in the chapters of this book dealing with the respective treatment modalities.

In the everyday clinical reality of pediatric oncology as practiced today, we cannot yet speak of an integrative pediatric oncology which chooses from the overall spectrum of treatment options available (conventional and complementary methods), the treatments that are best for the individual patient concerned. There are few exceptions which confirm this rule. One of the most important prerequisites for an integrative approach which would be desirable at least in the interests of the patient is that the treating pediatric oncologists do not simply dismiss the

topic of CAM, that they keep an open mind and communicate critically but openly with both patients and parents as well as with CAM practitioners.

On the basis of the scientific literature available on this topic, this chapter will look at the attitudes, opinions, and fears of pediatric oncologists regarding the topic of CAM. We will also look at the topic of communication about CAM and the factors which influence this (e.g., information, qualification, and personal experience). As there are currently only two published scientific studies on the attitudes and opinions of pediatric oncologists on the topic of CAM (Roth et al. 2009; Längler et al. 2012), we will also need to refer to the results of other publications which touch on this topic (studies involving adult oncologists and pediatricians).

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## 3.2 Communication About CAM

It is known that the topic of CAM is not a routine part of the doctor-patient consultation and is consequently not always addressed by the physician and/or the parents. Whether the doctor and parent talk about planned or performed CAM treatment of a child with cancer depends on various factors. For example, an Israeli study in a pediatric population showed that 61 % of parents whose children were treated in a hospital with a CAM focus told the hospital doctors about previously performed CAM treatments compared with only 19 % of parents whose children are treated in a conventional hospital. In a 2004 survey conducted among members of the American Academy of Pediatrics (AAP) (Kemper and O'Connor 2004), 87 % of the respondents reported that they had generally been approached by patients about CAM in the last three months. We cannot infer from this in total how often US American parents talk to their children's pediatricians about their use of CAM.

Only 17 % of parents of children with cancer in Canada reported that they discussed CAM use with their pediatric oncologist (Martel et al. 2005). In Europe, disclosure rates of 60 % were reported in a general pediatric population in Italy

(Menniti-Ippolito et al. 2002) and of 71 % in a pediatric oncological population in Germany (Längler et al. 2008). It is noteworthy that in practically all populations studied in the majority of the cases the discussion with the doctor about CAM (if it took place at all) was initiated by the parents. On the other hand, parents' feelings of having been well advised about CAM correlate positively with the degree to which the treating physician plays an active role in talking about CAM.

The overwhelming majority of American pediatricians (80 %) are of the opinion that doctors should actively ask parents/patients about past or ongoing CAM treatments (Sawni and Thomas 2007). However, only 37 % of the respondents actually do this in their daily practice. In the Netherlands, 28 % of pediatricians report that they actively bring up the topic of CAM when taking the history (Vlieger et al. 2010). American and German pediatric oncologists actively address the topic of CAM in 42 and 40 % of their consultations, respectively (Roth et al. 2009; Längler et al. 2012). About three-quarters of the pediatricians believe that parents who are using CAM in their children would actively disclose this to their pediatrician (Sikand and Laken 1998).

When doctors are asked about their communication about CAM, they confirm the situation reported by parents/patients, that is, that in the majority of cases, talking about CAM is initiated by the parents/patients. This applies in adult oncology and general pediatrics as well as in pediatric oncology. Practically all US American pediatricians ask the large majority of parents about the use of prescription and nonprescription medicines (Kemper and O'Connor 2004). However, a considerably smaller number of doctors asked specifically about use of CAM practices: 20 % asked about the use of herbal medicines, 17 % about the use of special diets and of dietary supplements. Less than 5 % of the responding pediatricians actively asked about other often frequently used CAM modalities such as chiropractic, massage, acupuncture, homeopathy, and mind-body therapies. In a survey among US American pediatric oncologists, the reason given by 49 % of the respondents for not asking their patients actively about CAM contrary to

better judgment was lack of time. About an equal number (47 %) also named lack of knowledge about CAM as the reason for not actively addressing the subject themselves (Roth et al. 2009). Unfortunately no other study has investigated this very important question of why doctors do not ask patients about their use of CAM.

Further, well-investigated factors which influence the communication behavior of the doctors are the doctor's individual level of training and personal experience of CAM use either themselves or by family members. A study in the UK showed that pediatricians address the topic of CAM with patients/parents significantly more often with increasing seniority: 27 % of juniors versus 75 % of consultants (Fountain-Polley et al. 2007). The opposite is observed among German pediatric oncologists. In general younger female pediatric oncologists with less professional experience have a more positive attitude to CAM (Längler et al. 2012). German pediatric oncologists who have personal experience of CAM use either themselves or by family members actively bring up the topic of CAM with patients/parents significantly more often than pediatric oncologists without personal CAM experience.

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### 3.3 Doctors' Estimations of the Frequency of CAM Use by Their Patients

Despite methodological limitations, doctors' estimates of the frequency of CAM use by their patients can to some extent be compared with the figures obtained when patients are asked directly about the frequency of CAM use. The result of this comparison can be seen as a further measure of the quality of doctor-patient communication on the topic of CAM, but its value should not be overrated.

In a survey conducted some time ago among pediatricians in the USA (Sikand and Laken 1998), the respondents were of the opinion that fewer than 10 % of their patients used CAM. Nine years later, fellows of the American Academy of Pediatrics (Sawni and Thomas 2007) were of quite a different opinion, believing that about



96 % of their patients used CAM. The actual rate of CAM use among children in the USA is about 50 % depending on the population studied (Jean and Cyr 2007). In Germany, on the other hand, the subjective estimates of pediatric oncologists about the frequency of CAM use by their patients (on average the German pediatric oncologists reported that 41 % of their patients used CAM) approximately matched the actual frequency of CAM use of 37 % reported by the parents (Längler et al. 2008; Längler et al. 2012).

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### 3.4 Personal Experience of CAM

Attitudes and opinions on CAM were influenced, among other things, by personal positive or negative experience of the use of CAM. The most direct experience a doctor can have of CAM is when it is used to treat his or her own illness or the illness of a close family member. Of course, this presupposes a fundamentally positive attitude to CAM; otherwise, CAM use in such a situation would not be considered. It is known that the frequency of CAM use by doctors is generally lower than in the respective general population. A comparative survey of oncologists in the USA and China in 2008 showed a very low rate of personal CAM use by oncologists of only 18 % (Lee et al. 2008), whereas the CAM usage rate in the general population in the USA is about 33 % (Barnes et al. 2008). In the UK, 22 % of oncologists reported personal experience of CAM (Lewith et al. 2001). Pediatricians, on the other hand, more often have personal experience of the use of CAM than adult oncologists, for example. In the USA, the increase in CAM use in the general population is paralleled by a trend toward an increase in CAM use by pediatricians from 34 % in 1998 (Sikand and Laken 1998) to 49 % in 2007 (Sawni and Thomas 2007). In European surveys, doctors also reported relevant CAM experience for treatment of personal illness or illness in the family: 39 % of pediatricians in the Netherlands have personal experience of CAM (Vlieger et al. 2010). As many as 46 % of German pediatric oncologists

report personal CAM use (Längler et al. 2012) which is substantially higher than the CAM usage rate of 37 % in pediatric oncological patients reported for Germany in 2004 (Längler et al. 2008). The CAM practices most often reported by the respondents are nonmedication, body-based methods such as massage. In Germany, a strikingly large number of pediatric oncologists (45 %) reported experience with acupuncture. Pediatric studies from other European and non-European countries do not report a comparable frequency of acupuncture use by pediatricians. In Europe, homeopathy is the most important medication treatment used for CAM self-medication by doctors (30 % among pediatricians in the Netherlands and 26 % among pediatric oncologists in Germany).

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### 3.5 CAM Treatments Recommended by Doctors for Their Patients

There are various studies in which doctors provide information about their own CAM prescribing. In principle, it is not surprising that in surveys of nonselected populations of doctors, only a minority actively recommend CAM use to their patients. Nor is this active prescribing/recommending of CAM therapies influenced by the doctor's personal experience of CAM use (see above). Here, doctors appear to make a clear distinction between the private and the professional. If we look at the minority of doctors who actively recommend CAM practices to their patients, we obtain an inhomogeneous picture with regard to the spectrum of methods recommended. This picture is markedly influenced by local and cultural factors. For example, in a survey of Japanese oncologists the respondents, if they used or recommended CAM at all (8 %), most often recommended use of Chinese herbs in the treatment of their patients (Hyodo et al. 2003). Pediatricians in the Netherlands who actively prescribe CAM treatments most often use mind-body therapies, homeopathy, and acupuncture (Vlieger et al. 2010).

The spectrum of CAM therapies actively recommended or in some cases prescribed by US American pediatric oncologists is dominated by dietary supplements, vitamins, prayer, massage, and guided imagery (Roth et al. 2009). Quite a different picture emerges when we look at the CAM therapies which some German pediatric oncologists actively recommend or offer in their institutions: nonmedication therapies such as art therapy (45 %), music therapy (54 %), massage (53 %), and external applications (52 %) predominate here. However, medication therapies such as mistletoe therapy (32 %), homeopathy (30 %), and anthroposophic medicine (24 %) are also relatively often actively used in the institutions of the responding doctors (Längler et al. 2012).

In summary, we can see that at most a minority of pediatricians or pediatric oncologists actively recommend and/or prescribe CAM treatments for their patients or offer them in institutions where they work. This may be due particularly to a generally rather skeptical attitude toward CAM. However, at the same time, the responding doctors also confirmed that there is a competence deficit (see below). The CAM treatments preferred in these situations by the respective doctors vary widely in the populations studied.

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### 3.6 Referral of Patients to CAM Specialists

The majority of the survey respondents in the described populations (pediatric oncologists, pediatricians, oncologists) have a critical or negative attitude to CAM treatments. In their daily practice, these doctors – if they address the topic at all (see above) – are more likely to advise patients/parents against CAM use. But even the doctors who are in principle more open toward CAM treatments are in many cases not sufficiently qualified to offer or prescribe the CAM treatments wished for by their patients/parents. Only a very small percentage of German pediatric oncologists (4 %) consider themselves sufficiently qualified to advise patients/parents about CAM

in such a way that referral to an appropriately qualified CAM practitioner would be superfluous. Apart from a personal lack of appropriate qualification by the physicians themselves, the availability or nonavailability of individual CAM treatments in the respective institution may also influence prescribing patterns. One way out of this dilemma is the possibility of referring patients/parents wishing for a specific CAM treatment to an appropriately qualified CAM practitioner. However, it should be emphasized that there are few practitioners who have a CAM qualification in addition to their medical specialty (in this case pediatric oncology). Therefore, in most cases, close, trusting, and respecting cooperation between the pediatric oncologist and the CAM practitioner will be the only solution. In the USA, 42 % of pediatric oncologists report that they refer patients/parents asking for a particular CAM treatment to an appropriately qualified CAM practitioner. The treatments most often used are massage and acupuncture (Roth et al. 2009). In Germany, pediatric oncologists report that they use this possibility of concomitant treatment by a qualified CAM therapist in as many as 57 % of the cases in which patients/parents actively ask for such treatment (Längler et al. 2012). On the other hand, about one in ten German pediatric oncologists actively advises such patients/parents against CAM treatment. Whether the patients/parents follow this advice has not yet been studied. The percentages of pediatricians of other disciplines and general pediatricians who would refer patients/parents asking for CAM treatments to a CAM specialized therapist are similar to that reported by German pediatric oncologists (Sawni and Thomas 2007; Sikand and Laken 1998). The principle willingness of the doctors to refer patients/parents to a CAM practitioner increases the more conventional treatments have already failed or not produced the desired effect in the treatment of the patient concerned. Similarly to communication about CAM (see above), referral to a CAM practitioner also appears to be influenced by the doctor's personal experience of CAM use. In a survey among office-based doctors in Denver, Colorado,

a significant correlation was found between referral to a CAM therapist and personal experience of CAM (Corbin Winslow and Shapiro 2002).

### 3.7 Concerns About CAM Use by Patients

The attitudes and opinions of doctors regarding requests for CAM use by their patients are significantly influenced by their worries and fears. These in turn vary widely and are determined by diverse factors. Concerns about feared side effects of the CAM practices often predominate, as well as about the possibility of hitherto uninvestigated interactions with necessary concomitant conventional therapy. Thus, two-thirds of German pediatric oncologists report that they worry about possible side effects or interactions in the case of CAM use by their patients (Längler et al. 2012). This concern is considerably more marked among doctors who have no personal experience of CAM use (Kemper and O'Connor 2004). A concern voiced similarly often by pediatricians and pediatric oncologists is that CAM use might delay or even prevent a necessary conventional treatment. There are currently no objective data on whether and to what extent use of CAM prevents conventional therapy. Our own unpublished data indicate that, in Germany at least, this fortunately only occurs in very rare isolated cases. An important factor ensuring that a planned CAM treatment does not prevent a conventional treatment appears to be the quality of the doctor-patient communication (see Chap. 13). The fear very often reported by 74 % of German pediatric oncologists that the sometimes considerable additional costs for CAM treatment would place an inappropriate burden on their patients (Längler et al. 2012) stands in contrast to the fact that 75 % of parents of children with cancer in Germany who have used CAM report that they spent less than €2000 (Längler et al. 2008). In our opinion, it is important for both parties (doctors and patients) that any concerns and fears with regard to requested CAM treatment are addressed and discussed openly and with respect.

### 3.8 Effects and Side Effects of CAM Use Observed by Doctors

In the majority of cases, the opinions of doctors on the effects of CAM treatments in their patients are negative ones. Either the doctors assume that if there is any effect, this is attributable to placebo action (Lewith et al. 2001), or they are of the opinion that CAM is ineffective, as reported by 82 % of responding Japanese oncologists (Hyodo et al. 2003), for example. However, in the field of pediatric oncology specifically, there are a significant number of doctors who believe that CAM treatments in general or specific individual CAM practices may have a positive effect. The presumed or observed positive effect of CAM treatments in pediatric oncology refers particularly to symptom control and quality of life and less to a direct effect on the cancer. In the USA, for example, pediatric oncologists were of the opinion that massage (74 %), prayer (74 %), meditation (67 %), guided imagery (65 %), yoga (57 %), and acupuncture (45 %) might improve the quality of life of their patients. On the other hand, a majority of American pediatric oncologists believe that dietary supplements, herbal drugs, special diets, vitamins, and chiropractic are dangerous (Roth et al. 2009). Methods regarded as possibly effective by German pediatric oncologists include acupuncture (63 %), external treatments (47 %), homeopathy (46 %), massage (43 %), mistletoe therapy (40 %), music therapy (40 %), and anthroposophic medicine (34 %). Spiritual healers (33 %), healing touch (21 %), osteopathy (23 %), and dietary supplements (22 %) are considered dangerous (Längler et al. 2012). In various survey populations, it stands out that doctors generally perceive CAM treatments which they class as being possibly effective as having fewer side effects (Sawani and Thomas 2007; Längler et al. 2012; Sikand and Laken 1998). Until the still largely open questions of the reported concerns and fears have been systematically studied for individual CAM treatments, an individual benefit-to-risk assessment must be used as the basis for an informed decision in each particular case.



### 3.9 Doctors' Qualification and Training

A majority of German pediatric oncologists (87 %) are of the opinion that doctors should have more opportunity for specialization in CAM. This applies to both undergraduate and postgraduate (specialty) training (Längler et al. 2012) and reflects the fact that worldwide there are only few doctors who are formally and/or practically qualified both in a conventional medical specialty and in one or more CAM practices. Conversely, it also means that most oncologists and pediatric oncologists do not consider themselves sufficiently qualified to prescribe or use specific CAM treatments. This was seen both in the field of adult oncology (87 %) (Lewith et al. 2001) and in pediatric oncology (48 %) (Längler et al. 2012). Hence, it is not surprising that more than half of the American pediatric oncologists would like more training in CAM treatments in general as well as in specific CAM treatments (particularly dietary supplements, herbal drugs, special diets). Where such or similar further training or continuing education is offered, however, the pediatric oncologists reported that in practice, this is only utilized by a minority (Roth et al. 2009). Around 8 % of German pediatric oncologists report that they “often” attend continuing education events on CAM and a further 47 % “sometimes” (Längler et al. 2012).

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### 3.10 Summary

According to the published data, attitudes and opinions on CAM among doctors in general and pediatric oncologists in particular are influenced chiefly by the following factors:

- Younger doctors usually have a fundamentally more positive attitude to CAM than older

doctors. The reasons for this are largely unknown. In apparent contradiction to this is the fact that doctors with longer professional experience have a more positive attitude to CAM than doctors with less professional experience.

- Doctors with a lower level of specialization in their field have a more positive attitude to CAM than doctors with a higher level of specialization.
- Women often have a more positive attitude to CAM than men. However, this was not verified in all studies.
- Both use and prescribing of CAM and the willingness to refer patients to a practitioner specialized in CAM are more marked in doctors with personal experience of specific CAM treatments (this applies both to treatment of personal illness and acquisition of competence in the use of a treatment method in their specialty) than in doctors without CAM experience.
- Doctors who have a generally more positive attitude to CAM practice a more open and active style of communication on the topic of CAM with their patients.

For a genuinely integrative pediatric oncology in which individual treatment decisions take into account the individual needs of patients/parents on the basis of existing scientific evidence, we need open discussion of the needs and concerns of both the treating pediatric oncologists and the patients/parents. This dialogue can be positively fostered by appropriate specialization in CAM treatments by pediatric oncologists and by personal experience of individual CAM treatments where desired. In the end, decisions should be guided not by personal opinions and attitudes but rather by concrete data and objective personal experience (Table 3.1).

**Table 3.1** Published data on attitudes and beliefs of physicians regarding CAM

Author	Year	Study population	Country	Number of respondents
Lewith	2001	Members and fellows of the Royal College of Physicians	UK	12,000
Corbin Winslow	2002	Physicians in Denver, Colorado	USA	751
Kemper	2007	Clinicians, nurses, practice nurses, and physician assistants at the tertiary care medical center	USA	
Risberg	2004	Oncologists, nurses, radiotherapists, and practice nurses	Norway	828
Lee	2008	Comparison between oncologists in the USA and China	USA/China	249
Hyodo	2003	Hospital oncologists in Japan (randomly selected from the Japanese oncology literature) and 1,118 office-based oncologists. 62 % of the respondents were oncological surgeons, 29 % medical oncologists	Japan	2,118
Kemper	2004	Members of the American Academy of Pediatrics in the Michigan region	USA	1,600
Sawni	2007	Fellows of the American Academy of Pediatrics	USA	3,500
Sikand	1998	Pediatricians	USA	860
Fountain-Polley	2007	Doctors in the pediatric department of a district general hospital and in a tertiary center children's hospital	UK	49
Vlieger	2010	Members of the Dutch Pediatrics Society	Netherlands	1,450
Roth	2009	Pediatric oncologists randomly selected from the Internet	USA	358
Längler	2012	Doctors belonging to the German Society of Pediatric Oncology and Hematology	Germany	660

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Alfred Längler and Georg Seifert

## Contents

<b>4.1</b>	<b>Background</b> .....	29	<b>4.6</b>	<b>Anthroposophic Treatment</b> .....	33
<b>4.2</b>	<b>The Anthroposophic View of the Human Being</b> .....	30	4.6.1	Practical Application of Anthroposophic Treatment .....	34
<b>4.3</b>	<b>The Fourfold Structure of the Human Organism</b> .....	30	<b>4.7</b>	<b>Anthroposophic Pharmacy</b> .....	34
4.3.1	Physical Body .....	30	<b>4.8</b>	<b>Non-medication Treatments</b> .....	35
4.3.2	Etheric Body .....	31	4.8.1	Treatments for External Use: Compresses and Application of Oils and Ointments .....	35
4.3.3	Astral Body .....	31	4.8.2	Rhythmic Massage .....	35
4.3.4	Ego Organization .....	31	4.8.3	Eurythmy Therapy .....	36
<b>4.4</b>	<b>Functional Threefoldness</b> .....	32	4.8.4	Art Therapy .....	36
4.4.1	Nerve-Sense System .....	32	<b>4.9</b>	<b>Research Overview</b> .....	37
4.4.2	Metabolic-Limb System .....	32	4.9.1	General .....	37
4.4.3	Rhythmic System .....	32	4.9.2	Mistletoe Therapy .....	37
<b>4.5</b>	<b>The Concept of Health and Illness in Anthroposophic Medicine</b> .....	32	<b>4.10</b>	<b>Anthroposophic Medicine in Pediatrics</b> .....	38
			<b>4.11</b>	<b>Anthroposophic Medicine in Pediatric Oncology</b> .....	39
			4.11.1	Practical Application of Anthroposophic Medicine in Pediatric Oncology/Practical Recommendations .....	39
			<b>4.12</b>	<b>Open Questions</b> .....	40
			<b>References</b> .....		42

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## 4.1 Background

Compared with other traditional healing systems, anthroposophic medicine is a relatively young branch of medicine which goes back only about 90 years. It was founded in the 1920s by the natural scientist Rudolf Steiner and the physician Ita Wegman. Translated more or less literally,

anthroposophic medicine means human medicine (*anthropos* (Gr.)=human being; *sophia*=wisdom). It describes a concept of holistic and integrative medicine which places the human being, with all his or her possible forms of knowledge and experience, at the center of its diagnostic and therapeutic endeavors. Like other traditional healing systems such as traditional Chinese medicine and ayurvedic medicine, for example, anthroposophic medicine is based on a spiritual worldview and view of the human being. An important characteristic of this worldview is the joint evolution of the universe, the earth and the human being. Other fields apart from medicine in which anthroposophic knowledge and insights are applied include biodynamic farming, Waldorf education with Waldorf kindergartens and Waldorf schools, educational institutions, and communities for people with special needs and in certain areas of economic life, for example, in banking and law.

Anthroposophic medicine extends the possibilities of conventional medicine by adding further therapeutic approaches. It can only be practiced by physicians who have already completed their training in conventional medicine and are therefore qualified doctors.

Where anthroposophic medicine and treatment are not sufficient to stimulate the patient's self-healing powers, the anthroposophic doctor will employ all necessary conventional treatment procedures that are appropriate for the patient. The primary approach and starting point of anthroposophic medicine is salutogenesis. This means that, in the healing process, the primary aim is to stimulate the body's own physiological responses rather than using medication to block or take over misdirected processes or functions.

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## 4.2 The Anthroposophic View of the Human Being

The anthroposophic understanding of the human being, the basic principles of which are outlined below, forms the basis for an integrative understanding of illness (= diagnosis), encompassing all the dimensions of the human being. This understanding of illness in turn provides the basis

for appropriate treatment of the patient within the context of anthroposophic medicine.

In anthroposophic medicine, the human being is regarded as having a fourfold structure consisting of four so-called constituent elements, as well as a threefold structure, describing the functional interactions between these constituent elements.

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## 4.3 The Fourfold Structure of the Human Organism

The four constituent elements of the anthroposophic concept of the human being are reminiscent of the Aristotelian theory of the four elements in which the different states of matter were said to correspond to the different natural kingdoms. However, this does not mean that we wish to show an affiliation with ancient prescientific systems. Our intention is, rather, to provide a terminological basis for an interdisciplinary and integrative epistemological approach to health, illness, and healing.

In the final instance, this fourfold structure describes different levels of the human being which, only when taken together, permit a holistic manner of approach which opens up an added perspective. For each of these different dimensions of being, the means of acquiring knowledge of or perceiving the respective dimension is different and is specific to each constituent element (Steiner 2005).

### 4.3.1 Physical Body

The physical body is the constituent element which is completely accessible to perception with the physical senses. It is the basis of the material, three-dimensional form of the human being, which is described in anatomy. It is subject to the laws of the inorganic mineral world (gravitation, mechanics, decay and breakdown of structures). It is characterized by processes of dying. It can be described by measurements such as height and weight, by chemical analyses such as laboratory values, and by the shaping of the organs. As the physical body is permeated throughout life by the other constituent elements, it can only be

perceived in isolation in the lifeless state. In terms of Aristotle's four-element theory, the corresponding state of matter is the solid state. The physical body is the element that the human being has in common with the inorganic mineral kingdom.

### 4.3.2 Etheric Body

The etheric body can be perceived in the organized form of the physical body. This organized form is the result of the coordinating growth processes of different tissues and is expressed, for example, in the formation of the face. The predominant processes in the etheric body are of a biochemical and physiological nature. They are the foundation of all healing and recovery and in the final instance, the basis of the human being's salutogenic potential. The etheric body can be described by assessment of vitality but also by a description of growth, development, and capacity for regeneration. Since, in terms of the Aristotelian four-element theory, the corresponding state of matter is the liquid state, description of the acid/base/electrolyte and fluid balance also provides information on the organization of the etheric body. The etheric body in the human being corresponds to the plant form of life, showing growth and life processes but without emotional activity or feelings, that is, without soul forces. In the etheric body, in contrast to the lifeless mineral substances, metabolic processes take place which are on a higher level than the physical body. Beyond the individual, human being formative powers are also active in the etheric body which lead to manifold differentiation of the etheric body. The etheric body manifests in a temporally highly complex interplay of individual physiological processes which are the basis of all vital and growth processes. According to the anthroposophic path to knowledge, the etheric body can be perceived with the powers of imagination.

### 4.3.3 Astral Body

The knowledge that perceives the astral body is a sensate knowledge which, according to the

anthroposophic path to knowledge, uses the faculty of inspiration. The astral body is subject to the laws of the aeriform or gaseous processes. The forces and laws governing the astral body are those which permit movement, language, consciousness, and emotional expression. The astral body is the precondition for feelings and emotions and forms the physical basis for emotional processes. Physiological expressions of the astral body include, for example, muscle tone, the play of the muscles, the manner of breathing and of speech, the spectrum of emotional expressions, and facial expression. The presence of an inner emotional world is bound to the existence of an astral body. It is the carrier of the world of consciousness and the emotional life of the human being. The activity of the astral body is characterized by processes of breakdown or degradation.

In terms of the Aristotelian four-element theory, the state of matter corresponding to the astral body is the gaseous state. Human beings have the astral body in common with animals, which, depending on the animal species, are also capable of experiencing feelings of pain or fear.

### 4.3.4 Ego Organization

The "I" or ego is the element responsible for the spiritual, self-conscious, and individual processes in the human being. It is thus the vehicle of thinking and remembering. The human ego organization can be perceived via a substantive knowledge through the faculty of intuition. It is expressed in speaking, standing, and walking, insofar as these are expressions of the individuality of the person concerned. In terms of the Aristotelian four-element theory, the state corresponding to the ego organization is heat. Physiologically, the ego organization expresses itself in all human bodily processes associated with heat. Generation of heat, regulation, and maturation of the ability to maintain a constant body temperature are processes of the ego organization. The intervention of the ego in the rest of the body expresses itself in varying modulation of heat processes. The ego as individual spiritual center represents the individuality of the human being. The ego is what

distinguishes human beings from animals and makes them individuals. The ego is also what distinguishes one human being from another.

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## 4.4 Functional Threefoldness

The functional interaction of the four constituent human elements becomes clear in the threefold organization which is a functional and morphological reflection of the polar structure of the human being. The threefold organization presents a different perspective from that of the four constituent elements. It shows the functional interaction of the four levels of the constituent elements and thus provides a possible view of the development of disease, as well as a model for the preservation and/or generation of health. This threefold organization can already be seen in the early embryonic phase, for example, in the polarity of the entoderm and ectoderm between which the mesoderm then develops. The chief expression of the threefold organization is to be found in the mental activities of thinking, feeling, and willing (Steiner 2004).

### 4.4.1 Nerve-Sense System

The activities of the clear-waking consciousness as the basis of comprehension of spiritual content are concentrated in the upper pole of the human being, specifically in the region of the head. The prerequisite for concentrated thinking is stillness and an alert state of consciousness. The head (which is the seat of important organs of sense but above all also of a large part of the central nervous system, protected by the spherical construction of the cranium) is where the activities of the nerve-sense system are for the most part located and is characterized largely by a clearly structured form.

### 4.4.2 Metabolic-Limb System

Quite in contrast to the stillness of the nerve-sense system, the metabolic-limb system is characterized

by constant movement. This movement is partly of a distinctly intentional nature and thus closely related to the mental quality of willing. In part, however, it is also very unconscious. This applies particularly to the movement of the digestive organs. In the metabolic-limb system, the human being is asleep. The activity of the metabolic-limb system can be described as processual and dynamic. The life forces which are here still fully available provide an enormous capacity for regeneration even in adulthood. In contrast to the spherical form which predominates in the nerve-sense system, the metabolic-limb system is characterized largely by radial structures. This can be seen most clearly in the shape of the extremity bones.

### 4.4.3 Rhythmic System

In health, the mediator between the two functional poles, nerve-sense system and metabolic-limb system, is the rhythmic system. It displays a rhythmic structure itself, in the form of vertebral column and thoracic cage. The state of consciousness corresponding to the rhythmic system is that of dreaming. This is where the emotional quality of feeling finds its echo. The rhythmic system moves in the direction of waking up toward the nerve-sense system in inspiration with an increase in sympathetic tone and in the direction of falling asleep toward the metabolic-limb system in expiration with an increase in parasympathetic tone. However, this rhythmic system is not the passive product of the action of the nerve-sense system and the metabolic-limb system, but itself has an actively ordering function in the interaction of the polar systems with the heart as central organ of the rhythmic system.

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## 4.5 The Concept of Health and Illness in Anthroposophic Medicine

While in conventional medicine, the understanding of illness is usually based on causal analysis, in anthroposophic medicine, the understanding of illness is oriented toward disease processes



and disease typologies. The basis of an anthroposophic understanding of illness and health is the understanding of the constituent elements and their interaction in the threefold organism. A tendency to become ill arises when an imbalance develops in the threefold organism, and this imbalance can no longer be compensated by a person's salutogenic powers. Illness occurs where physiological processes take place in an unphysiological location. In concrete terms, this means that predominance of the nerve-sense system in a place where it does not belong results in a tendency to diseases characterized by loss of vitality and sclerosis. The ultimate form of such a sclerosis is cancer, in which parts of the organism withdraw from the control of the overall organism and lead a life of their own which destroys the body.

Inflammation, on the other hand, is the expression of predominance of the metabolic-limb system in a place where it does not belong. If this tendency to inflammation spreads into the periphery, into the sensory organization, this results in the development of allergies. It is often the case that a disease itself triggers the process in the organism which can lead to recovery (salutogenesis), as in the development of fever in overcoming inflammation, for example. In this respect, it is part of the treatment principle of anthroposophic medicine to activate and support these disease-overcoming processes and not to misinterpret and suppress them as expressions of the illness (Steiner and Wegman 2000).

In order to obtain a diagnosis based on the constituent elements of the human being in terms of anthroposophic medicine, various aspects related to the illness must be taken into account. These are in particular:

- Constitution
- Clinical picture, including diagnosis in terms of the constituent elements
- History
- Biography and biographical context

Thus, the anthroposophic doctor moves from understanding the nature of the disease in terms of the constituent elements to the appropriate remedy for the patient.

In the course of the joint evolution of the human being and the natural world, a close

relationship developed between the human being and nature which forms the basis for the pharmaceutical approach used in anthroposophic medicine.

In principle anthroposophic pharmacy uses substances from minerals, plants, and animals. Generally speaking, these pharmaceutically processed natural substances act on the different levels of the fourfold human being:

- Mineral medicines act on the ego organization.
- Plant medicines act on the astral body.
- Medicines of animal origin act on the etheric body.
- Medicines of human origin (e.g., red cell concentrates), act directly on the physical body and temporarily take over its function.

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## 4.6 Anthroposophic Treatment

The primary aim of anthroposophic treatment derived from an understanding of the human being based on spiritual science is to promote future health rather than to restore the previous state which existed before the illness. Thus, anthroposophic medicine is a medicine that promotes development and that gives patients the assistance they need to enable them to deal with the task posed by the illness themselves. Ideally, healing involves three dimensions:

1. Development of the spirit
2. Maturation of the soul (eurythmy therapy, art therapies)
3. Recovery of the body (the medicines support the powers of healing which, although rudimentarily present, are not yet sufficiently effectual)

Two basic principles of action can be distinguished in anthroposophic medicine:

1. A treatment principle based on the disease process (lessening)
2. A treatment principle based on the healing process (enhancing)

In contrast to this, conventional medicine with its primarily pathogenetic orientation modifies the manifestation of disease by prophylaxis, control, suppression, and replacement but does not address the actual powers for overcoming illness.



### 4.6.1 Practical Application of Anthroposophic Treatment

The raw materials that form the basis of the anthroposophic medicines are prepared using different pharmaceutical principles (Simon 2011):

- In the form of unpotentized preparations from the whole plant as in phytotherapy (e.g., mistletoe preparations, Cardiodoron®, Bryophyllum)
- In potentized form as in homeopathy

When using potentized medicines, the choice of potency can steer the effect in the direction of one or other of the three functional systems:

Nerve-sense system	High potency	D20-D30
Rhythmic system	Medium potency	D10-D12
Metabolic-limb system	Low potency	D1-D6

The choice of the route of administration can also influence which functional system is addressed:

Nerve-sense system	External application
Rhythmic system	Parenteral administration (subcutaneous, intravenous)
Metabolic-limb system	Internal use

#### 4.6.1.1 Mineral Medicines

Among the mineral medicines, the seven planetary metals, which bear a close evolutionary relationship to the seven main organs of the human being, occupy a central position in anthroposophic medicine:

Lead/plumbum	Spleen
Tin/stannum	Liver
Iron/ferrum	Bile
Gold/aurum	Heart
Copper/cuprum	Kidneys
Mercury/mercurius	Lungs
Silver/argentum	Brain

#### 4.6.1.2 Plant Medicines

A threefold structure similar to that described above with regard to the organization of the human being can also be found in plants.

In the root organization, we find characteristics of the human nerve-sense system. In the leaf organization, we find a close relationship to the human rhythmic system. In the flower organization, we find a relationship to the human metabolic-limb system.

In addition to the actual substantive language of the plant characterized by its constituents, choice of the appropriate remedy is also guided by the form, diction, and temporal development of the plant.

#### 4.6.1.3 Medicines of Animal Origin

Animal substances are also used in various forms in anthroposophic medicine. Typical examples are pharmaceutical preparations from the wood ant (*Formica*). Here the principal feature is poison production with a predominance of the astral organization. *Formica* is therefore used, for example, in diseases with a tendency toward formation of deposits (e.g., in cancer). In contrast to this, the poison of the honeybee (*Apis*) is used in inflammatory processes, for example, for adjunctive treatment of sepsis. While the action of *Formica* is more in the direction of the astral body, the action of *Apis*, with its relationship to heat, focuses more on the ego organization.

## 4.7 Anthroposophic Pharmacy

The basis of anthroposophic pharmacy is the high quality of the raw materials selected for the pharmaceutical process. Plant raw materials are sourced either from biodynamic agriculture or, in the case of plants which cannot be cultivated, collected in the wild. In addition to the growing conditions, particular importance is attached to the harvesting process, including choice of the right harvesting time. The more perfect the physical form produced by the natural process and the greater the purity of the selected substance (this applies particularly to mineral preparations), the more ideally the raw material meets the criteria of a starting substance for anthroposophic medicines.

The raw materials obtained in this way are subjected to different pharmaceutical processes depending on their intended use. These include:

- Heat processes:
  - Liquid: maceration, digestion, infusion, decoction, and distillation
  - Dry: roasting, carbonization, and ashing
- Rhythmic pharmaceutical processes:
  - Potentizing: Rh (rhythmic) processes
  - WALA process
- Metal processes:
  - Metal mirrors.
  - Metal mirrors obtained by reduction.
  - Metal mirrors obtained by distillation (Metallicum praeparatum).
    - Metal mirror foils.
  - Vegetabilized metals: Plants treated with a diluted metal substance according to a special procedure are processed into a mother tincture.
  - Solutio: mineral compositions according to the model of a plant.

In addition to these medicines, which are usually made by one of the two manufacturers of anthroposophic medicines Weleda and WALA, the experienced anthroposophic doctor will also use medicines from other manufacturers in his daily practice where this is appropriate.

## 4.8 Non-medication Treatments

### 4.8.1 Treatments for External Use: Compresses and Application of Oils and Ointments

Compresses and other external treatments are an integral part of anthroposophic medicine. Used properly, they can alleviate many symptoms, such as nervous or muscular tension, for example, as well as digestive problems. Compresses also convey an intense feeling of comfort, well-being, and healing. There are many different forms of external treatments which can be used in the area of therapeutic nursing care. These are used particularly to address dysregulations in the nerve-sense

system. Medicinal oils such as *Solum uliginosum* comp. or plant ointments in the form of composition medicines are applied in the form of wraps or compresses or by rhythmic massage for alleviation of nervous anxiety or pain, for example, of the musculoskeletal system. Anthroposophic external treatments are often used in cachectic patients, patients suffering from exhaustion or chronic pain, and patients with vegetative disturbances (Sonn 2004). In anthroposophic hospitals, the nurses use wraps, compresses, and rhythmic massage with oil or ointments in their patients. Touching the patient in this way is also a form of human contact that is in itself important for the patient's healing process.

Typical examples of external treatments used in pediatric oncology

Indication	Treatment
Restlessness, anxiety (general)	Rhythmic massage of the back, e.g., with <i>Solum</i> oil
Abdominal pain (e.g., in steroid treatment or vincristine neuropathy)	Moist warm abdominal wrap with <i>Oxalis</i> essence
Neuropathic pain	Rhythmic massage of the extremities, e.g., with rosemary oil
Nausea, lack of appetite	Moist warm abdominal wraps with yarrow
Palpitations, anxiety	Piece of cloth spread with <i>Aurum/Lavandula</i> ointment placed over the heart

### 4.8.2 Rhythmic Massage

The rhythmic massage developed by Dr. Ita Wegman (RTM) is a special form of therapeutic massage used in anthroposophic medicine that was developed on the basis of classical massage (Batschko 2011). The aim of RTM is to correct disturbed rhythms of the different constituent elements. Rhythmic massage acts primarily on the fluid currents and breathing of the entire organism and on the body's heat balance. The specially and intensively trained hands of the rhythmic massage therapist stimulate the flow of fluid in the body via

the connective tissue, thus releasing pathologically solid and compacted structures and allowing them to flow freely again. Rhythmic massage therapists use mainly circular, round, and undulating movements with a quality of touch which differs substantially from that of classical massage. RTM can be used for conventional massage indications such as back pain, muscle pain (muscle tension), or degenerative muscle disease (muscle wasting through inactivity). RTM is also used in chronic or psychosomatic illnesses, depression, cancer, or developmental disorders in children. It is often combined with pharmacological and art therapies. The duration depends on the patient's age and medical history and the duration of the illness.

RTM is prescribed by the doctor and performed by rhythmic massage therapists according to an individually drawn-up treatment plan. A treatment unit lasts 45–60 min (including resting for 20–30 min after the massage). A treatment cycle consists of 6–12 units.

Although RTM has been used since the 1920s, there have been few systematic studies to date. RTM is therefore used and prescribed mainly on an empirical basis (Hamre et al. 2007a).

### 4.8.3 Eurythmy Therapy

Eurythmy therapy is a form of movement therapy which is prescribed for many medical indications. The basic elements of eurythmy therapy are the sounds of our speech transformed into movement which are employed in a specific manner depending on the indication and the therapeutic goal. In eurythmy therapy, the formative dynamic which is contained in the process of articulation, that is, in the uttering of vowels and consonants, is translated into movement and becomes experienceable. While our inner feelings are reflected in our facial expressions and gestures, the movements of eurythmy therapy act in the reverse direction, that is, from the outside inwards. Each sound, each movement bears a certain relationship to the processes in the organism. Eurythmy therapy is thus employed specifically to influence the functions of individual organs and organ systems. Eurythmy therapy is prescribed by the doctor and performed by

eurythmy therapists according to an individually drawn-up treatment plan. A treatment unit lasts 60 min. A treatment cycle comprises 10–15 units. In the case of chronic illnesses and developmental disorders, treatment over a longer period of time may also be necessary.

There are few clinical data on eurythmy therapy to date, but the treatment has been practiced on an empirical basis for a long time with very positive results. The few studies on eurythmy therapy that have been performed show promising initial results (Büssing et al. 2008). One of the few cohort studies showed a significant reduction in symptoms, for example, in cervical spine syndrome, attention deficit hyperactivity syndrome, disturbance of social behavior, chronic pain, and depression, as well as improvement of health-related quality of life. In a controlled comparison (Hamre et al. 2007b), it was found that patients with chronic back pain who received various anthroposophic treatments reported comparable successes to patients who had received conventional physiotherapy.

First, controlled clinical studies on eurythmy therapy showed that it can stimulate heart rate variability, considerably more effectively and lastingly than physical exercise (Seifert et al. 2009). Further, initial studies have shown that the use of eurythmy therapy in people suffering from stress improves quality of life and coping (Kanitz et al. 2011), can make sleep more refreshing (Kanitz et al. 2012b) and/or reduces daytime tiredness, and can also increase heart rate variability over a prolonged period (Seifert et al. 2011a).

In pediatric oncology, eurythmy therapy is often used during aftercare. A pilot study showed neurological and cognitive improvements in children with medulloblastoma (Kanitz et al. 2012a), so that eurythmy therapy can be considered as an adjunctive treatment option for various complaints in pediatric oncology.

### 4.8.4 Art Therapy

Anthroposophic art therapy uses various painting and drawing techniques. The emphasis is less on the result than on the inner process stimulated in the patient by, for example, the light–dark

techniques of charcoal drawing, by the techniques of watercolor painting, and by painting with pastels. The aim is to encourage a development process and use this for the therapeutic process.

Only one international study on anthroposophic art therapy, which is used in 28 countries, has been published to date (Hamre et al. 2007c). This study reported that after an average of 15 art therapy interventions over an average period of 161 days patients experienced a sustained improvement of chronic symptoms and improved quality of life. Art therapy is another important component of anthroposophic medicine which is based on long-standing experience and can be used for a wide range of indications.

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## 4.9 Research Overview

### 4.9.1 General

The main areas covered by the available scientific literature on anthroposophic medicine are on the one-hand basic epistemological principles (Heusser et al. 2012), on the other hand, clinical application, including particularly a wealth of individual case reports and smaller case series. Numerous clinical studies, some of them randomized, have been published particularly on the topic of mistletoe therapy. In addition, in recent years in particular, there have been increasing numbers of clinical studies from the field of health-care research which look retrospectively at anthroposophic medicine in the setting of routine daily practice. A systematic and detailed overview of clinical research on anthroposophic medicine can be found in the book Kienle/Kiene/Albonico *Anthroposophic Medicine: Effectiveness Utility, Costs, Safety* (2008). In the form of a health technology assessment (HTA), the authors reviewed a total of 189 clinical studies on anthroposophic medicine (17 randomized controlled trials, 22 non-randomized controlled trials, 44 retrospective comparative studies, 106 cohort studies) with regard to quality, practical relevance, and data extraction. A further 2,090 individual case reports have been published.

### 4.9.2 Mistletoe Therapy

Mistletoe plays a central role within the overall concept of anthroposophic supportive therapy in cancer. There is a relatively large body of clinical data on the use of mistletoe extracts (Kienle and Kiene 2003).

Mistletoe extracts have been used for adjunctive therapy in cancer therapy for more than 80 years. This clinical use of mistletoe extracts was initially based largely on empirical evidence, that is, the efficacy was inferred mainly from individual case reports and experience. In the meantime, numerous clinical and preclinical studies on mistletoe have been published, although not all meet the methodological standards required today.

Since the beginning of mistletoe therapy, as well as in subsequent studies, it has often been reported that mistletoe extracts have a positive influence on general well-being. However, this question has only been addressed in a few later studies and then usually as secondary question. All investigations except one showed a positive effect of the mistletoe treatment (Kienle and Kiene 2007, 2010).

In the studies in which mistletoe extracts were used with the aim of reducing treatment toxicity during or after chemotherapy, bone marrow regeneration was often examined in addition to quality of life, and in some cases, positive changes were found (Kienle and Kiene 2010).

The majority of the studies published showed a positive outcome of mistletoe treatment for reduction of treatment toxicity. For example, in a randomized placebo-controlled study in 46 patients with advanced breast cancer, Heiny et al. examined the influence of mistletoe treatment during palliative chemotherapy (carboplatin, vindesine, epirubicin). They found a significantly less marked decrease in white blood cells from the second chemotherapy cycle onward, as well as significantly less deterioration in quality of life and significantly less increase in anxiety (Heiny and Beuth 1994).

A randomized study in 107 patients with advanced colorectal cancer (Heiny et al. 1998), comparing the cytotoxic drug 5-FU without mistletoe versus 5-FU with mistletoe, showed a

significantly lower rate of WHO grade III mucositis in the mistletoe group (25.8 % vs. 17.9 %,  $p=0.03$ ). Leukopenia also occurred more often in the control group (38.8 % vs. 32.1 %,  $p=0.03$ ). However, the validity of the study is limited by a dropout rate of 26 % which was not further explained.

In a prospective randomized study in 233 patients (breast cancer, ovarian cancers, NSCLC), Piao et al. (2004) showed a marked improvement of three quality of life indices (FLIC, TCM, KPI) during chemotherapy. Pain reduction, physical status, physical activity, subjective well-being, and appetite were consistently rated as significantly better in the mistletoe group. The reduction of treatment associated side effects was almost 50 %, and weight gain in the patients in the mistletoe group was significant.

A retrospective-controlled cohort study of Hannover Medical School on the benefit of long-term mistletoe therapy parallel to adjuvant chemotherapy in primary, nonmetastatic breast cancer showed a significantly lower rate of adverse drug reactions in the mistletoe group (16.2 %) compared with the control group (54 %) and a longer recurrence free interval (Schumacher et al. 2003).

In a randomized double-blind study in healthy subjects, Stoss et al. (1998) showed a significant increase in neutrophil, granulocytes, and monocytes 24 h after subcutaneous administration of mistletoe extract (neutrophils 3,225–8,514,  $p=0.001$  and monocytes from 390 to 706,  $p=0.001$ ). Other investigations, also in cancer patients, have shown similar effects (Hajto et al. 1997; Stein and Berg 1998a, b; Hajto and Lanzrein 1986; Stoss et al. 1998), but it has not yet been possible to attribute this to a particular constituent (Stein et al. 1999). The effect is probably caused by increased mobilization of granulocytes from the bone marrow rather than an actual increase in production.

The only investigation (Lukyanova 1994) on the use of mistletoe extracts in pediatrics was performed with the aim of reducing recurrent airway infections in 25 immunosuppressed children from the 30-km zone of the Chernobyl region after the reactor disaster. A 5-week course of

treatment with mistletoe led to a prolonged reduction in the rate of respiratory tract infections during the treatment period and thereafter. Immunologically there was a significant increase in phagocytic cells, both T and B lymphocytes.

In summary, we can say that mistletoe extracts have definite biological activity and that there are several clinical studies which show that subcutaneous treatment with mistletoe extracts can be used to treat side effects of chemotherapy or symptoms of cancer. A direct anticancer efficacy of subcutaneously administered mistletoe extracts has not been demonstrated to date.

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#### 4.10 Anthroposophic Medicine in Pediatrics

In a prospective multicenter observation study, Jeschke et al. (2011) investigated the prescribing behavior, diagnoses, and non-pharmacological therapies of anthroposophic doctors in Germany. The study covered a total of 33,000 patients, 56 % of whom were children. The average duration of treatment was 8.1 min. The most common diagnoses were upper respiratory tract infections, otitis media, and bronchitis. Anthroposophic medicines accounted for 41.8 % of all medicines prescribed. Of 5,289 non-pharmacological treatments prescribed, 27 % were anthroposophic treatments.

In a cross-sectional survey in a pediatric emergency department in Switzerland, Zuzak et al. (2010) found that 24 % of all CAM users used anthroposophic medicine.

In a prospective cohort study comprising 233 patients from 72 anthroposophic medical practices, Hamre et al. (2007a) showed that although patients treated by anthroposophic doctors initially had longer consultations, in the long term, there was a lasting improvement in both the symptoms of the chronic illness and quality of life. This study included children, 23 % of the patients were between 0 and 19 years. The greatest treatment effect occurred in the first 6 months.

Swartz et al. performed several epidemiological studies investigating the influence of an

anthroposophic lifestyle on the development of allergic disorders and atopy in children (Alm et al. 1999). They were able to show that children with an anthroposophic lifestyle (defined on the basis of fewer vaccinations, less use of antipyretics and antibiotics in the first 12 months, consumption of fermented vegetables containing live lactobacilli) had a lower risk of allergies and atopic sensitization than children in a reference population. The observed protective effect against allergies and atopy was, however, most marked in children who had grown up on a farm.

No prospective controlled studies on the use of individual anthroposophic medicines or anthroposophic treatment procedures in defined diseases have been published in the international scientific literature to date.

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## 4.11 Anthroposophic Medicine in Pediatric Oncology

In pediatric oncology in Germany, 27 % of all parents who use some form of complementary or alternative medicine (CAM) use anthroposophic medicine. In a nationwide survey among parents in Germany, Längler et al. (2010) showed that, compared with other CAM procedures, anthroposophic medicine stands out as being characterized by a particularly long duration of use and a high level of patient satisfaction and physician loyalty.

A retrospective-matched pair analysis investigated the safety of concomitant use of anthroposophic supportive therapy (AST) with regard to any impact on the efficacy of the intensive therapy in children with brain tumors. The study showed that, in terms of event-free survival and overall survival, there were no advantages or disadvantages for either group. Although the anthroposophic supportive treatment was used for treatment of the side effects of chemotherapy and radiation therapy, it was not possible to obtain any data retrospectively on the actual efficacy of anthroposophic supportive therapy with regard to the side effects of the primary treatment (Seifert et al. 2011).

In addition there are some case reports on the use of mistletoe preparations, occasionally accompanied by other anthroposophic medicines and treatments in children with cancer.

### 4.11.1 Practical Application of Anthroposophic Medicine in Pediatric Oncology/Practical Recommendations

There is currently only one pediatric oncological center worldwide which treats children both conventionally according to the current treatment guidelines of the medical societies and adjunctively with anthroposophic treatment procedures (Gemeinschaftskrankenhaus, Herdecke, Germany). However, in Europe, particularly in German-speaking countries, there are many doctors offering anthroposophic medicine especially in the outpatient setting (Längler and Zuzak 2012).

Many office-based anthroposophic pediatricians, particularly in German-speaking countries (Germany, Switzerland, Austria), use complementary medicine to treat children receiving treatment in conventional pediatric oncological institutions.

The main type of concomitant anthroposophic treatment used in children with cancer is subcutaneous mistletoe therapy. In addition, some typical anthroposophic medicines derived from the fundamental anthroposophic understanding of the cancer may be used alongside the conventional treatment (Table 4.1). While on the one hand, anthroposophic medicine is used with the aim of reducing the toxicity of the conventional therapy; it also has a place in follow-up care. Also, there are a number of medicines which can be used as required depending on the specific clinical situation. In Table 4.2, we present a selection of medicines which have proved empirically effective and are often used. They should be regarded as suggestions which can be modified depending on the experience of the user. At any rate, as discussed in more detail above, the aim underlying treatment with anthroposophic medicine is always to enhance the salutogenic forces



**Table 4.1** Medication in cancer

Medicine	Indication	Dose < 4 years of age	Dose ≥ 4 years of age
<i>Mistletoe extract, subcutaneously, ampoules</i>	Malignant diseases	Twice weekly as subcutaneous injection	
<i>Cichorium 5 % globuli p.o.</i>	Stimulation of the rhythmically mediated processes in the organism in terms of harmonization	5 globuli 3 times daily	7 globuli 3 times daily
<i>Oxalis folium</i> Rh D4 dilution p.o.	Stimulation and harmonization of metabolic processes and of excretory and digestive functions	5 drops 3 times daily	7 drops 3 times daily
<i>Phosphorus</i> D8+D30 globuli p.o	Together with phosphorus D30, strengthening of regenerative powers and harmonization of the rhythm of waking and sleeping	D8: 5 globuli in the morning daily D30: 5 globuli in the evening daily	D8: 10 globuli in the morning daily D30: 10 globuli in the evening daily
<i>Ratanhia comp.</i> mouthwash	For oral care several times daily during chemotherapy and for manifest mucosal lesions	30 drops in 100 ml water	
<i>Aurum/Prunus D9/D5 i.v.</i> Infusion before each chemotherapy	Aurum: protection and shield for the life organism Prunus: strengthening of immune defenses	1 ampoule of each daily before the chemotherapy	
<i>Nux vomica D4 i.v.</i> Infusion before each chemotherapy	For functional gastrointestinal disorders with nausea and/or vomiting		

in the sick child and thus encourage long-term recovery from the cancer.

In addition to the medicines shown in the above tables, the non-pharmacological treatment methods of anthroposophic medicine described above can be used in terms of integrative pediatric oncology. In the Gemeinschaftskrankenhaus Herdecke/Germany, wraps, application of oils and ointments, and rhythmic massage are used for symptomatic treatment (pain, restlessness, tension) parallel to conventional chemotherapy. Depending on the indication, the children and adolescents are also prescribed art therapies and/or eurythmy therapy particularly during the inpatient treatment phases.

Generally speaking, as we have said above, anthroposophic medicine sees its role, particularly in the field of pediatric oncology, as an adjunct to conventional medicine, in the sense of integrative medicine. The precondition for this kind of integrative use of anthroposophic treatments in pediatric oncology is both a sound knowledge of the conventional pediatric oncological treatment principles and treatment guidelines and an extensive

training and experience in anthroposophic medicine, in this case specifically in children.

## 4.12 Open Questions

The frequency of use of anthroposophic medicine in children in Europe has been relatively well studied and documented. Figures on use specifically in pediatric oncology are only available for Germany. It can be assumed that in practically all European countries, and undoubtedly also in some non-European countries, children with cancer receive additional pharmacological or non-pharmacological treatment with anthroposophic medicine concomitantly with or after completion of their conventional therapy. Here, there is an urgent need for research with differentiated documentation of the treatment methods used and their effects. As this is a treatment system with numerous combinations of different medicines and treatments, a systematic prospective scientific evaluation should be carried out at least for some typical medicines or treatment methods. Such an



**Table 4.2** Medication for use as required

Symptom	Medicine	Start	End	Dose < 4 years of age	Dose > 4 years of age
Lack of appetite	Magen globuli	<i>As required</i>	Normalization of eating behavior	5 globuli 3 times daily	10 globuli 3 times daily
Abdominal pain, digestive disorders	Oxalis ointment 30 %	<i>As required</i>		Moist warm abdominal wrap as required or regularly at midday.	
Temperature above 38.5 °C	Argentum met. prp D30 infusion	For fever above 38.5 °C before each i.v. antibiotic administration	24 h after fever has subsided	1 ampoule as short infusion	2 ampoules as short infusion
Neutropenia	Lachesis D8 dilution	Granulocytes below 500 µl	Granulocytes above 500 µl	5 drops 3 times daily	10 drops 3 times daily
Beginning mucositis	Calendula D3 globuli	Signs of beginning mucositis	Mucosal regeneration	5 drops 3 times daily	10 drops 3 times daily
After infections, mucositis	Meteoreisen globuli	For 1 week after administration of i.v. antibiotics		5 globuli 3 times daily	10 globuli 3 times daily
Nausea in spite of antiemetic treatment	Nux vomica D4 globuli	Additionally in case of nausea in spite of antiemetic treatment		3 globuli 3 times daily to hourly	5 globuli 3 times daily to hourly
Side effects of steroids	Bryophyllum 50 % Trituration	Psychological and somatic side effects	End of steroid administration	1/2 teaspoon 3 times daily 1	1 teaspoon 3 times daily 1
Sleep disturbances	Bryophyllum 50 % Trituration	For sleep disturbances daily as required		1/2 teaspoon	1 teaspoon
Restlessness, anxiety	Bryophyllum 5 %	Waking phases after sedation, anesthesia, or bone marrow aspiration		5 ml as short- intravenous infusion	10 ml as short- intravenous infusion
Restlessness, anxiety	Aurum valeriana comp. Globuli	Before procedures such as lumbar puncture, bone marrow aspiration, and anesthesia		Up to 5 globuli every 2 h	Up to 10 globuli every 2 h
Restlessness, emotional instability	Solum oil	Examination of very anxious children <i>As required, best at bedtime</i>		Rub oil into individual body parts (e.g., extremities, back) As required, ideally in the evening	

evaluation must address not only questions of efficacy but also questions of adverse effects and interactions with conventional medication.

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Clare O'Callaghan and Trygve Aasgaard

## Contents

<b>5.1 Arts Therapies</b> .....	45
5.1.1 Visual Art Therapies .....	47
5.1.2 Music Therapy .....	48
5.1.3 Legacy Work .....	54
5.1.4 Contraindications .....	54
<b>References</b> .....	55

## 5.1 Arts Therapies

The concept “arts therapies” includes the individual therapies of drama, art, music, dance, and poetry. “Expressive arts therapy”/“creative arts therapy” is an intermodal discipline whereby the therapist and client move freely between drawing, music making, writing, art creation, movement, and talking. Each form of therapy has unique properties and inherent differences. While expressive therapies, as a rule, include both non-verbal and verbal elements, focus on artistic activities gives clients opportunities to express themselves without words (Malchiodi 2005). This can be especially important for children having trouble using words to describe feelings, which is common for those under eight or nine, particularly if traumatized (Carey 2006).

Children with serious life-threatening illnesses will make sense of their experiences with their available resources and, even when not communicating, can think or worry about their situation (Aasgaard and Edwards 1999). When overwhelmed or distressed, they may find it difficult to talk about their feelings or lack the developmental capacity to verbalize them. It is vital for children to have the opportunity to deal with feelings and thoughts related to arduous cancer illness and treatment experiences. This chapter introduces art therapies in pediatric oncology. Following a description of the use of visual art modalities, music therapy will be highlighted because numerous pediatric

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oncology music therapists are now employed, including in Norway, Australia, USA, Germany, and Sweden.

It is important to remember that a general presence of the arts in pediatric oncology is important, just as it is in children's daily lives. Children normally sing, play, or draw, and, when very sick and hospitalized, they need opportunities to continue being creative and artistic without the "therapy" tag being attached! Hence, artistic expression by young cancer patients should continue to be encouraged by family, friends, and staff caregivers. This chapter, however, will focus on the use of visual art and music with a trained therapist, to extend children's capacity to understand and deal with life-threatening conditions and, in some cases, coping among their family members.

Arts therapists are often university trained. This may encompass bachelors training in one of the arts modalities. Alternately, one may train in an arts modality or health profession as an undergraduate and then receive postgraduate training in arts therapy at masters or Ph.D. levels. National registration bodies exist in some countries for various arts therapies. For example, in 1999, the art, drama, and music therapy professions became state registered in Great Britain. In Australia, arts therapy (including art making, drama, and movement) and music therapy have separate professional associations and registration procedures (AMTA n.d.; ANZATA 2009).

Arts therapies are widely described as complementary therapies which are directed at enhancing physical, mental, and spiritual well-being. In cancer and palliative care, art therapies allow less verbally skilled children to more comfortably express fears and concerns through metaphorical representations of their experiences (Breitbart et al. 2004). They can offer an experience of self-understanding which eludes verbal definition but which finds expression in creative form (Ryan 2009). Arts therapies may also provide avenues whereby children develop psychological insights (Breitbart et al 2004), feel safe talking about them, and be a means of emotional and physical release. Furthermore, art therapies can provide accessible and enjoyable modalities which alleviate stress during adverse diagnostic

and treatment procedures and during the unpleasant routines of daily hospital life. This can be especially important for bedbound patients who would otherwise be very active and for those with cognitive and physical impairments.

Previous dominance of experimental methods, and concern that children expressing opinions was distressing and consequently ethically unsound, has resulted in a paucity of research examining children's perspectives (Greig et al. 2007). The 2004 Children's Act in England and Wales and the 2007 Australian National Statement on Ethical Conduct in Research Involving Humans indicate that research is, however, essential to advancing young people's well-being, and appropriate research methods are vital (Greig et al. 2007; NHMRC, 2007). The scant research examining art therapies in pediatric oncology is mostly found in music therapy, which will be discussed later. More of the visual arts therapy research is found in adult palliative care, an overview of which is elsewhere (Wood 2010). Interdisciplinary projects are common.

Quantitative, qualitative, and mixed methods research have been used to examine art therapies in pediatric oncology, and, arguably, all approaches can provide important and logically (or conceptually) generalizable insights into their effects on children's subjective experiences. This means that findings from studies in well-described contexts can provide insight into what comparable (art therapy) interventions may offer comparative populations (Kitto et al. 2008; Popay et al. 1998). Randomized controlled trials (RCTs) are often regarded as providing high-quality predictive evidence; however, when examining subjective outcomes on non-blinded research participants, including those receiving art therapy interventions, the evidence obtained may not be of high quality (see Table 5.1). Furthermore, it is arguably unethical to withhold offering potentially supportive care to people with life-threatening conditions assigned to nonexperimental group conditions in trials (Keeley, 1999). Arguably qualitative research, which examines participants' subjective experiences, is more aligned with the principle of patient-and-family-centered care (Kvåle and Bondevik 2008).

**Table 5.1** Factors which may reduce the quality of arts therapy RCT findings on subjective outcomes in non-blinded participants

Art therapies are not standardized treatments. Therapists tailor their approach according to assessed needs
Patient and therapist relationships are associated with therapeutic gain (Kain et al. 2004)
Finding representative samples with even distribution of confounders in treatment groups is difficult in people with life-threatening conditions because of variations in patients, including diagnoses, medications, and backgrounds
RCTs include standardized measurement scales which may provide information important to the researcher but not necessarily the patient (McGrath 2000)

## 5.1.1 Visual Art Therapies

### 5.1.1.1 General Aims

A general aim of art therapy (also called *arts therapy*) is to improve and enhance physical, mental, and emotional well-being of individuals of all ages. It encompasses the use of art materials (e.g., pictures, sculpture, sand), drama, movement, and music in a supportive therapeutic relationship with a trained therapist (Wood 2010). The creative process, which underpins therapeutic change, is more important than the artistic product. Art therapy works by accessing imagination and creativity and may contribute to increased self-awareness and acceptance, including recognition of the individual's abilities. The American Cancer Society (2008) promotes "art therapy" for children on their website:

Artwork may also be used as a diagnostic tool, particularly with children, who often have trouble talking about painful events or emotions. Art therapists say that often children can express difficult emotions or relay information about traumatic times in their lives more easily through drawings than through conventional therapy.

Art therapy can involve individuals or groups, and preexisting artistic skills are not needed for involvement.

### 5.1.1.2 Practice Examples

Various art therapy practices have been described by Tracy Councill (1999). Councill uses art-based assessments in evaluating how children are coping with their cancer. She adapted a "bridge drawing" tool (from Hays and Lyons 1981) for use with children from 6 years to adults, to help each client express how she or he has overcome obstacles and can link two periods of life:

The child is instructed to 'draw a bridge going from one place to another'. With an older child, the

therapist may also ask the child to depict going from past to future and placing oneself on the bridge, offering an opportunity for expressing concerns at times of transition. After the drawing is completed, the therapist may wish to consider any or all of the following characteristics: direction of travel, placement of self, places on each side of the bridge, solidity of bridge attachments, emphasis by elaboration, bridge construction, type of bridge, matter under the bridge, vantage point of the viewer, axis of the paper, consistency of gestalt, and, of course, the child's associations to the drawing. (Councill op.cit.p. 80)

Councill illustrated this technique in a case presentation of a young teenage boy with leukemia. Previous to his cancer diagnosis, "Mike" had a complicated social and personal history including depressive symptoms and bizarre behavior. Throughout cancer treatment, he was involved with art therapy and demonstrated artistic talent in pictures which expressed threat, fear, and suicidal ideation. Mike, however, did not make any "self-destructive gestures" following these drawings. Councill suggested that the drawings, which Mike said were about his impending bone marrow procedure, indicated that Mike felt threatened by the procedure. Although the leukemic disease was successfully treated, Mike then developed neurological disturbances related to a post-traumatic stress disorder. Mike was invited to make a bridge – drawing to express "how he bridged the gap between the period of his cancer treatment, his life at present, and the hopes for the future (ibid p.87)." In Mike's drawing, the left part of the bridge was full of holes and broken boards. The middle section appeared solid, but the bridge ended abruptly, leaving the right quarter of the page completely blank. The drawing was believed to illustrate Mike's shaky past, relatively safe and solid presence, but unknown and perhaps nonexistent future.

Favara-Scacco (2005) described art therapy in a pediatric oncology unit in Catania (Italy) where



the children's families are also included in ongoing therapy, including during the terminal phase. The author's therapeutic repertoire contains puppetry, storytelling and dramatization, drawing, the making of paper-trees, etc. Favara-Scacco (2005) stated that:

the child is given the opportunity to choose, to express his will about which creative activity to undertake and which materials to use. But he is also given a chance to say 'no' to something within the hospital setting. Decision making facilitates children's capacity to maintain their identity, helping them feel more in control. (p. 121)

### 5.1.1.3 Research

Art therapy within pediatric care is mostly described in relation to children with psychiatric and educational difficulties, where outcome research has been conducted (Gilroy 2006). Nonetheless, its presence in pediatric oncology is emerging. In a qualitative study, 32 children with leukemia, aged 2–14 years, received art therapy before, during, and after bone marrow aspiration and lumbar puncture procedures. Sessions consisted of coping-related clinical dialogues, visual imagination to activate alternative thought processes, medical play to offer control over “threatening reality,” and both structured and free drawings to contain anxiety and to externalize confusion and fears. During and after the art therapy program, the children exhibited less resistance and anxiety and more collaborative behavior. Their parents also reported their belief that the children were better able to manage the painful procedures when involved in the program (Favara-Scacco et al. 2001).

Rollins (2005) conducted an international study on drawing as a communication tool for children (between 7 and 18 years) with cancer. Participants were 11 children from the United States and 11 from the United Kingdom. The study had three foci: (a) to explore and compare the nature of stressors of everyday life and disease that children with cancer in the United States and the United Kingdom experience, (b) to explore and compare the coping measures they use to manage these stressors, and (c) to examine the use of drawing to enhance communication. Quantitative and qualitative methods were used within a grounded

theory approach and included drawing to accompany the traditional grounded theory methods of interview and observation. Findings indicated that the children, regardless of their ethnicity and other cultural components, responded to the childhood cancer experience in a similar manner: Their use of drawing enhanced nonverbal and/or verbal communication through the “campfire effect.” This means that the children seemed more comfortable interacting with each other when their attention was focused on another activity. Rollins (2005) also suggested that pediatric nurses learn to facilitate drawing among young cancer patients, to help the children communicate with others.

## 5.1.2 Music Therapy

### 5.1.2.1 General Aims

Music Therapy is the clinical and evidence-based use of music interventions to accomplish individualized goals (physical, emotional, cognitive and social) within a therapeutic relationship .... Through musical involvement in the therapeutic context, clients' abilities are strengthened and transferred to other areas of their lives. Music therapy also provides avenues for communication that can be helpful to those who find it difficult to express themselves in words. (AMTA 1999)

Music therapists have received extensive university training in music therapy methods, performance skills, music history and theory, psychotherapeutic theories, counseling techniques, and biopsychosocial knowledge. Through working as multidisciplinary team members, music therapists endeavor to promote holistic patient care. Music therapists assist people dealing with arduous illnesses and treatments through creative music involvement. Participants do not need any music background, and the focus is on the creative process rather than musical outcomes (O'Callaghan 2010).

### 5.1.2.2 Aims of Music Therapy in Pediatric Oncology

#### Why Is Music Important?

Music is a central part of how most young people engage with their inner and outer worlds. Infants' babbling and cooing with significant people is



**Table 5.2** Music therapy aims for pediatric oncology patients

Opportunities for playful “normality” even when severely unwell or incapacitated (Aasgaard 2002)
Alleviation of distress during diagnostic and treatment procedures such as radiotherapy (Barry et al. 2010; O’Callaghan et al. 2007)
Alleviation of uncomfortable and distressing physical symptoms (Standley and Hanser 1995)
Support endurance through rehabilitation interventions (Standley and Hanser 1995)
Enhanced communication, including with family members, friends, and staff caregivers (Davieson and Kennelly 2000)
Enabling the child’s sense of being heard and known which can transduce into creative self-awareness and strength (O’Callaghan et al. 2007)
Increased self-esteem through successful music-based achievements
Increased feelings of autonomy and coping (Robb 2000)

musical and used to explore and culturally adapt in their environments (Neelly 2007). Most American children between the ages of 2 and 18 years old use media, which includes music, for at least seven hours each day (Penn and Clarke 2008). In two US ethnographic studies, music’s meaning for “healthy” children aged 4–12 (Campbell 1998) or 13 (Crafts et al. 1993) years old was examined through observations and interviews. Through the imagery and moods that music elicited, children related to their worlds. Music also carried culturally transmitted values from family members, friends, teachers, and others they came into contact with. Music reflected what the children believed and helped with communication, safely expressing emotions, releasing kinesthetic energy (Campbell 1998), and enabling solitude and social interaction (Crafts et al. 1993). Research interviews with pediatric cancer patients and their parents also revealed how the children’s personal music usage and music-based interactions with family and friends helps to “normalize” and promote the children’s resilience when dealing with cancer (O’Callaghan and Jordan 2011). It therefore makes sense to offer music as a therapeutic modality to children diagnosed with cancer, to help them deal with tests, treatments, life “after cancer,” or the end of life.

This section describes the role of music therapy in pediatric oncology, focusing on styles of working with individuals and groups, including family members and staff. Through helping pediatric caregivers, children also benefit. Related research is also outlined.

### How Music Therapists Practice

Almost two decades ago, Barbara Griessmaier and Wolfgang Bossinger (1994) produced a pioneer text on music therapy in pediatric oncology. This comprehensive description illustrated how music therapists gradually become integrated in the daily life of the hospital ward and develop versatile practices within a framework of specific hygienic measures and strict regimens of treatment and care. Focus on pediatric oncology and end-of-life care has continued in the music therapy literature, especially over the past decade. When normal outlets for expression are disrupted through illness and hospitalizations, music therapy can be a vehicle for children to creatively express their feelings, concerns, and questions and further understand their experiences (Aasgaard and Edwards 1999). Developmental, neurological, educational, and psychological perspectives inform music therapy programs directed at addressing children’s vulnerabilities and promoting more adaptive and enjoyable lives. Music therapists assess the child’s vulnerabilities and strengths before and during sessions and offer techniques including song writing, music improvisation, therapeutic music lessons, relaxation, live performance, and singing (Aasgaard 2002, 2004, 2005; Dun 2007; O’Callaghan et al. 2007). Sessions often include families in inpatient (Aasgaard 2004) and outpatient settings (Dun 2007; O’Callaghan et al. 2007) in individual and group sessions. Further music therapy aims in pediatric oncology include those listed in Table 5.2. Music therapists tailor their approach to the child’s (and perhaps family’s) assessed

need, developmental level, and interests, as illustrated in the following sections.

### 5.1.2.3 Practice Examples

#### Focus on the Family

Infants, that is, preschoolers, need responsive and sensitive caregiving by parents or guardians to develop a sense of security and ongoing emotional health (Ainsworth 1985). When parents are so distressed by the infant's cancer diagnosis and need for treatments, parents may find it difficult to be emotionally available to the infant. As so much effort goes into keeping children alive during cancer treatment, opportunities for playful and "normal" exchanges between parents and infants reduce, further rendering the infant vulnerable. The infant's neurobiological responses to trauma may also affect their emotional and social functioning (Perry et al. 1995). Professionals need to assist healthy family connectedness wherever possible (Boog and Tester 2008). Music therapists can assist this through helping the infants, parents, and siblings to musically sing and play together. When an infant-parent dyad is unable to engage, because of the difficult cancer treatment experience, the therapist may be able to bring fun, play, and creativity to the child, reigniting the child's own playfulness and, possibly, the parent and infant's shared play through role modeling (Thomson Salo and Paul 2004).

Beth Dun (2007) describes her role as a "bricoleur" at the Royal Children's Hospital in Melbourne, Australia: one who "joins children (and parents) on their journeys ... (being) in the moment with them meeting their immediate and emerging needs, ... throughout that journey and creating possibilities (Dun 2007, p. 1)." She described how she helped a mother reassure and support her 5-year-old daughter who was waiting for a bone marrow transplantation. As the daughter huddled into her mother, Dun sang well-known songs and the mother began to rock her back and forth. Eventually, the young cancer patient took an interest in Dun's duck castanets and started to smile and musically interact with her mother.

At the Norwegian National Hospital, Oslo, music therapists often initiate musical activities

with the young cancer patient and parents (at times also with visiting brothers or sisters) during the very first days of hospitalization. The word "therapy" is not emphasized, but the families are told that the music therapist may assist them if they want to make and record songs, learn to play (better) various instruments, or simply want to spend some time making music together. Parents of children with leukemia often say they appreciate the continuous resource-oriented cooperation with the music therapist during the many inevitable scheduled (and unscheduled) periods of treatment (Aasgaard 2004). The music therapist may also provide songbooks, CDs, and instruments (or encourage families to bring "their own music") to the sickroom.

Catherine Sweeny-Brown (2005) illustrated how a music therapist can also support the parent-infant dyad, when the child has advanced illness, through her work with James who became blind when 9 months old because of a tumor. Toward the end of his life, when 4-year-old, James was irritable and in severe pain but relaxed and slept for short periods when the parents held him, while Catherine sang or played the flute.

#### Music Therapy Related to Aversive Treatment Procedures and Symptoms

Children with cancer can feel anxious, isolated, pain, fear, embarrassment, and experience disrupted development (Hilliard 2006; Kazak and Baxt 2007) when exposed to possibly frightening hospital environments and aggressive, sometimes painful, treatments (Kazak and Baxt 2007). Music therapy may promote endurance and resilience as they try to cope. A radiation therapist, David Willis, established a closed-circuit television (CCTV) system in a radiation bunker at Peter MacCallum Cancer Centre (Peter Mac), Australia; music therapists have played music for children during treatment, alleviating their anxiety so that sometimes anticipated anesthesia is not needed. Diagnosed with ependymoma, four-year-old Laura experienced adverse reactions to some anesthetic agents and cried for hours after radiation planning and initial treatment. After watching the music therapist, Pip Barry, or her mother via the CCTV, however,

Laura tolerated treatment without anesthesia or sedation and, her mother said, Laura's confidence increased (Willis and Barry 2010). O'Callaghan et al. (2007) also described music therapy in Peter Mac's pediatric radiotherapy waiting area. In two case studies of children who had head and neck tumors, an 11-year-old girl and 13-year-old boy, music therapy arguably reduced pain, anxiety, and gastrointestinal symptoms. Their radiation oncologist believed that this enabled reductions in analgesia for both patients and reduced steroids for the girl. Staff also said that it took less time to prepare the calmer boy for radiotherapy treatment. Music therapy methods used included therapeutic music lessons, music improvisation, and song writing, and family members were also involved (O'Callaghan et al. 2007). Song writing also helped a nine-year-old boy with a medulla glioblastoma deal with chemotherapy-related hair loss when he laughed and created the lyrics, "It falls out on the (billiard) table and makes the game unfair," for his song (O'Callaghan 2005, p. 122).

As a rule, music therapists work in close cooperation with medical staff and nurses when the task is to alleviate unpleasant symptoms related to sickness or treatment (procedures). Ærø and Aasgaard (in press) discuss potential explanations of why a musical activity may facilitate an unpleasant procedure. Point of departure is a situation related to the daily management of a central venous catheter (CVC). A one-year-old boy was loudly protesting against the nurse's attempts to change an adhesive tape securing the right position of the CVC. The screaming and constantly turning and twisting infant made this quite simple procedure difficult to perform correctly, and the mother's cautious strokes did not seem to help. A music therapist in the ward was being asked to assist; she positioned herself at the side of the bed and started playing a little lyre while she sang a familiar children's song. The boy stopped crying, his body seemed to relax, and he stretched his right arm to touch the strings. The nurse attended to the CVC, and the music therapist presented a little castanet frog who started "talking" to the boy. The boy had started smiling and was responding verbally while checking if his mother also

saw the frog. The procedure then came to an end. It seemed to become a rather pleasant experience for the patient – and the adults standing beside. If we *assume* that the music therapy intervention made a temporary positive change (a more "happy" and relaxed young patient), we still do not know for sure *what* component in the intervention caused the change. It could have been the actual instrumental and human sounds, the form of the instruments, the chosen song, or a combination of these elements. And what happened? Did the music-related elements, first of all, *disconnect* the boy from what was going on during the procedure, or did the boy *connect* his mental and bodily attention to new, pleasant stimuli? Did the musical intervention also influence the nurse and the mother in some way which the child could notice? These questions are provided to show the potential complexity of a music therapy intervention and the problem of understanding "music" as a single variable.

### Music in the Pediatric Ward Environment

When a pediatric hospital (ward) explicitly includes a "healing" or "therapeutic" environment in its overall policy for treatment and care, musical concerts and activities may be presented as a major social and aesthetic element. Organizations like *Musique et santé* and *Arts in Health* act as a link between health institutions, music therapists, and musicians, many from professional orchestras. In the United Kingdom, the Royal Liverpool Philharmonic Orchestra (Liverpool Philharmonic: Backstage: Musician in Residence 2011) has a "musician in residence" program across various health institutions, including periods at the cancer ward of one of Europe's largest children's hospitals, Alder Hey.

Music therapists in cancer care do not always work with individual patients but may also be involved with groups of children in music-related activities in the open spaces (halls, corridors) of the hospital (Aasgaard 1999, 2004) or with internal TV productions (Dun 1999). Twice weekly, musical events take place at the entrance of the pediatric oncology ward at the Norwegian National Hospital. Patients, relatives, medical doctors, and nurses have a sing-along and perform music for

those who might want to watch and listen. Often patients' own created songs are presented, at times with the child-songwriter as soloist (Aasgaard 2005). Radiation staff have also reported that witnessing and talking with children about their music therapy involvement can be a "happy and positive" experience (Barry et al. 2010, p. 252). Music therapy's presence in pediatric oncology can clearly improve the quality of staff caregivers' work life.

### Music Therapy in Pediatric End-of-Life Care

Music therapy has become an integrated part in several palliative care and hospice programs for children. This emerging field of practices and related research is also given particular attention in the literature (Aasgaard and Edwards 1999; Daveson and Kennelly 2000; Hilliard 2003, 2006; Pavlicevic 2005; Knapp et al. 2009; Lindenfelser et al. 2008). Pavlicevic (2005) presents the particular role of music therapists in pediatric hospices:

What you read in this book are stories of children singing and playing music in their own way. They are facilitated by music therapists whose special skill is to invite and support children's breathing, their movements, the quality of their stillness or restlessness, their vocal sounds and their music making, no matter how unconventional or idiosyncratic, and no matter how minute. Music therapists know how to listen and to create great beauty, intimacy and magic ... and the feeling of being heard. (p. 16)

Some hospices also provide care for terminally ill children in their own homes. Hilliard (2003) underlined the necessity of an interdisciplinary approach when illustrating how music therapy treats the psychosocial, physical, and spiritual needs of terminally ill pediatric patients in home hospice care. Music therapy referrals enabled two girls with brain cancer, 10 and 14 years old, to share positive and "normal" type musical interactions with their families. As one of the girls cognitively deteriorated, and her siblings had trouble finding ways of interacting with her, the music therapist helped the siblings to write songs and observed the children smiling as they sang them to their sister before she died (Hilliard 2003).

Involvement in musical activities offers children opportunities to preserve and express "normal" and healthy parts of themselves. Furthermore, many children with life-limiting illnesses appreciate, even if only temporarily, the chance of expanding their role repertoire, from that of a *homo patiens* who suffers and patiently accepts his fate, to a creatively expressive and socially interactive being. When the young patient becomes more or less permanently bedbound, the music therapist may still have a repertoire of activities to nurture fantasy and pleasant experiences. Children often preserve their sense of humor, even at times when they otherwise are challenged by fatigue and various unpleasant symptoms. One nine-year-old girl liked to perform "naughty" versions of well-known songs as long as she was able to speak. Some children – otherwise severely marked by end-stage illness – clearly appreciate taking part (some way or another) in song games or recording sessions (Aasgaard 2001).

Singing or listening to a familiar song or melody can foster security and strengthen bonds between those present. The music therapist often supports interplay of musical acts between patient, family, and professional carers. When death is imminent, singing can be a complement to talking, sometimes a substitute, or a deeply meaningful way of communication on its own. The music therapist can accompany, sing, or play with or for the patient or family. Daveson and Kennelly (2000) described family-centered music therapy whereby a 12-year-old boy with end-stage cancer was in an intensive care unit. His younger brother chose songs, including "I'll say a little prayer for you" and "How do I live without you," to be sung at the patient's bedside. After the younger brother described their shared memories, he took his dying brother's hand and said, "I bet you enjoyed that."

#### 5.1.2.4 Research

Table 5.3 outlines research on music therapy's effects on children hospitalized with cancer or receiving palliative care, illustrating how studies encompass quantitative, qualitative, or both (mixed) quantitative and qualitative designs. Quantitative research into music therapy's effects

**Table 5.3** Music therapy research in pediatric oncology and palliative care<sup>a</sup>

Author/year	Approach	N/ages	Music exp	Findings
Pfaff et al. (1989)	Repeated measures Self-report face scales; OSBD	6 pts; 7–15	Music relaxation	No significance in pain, distress, and fear but positive trends
Robb (2000)	Crossover Affective face scale self-report measure; behavioral observations	10 pts; 4–11	MV cf other conditions	Music therapy produced significantly higher supportive environmental elements and engaging behaviors (unsustained) than reading and standard conditions
Barrera et al. (2002)	PP FACES children self-report; Play PS parent rating; satisfaction questionnaires (open-ended for children and likert for parents and staff with comments added)	65 pts; 0.5–17	MV	Significant improvements in children's feeling ratings and parents' play performance ratings for preschoolers and adolescents; positive well-being comments
Robb et al. (2003a, b)	Descriptive case study and RCT; PP CDI, STAI (children); lyric analysis (inductive) including inter-raters; semi-structured survey	6 pts; 9–17	SW and video production cf game	Described how depression and anxiety varies with treatment stage; anxiety dropped in 3 music and 1 control condition; both conditions improved mood; lyrics included coping, positive physical status, family support
Aasgaard (2002, 2005)	Interpretive naturalistic inquiry. Maximum variation sampling. 19 songs' lyrics and histories thematically analyzed	5 pts; 4–15	SW	Meaningful aspects in song-life histories: expression, pleasure, achievement. Lyric themes: hospital world, cancer experiences and themes not related to sickness, included nonsense verses
Amadoru et al. (2007) (palliative)	Phenomenology Open-ended interviews	4 staff	MV	MT helps children in hospices and their families to communicate and express feelings and emotions
Lindenfels et al. (2008) (palliative)	Phenomenological interviews and analysis	7 <sup>b</sup> bereaved parents of <13	MV	MT altered child's and family's perception of their adverse situation; promoted remembrance and communication
Robb et al. (2008)	Non-randomized; repeated measures; Behavioral coding by observers	83 pts; 4–7	ML; cf AM; cf audio story	Active music engagement group: significant higher coping and initiation behaviors and positive facial affects
Barry et al. (2010)	Mixed methods. RCT including Kidcope and semi-structures questionnaires and interviews	11 pts; 6–13 and 22 staff and 11 parents	MT CD creation before and listened during RT	Qualitative data indicated that MT CD creation was a developmentally fun and engaging intervention which helped children to cope with radiotherapy; however, findings on Kidcope questions were insignificant between groups
O'Callaghan et al. (2011, in press)	Constructivist. Grounded theory methodology. Semi-structured interviews with children and parents. Focus group with music therapists	26 pts; 3–14 and 28 parents and 4 music therapists	MV	MT often (but not always) alleviated children's distress. The positive effects could transfer into children's home lives and vicariously support families as parents model therapists' behaviors

<sup>a</sup>Based on Tables 2–4 in O'Callaghan (2009)

<sup>b</sup>The seven children of these parents had brain tumors (5) or chronic conditions (2)

*Outcome Measure (Inventories) Abbreviations:* CDI Children's Depression Inventory, Kidcope Kidcope measurement tool, OSBD Observational Scale of Behavioral Distress, STAI Stait-Trait Anxiety Inventory

*General Abbreviations:* AM active music making by patients, Exp experience, Cf compared to, ML music listening, MT music therapy, MV variety of music therapy techniques, PP (pre-post method) patient exposed to one treatment; outcome measured twice, Pts patients, RCT randomized controlled trial, RT radiotherapy, SW song writing



indicated that children displayed or experienced improved mood (Barrera 2002; Robb and Ebberts 2003a), engagement with others (Robb 2000), and coping and initiation behaviors (Robb 2008). These studies involved rating scales, pre-post evaluations, and research trials. Qualitative research examines patients' experiences through inviting the patients, their family members, and/or staff caregivers to describe music therapy's role in the children's lives. While an earlier review on pediatric oncology research also included program descriptions and case studies under the "qualitative research" header (Hilliard 2006), qualitative research in music therapy now commonly depicts systematic research processes. In pediatric oncology, these include (a) a grounded theory study which found that music therapy often alleviates children's distress and that parents could role model music therapists' behaviors to help their children through cancer treatment (O'Callaghan et al. 2011, *in press*), (b) phenomenology studies which found that parents perceived that music therapy positively altered their (now deceased) children's perception of their illness experience (Lindenfelser et al. 2008) and that pediatric hospice staff perceived that music therapy helped parent-child communication (Amadoru and McFerran 2007), and (c) lyric analyses of pediatric oncology patients' song writing which suggested that the children feel supported (Robb and Ebberts 2003b) and experience pleasure and achievement (Aasgaard 2002, 2005) when engaged in the songwriting process. Finally, mixed methods research is intended to provide a better understanding of a research phenomenon than if one dataset is used alone (Creswell and Plano Clark 2007). A small mixed methods study found that music therapy CD creation supports children through radiotherapy treatment through creating a playful and engaging therapeutic context (Barry et al. 2010), despite insignificant differences between the intervention and control group on a coping scale.

### 5.1.3 Legacy Work

Legacies include both physical items and memories which help to validate a life and support adaptation (Coyle 2006) and creative living

(Boog and Tester 2008) until people die. At the end of life, children may find the experience of creating a parting gift a helpful way of affirming their own life (Daverson and Kennelly 2000). The bereaved can also be supported in their grief through legacies which become cherished and comforting reminders of the lost person (Boog and Tester 2008). Focus on helping people to create legacies at the end of life has mostly involved adult care (Allen et al. 2008; Boog and Tester 2008; Chochinov 2002; Coyle 2006; O'Callaghan et al. 2009); however, cherished reminders of children who have died are also important to foster. Positive memories of music therapy sessions shared with dying children supported parents' positive remembrance of them when bereaved (Lindenfelser et al. 2008). Children's song compositions, which may include their singing voices, and art creations could also become important mementos for parents and families. In the authors' songwriting work with dying children, the children are invited to record their singing and musical compositions, or make sound effects and play instruments, so that they can hear themselves in the performances, and hopefully feel a greater sense of "ownership" and pride. These audible mementos can become important connections for the bereaved if the children sadly die. Preloss (also called "pre-bereavement") care, such as helping dying patients to share meaningful experiences with those who will mourn their loss, can support the bereaved following the patients' deaths (Magill 2009; Reid et al. 2006). More research on this form of care is needed across the lifespan to support all who grieve, especially parents and siblings of children who die.

### 5.1.4 Contraindications

As long as children have a choice about their involvement in arts therapies, it is unlikely that there would be any adverse effects. One needs to ensure that children are given opportunities to experience a sense of success and mastery, and arts therapists are trained to help children participate to the maximum level of their abilities and to help compensate for their developmental or illness-related vulnerabilities as needed. For

example, to support creative efforts, a child with word-finding difficulties related to neural involvement may be given “yes/no” and multiple-choice questions [e.g., Would you like to write a song? (If yes) Would you like to write a song about the hospital or you?] for their song writing, rather than open-ended invitations (e.g., “What kind of song would you like to write today?”). It is important to be aware, however, that children with neural involvement may be more sensitive to noise. Also, using favorite music to help children through adverse procedures may sometimes trigger adverse memories when it is heard after treatment (O’Callaghan et al. 2011). Benefits gained from using such music may need to be weighed against this possible outcome. Children with physical impairment may also find it frustrating to be involved in creating art and music when they feel their “performance” is unsatisfactory, including if they have previously played musical instruments at proficient levels. While some may refuse involvement in the therapy, others may participate when the activity is offered as an enjoyable way of doing physical exercise.

### Conclusion

Art therapies can help children and their families cope with the often distressing hospitalizations and treatments needed when children are diagnosed with cancer. Familiar art and musical modalities may comfort when children are frightened. Creative and often nonverbal endeavors within a therapeutic relationship can also allow children to symbolically express apprehension, fear, uncertainty, frustration, and anger, as well as experience fun. Through witnessing, “mirroring” (copying), and extending (offering new artistic visual and musical ideas), therapists convey that children are known for their healthy identity, alongside illness experience. Children can develop insight, improved self-esteem, and increased capacity for self-soothing as they feel “heard” and validated, master new meaningful skills, and accomplish therapeutic products (artworks, song compositions on CDs, etc.). Parents, siblings, friends, and staff may also engage in the creative therapeutic processes, which can help them deal with the

cancer’s effects, and also find ways of supporting and having “normal” type relationships with the children.

Research demonstrates that children and parents often want, are grateful for, and satisfied with music therapy services for the children in oncology (O’Callaghan et al. 2011) and palliative care (Knapp et al. 2009) contexts. It is likely that visual arts therapies are regarded in a comparable manner. Developments in DVD creation for therapeutic purposes with young cancer patients (Robb and Ebberts 2003a), such as involving children in producing educational videos and souvenir movies about their radiotherapy treatments (Willis and Tongs 2009), suggest that art therapy modalities are evolving in pediatric oncology, propelled by staff committed to supporting children and their families through potentially devastating challenges associated with life-threatening illness. Managers of pediatric oncology and palliative care services are urged to include creative arts therapists in their treatment teams, to support and improve the life quality of children with cancer and their families, and to also allow legacies to comfort the bereaved if the children sadly die.

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Birthe Repenning, Tim Schütze, and Alfred Längler

## Contents

<b>6.1</b>	<b>Introduction</b> .....	59	<b>6.5</b>	<b>Homeopathic Practice in Pediatric Hemato-Oncology</b> .....	67
<b>6.2</b>	<b>History and Methodology</b> .....	60	6.5.1	Constitutional treatment.....	67
<b>6.3</b>	<b>Use of Homeopathy and CAM in Pediatric Hemato-Oncology Worldwide</b> .....	62	6.5.2	Symptomatic treatment.....	68
6.3.1	Europe.....	63	6.5.3	Dilutions and Dosing.....	69
6.3.2	North America.....	63	<b>6.6</b>	<b>Adverse Effects of Chemotherapy</b> .....	69
6.3.3	Middle East.....	63	6.6.1	CINV.....	69
6.3.4	Asia.....	63	6.6.2	Constipation.....	70
6.3.5	Circumstances of CAM use.....	63	6.6.3	Stomatitis.....	71
<b>6.4</b>	<b>Overview of Homeopathic Research</b> .....	64	6.6.4	Fever.....	71
6.4.1	Efficacy of Homeopathy in General.....	64	6.6.5	Anxiety and Aggressivity.....	71
6.4.2	Efficacy of Homeopathy in Hemato-Oncology.....	66	6.6.6	Support During Chemotherapy.....	72
			6.6.7	Stabilization in Chemotherapy-Free Intervals.....	72
			<b>6.7</b>	<b>Adverse Effects of Radiotherapy</b> .....	72
			<b>6.8</b>	<b>Adverse Effects of Surgery/Medical Interventions</b> .....	72
			<b>6.9</b>	<b>Cancer-Related Pain</b> .....	73
			<b>6.10</b>	<b>Palliative Homeopathic Treatment</b> .....	73
			6.10.1	Incurable Disease and Terminal Illness.....	73
			6.10.2	Terminal Care.....	74
			<b>6.11</b>	<b>Perspectives</b> .....	74
			<b>References</b> .....		75

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## 6.1 Introduction

Homeopathy is a 200-year-old holistic medical system that mobilizes the organism's self-healing powers. It falls into the category of complementary and alternative medicine (CAM).

The German physician C.F. Samuel Hahnemann discovered homeopathy in 1796 and continued to

develop its basic principles in the subsequent years. He saw disease as the result of a disruption in the vital force, the name he gave to the life force inherent in all mental and bodily functions. Homeopathic treatment is based on the law of similars (“*similia similibus curentur*”) meaning that a substance that is able to provoke symptoms in a healthy person can cure the same symptoms in an ill person when administered in highly diluted form.

Homeopathic remedies essentially originate from plants, minerals, and animal substances, which undergo a defined preparation process of serial dilution and succussion called potentization. The choice of the appropriate remedy is made on the basis of a thorough history and matches the characteristics of the patient and the remedy. The treatment can be symptomatic or constitutional.

Conventional treatment in pediatric hematology has made remarkable progress in the last 20 years in terms of survival rates and supportive therapy. Nevertheless, adjunctive homeopathic treatment among pediatric cancer patients is common. Usage rates worldwide are inconsistent. A great deal of research has been done on different forms of homeopathy, and different study types have been employed to assess its clinical efficacy. There are few studies investigating the effect of homeopathic treatment in adult hematology, and even fewer have been conducted in children. Altogether, the current scientific literature is promising, but the evidence is not entirely convincing. However, in practice, complementary homeopathic therapy appears to help diminish treatment-induced adverse effects and strengthen the overall condition of the cancerous child, thus possibly contributing to the healing process.

In the following chapters, we will begin with a short history of the origins of homeopathy, followed by a description of the basic principles of homeopathic theory and the process of potentization of homeopathic remedies. After this, we will present an outline of homeopathy and CAM use in pediatric hematology worldwide and an overview of homeopathic research.

Finally, we provide practical suggestions for use of homeopathic medicines in pediatric hematology, detailing indications for constitu-

tional treatment and for symptomatic treatment of adverse effects of chemotherapy, radiotherapy, and surgery, treatment of cancer-related symptoms and for use in palliative situations.

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## 6.2 History and Methodology

The Greek origins of the word homeopathy are *hómoios*, meaning similar, and *páthos*, meaning suffering or disease. Over 2,400 years ago, Hippocrates first expressed the idea of like curing like, but never developed it further.

Dr. C. F. Samuel Hahnemann (1755–1843), a German pharmacist and physician, introduced homeopathy in 1796. Frustrated by medical practice in those days (bloodletting procedures, syphilis treatment by quicksilver, etc.), which produced only moderate healing effects but often severe side effects, he had stopped practicing his medical profession some years ago. Mastering seven languages, he supported his family by translating chemical works and thereby discovered the principles of homeopathy in the laws of nature.

At that time, malaria was conventionally treated by cinchona bark. Hahnemann translated a medical essay by the Scottish physician and chemist William Cullen into German and found himself skeptical of a theory concerning the properties of cinchona bark. He decided on a self-experiment: he ingested cinchona bark twice a day and after each ingestion experienced for 2 or 3 h periodic fever and other symptoms that were similar to malaria symptoms. This led him to postulate that healing in fact occurred through similarity, calling this hypothesis the law of similars (“*similia similibus curentur*”: like cures like). In other words, he believed that the presenting symptoms of a sick person could be cured by the same substance that would cause similar symptoms in a healthy person. Subsequently, Hahnemann further explored what was later to become the fundamental principle of homeopathy. He conducted innumerable experiments on himself and other healthy persons and meticulously documented his findings.

The process of systematically testing a substance on healthy human beings and observing the symptoms elicited by this substance is called remedy proving. Remedy provings are still part

of fundamental homeopathic research and serve to explore the characteristics of new or poorly known remedies. They are ideally conducted in a double-blind setting. The remedy is administered repeatedly to healthy participants, for example, once a day, mostly in a 30C dilution. Depending on individual sensitivity, each participant will subsequently present several, varying physical, emotional, and mental symptoms which are all part of the totality of the remedy profile. The collection of all symptoms that emerge at the same time gives us the symptoms which are potentially curable by the same homeopathic remedy in diseased patients. The listing of all available remedy profiles can be found in books called *Materia Medica*. Today, homeopathy has some two to four thousand remedies, whereas in Hahnemann's day, it was about a hundred. Some of them have a very wide spectrum of symptoms and are frequently indicated in daily practice; they are called polychrests (calcium carbonicum, lycopodium, natrum muriaticum, nux vomica, phosphorus, sepia, sulfur, and several others). Hahnemann also created the first so-called repertory, an index of symptoms listing the respective remedies associated with each symptom. These repertories are still regularly and critically revised today.

Hahnemann resumed his medical practice and began treating his patients with homeopathic dilutions of the previously explored substances. He would, for example, administer one or several doses of highly diluted Belladonna to a child presenting a sudden high fever with a swollen red and steaming face, wide pupils, a rash of the body, maybe confusion, or even febrile convulsions.

To minimize side effects, he further experimented on the dosage and dilution of the administered remedies, concluding that a combination of serial dilution and succussion of the substance led to a profile of the respective plant, mineral, or animal remedy with the greatest effect and least side effects. This special process of preparation is called dynamization or potentization.

The most commonly employed potencies today are the C (centesimal, dilution 1:100) and Q potencies (quintamillesimal, dilution 1:50,000), sometimes D potencies (decimal, dilution 1:10), the number after the letter indicating the number of dilution series conducted.

To produce a 3C dilution, for instance, several steps have to be taken: for plant and animal remedies, firstly, a mother tincture has to be prepared. The respective substance, for example, one or all parts of a plant or animal, is dissolved in a mixture of alcohol and water. This tincture is left to stand for 2–4 weeks, during which time the preparation is shaken occasionally and is then strained. Mineral remedies must be finely ground before further preparation. Subsequently, the substance is diluted to one part in 100, that is, one drop of the mother tincture in 100 drops of alcoholic solution, followed by vigorous shaking by ten hard strikes against an elastic body (succussion) or, for insoluble solids, one part to 100 parts of lactose followed by grinding for 1 h in a mortar (trituration). This gives a 1C dilution. To obtain a 2C dilution, one part of this solution is diluted in a further hundred parts of solvent with subsequent shaking or grinding, and then again, one part of the resulting solution is diluted by a factor of one hundred to obtain a 3C dilution. The result is one part of the original substance in 1,000,000 parts of the solution. Dilutions following the quintamillesimal scale, produced from a 3C dilution, are diluted in a ratio of 1:50,000 parts and require 100 succussions at each dilution step.

According to the Avogadro constant, from a dilution of 24D or 12C (reaching a dilution ratio of  $1:10^{24}$ ) onward, the remedy statistically contains less than one molecule of the substance present in the mother tincture.

Homeopaths assume that this process of serial dilution and succussion leads to transfer of the information and energy of the specific substance to its supporting medium. Moreover, Hahnemann observed that the higher the dilution of the homeopathic remedy, the stronger its effect becomes and the longer the effect lasts.

Over several decades, Hahnemann recorded his theoretical and methodological findings in the *Organon of the Art of Healing*, later entitled the *Organon of Medicine*. The work was constantly revised and six editions were published, the last one long after his death.

Hahnemann described what he called the vital force, the life force which perpetuates vital harmony in our organism. While defining acute



disease in the same manner as it is commonly described today, he developed his own concept of chronic disease. Convinced that the vital force in each of us could not overcome chronic illness on its own, he described three miasms which he regarded as the underlying cause of chronic disease: psora (scabies), sycosis (gonorrhea), and syphilis. Today, homeopathy has many different streams in many parts of the world, and other miasms, such as the tubercular or the cancer miasm, have been described.

In classical homeopathy, the remedy is chosen on the basis of the law of similars, and apart from exceptional cases, only one remedy is prescribed at a time. The ambition, in particular for chronic illness, is to find a constitutional remedy for the patient, that is, a remedy acting on a profound level that is able to lead the patient back to his<sup>1</sup> inner balance and restore his health to a remarkable degree. Several constitutionally acting remedies, sometimes following each other or alternating during the course of the treatment, can bring a benefit for the patient. With this procedure, it is necessary to exactly judge the organism's reactions to one remedy at a time, which is impossible once several remedies are involved. Ideally, a remedy which seems to really fit the patient on all levels and is able step by step to heal his affections can eventually be found; this remedy is called the *similimum*.

In the case of acute or intercurrent illness, the *similimum* may help if it has been found earlier. Also, symptoms emerging in acute illness can provide clues that help to find a constitutional remedy.

Otherwise it may be necessary to prescribe a different individual remedy matching the acute symptoms, especially the modalities (i.e., the aggravating or ameliorating factors of a symptom), accompanying factors such as thirst or fear, or the causing factor, for example, in an epidemic or in the case of symptoms occurring on account of an anticancer treatment.

Two patients with the same diagnosis, for example, stomatitis, would probably get different homeopathic remedies: One patient will describe splinter pain and excessive salivation; another patient will be complaining of burning pain and asking for cold drinks or ice cream.

Nevertheless, there is such a thing as what homeopaths call proved indications. For example, for headache or lumbar pain following a lumbar puncture, most practitioners will prescribe *Ledum palustre* in the first instance. One can say that in this case, the impact of the cause of the condition overrides any need to individualize the treatment, which will still have to be done subsequently in the few percent of cases where *Ledum* fails to cure the complaints.

In complex remedy homeopathy, several remedies or fixed combinations of remedies are prescribed at a time, for example, a mixture of several remedies for sore throat or hay fever. These preparations are undoubtedly less effective than a well-chosen single remedy, but can have their justification, for example, when there is lack of time or when symptoms do not draw a clear picture of a single remedy.

Isopathy means prescribing Vincristinum for a patient receiving a vincristine-containing chemotherapy, for example, or cisplatin for a patient receiving a cisplatin-containing chemotherapy, to alleviate possible or confirmed side effects. In classical homeopathy, this approach is neglected in favor of the search for a remedy acting on a deeper level, unless maybe a patient reacts in an extremely unfortunate manner to one or the other substance, developing a multitude of side effects (Geißler and Quak 2005; Hahnemann 1842).

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### 6.3 Use of Homeopathy and CAM in Pediatric Hemato-Oncology Worldwide

The use of complementary and alternative medicine (CAM) and, in particular, homeopathy in pediatric hemato-oncology is quite well documented for Europe and North America, but less so elsewhere.

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<sup>1</sup>To avoid the cumbersome repeated use of “he/she”, “he or she”, “his or her” etc., the pronouns “he”, “his”, etc., are used inclusively and should be understood as referring to both genders.

### 6.3.1 Europe

Especially in Europe, homeopathic treatment in pediatric hemato-oncology is widespread. According to available publications from Germany, the Netherlands, France, Italy, Great Britain, and Turkey, CAM usage rates vary from 12 % (Italy) to 49 % (Turkey) (Clerici et al. 2009; Grootenhuis et al. 1998; Gözümler et al. 2007; Johannessen et al. 2008; Längler et al. 2005; 2007, 2008; Molassiotis and Cubbin 2004; Molassiotis et al. 2005; Simon et al. 2007). The largest population-based study on the prevalence of CAM usage in pediatric oncology in Germany, published by Längler et al. in 2008 and analyzing questionnaires from 1063 families, reports an overall CAM usage rate of 35 %, of whom 45 % used homeopathy (Längler et al. 2007, 2008). In the surveys from the Netherlands and Italy, homeopathy accounts for the largest proportion of CAM use in pediatric hemato-oncology (Clerici et al. 2009; Grootenhuis et al. 1998). In Great Britain, homeopathy use amounts to 6 %.

### 6.3.2 North America

In North America, the percentage of children with malignancies using homeopathic remedies varies from 1 to 25 %, according to data from Canada, the United States, and Mexico.

Mexico shows the highest usage rate of CAM with 70 % of 110 families questioned in a survey in 2005 reporting CAM usage, of whom 25 % reported the use of homeopathic medicine (Gomez-Martinez et al. 2007).

A large-scale, retrospective, population-based study in Canada investigated the usage rates of complementary and alternative treatments among 366 pediatric cancer patients in 1998, reporting CAM use by 42 % and homeopathy use by 17 % (Fernandez et al. 1998).

In 1997, a survey in the United States about CAM use was conducted in a small cohort of 81 pediatric oncology patients: 65 % of the children were using CAM methods, of whom only 1 % reported usage of homeopathic medicine. Two other surveys of comparable size conducted in

the USA in 2001 and 2003 report CAM usage rates of 41 and 73 %, respectively, without any use of homeopathy worth mentioning (Friedman et al. 1997; McCurdy et al. 2003; Neuhausner et al. 2001).

### 6.3.3 Middle East

One study was found describing the usage rate of homeopathy among pediatric oncology patients in Haifa, Israel: a cross-sectional descriptive study conducted in 100 pediatric oncology patients in 2003 showed that 61 % had used complementary and alternative treatments, including up to 28 % who had used homeopathy (Weyl Ben Arush et al. 2006).

### 6.3.4 Asia

According to two studies conducted among pediatric oncology patients in Taiwan in 2000 and in Malaysia in 2009, there are high rates of CAM use among pediatric oncology patients in Asia, ranging between 73 and 85 %, but no significant use of homeopathic remedies was observed (Hamidah et al. 2009; Yeh et al. 2000).

### 6.3.5 Circumstances of CAM use

Parental reasons given for using homeopathy as a complement to conventional anticancer treatment are physical stabilization, strengthening of the immune system, improving the tolerability of the conventional treatment, detoxification, and relaxation (Kruse 2005; Längler et al. 2005, 2007, 2011). Homeopathy has been observed to reduce use of antiemetics and analgesics in pediatric hemato-oncology and to lead to better mental stability of the patients and other family members (Pichler 2007a) while notable patient satisfaction has been reported for adult homeopathy users in general (Marian et al. 2008).

A significant number of CAM users do not inform their oncologists about the complementary treatment, but rather act on their own initiative



**Table 6.1** Systematic reviews on the efficacy of homeopathic medicines (selection)

Reference	Homeopathic treatment	Health condition	No. of trials	Conclusion
Hill (1990)	All	All	40	(+)
Kleijnen (1990)	All	All	105	(+)
Walach (1997)	All	All	41	(-)
Linde (1997)	All	All	89	(+)
Cucherat (2000)	All	All	17	+
Milani (2002)	All	All	127	+
Mathie (2003)	All	All	93	(+)
Dean (2004)	All	All	205	(+)
Shang (2005)	All	All	110	-

Reviews with a general scope (Lüdtke 2009)

+ = positive, (+) = tentative positive, 0 = inconclusive, (-) = tentative negative, - = negative

(Clerici et al. 2009; Längler et al. 2007). In most cases, parents have had prior experience of using homeopathy in their children before administering it for the child's cancer. According to the aforementioned study from Germany, 94 % of homeopathy users would recommend this therapy to other parents with a comparably sick child (Längler et al. 2011).

## 6.4 Overview of Homeopathic Research

In general, a great deal of research has been done on different types of homeopathy and different study types have been employed to assess its clinical efficacy. Besides this, basic research on the mechanism of action of homeopathy can be found.

There are few studies investigating the effect of homeopathic treatment in hemato-oncology, and these almost exclusively involve adults. Except for one study discussing homeopathic treatment of chemotherapy-induced stomatitis in children and young adults, no pediatric homeopathic trials addressing either symptomatic treatment of cancer symptoms or treatment-induced side effects or constitutional treatment exist.

However, some more or less detailed pediatric case reports can be found.

Homeopathic remedy provings, even if atypical for the scientific world, represent another

important component of homeopathic research (see above).

### 6.4.1 Efficacy of Homeopathy in General

#### 6.4.1.1 Meta-analysis

Since 1990, at least ten systematic reviews on homeopathy have been published, each setting up slightly different quality criteria for inclusion and covering between 17 and 205 trials. Most of them found some degree of superiority of homeopathy over placebo; almost all of them conclude that homeopathy has to be investigated further to yield more distinct results (Table 6.1).

#### 6.4.1.2 Randomized Controlled Trials

Several studies on specific clinical questions have been conducted in children as follows:

##### Postoperative Pain and Agitation

In 1990, Alibeu conducted a study demonstrating the effectiveness of Aconite 4C for relief of postoperative pain and agitation, with 95 % positive results in a population of 50 children presenting typical symptoms for the remedy (Alibeu and Jobert 1990).

##### Diarrhea

In 2003, Jacobs published the combined results and meta-analysis of three clinical trials dealing

with individualized homeopathic treatment for childhood diarrhea, showing a statistically significant advantage of homeopathy over placebo (duration of diarrhea 3.3 versus 4.1 days) (Jacobs et al. 2003). Interestingly, when the same author reconducted a similar study using a homeopathic combination remedy containing the five most frequent homeopathic remedies for childhood diarrhea in 2006, no significant results could be obtained (Jacobs et al. 2006).

### Acute Otitis Media

Three trials exist showing benefits of homeopathic treatment for acute otitis media (AOM): Jacobs et al. found trends toward better efficacy of homeopathic treatment over placebo in a trial conducted on 75 children aged 18 months to 6 years in 2001, with a significant improvement of subjective symptoms (Jacobs et al. 2001). Friese et al. compared homeopathic and conventional treatment in 131 children aged 6 months to 11 years and found a significant advantage of the homeopathic therapy with regard to pain duration and number of relapses over 1 year (Friese et al. 1997). In 2001, Frei and Thurneysen administered a first individualized homeopathic treatment to 230 children with AOM and judged pain control after 12 h and after 18 h with a second homeopathic remedy, finding resolution rates 2.4 times faster than in placebo controls (39 and 72 %, respectively) (Frei and Thurneysen 2001a).

### ADHD

In 2001, Frei and Thurneysen conducted a study on 115 patients aged 3–17 years with a Conners Global Index (CGI) of 14 or higher, showing homeopathy to be a valuable alternative to methylphenidate for children, particularly preschoolers, affected by attention deficit hyperactivity disorder (ADHD) (Frei and Thurneysen 2001b).

#### 6.4.1.3 Prospective Observational Studies

##### Acute Respiratory Infections

In 2001, Riley et al. compared homeopathic and conventional treatment for upper and lower respira-

tory complaints in a multicenter outcome study with 465 children and found homeopathy at least as effective, with better recovery and less side effects in the homeopathy group (Riley et al. 2001).

##### Chronic Illness

Witt et al. published the results of an observational study in 103 homeopathic primary care practices in Germany and Switzerland, assessing the health status of 3,709 chronically ill patients (including 819 children) after 8 years of homeopathic treatment. The most frequent diagnoses in adults were allergic rhinitis and headache, and in children, atopic dermatitis and multiple recurrent infections. Results showed significant improvement of health scores (complaint severity, physical, and mental quality of life) after 2 and 8 years compared to baseline scores (Witt et al. 2008).

##### Overall Mortality

A comparative observational study published in 2011 by Kooremann and Baars showed that patients cared for by GPs with additional CAM training (homeopathy, anthroposophic medicine, or acupuncture) had 0–30 % lower healthcare costs and mortality rates, depending on age groups and type of CAM (Kooreman and Baars 2011).

##### Disabled Children

In 1993, Riley et al. found a convincing effect of individualized homeopathic treatment on the impetus and behavior of 40 handicapped children in a prospective trial (Riley et al. 1993).

#### 6.4.1.4 Basic Research

Lenger et al. found magnetic photons to be responsible for the active mechanism in homeopathic remedies in 2006 (Lenger et al. 2008).

Frenkel et al. recently demonstrated biological activity of ultra-diluted homeopathic remedies, showing cytotoxic effects of *Carcinosinum* 30C, *Thuja* 30C, *Conium* 3C, and *Phytolacca* 200C on two human breast adenocarcinoma cell lines (MCF-7 and MDA-MB-231) in vitro (Frenkel et al. 2010).

## 6.4.2 Efficacy of Homeopathy in Hemato-Oncology

### 6.4.2.1 Randomized Controlled Trials (RCTs)

In 2009, a Cochrane review assessed eight controlled trials (RCTs, seven placebo-controlled and one compared to an active treatment), dealing with homeopathic treatment for adverse effects of chemotherapy (3), radiotherapy (3), and menopausal symptoms associated with breast cancer treatment (2) (Kassab et al. 2009). Two studies with a low risk of bias showed a benefit of the homeopathic treatment:

One study conducted in 2001 by Oberbaum et al. demonstrated superiority of Traumeel S® (a complex homeopathic remedy containing extracts of *Arnica montana*, *Calendula officinalis*, *Achillea millefolium*, *Chamomilla recutita*, *Symphytum officinale*, *Atropa belladonna*, *Aconitum napellus*, *Bellis perennis*, *Hypericum perforatum*, *Echinacea angustifolia*, *Echinacea purpurea*, *Hamamelis virginiana*, *Mercurius solubilis*, and *Hepar sulfuris*) as a mouthwash over placebo for chemotherapy-induced stomatitis in children and young adults (32 patients aged 3–25) undergoing stem cell transplantation, with significant reduction of severity and duration of stomatitis (Oberbaum et al. 2001).

The second study published in 2004 by Pommier et al. and including 254 participants demonstrated superiority of topical undiluted *Calendula officinalis* over trolamine (Biafine®) for prevention of grade 2 or higher acute dermatitis during irradiation for breast cancer (41 % vs. 63 %), accompanied by less frequent interruption of radiotherapy, as well as significant reduction of radiation-induced pain (Pommier et al. 2004).

Two other studies with an unclear risk of bias reported positive results:

Balzarini et al. examined the effect of *Belladonna 7C* and *X-ray 15C* on skin reactions (breast skin color, warmth, swelling, and pigmentation) during and after radiotherapy for breast cancer in 66 patients. While during irradiation, there was a nonsignificant trend toward better efficacy of the homeopathic treatment compared to placebo; in the recovery phase, the active

treatment showed a statistically significant benefit with particular effectiveness on the heat of the skin (Balzarini et al. 2000).

Jacobs et al. set up a small study looking at homeopathic treatment for menopausal symptoms in breast cancer survivors over 1 year, finding no significant effect of homeopathic treatment on severity and frequency of hot flushes (only an initial positive trend in the single remedy group), but a significant improvement of general health scores in the single remedy and in the combination remedy group (Jacobs et al. 2005).

The remaining four studies reported negative results (Kassab et al. 2009). Serious adverse effects or interactions attributable to the homeopathic medicines have not been reported.

### 6.4.2.2 Prospective Observational Studies

Rostock et al. conducted an observational cohort study in adult cancer patients in 2011, finding significant improvement of quality of life at 3 and 12 months and a trend toward improvement of fatigue syndrome in the group treated complementarily by homeopathy, although matched pairs with patients of the same tumor entity and comparable diagnosis could hardly be formed, and thus, direct comparison was not possible (Rostock et al. 2011).

### 6.4.2.3 Case Reports

Pichler and Takács give detailed case reports of a 4- and 8-year-old boy with ALL, both receiving constitutional treatment as a complement to the conventional therapy with episodes of symptomatic treatment (Pichler 2007b; Leukämie et al. 2007).

In many countries such as India, Pakistan, and parts of South America, where an important part of the population does not have access to high quality conventional therapy, homeopathy and other CAM treatments have a long tradition and are provided affordably. Homeopathy is thus widely used even for severe pathologies. With the growing interest of the western world in treating severe pathologies by homeopathy, some case reports from these countries have been published in recent years: Ramakrishnan and Coulter (who

employ a method derived from classical homeopathy) give several case reports of children who were cured of their malignancies by homeopathy without or after failure of conventional treatment: 2 children with brain tumors (an 8-year-old boy with recurrent parietal grade III glioma and a 10-year-old boy with recurring grade II astrocytoma; cases 9 and 10), 3 children with leukemia (a 1 1/2-year-old girl with ALL, a 6-year-old boy with CML, and a 3-year-old boy with AML; cases 59, 60, and 62), and an adolescent with a 6-cm Ewing sarcoma of the left calf (case 96). Another case is described concerning a 6-year-old boy with AML who died in the 5th month of treatment (case 103) (Ramakrishnan and Coulter 2001).

In the United States, the NCI initiated a BCS (best case series) program, evaluating fourteen case records of completely regressed lung and esophageal carcinomas of adult patients treated by homeopathy according to Banerji's protocol. In four of these cases, diagnosis and radiographic responses were independently confirmed. These results have led to the conduct of an observational study (Banerji et al. 2008).

#### 6.4.2.4 Adverse Effects of Homeopathic Remedies

Adverse effects of homeopathic treatment are rare and occur on a different level than, for example, adverse effects of phytotherapeutic, that is, substantial treatment. This is due to the fact that in most of the dilutions employed, few or no molecules of the original substance are left. A complementary homeopathic treatment does not interfere with a conventional anticancer treatment, in particular, with chemotherapeutic drugs. Nevertheless, potential reactions to the homeopathic remedy can be misunderstood as side effects: for example, if in the course of a constitutional treatment a transient diarrhea or skin eruption is observed, in homeopathy this is seen as an elimination reaction of the organism in which disease is transferred from an interior to a more exterior level. Such a reaction is highly indicative of a good healing process.

Provided that the rules of homeopathy are respected, genuine adverse reactions are exceptional and are most likely to occur either in highly

oversensitive patients or in the sense of a remedy proving in consequence of repeated administration of a nonsuitable homeopathic remedy over weeks, months, or years (Geißler and Quak 2005; Hahnemann 1842). Publications uncritically judging all sorts of reactions, including treatment errors, as CAM side effects, and thus handicapping any serious CAM approach by serious CAM practitioners, have to be seriously questioned (Seifert et al. 2011).

## 6.5 Homeopathic Practice in Pediatric Hemato-Oncology

Today's results of conventional anticancer treatment in pediatric hemato-oncology in countries providing modern standards of treatment combining chemo-, radio-, operative, and biological therapy are convincing. However, about a third of the children remain uncured or relapse, and numerous side effects reduce their quality of life during and after treatment. Complementary homeopathic therapy can bring much additional benefit in the in- or outpatient setting, improving mental stability and the body's immune defenses and relieving cancer symptoms, as well as numerous symptoms due to side effects of conventional treatment.

A specific homeopathic treatment for cancer does not exist. Homeopathic treatment in pediatric hemato-oncology can be put into practice on different levels:

### 6.5.1 Constitutional treatment

A basic or so-called constitutional treatment in classical homeopathy acts on a profound level. It takes into account the personal constitutional profile of the child, that is, its symptoms on the physical, emotional, and mental level, and so helps to strengthen his overall condition. It may help to enhance immunologic competence, to preserve a better appetite, to increase mental stability, to encourage better tolerance of the conventional treatment, and in the long term, to prevent relapse. In fortunate cases, it may directly influence the cancer.

A homeopathic therapy on this level should begin as early as possible. To obtain a clear and unclouded picture of the symptoms, the history should ideally be taken before the onset of conventional treatment, that is, before a chemotherapy or radiation syndrome overlaps the cancer syndrome. To execute this treatment, a well-grounded training in classical homeopathy is required. For this reason, as well as because of the almost inexhaustible range of homeopathic remedies, the present description of constitutional therapy will concentrate only on its principles as well as some examples.

### 6.5.2 Symptomatic treatment

A symptomatically oriented treatment acts on a more superficial level. Acute disorders, that is, mostly side effects of the conventional anti-cancer treatment or cancer symptoms, can be influenced. Adverse effects of chemotherapy can be chemotherapy-induced nausea and vomiting (CINV) and loss of appetite, stomatitis, constipation, +/- intestinal obstruction, and neutropenic febrile episodes including sepsis, fatigue, insomnia, bad temper, aggressivity, and anxiety. Radiotherapy can cause radiodermatitis, digestive problems as well as fragilization of the irradiated zone in general and with regard to secondary tumors. Side effects of surgery include postoperative pain, wound healing, and innervation problems. Influenceable cancer symptoms are mainly pain and fatigue.

Homeopathic therapy on this level can be initiated instantly or subsequently and can be conducted by any person fully respecting the general rules of homeopathy.

Homeopathic constitutional therapy begins with a thorough history, taking into account all the child's symptoms from pregnancy, birth, infancy, and early childhood onwards and including nutrition, development, children's diseases, vaccinations, local organic symptoms, and current complaints including their modalities, eating habits, food and drink preferences, aversions and intolerance, bowel and bladder habits, perspiration, sleep, menstrual patterns and sexual life

(if of appropriate age), dreams, personal habits, emotional and mental symptoms, fears and desires, as well as a social and family history, and is completed by the physical examination of the child. The focus typically lies rather on individual symptoms than on pathognomonic symptoms of the disease.

Although it is always beneficial to know the constitutional background of the child and its family when initiating a homeopathic treatment in addition to a conventional therapy, a symptomatically oriented treatment can frequently be realized with much less time and effort. In some cases, several acute conditions emerging under conventional therapy will indicate the same remedy and so contribute to finding a constitutional remedy. If, for example, a child shows phosphorus symptoms for CINV, again phosphorus symptoms for stomatitis, and is in general rather anxious, demanding constant company and comfort, phosphorus might be the constitutional remedy.

Also, with the aim of encouraging the child's recovery and preventing relapse, a constitutional homeopathic treatment can still be initiated once the conventional therapy, maybe in combination with a symptomatically oriented homeopathic treatment, is finished and should in any case continue lifelong.

The best prognosis can be observed in cases in which the cancer symptoms, the symptoms associated with the conventional treatment and the constitutional symptoms the child presents, all point to the same homeopathic remedy. In all other cases, several remedies will be needed.

To treat acute, isolated symptoms of a child undergoing a conventional anticancer treatment, the homeopath nevertheless has to collect all the factors describing the present complaint or condition.

For a symptomatic CINV treatment, for example, the following circumstances must be explored: cause of the condition (chemo-/radiotherapy), time of onset and time of main complaints (day, night, morning, afternoon, etc.), description of the nature of nausea and vomiting (frequency, color, relief, or not after vomiting, relation to meals or drinks), thirst and appetite, food and

drink preferences (especially when altered since treatment onset), susceptibility to odors, noise, light, etc., modalities (cold/hot drinks or applications, lying down/moving, privacy/company, comfort, etc.), body temperature, humor, fears and other mental symptoms, appearance of the tongue, and any other concomitant factor since the onset of therapy-related complaints.

A symptomatic stomatitis treatment, as another example, requires information about the current state of the mucosa (aphthae, color, swelling; early or advanced grade), concomitant factors such as salivation, characteristics of the pain (burning, stinging, pulsatile), sensations such as dryness or warmth, food and drink preferences, modalities, and mental symptoms (weeping, irritability, desire for company, etc.), as well as any distant symptoms occurring at the same time (inflammation of the anus, changes in the urine) (Geißler and Quak 2005; Hahnemann 1842; Pfeiffer et al. 2004; Takács 2007; Wurster 2005).

### 6.5.3 Dilutions and Dosing

Complementary homeopathic treatment in pediatric hemato-oncology necessitates more frequent administration of the remedies than in treatment for other chronic illness. This is due to the fact that the organism has to face a strong influence from the cancerous condition on one hand and from the treatment on the other side. The dilutions employed depend on the level of treatment.

Acute disorders (side effects, cancer pain, etc.) will be treated with 6C, 12C, or 30C potencies. 6C dilutions are generally administered three times a day and 12C dilutions twice a day, while a 30C dilution is given once a day as long as the maintaining cause is present, that is, on each chemotherapy day, for example. In very acute conditions (pain, panic, intense nausea), a 30C potency can be dissolved in half a glass of tap water and one teaspoonful administered every 10 min after vigorous stirring, until amelioration is noticed. Q potencies can be used up to once daily depending on the clinical picture, when the remedy indicated is chosen mainly on the basis of mental symptoms and could potentially turn out to be a

constitutional remedy, such as *Arsenicum album*, *Phosphorus*, *Sulfur*, or other polycrest remedies.

Constitutional treatment accompanying a conventional anticancer treatment will mainly be conducted with daily Q potencies. In the long term, especially once conventional treatment is finished, higher C-potencies (30C, 200C, 1000C (= M), 10000C (= XM), etc., according to Kent's scale) given every few weeks or months only can be used.

The following chapters introduce the homeopathic remedies most often used in pediatric (and adult) hemato-oncology. We first describe remedies to diminish side effects of chemotherapy, radiotherapy, and surgery, then remedies used to influence cancer symptoms directly. Finally, we discuss the principles and practice of palliative homeopathic treatment.

Different homeopathic remedies cover different types of acute conditions or reactions expressed by the patient. For each remedy, several characteristics and modalities (> indicating amelioration by; < indicating aggravation by) are given.

However, the attending physician has to keep in mind that, in general, each patient will only present a few of the mentioned symptoms at a time (Czimmek 2007; Geißler and Quak 2005; Hahnemann 1842; Kruse 2005; Phatak 2004; Pfeiffer et al. 2004; Pichler 2007a, b; Takács 2007; Wurster 2005):

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## 6.6 Adverse Effects of Chemotherapy

### 6.6.1 CINV

- *Arsenicum album* (= arsenic) 30C (as required, stop when amelioration occurs) or Q  
*Arsenicum album* is a very important remedy for patients with malignancies. A patient requiring this remedy suffers from intense nausea, retching, and liverish or blackish vomiting, accompanied by dryness of the mouth and thirst, he will drink in small sips. He may have a burning pain in the abdomen or along the esophagus. Nervousness and restlessness



make him move constantly. He feels chilly, weak, and anxious, not wanting to stay on his own. Children demand their parents to stay close to them. Amelioration by external application of warmth and by warm drinks and food, aggravation often in the night between 1 and 3 o'clock.

- Cadmium sulfuratum 30C

This remedy has many similarities with Arsenicum album, but the patient is essentially not chilly but rather warm-blooded and less anxious. He demands cold water but immediately regurgitates it. The vomit is black like coffee grounds. The patient's nausea makes him lie quietly without moving. He can faint when getting up. His eyes are half-open when he sleeps.

- Phosphorus (= phosphorus) 12C, 30C (do not repeat frequently), or Q

Phosphorus is a very useful remedy for cancer patients who have a lot of fears and always want to be in company. The child wants to be in its parents' arms and cries for all possible reasons. Nausea and/or vomiting occur a few minutes after drinking or eating; the vomit is of yellowish color, can be painful or blood-tinged, and can be caused by putting the hands in warm water. The child has a strong demand for cold drinks or ice cream, which improve its stomach ache, and salty, sour, or savory food. Consolation and stroking bring relief. Phosphorus is also indicated in radiotherapy-induced and post-operative nausea and vomiting (see below).

- Nux vomica (= poison nut) 30C each day before chemotherapy

Nux vomica is the most common and best known remedy for nausea and vomiting including CINV. The patient has gastric spasms with loss of appetite and a bitter or putrid taste in the mouth. He is oversensitive to odors, sometimes to noise, music, or light. He may not be able to vomit but feels better after vomiting, rather being cold and having chills when taking his hands out from under the blanket. The child is in an irritable and impatient mood and wants to be left alone,

does not want to communicate. Accentuation early in the morning.

- Ipecacuanha (= ipecac) 30C (stop when amelioration occurs)

This patient suffers from destructive and permanent nausea and feels disgust for any food, not feeling relieved after vomiting. He has a remarkably clean tongue which is a keynote for Ipecacuanha. His face may be bluish. Aggravation in the warmth, by vomiting and bending down.

- Sepia (= cuttlefish) 30C

Dreadful nausea with feeling of emptiness in the stomach and vomiting of milky liquid may call for sepia. The patient has a desire for sour food. CINV is aggravated in the morning, by food odors and thinking of food and ameliorated by eating.

- Okoubaka (= African tree bark) 6D or 6C

Okoubaka is a remedy for intoxication in general and can help if the patient shows rather unspecific symptoms during chemotherapy.

- Tabacum (= tobacco) 30C

Severe nausea and vomiting in combination with weakness, paleness, icy chilliness, and intermittent pulse are characteristic for Tabacum. The abdomen is inflated and cold, but the patient does not want to have it covered.

- Sulfur (= brimstone) 30C or Q

Sulfur as a major remedy is indicated when the patient shows a rather optimistic and cheerful attitude despite his difficult situation and has increased appetite during the chemotherapy. CINV is accompanied by a feeling of hotness over the whole body. The patient is sensitive to odors and may have odor hallucinations.

- China (= cinchona bark) 30C

China, the substance which led Hahnemann to discover homeopathy, is needed in case of significant weakness following loss of bodily fluids, for example, vomiting and diarrhea (undigested, painless, weakening stools with much flatus). The patient presents cavernous eyes with dark circles around, throbbing in the head, and carotid arteries and aching limbs. < light touch, > fierce pressure.

Besides these remedies, other remedies can be useful if the patient presents characteristic and corresponding symptoms.

### 6.6.2 Constipation

- Nux vomica (= poison nut) 30C each day before chemotherapy  
Nux vomica can be useful in chronic constipation when the child easily produces side effects in reaction to administered conventional medication and shows the characteristic mental pattern of this remedy (see above).
- Opium 200C  
Opium can probably reduce the bowel inactivity induced by chemotherapy or opioids, or sometimes even help in case of (iatrogenic) intestinal obstruction or post-operative ileus.

### 6.6.3 Stomatitis

- Borax (= sodium borate) 6C  
Borax is often useful as a first remedy. The gingiva is swollen and florid with aphthae, a sensation of warmth and increased salivation. Irritable or anxious and jumpy child.
- Calendula (= marigold) 6C  
Incipient stomatitis with mucosa breaking open, uncharacteristic.
- Lachesis (= poison from Buschmeister snake) 12C  
Swollen purple gingiva, aphthae/ulcers, burning pain, and threatening sepsis are characteristics of Lachesis. The child cannot bear constriction or touch, < after sleep.
- Mercurius solubilis (= quicksilver) 12C  
Intense viscous salivating, the child cannot swallow its saliva, has bad breath, and purple, bleeding ulcers. The tongue is swollen and shows dental imprints and cervical lymph nodes are equally swollen and hard.
- Nitricum acidum (= nitric acid) 12C  
Extensive stomatitis with splinter pain and intense, maybe bloody salivating in combination with inflammation of the throat and anus,

and stinking urines suggests Nitricum acidum. The child is weak and irritable.

- Phosphorus 12C  
Easily bleeding gums, epistaxis, pain like fire in a weepy child asking for cold drinks and ice cream calls for phosphorus.
- Arsenicum album 30C  
Significant stomatitis with burning pain, > warmth or warm drinks, the child does not want to be alone.
- Euphorbia peplus (= wood spurge) 12C  
Very severe stomatitis.

### 6.6.4 Fever

- Aconitum (= monkshood) 30C  
Sudden and intense “dry” fever, rather without perspiration, often beginning in the night, accompanied by anxiety and restlessness, paleness of the face when sitting up.
- Belladonna (= deadly nightshade) 30C  
Intense fever with sweating, often beginning in the early afternoon, red and steamy face but cold hands and feet, usually with perspiration, widened pupils, pulsating pain, possible hallucinations, or even febrile convulsions.
- Pyrogenium (= putrefaction product) 30C  
Threatening or apparent sepsis, chills, temperature fluctuating quickly, high fever with low pulse or moderate fever with high pulse (discordant temperature and pulse).
- Ferrum phosphoricum 6C  
Moderate fever of gradual onset, face changing between pale and red, possible epistaxis, rather cheerful child.

### 6.6.5 Anxiety and Aggressivity

- Aconitum 30C  
Sudden and intense panic, often in the night around midnight, or anxiety and agitation following anesthesia, before medical interventions (change of dressing, lumbar puncture), the child is “out of control”.

- Arsenicum album 30C  
Generally “nervous” child, easily troubled and afraid, always wanting a parent to be there, but not necessarily needing physical contact. Anxiousness especially between midnight and 2 o’clock in the morning, with restlessness bringing the child out of bed, or fear of death.
- Nitricum acidum 30C  
Irritable and resentful, “corrosive”, taciturn, repulsing sympathy. Stomatitis.
- Stramonium (= thorn apple) 30C  
Aggressivity and delirium, hallucinations, nightly fears of darkness and animals.
- Pulsatilla (= pasque flower) 30C  
Easily weeping child, of rather fair complexion and blond or red hair, demanding consolation continuously.
- Ignatia (= ignatia bean) 30C  
Grief after troubling incident, sobbing child with trembling lower lip, exaggerated or almost hysterical reaction.

### 6.6.6 Support during Chemotherapy

In a more general manner, there are also remedies which can strengthen the child’s immune defenses, appetite, etc., during the chemotherapy, even if there are no specific symptoms to be observed, or during the chemotherapy-free intervals (see above for detailed description of the remedies that have already been mentioned).

- Okoubaka 6C  
“Detoxification”, system cleansing
- Nux vomica 30C  
Limitation of medication side effects
- Phosphorus 12C

### 6.6.7 Stabilization in Chemotherapy-Free Intervals

- Chininum arsenicosum 6C  
Loss of appetite, weakness, anxious attitude can boost leuko- and thrombopoiesis.
- Chininum sulfuricum 6C  
Loss of appetite, weakness, indifferent attitude, can boost leuko- and thrombopoiesis, especially indicated in case of tinnitus or deafness.

- Ferrum phosphoricum 6C
- Okoubaka 6C

## 6.7 Adverse Effects of Radiotherapy

- Phosphorus 30C (do not repeat often) or Q  
Most frequent remedy for (high frequency) radiation sequelae. The patient presents tickling cough, vertigo, a feeling of hotness in the whole body (especially between the shoulder blades and along the spine), diarrhea with undigested pieces or mucus, and audible bowel sounds. He longs for refreshing food, cold drinks, and ice cream. The child needs physical contact with its parents and frequently presents clairvoyant dreams.
- Radium bromatum 30C some hours before irradiation  
 $\alpha/\beta/\gamma$ -radiation. Complaints are ameliorated by warmth, hot bath and movement, and aggravated by rest. The patient suffers from pruritus of the skin with scaly eruptions, watery or bloody diarrhea, venectasia of the tongue, and radiation sickness with exhaustion and fatigue. He presents enhanced work enthusiasm (like Mme Curie) and may report clairvoyant dreams.
- X-Ray (= x-radiation) 30C before irradiation  
 $\gamma$ -radiation. Main complaints are burning of the skin after irradiation, cracked skin, especially on the palms of the hands and feet, radiogenic fibrosis, limited elasticity, improved by warmth. The patient suffers from drowsiness in the head, somnolence, headache, and paresthesia of the extremities. He feels as if magnetized or on adrenalin and expresses a desire to be alone. Motion aggravates.
- Silicea (= silica) 30C  
Appropriate remedy for sequelae of low frequency irradiation.
- Causticum (= caustic lime) 30C  
Burning after (x-)radiation, warts appearing within the irradiated area, constriction of muscles and tendons, burning and rawish sensation of the mucous membranes may indicate Causticum.  
Other potentially useful remedies: Fluoricum acidum, Strontium carbonicum, Cadmium

sulfuratum, Cobaltum nitricum, Kreosotum, Lachesis, Nux vomica, Sol.

For prevention of radiotherapy side effects, for example, accompanying a 6-week period of daily radiation, one dose of Radium bromatum 30C can be given once a week. Instead, preventive doses of Phosphorus 30C can be indicated if the typical mental symptoms are present.

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## 6.8 Adverse Effects of Surgery/ Medical Interventions

- Arnica 200C  
Arnica is a nonspecific injury remedy for sequelae of operations including pain, wound healing problems, extensive hematoma, etc.
- Staphysagria (= stavesacre, palmated larkspur) 30C or 200C  
Laceration/cutting damage can lead to healing problems curable by this remedy (e.g., cerebrospinal fluid leakage after brain surgery). Equally indicated in postoperative urinary retention (if occurring after catheterization, try Aconitum; if occurring in combination with postoperative hypomotility, try Opium).
- Hypericum (= St. John's wort) 200C  
Hypericum is a typical remedy for nerve damage with resulting darting pain, neuropathic pain, postoperative an- or hypesthesia, paralysis (incontinence).
- Ledum (= marsh tea, wild rosemary) 30C or 200C  
Ledum is an excellent remedy for treating post-lumbar puncture sequelae such as back pain, headache, vertigo, visual disorder. In case of failure, repertorization of the symptoms will indicate another remedy.

After an important surgical intervention, one dose of Arnica 200C can be given preventively, as well as one dose of Hypericum 200C 24–48 h later if the operation has been conducted in a very innervated area or if nerves have been damaged or even removed.

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## 6.9 Cancer-Related Pain

- Aconitum 30C or 200C dissolved (see below)

Aconitum is in order in case of sudden and intense pain, often in the night about midnight; the child is terrified, restless, “out of control”.

- Arsenicum album 30C or 200C dissolved  
An agonized, weak, and anxious child or adolescent, with a strained expression, burning pain accompanied by restlessness, not finding its position in bed, and fear of death driving it out of bed, calls for Arsenicum album. The patient complains of dryness of the mouth, drinks in little sips, and is critical and dictatorial, saying that medicine is useless. Exacerbation at nighttime (often after midnight or about 2 o'clock in the morning), > warmth, warm applications, hot bath.
- Belladonna 30C or 200C dissolved  
Belladonna is indicated in sudden intense pulsating or radiating pain, driving the patient mad, with heat, rash, and burning, heat of the head with rather cold extremities, widened pupils. > firm touch or pressure (child puts hands on the painful region), < light touch, slightest commotion.
- Chamomilla 30C or 200C dissolved  
Chamomilla is a minor remedy that can be useful for intense radiating neuropathic pain accompanied by restlessness and irritability.
- Nux vomica 200C  
Patients who have been taking analgesics for some time may develop a Nux vomica picture: the child or adolescent is restless, capricious, oversensitive to noise, light, odors, has a low pain tolerance, does not want to be touched, and criticizes everything and everyone.

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## 6.10 Palliative Homeopathic Treatment

### 6.10.1 Incurable Disease and Terminal Illness

Homeopathy can generally be effective at any moment of a disease. However, depending on the stage of disease, the approach of homeopathic treatment can be with curative or palliative intent.

Certain conditions entail a reduction of the vital force of the organism and have to be considered

incurable. In hemato-oncology, this concerns mainly patients presenting advanced cancers with missing or irreversible damage to/destruction of vital organs (liver, kidneys, lungs).

In these cases, homeopathic treatment can still be of valuable use, assuring a better physical and mental quality of life (e.g., better appetite, sleep, less pain) and sometimes being able to maintain the patient's fragile balance for a considerable period of time.

However, at this stage, several rules have to be respected, in order not to overburden the powers of the enfeebled organism:

Deeply acting constitutional remedies (in particular, antipsoric remedies) should be avoided or administered with great caution, as the organism may be too weak to build an adequate response, and consequently the vital force would be weakened even further. Instead, partially acting, often plant remedies can still improve several troubling symptoms. Suppression of minor peripheral complaints, in particular skin eruptions, should be avoided.

The most appropriate potencies to use are Q or 30C potencies. The 200C potency should only be employed dissolved in water, and even then very carefully. Higher potencies should be avoided for the reasons explained above.

### 6.10.2 Terminal Care

Homeopathic remedies can do astonishing services in terminal care situations dominated by pain and agony, often appeasing and allowing the patient to fall asleep calmly. The indicated remedy is preferably to be administered dissolved in water in hourly sips (vigorous stirring before each sip) as long as the condition persists.

- Antimonium tartaricum (= potassium antimonyl tartrate) 30C or 200C teaspoon-wise  
Remedy for death-rattle, audible from afar, with much mucus but little expectoration.
- Arsenicum album 200C teaspoon-wise  
Arsenicum album is the most useful remedy in terminal care; it can free the patient from his fear of death. The patient is restless, notably during the night, shows a pale, hippocratic face with anxiously wide-opened eyes, has

intense fear when being alone and wants someone to stay with him. He is chilly and asks for hot drinks (drinking in small sips), application of warmth or blankets (a similar patient who is hot and asking for cold drinks, application of cold and open windows may need Secale). Burning pain and bluish or blackish spots on the skin may appear.

- Carbo vegetabilis (= wood charcoal) 200C teaspoon-wise  
Carbo vegetabilis is in order for a patient desiring open windows and fanned fresh air, although his body is covered in cold sweat and his knees or lower legs are ice cold and bluish. He is lying still with an inflated abdomen and is afraid of suffocating.
- Lachesis 200C teaspoon-wise  
Indicated in choking fits which make the patient startle from his sleep or occur after drinking. He throws off the blanket and cannot bear constriction of the throat or abdomen, suffering from abundant sweats, hot flushes, and palpitations.
- Opium 30C or 200C teaspoon-wise  
Appropriate remedy for comatose patients with puffy expiration, open eyes and mouth, red face, almost happy facial expression. Respiration is discontinuous, the patient may be moaning or weeping in his sleep. Bladder palsy.
- Phosphorus Q or XM one single administration, repeat only exceptionally!  
Intense fear and weakness, the child seeking encouragement, massage, and the parent's hand call for phosphorus. Burning heat of skin and body with red mottled face, hectic fever, and longing for cold drinks. The patient may see things gray or with a green halo and may show bloody expectoration or diarrhea when coughing. He cannot lie on his right side.
- Rhus toxicodendron (= poison ivy) 200C teaspoon-wise  
Extreme restlessness but little or no fear (in contrast to Arsenicum album) is typical for Rhus toxicodendron.
- Tarentula cubensis (= cuban tarantula) 30C teaspoon-wise  
This remedy corresponds to agony in the last moments of life, with intense burning or

stabbing pain, death struggle, nervousness with constant motion of the feet, and hot sweats.

## 6.11 Perspectives

Scientific medicine has achieved indispensable progress in pediatric cancer therapy, however, with treatments entailing numerous adverse effects and thus significant loss of quality of life. Homeopathy can diminish these side effects and strengthen the overall condition of the child, and should be regarded as a respectable complementary therapy in pediatric hemato-oncology.

Further scientific research should be performed to promote and facilitate homeopathic practice as an integrative part of pediatric cancer care.

Homeopathy practitioners should be encouraged to practice responsibly and openly and to contribute to and participate in the scientific discussion. Hemato-oncologists should be encouraged to open their minds to appropriate complementary methods and to enter into an open and critical dialog with CAM-competent colleagues, in order to ensure qualified guidance and maximum well-being for each child and its family.

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Janice Post-White and Deborah Hughes Ndao

## Contents

<b>7.1 Theory/Background</b> .....	79
7.1.1 Cultural Considerations .....	80
<b>7.2 Research Overview</b> .....	81
7.2.1 Cognitive-Behavioral Therapies .....	81
7.2.2 Expressive Arts .....	86
7.2.3 Physical/Movement-Based Mind-Body Therapies .....	88
7.2.4 Sensory Therapies.....	90
7.2.5 Biofield Therapies (Energy, Circulation, Environment) .....	95
<b>7.3 Practice/Application</b> .....	96
<b>7.4 Open Questions</b> .....	100
<b>References</b> .....	101

## 7.1 Theory/Background

Mind-body therapies premiered in children with cancer in the 1980s when Dr. Leora Kuttner, a pediatric clinical psychologist in British Columbia, Canada, revolutionized acute pain management through her pioneering use of breathing strategies, bubble blowing, pop-up books, music, hypnosis, guided imagery, and medical play for children undergoing lumbar punctures, bone marrow aspirations, and chemotherapy. Dr. Kuttner believed that anxiety was a natural response by children in pain and that mind-body therapies helped the child “work through the fear to overcome the pain” (Kuttner 1985, 2010). Mind-body therapies are the only category of complementary and alternative medicine (CAM) that has been studied for its use in reducing the distress of procedure-related symptoms in pediatric oncology (Landier and Tse 2010). Today, mind-body therapies are often used in conjunction with conventional medical care to manage symptoms, reduce anxiety and distress, provide distraction, and offer therapeutic healing (Ladas et al. 2006; Rheingans 2007).

Anxiety and fear are universal responses to cancer. In a small study conducted in China, nearly all children had some degree of sadness and worry on admission to the hospital (Li et al. 2010). Pain, nausea, and insomnia often cluster together with anxiety. The advantage of mind-body therapies is their usefulness in addressing multiple symptoms triggered through emotion and stress-related responses.

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Children respond to different therapies, depending on age, developmental stage, personal preferences, and energy level. Parents sometimes choose mind-body therapies to allow choice and control in managing their family's health care (O'Keefe et al. 2009). In a large survey of CAM use among children and adolescents, more adolescents than young children used mind-body therapies (Birdee et al. 2010). CAM use was higher when the child had anxiety, distress, insomnia, or nausea/vomiting and when the parents were college educated or used CAM for themselves (Birdee et al. 2010). In cancer survivors, CAM is used similarly across ethnic groups, with some variation among subgroups (Hsiao et al. 2006). Biofeedback, yoga, and hypnosis were the most commonly selected therapies in 129 children with chronic pain; use of therapies correlated with greater interference with activities (Tsao et al. 2007). In children with cancer, mind-body therapy use ranked among the most commonly used integrative therapies for supportive care (Kelly 2009; Landier and Tse 2010; McLean and Kemper 2006). In a review of 25 studies of CAM use in pediatric cancer, mind-body therapies were used by 9–27 % of children in five studies ( $n=611$ ), and massage was used by 2–17 % of children in five other studies ( $n=779$ ) (Bishop et al. 2010).

Parents and siblings also benefit from the use of mind-body therapies. Posttraumatic stress was related to uncertainty and anxiety in parents (Santacroce 2002) and was reported to influence how children adjust emotionally as adults (Bernardon and Pernice-Duca 2010). Emotional attachment theory purports that parents may react to the overwhelming stress of having a child with cancer by responding impulsively and reactively, or through detachment, which does more to assuage their own emotional distress than to help their child feel secure or emotionally able to process the events. Interventions that help the family openly talk about their child's illness and their approach to care improve communication and reduce externalizing and internalizing symptoms in children (Bernardon and Pernice-Duca 2010). Cognitive-behavioral therapy, narrative family therapy, and journaling for the older child,

siblings, and parents, and drawing, music, drama, and telling stories in younger children, can help the family reframe the situation to emphasize survival, acceptance and understanding, and the perception of the cancer as a shared and conquerable event. Interventions that help center the parent emotionally promote responsiveness, warmth, active listening, and acceptance of the child's situation and fears, which facilitates resiliency.

Mind-body therapies also directly modify psychological and physiological stress responses. A complex network of neurohormones and cytokines respond to emotional states and influence behavior, neural and endocrine function, and immune processes of adaptation. This psychoneuroimmune model asserts that stressors lead to a stress response through psychological tension, which activates the sympathetic branch of the autonomic nervous system. Consistent with Antonovsky's salutogenic model of health (1979), mind-body therapies that help the family and child reframe the situation as controllable and manageable and perceive available support and resources can empower families to find meaning and make sense of the situation. Although the stressor itself cannot always be controlled, children and adults can modify their response to the stressor to better adapt to the situation. Mind-body therapies also help control symptoms by reducing reactive physiologic tension and can foster emotionally centered responses, decisions, and empathic and supportive communication and participation among family members. Mind-body therapies provide more than distraction and relaxation.

### 7.1.1 Cultural Considerations

Central to many cultures and whole medical systems, illness is often believed to manifest as a result of physical, emotional, spiritual, or psychological imbalance; mind-body healing is believed to restore balance to promote health and wellness. Mind-body therapies that can evoke a spiritual, mystical, or an existential experience, such as prayer, meditation, and dance, are often debated by CAM researchers as to whether or not

to be considered CAM due to potential associations with more formal and organized religious institutions. But these practices reflect fundamental mind-body health beliefs, whether religiously or spiritually based, that are often integral to patients and families' understanding of their or their child's diagnosis and symptoms. Because both religion and spirituality are significantly associated with the adjustment and management of symptoms among cancer patients (National Cancer Institute 2011), it is vital to consider these therapies in providing culturally appropriate patient care.

As an example, the Integrative Therapies Program for Children with Cancer (ITPCC) in the Division of Pediatric Oncology at Columbia University Medical Center, Morgan Stanley Children's Hospital of New York-Presbyterian, emphasizes culturally appropriate care among its diverse patient population by tailoring the delivery of integrative therapies. The ITPCC specializes in clinical care, research, and education and is dedicated to providing free integrative therapies and educational services to children with cancer and their families living through and beyond cancer treatment. Acknowledging patients' and families' reliance on spirituality and cultural practices, ITPCC strives to offer integrative therapies to both the patient and the caregiver that enhance spiritual well-being, such as mindfulness-based stress reduction, meditation, yoga, and expressive art therapies. On the other hand, for those families who may find biofield therapies to conflict with their religious and spiritual beliefs, these therapies are omitted from patient care.

Research has shown that families' choices about health care are often determined by illness characteristics, health beliefs, ethnicity, and the availability of biomedical and traditional medicine health-care providers (Goldman et al. 2002). In a recent survey among children with cancer in Guatemala, when asked about presenting symptoms at diagnosis and their causes, respondents frequently reported *susto* (fright) as the primary reason they or their child had an onset of symptoms (Ndao et al. 2009). Referred to as a culturally bound health problem, *susto* is regarded as a

Latin-American folk illness that is manifested by the stress response and is often treated with prayer, massage, or other relaxation techniques (Weller et al. 2008). Additionally, although not specific to mind-body therapies, perceptions about CAM among Chinese immigrant parents of children with cancer residing in Canada reveal strong health beliefs grounded in Chinese medicine and an understanding of yin-yang balance (Watt et al. 2011). As well, a descriptive study among African American, Somali, and Hmong children residing in the United States demonstrated that ethnicity influences a child's preference for essential oils, perhaps due to the familiarity of smells (Fitzgerald et al. 2010). These studies further demonstrate that with increasing migration and cultural diversity, the globalization of mind-body health beliefs is being introduced and disseminated in new ways.

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## 7.2 Research Overview

The use of specific therapies is determined by the child's interests and receptiveness, energy level, symptoms and indications/reasons for use, and developmental age/stage. Although studies evaluate singular therapies and specific outcomes, mind-body therapies often are used together to facilitate a whole system approach to healing. The goal of measuring outcomes of individual therapies is to determine the strength of the evidence (efficacy) and the risk-to-benefit ratio (safety). There are few studies specific to pediatric oncology, and many of the findings extrapolate evidence from studies in adult patients with cancer (Table 7.1).

### 7.2.1 Cognitive-Behavioral Therapies

Imagery, hypnosis, and meditation are cognitive mind-body therapies that involve a change in the perceptual awareness of the situation. Stress results when a situation is perceived as threatening, such as a painful procedure or separation from a parent. Cognitive mind-body therapies modify the child's perception of the event as

**Table 7.1** Mind-body therapies used in pediatric oncology

<i>Cognitive therapies</i>
Meditation, meditation-based relaxation response (MBSR)
Guided imagery, visualization, self-hypnosis, biofeedback
Humor
<i>Expressive therapies</i>
Expressive writing, narrative writing
Storytelling, support groups, counseling
Art, music
<i>Physical/kinesthetic therapies</i>
Dance, movement
Yoga, tai chi, Qigong
Feldenkrais
<i>Sensory therapies</i>
Aromatherapy
Bach flower remedies
Massage/touch, reflexology
<i>Biofield therapies</i>
Healing touch, therapeutic touch, Reiki
Magnetic therapy
Polarity therapy

manageable by allowing some control and mastery over the situation. The situation does not change, but the child learns that he can control how he responds to the stressful event. Parents can be taught how to coach the child, which empowers them with an active role in helping their child adapt to stressful situations and painful procedures (Christensen and Fatchett 2002).

### 7.2.1.1 Relaxation and Distraction

*Relaxation* and distraction are behavioral therapies often used in combination with cognitive therapies to decrease procedural pain, fear, and distress. Physically releasing tension reduces anxiety and pain and allows some control over fear and discomfort. Systematically tensing and then relaxing groups of muscles, such as in progressive muscle relaxation (PMR), demonstrates to the child how to let the tension go and shows him what relaxed muscles feel like and, because of the concentration it requires, distracts from painful or stressful external events. Attention is focused on controlled breathing, along with tensing and relaxing muscle groups, which reduces

sympathetic nervous system response. Distraction diverts the brain's awareness and processing of pain signals and prevents the related anxiety and fear that contributes to distress and pain perception (Bantick et al. 2002; Petrovic et al. 2000).

Relaxation has been shown in case studies and small pilot studies to reduce acute anxiety experienced by children during stressful procedures (Landier and Tse 2010). In adults with cancer, four studies established that PMR reduced pain and one study found that PMR eased sleep disturbances, although several other studies did not see significant improvement (Kwekkeboom et al. 2010). Hypnosis and imagery appear to be more effective than relaxation alone for reducing pain (Lasseter 2006) and anxiety and insomnia in children with cancer (Ladas et al. 2006).

*Distraction* focuses the attention away from the painful procedure and is particularly effective for young children (Landier and Tse 2010). A systematic Cochrane review of the efficacy of cognitive-behavioral strategies for managing needle-related pain and distress in children determined that distraction and hypnosis had the largest effect sizes for treatment improvement over control conditions (Uman et al. 2008). Eleven studies of distraction ( $N=682$ ) showed reductions in pain, and five studies of hypnosis ( $N=163$ ) showed reductions in pain and distress. In studies assessing mind-body interventions for symptom management in children with cancer, distraction was effective in reducing overall distress (Zeltzer et al. 1984) and chemotherapy-induced nausea and vomiting (Redd et al. 1987; Zeltzer et al. 1984, 1991).

Various distraction techniques are used in practice, including kaleidoscopes, virtual reality glasses, party blowers and bubbles, breathing and blowing techniques, pop-up books, and video-games. The specific type of distracter is not as important as the fit with the interest of the child or adolescent. Effective distracters should be age appropriate, actively engage the child to interfere with perceptions of pain or distress, and enjoyable, in order to refocus attention away from the procedure.

In a randomized study of 50 children and adolescents with cancer undergoing port access or



venipuncture, self-selected distraction was used as an adjunct to topical anesthetic, and was more effective than topical anesthetic alone in reducing fear and distress, but not self-reported pain (Windich-Biermeier et al. 2007). Children ages 5–18 could choose between an *I Spy* book, bubbles, and vibration/acoustic music that could be heard and felt through the table, virtual reality glasses, or a videogame. The majority of children (72 %) chose the Gameboy Advance®. The authors concluded that children with chronic illness become experienced with managing painful triggers, and although the pain itself did not decrease with distraction, the perception of mastery and the repertoire of coping skills increased, along with parent perceptions of satisfaction. The self-regulatory skills learned through cognitive-behavioral strategies may help with symptom management throughout cancer treatment (Sencer and Kelly 2007).

### 7.2.1.2 Imagery and Hypnosis

*Imagery* uses the power of imagination to bring about change in physical, emotional, or spiritual dimensions (Fitzgerald and Langevin 2010). Imagery focuses the child's attention away from the procedure or distress by having her imagine a specific object or experience that brings positive physical or emotional benefits. Children often prefer imagery scenes that have some type of active play, such as riding a bicycle, playing a sport, swinging, or swimming (Hockenberry 1988). Symbolic images may be the most powerful healing images because they are drawn from the child's beliefs, culture, and meaning (Fitzgerald and Langevin 2010). Imagery uses all of the senses, requires active participation of the child, and is most effective for children over 8 years of age (Landier and Tse 2010).

Imagery can be general or specific, receptive or active, and outcome or process oriented (Achterberg 1985). In receptive imagery, the individual focuses awareness on and perceives messages from the body, whereas active imagery evokes thoughts and ideas that might lead to action. In outcome or end-state-oriented imagery, the individual envisions a goal, such as relief of nausea or pain. In process-oriented imagery,

the mechanism of the desired effect is imagined, such as imagining activated T cells coming to the rescue to fight off infection or a pain dial to dial down the pain, one number at a time. Imagery can be used to modify behavior through three steps: (1) increasing awareness of thoughts, feelings, reactions, and behaviors, (2) generating new thoughts or revising/reframing perceptions, and (3) changing actions and reassessing outcomes (Meichenbaum 1978). This change in perception and meaning of the problem contributes to a feeling of control.

The exact type of imagery used is not as important as the emotional immersion, in which an altered state of consciousness increases responsiveness to inner emotions or suggestions (Leuner 1984; Sheikh 1983). The body is thought to mimic neurohormonal responses to the mental images, as if they were actually occurring. As a result, the desired outcome may actually occur in response to the image (Milling 2008). Imagining a particular outcome helps to make it happen.

*Hypnosis* is similar to imagery but is more involved, with the goal to dissociate from the distress or painful experience through hypnotic induction, suggestions, and imagined fantasy (Uman et al. 2008). Hypnosis consists of focused concentration and absorption, an altered state of consciousness not always found in imagery, dissociation from environmental stimuli, and increased responsiveness to suggestion. Because of their ability to become absorbed in fantasy and imagination, children in general are more susceptible to hypnosis than adults (Saadat and Kain 2007). Both imagery and hypnosis use relaxation techniques to help focus attention and generate positive mental representations through recall of memories or creative imagination (Fitzgerald and Langevin 2010). Distraction, or a concerted effort to refocus away from the specific event, also may be used in imagery and hypnosis to reduce a specific symptom or achieve a desired outcome (Kwekkeboom et al. 2010).

Imagery and hypnosis have been extensively tested in children with cancer since the 1980s (Steggles et al. 1997). The effects of imagery and hypnosis on procedural pain and anxiety are now well established (Richardson et al. 2006), and

there is some evidence in five studies that imagery and hypnosis reduce anticipatory and chemotherapy-induced nausea and vomiting in children (Richardson et al. 2007).

Distraction, imagery, and hypnosis are the three most commonly studied mind-body modalities shown to be effective for managing procedural pain and related anxiety and distress in children (Landier and Tse 2010; Rheingans 2007; Wild and Espie 2004). Several systematic reviews (Landier and Tse 2010; Richardson et al. 2006; Uman et al. 2008) concur that hypnosis is more effective than distraction and is clinically beneficial in reducing procedure-related pain and anxiety. In a study of 30 children with leukemia undergoing bone marrow aspiration, hypnosis was more effective than cognitive-behavioral skills training in reducing anxiety, although both were equally effective at reducing pain (Lioffi and Hatira 1999).

Imagery also has been shown to be effective at reducing chronic pain conditions in children with recurrent abdominal pain (Weydert et al. 2006) and chronic functional abdominal pain (van Tilburg et al. 2009). Both studies found imagery more effective at reducing pain intensity and frequency and the disability from the pain, compared to breathing exercises (Weydert et al. 2006) or standard medical care (van Tilburg et al. 2009). Children and parents were trained in the techniques and then either participated in weekly sessions for 4 weeks (Weydert et al. 2006) or practiced at home for 8 weeks (van Tilburg et al. 2009). Compliance was high in both studies, and treatment effects were maintained for 2 months (Weydert et al. 2006) and 6 months (van Tilburg et al. 2009).

The majority of studies in imagery and hypnosis support their use for relieving pain. There is less evidence that imagery or hypnosis reduce other symptoms, such as fatigue and sleep disturbances. In one review of six studies in adults, two studies documented improvement in sleep in response to imagery and hypnosis, and one study documented improvement in fatigue with imagery (Kwekkeboom et al. 2010). In children with sleep disorders, relaxation and positive imagery

training was not beneficial in improving sleep behaviors, although younger children benefited from the parents changing their behaviors in response to training (Tikotsky and Sadeh 2010). In children undergoing stem cell transplant, Phipps and colleagues (2010) found no reduction of somatic distress or mood disturbance with relaxation/imagery or massage and humor therapy, compared to standard care. Imagery may be more effective for improving psychosocial and quality of life indicators, rather than specific outcomes (Roffe et al. 2005; Fitzgerald and Langevin 2010). Even though symptoms may not change, imagery used during treatment for cancer can restore confidence, self-esteem, and a sense of participation and control.

Van Kuiken (2004) found that imagery practiced up to 18 weeks increased the effectiveness of the intervention. Children and adults who have greater hypnotic ability also tend to have better outcomes when using imagery and hypnosis (Kwekkeboom et al. 2008; Lioffi et al. 2009). Four studies in children with cancer report less pain and anxiety in highly hypnotizable subjects (Hawkins et al. 1998; Hilgard and LeBaron 1982; Smith et al. 1996; Zeltzer and LeBaron 1982). Hypnotizability increases through early childhood, peaking between the ages of 7 and 14 years, and then leveling off into adolescence and adulthood (Olness and Kohen 1996).

As cognitive mind-body therapies, distraction, imagery, and hypnosis present minimal risk and are now well integrated into the conventional care of children (Weisberg 2008). Although they are still mind-body therapies, they are no longer considered alternative therapies because of their common integration into care (Berberich 2007).

### 7.2.1.3 Meditation and Mindfulness-Based Stress Reduction (MBSR)

Intended to enhance focus or attention, *meditation* is a general term that describes an array of practices that have been used by many different cultures and religious and spiritual traditions throughout history to promote health; most meditative practices share four common elements: a

quiet location, a specific and comfortable posture, focus on attention, and an open attitude (National Center for Complementary and Alternative Medicine 2010a). A physiological state of reduced metabolic activity that elicits both physical and mental relaxation, meditation, as described by Eastern philosophy and some Western religious and mystical traditions, can enable a practitioner to achieve a supposedly greater state of consciousness and thoughtless awareness (Rubia 2009). Sibinga and Kemper (2010) categorize the types of meditation practices as concentration, cultivating positive emotions or spiritual qualities, mindfulness, movement, and emptying. Within each of these categories is an array of practices; for instance, transcendental meditation or repetitive prayers are forms of concentration meditation, Buddhist metta and tonglen meditation are forms of cultivating positive emotions or spiritual qualities, and *MBSR* and Vipassana are forms of mindfulness (Sibinga and Kemper 2010). Mindfulness is often defined as the state of being attentive to and aware of what is taking place in the present (Brown and Ryan 2003), and a mindful perspective is needed to fully experience self-compassion, an emotional regulation strategy that transforms negative self-affect into positive self-affect (Neff 2003; Neff and Vonk 2009).

*MBSR* is one of the most popular forms of mindfulness meditation practice. *MBSR* brings together mindfulness meditation (guided meditation), deep breathing, relaxation, and gentle yoga and emphasizes the practical application of mindfulness in coping with stress and enhancing adaptive health behaviors (Kabat-Zinn et al. 1992). Developed in 1979 by Jon Kabat-Zinn at the University of Massachusetts Medical Center's outpatient stress reduction clinic, *MBSR*, a non-religious, structured group program, helps train practitioners to cultivate greater concentration and relaxation and to attend to a wide range of changing objects of attention while maintaining moment-to-moment awareness (mindfulness) (Kabat-Zinn et al. 1992).

Traditionally, the *MBSR* program consists of 26 h of instructor-led group session time over

the course of 8 weeks. During the program, participants are taught meditation fundamentals, relaxation techniques, and yoga. The leader-led sessions also include a discussion component where participants can talk about how they are progressing with their home practice and any challenges they are experiencing with the process. In recent years, *MBSR* programs have been tailored with abbreviated class time so as to assist with compliance and be realistic for the population served.

Preliminary research of *MBSR* programs suggests that the intervention fosters greater psychological and physical well-being and is positively associated with adaptive emotion-regulation strategies such as emotional awareness, acceptance, and letting go of negative thoughts. A meta-analysis of *MBSR* interventions concluded *MBSR* was a useful intervention for a broad range of chronic disorders and problems and had a strong level of support in enhancing general features of coping with distress and disability in everyday life as well as under conditions of extraordinary stress (Grossman et al. 2004). Though a meta-analysis of *MBSR* among cancer patients suggests more research is needed to conclude benefits of *MBSR* for physical health, the analysis demonstrated efficacy of *MBSR* for cancer patients in coping with psychosocial stresses brought about by disease, specifically in relieving anxiety, stress, fatigue, general mood, and sleep disturbance and improving psychological aspects of quality of life (Ledesma and Kumano 2009).

Though no studies have specifically studied meditation or *MBSR* among children with cancer, two reviews of meditation practices suggest that meditation practices reduce blood pressure and improve attention, behavior, and psychological functioning among children and youth (Sibinga and Kemper 2010; Black et al. 2009). Mindfulness training and *MBSR* have also been shown to improve parent-child interactions and moderate the role of attachment styles (Singh et al. 2009; Cordan et al. 2009). Specifically, in a trial evaluating *MBSR* for caregivers of children with chronic conditions, the majority of which were

asthma and diabetes; a significant overall reduction in stress-related symptoms and total mood disturbance was reported (Minor et al. 2006). Thus, MBSR interventions may provide caregivers with an adjunct stress-management intervention that may help in reducing stress and increasing mindfulness and self-compassion in the adjustment of and coping with their child's diagnosis.

## 7.2.2 Expressive Arts

Expressive arts, such as dance, movement, drama, music, art, drawing, and writing, allow children and adolescents with cancer to process and express their feelings about the course of the disease and treatment and to gain a stronger sense of self and ability to cope with hospitalization (Cohen and Walco 1999; Madden et al. 2010). Animal therapy also offers a unique connection that fosters expressive and interactive responses that can reduce distress and promote adaptation to the hospital environment (Gagnon et al. 2004). Creative arts focus on the psychological needs of the individual and are more than a distraction technique. In a descriptive pilot study, 16 children with brain tumors who received two sessions each of dance/movement, art, and music had less pain than an attention control group. An additional descriptive intervention group of 32 children receiving one session of combined creative therapies had improved mood states (Madden et al. 2010).

### 7.2.2.1 Drawing/Art

*Drawing* is an important means of communication for children. Several techniques encourage expression of feelings, issues, and problem-solving strategies for children with cancer. Combining drawing with writing has been particularly effective for exploring the young child's perceptions about health and illness (Rollins 2005). Although there is little research on the actual outcomes of art therapy, descriptive and qualitative studies demonstrate that the expression of feelings and insight into perceptions that emerge through art facilitates coping during painful procedures, enhances communication about children's hopes and fears, helps children to sort out their thoughts,

and increases self-esteem and active participation in healing (Favara-Scacco et al. 2001; Massimo and Zarri 2006; Rollins 2005). Several studies by Walsh and colleagues (2004, 2007) support the emotional benefit of art therapy for family caregivers of adult patients with cancer.

### 7.2.2.2 Music

*Music* has long been used to soothe children experiencing pain or anxiety in stressful situations. Although different kinds of music appeal to different children, and preferences change with the circumstances, physiologically, music has been shown to reduce tension, focus attention, regulate breathing, and increase oxygen uptake and heart rate variability (Kemper and Jennings 2005). Adults with cancer who listened to their choice of music before and during surgery had lower levels of intraoperative and postoperative cortisol and plasma levels of natural killer cell lymphocytes (Leardi et al. 2007). Music also facilitates emotional expression and communication and connectedness among families at all ages and stages of care (Burns et al. 2010; O'Callaghan et al. 2009; Sales et al. 2011; Standley and Hanser 1995).

Interactive music therapy empowers children and adolescents by allowing them to choose music preferences or create their own music, oftentimes merging music with video production. Several studies testing the use of music for children with cancer support its effects on reducing pain (Sahler et al. 2003) and lowering anxiety and improving mood states during radiation therapy (O'Callaghan et al. 2007), bone marrow transplant (Robb and Ebberts 2003), and hospitalization (Barrera et al. 2002) and before and after lumbar puncture (Nguyen et al. 2010). Music has long been used to reduce pain, or the perception of pain, in adults and children undergoing procedures, although not all studies show significant benefits (Danahauer et al. 2010; Kwekkeboom 2003). Art and music therapies are discussed in greater depth in Chap. 6.

### 7.2.2.3 Expressive and Narrative Writing

Pennebaker first introduced *expressive writing* as a way to improve health outcomes (Pennebaker and Beal 1986). Pennebaker's expressive writing

is a task-oriented “free write,” asking the writer to write continuously off the top of his or her head for 20 min. The conceptual basis for this expression relies on inhibition theory and cognitive change theory and proposes that expressive writing releases emotions and thoughts that would otherwise be inhibited, which helps the individual to reorganize their thoughts and to understand them in a new way.

While expressive writing is a “letting go” process, writing also may help people connect with how they *feel*, rather than what they *think* about the experience (Nicholls 2009). Nicholls proposes that developmental creative writing takes expressive writing one step further. By continuing to revise and reshape the writing, putting ideas, images, and feelings into words, the individual becomes emotionally connected to the material. Through interpretation and reflection, insight and understanding deepen, bringing about a change in perspective. Nicholls believes that mere disclosure or narration of events or difficult experiences does not by itself bring about cognitive change (2009). Instead, it is the interpretation of the personal significance of the events that gives the writing meaning. One strategy to access buried emotions is to write about the body’s sensations and response to a specific experience at the time it occurred and then to reflect at a later time on the importance of the event and the awareness it brings about. It is the ability of the individual to see himself or herself inwardly and to open up to what is sensed, but unknown, that results in a therapeutic change (Nicholls 2009).

Several other writing techniques also may be of value, including daily diary writing for ten days with a follow-up 1 week later (encouraging reflection); writing about an event in first person, second person, and third person, allowing psychological distance from the material; or writing in a group and sharing experiences. The Internet provides further incentive to write about and find meaning in health-related experiences (Smyth and Pennebaker 2008), with blogs and journals expanding communities of support (Murray 2009). Important to any writing process is having a safe place to write, with supportive people and a feeling of comfort and privacy.

Both the free write of expressive writing and the introspection fostered through reflective or narrative writing have a place in the emotional understanding of older children and adolescents with cancer. The abilities and developmental stage of the child and adolescent will drive the therapeutic approach.

There are very few studies testing the effects or benefits of writing. In children with cancer, Oppenheim et al. (2008) described examples of how children expressed their feelings, thoughts, hopes, and demands in a writing workshop aimed at helping them to regain their confidence and maintain their identity. Although outcomes were not formally assessed, the authors report that the workshop changed the way parents and caregivers saw and related to the children and adolescents. In nonhospital environments, a study of 359 adolescents in a school system found that expressive writing, used in combination with a psychoeducational program teaching emotion regulation, improved negative affect, grades, and number of days absent from school (Horn et al. 2011).

Several studies in adults provide evidence that patients with cancer have more positive mood states, less depression, and fewer physical symptoms in response to expressive writing (Carmack et al. 2011; Henry et al. 2010; Low et al. 2010). In one study of women with metastatic breast cancer, only women with low levels of emotional support or who had been recently diagnosed had fewer somatic symptoms and intrusive thoughts following four sessions of expressive writing, which was specific to their cancer-related emotions (Low et al. 2010). Several studies of students and patients attest that writing about emotional topics was more effective than writing about neutral topics (Danoff-Burg et al. 2010; Lu and Stanton 2010; Petrie et al. 2004), as was writing about positive thoughts and feelings (Henry et al. 2010).

Smyth and Pennebaker (2008) believe that at this time there is no conclusive evidence that expressive writing is more effective as a multiple-day intervention or that the specific writing topic influences the outcome. They admit that expressive writing works only some of the time and that



there likely are multiple interacting factors driving its effectiveness. The mechanism remains unknown, and it is not clear whether the effects are a result of the actual writing, the thinking time dedicated to the process or reflection after as a result of the writing, the social connection or feedback about the writing, or other intervening factors. Most studies have low effect sizes (Frattaroli 2006), many are qualitative in design, and few studies have been conducted in children or adolescents.

### 7.2.3 Physical/Movement-Based Mind-Body Therapies

Eastern and western movement-based mind-body therapies facilitate the mind's capacity to affect bodily function and symptoms through various forms of physical exercise or movement. Movement-based mind-body therapies often focus the mind on the body using an array of physical activities and breathing or meditative practices to instill relaxation and promote physical, mental, emotional, and spiritual well-being (Larkey et al. 2009; National Center for Complementary and Alternative Medicine 2010b). Often, these therapies are classified as mind-body exercise or the coupling of muscular activity with mindfulness, with the aim of achieving a self-contemplative mental state (La Forge 1997). In a controlled condition comparison study of expert and novice yoga participants exposed to a stressor prior to practice, experts had less interleukin 6 and C-reactive protein than novice participants, suggesting that yoga counteracts the inflammatory process of the stress response, which might have substantial health benefits if practiced regularly (Kiecolt-Glaser et al. 2010).

To date, there have been few clinical trials investigating movement-based mind-body therapies among children with cancer. Studies among other children groups as well as adults with cancer suggest the feasibility of these interventions and the potential of these therapies to help manage a variety of symptoms, including fatigue, quality of life, pain, and stress. Because these therapies have the potential to enlist the child

with cancer to become an active participant in managing their health and supporting their own rehabilitation, movement-based mind-body therapies are potentially appealing interventions among this population.

Some of the most frequently used movement-based mind-body therapies are yoga, dance/movement therapy, tai chi chuan, progressive muscle relaxation training, Feldenkrais Method®, and Pilates.

#### 7.2.3.1 Yoga

Originated in India thousands of years ago, *yoga* consists of asanas (physical postures), pranayama (breathing exercises), and meditation. Derived from the Sanskrit root “yuj,” meaning to bind or join together, yoga aims to connect body movement to the rhythm of the breath and promotes cardiovascular fitness, flexibility, strength, and concentration. Hatha yoga is one of the most commonly practiced forms of yoga. Different disciplines of Hatha yoga include Iyengar yoga, Ashtanga Yoga, vinyasa (power yoga), Kundalini yoga, and restorative yoga (supportive yoga). When considering teaching yoga to children and adolescents, Kaley-Isley et al. (2010) suggests modifying instruction according to age group and diagnostic considerations to support the alleviation of suffering from their condition and nurture the child's or adolescent's inherent capacity for mastery of the practice. Some suggested modifications include beginning with energizing poses for children and adolescents with anxiety whereas beginning with slow and calming poses for children and adolescents with depression and obesity (Kaley-Isley et al. 2010).

Only one study of yoga as an intervention among children with cancer and their caregivers has been conducted to date (Thygeson et al. 2010). Though hospitalized children (aged 7–12 years of age) reported no change in anxiety, both adolescents (aged 13–18 years of age) and caregivers showed improved anxiety following a 45-min session of yoga on an inpatient hematology/oncology unit. The yoga class consisted of seated meditation, warm-up and centering poses, standing poses, balancing poses, a cooldown, spinal twists, and a final resting pose.



Several nonsystematic and systematic reviews on yoga for adults with cancer have concluded that studies have demonstrated high satisfaction rates and some psychological benefits of yoga among both patients undergoing cancer treatment as well as survivors, though, because the methodological quality of many of the studies are low, the generalizability of yoga as an intervention for managing cancer-related symptoms is limited (Bower et al. 2005; Smith and Pukall 2009). These reviews have demonstrated that yoga may provide improvements in measures of sleep, quality of life, stress, energy, and mood. Furthermore, a systematic review also concluded that there is preliminary evidence that yoga may be beneficial for physical fitness and cardiorespiratory health among children (Birdee et al. 2009).

### 7.2.3.2 Dance/Movement Therapy

Involving direct expression through the body, *dance/movement therapy (DMT)* is the psychotherapeutic use of dance and movement to address the physical, emotional, social, and cognitive needs of individuals (American Dance Therapy Association 2009). With the premise that the body holds mental and emotional stress in the form of muscle tension and constrained body movement, DMT helps individuals express themselves through authentic movement to achieve greater self-awareness and well-being (Aktas and Ogce 2005). Thus, it is theorized that DMT may facilitate coping and promote physical activity among children with cancer.

To date, no randomized controlled trials have rigorously evaluated DMT among children with cancer. A recently published mixed-methods pilot study investigating creative arts therapy (CAT), an intervention which encompasses DMT, music, and art, found by parent report that child's hurt (problems with having a lot of pain) and child's nausea (becoming nauseated while thinking about medical treatment) significantly improved among a small sample of pediatric brain tumor patients (Madden et al. 2010). The CAT intervention consisted of six sessions, two sessions of each CAT modality. Additionally, in a small, randomized controlled, crossover pilot study, Sandel et al. (2005) showed that a 12-week

(18 session) DMT intervention using the Lebed Method, consisting of gentle movement to increase lymphatic circulation, significantly improved the quality of life among breast cancer survivors with a history of surgery.

### 7.2.3.3 Tai Chi Chuan

Sometimes referred to as “moving meditation,” *tai chi chuan (TCC)* originated in China thousands of years ago from martial arts and breathing practices. Consisting of a series of self-initiated continuous and rhythmical slow and gentle movements, TCC encourages the flow of qi, or vital energy, and is aerobically equivalent to moderate-intensity aerobic exercise (Mansky et al. 2006). Known for improving functional balance, TCC also encourages postural stability through movements that enhance control over the displacement of body mass and emphasize abdominal and lower-extremity muscle function and range of motion in the ankles, knees, and hips (Li et al. 2004). Because TCC requires sustained concentration, precision, and mechanical exactness, TCC facilitators working with children and adolescents suggest incorporating synergistic elements of other mindfulness-based practices, such as mindfulness-based stress reduction, to maintain interest in this age group for learning this therapy (Wall 2005).

A nonsystematic review of TCC trials among a number of populations supports the potential benefits of TCC to improve physical conditioning and reduce cardiovascular disease risk and psychological stress in adult cancer survivors (Mansky et al. 2006). In contrast, a systematic review of TCC as a supportive care intervention for cancer patients concluded there is not yet enough evidence to support the application of this intervention, though preliminarily recognized that TCC has shown improvements in self-esteem, total distance walked, and grip strength among adults with cancer (Lee et al. 2007b).

### 7.2.3.4 Progressive Muscle Relaxation Training

*Progressive muscle relaxation training (PMRT)* involves the systematic tensing and relaxing of different parts of the body, often progressing from

the feet to head (Baider et al. 1994). Originally developed by Edmund Jacobson in the 1920s and 1930s and later modified by other behavioral therapists, PMRT is often referred to as active relaxation. Where imagery-based relaxation techniques try to induce change on the physiological level through cognition, PMRT directly targets change through physical reactions (Lohaus et al. 2001). Facilitated either by a therapist or incorporated as part of self-care, PMRT may be augmented with breathing exercises and/or guided imagery. Although no studies have been conducted on PMRT among children with cancer, PMRT augmented with guided imagery has been found to be effective in several controlled trials in the clinical management of chemotherapy-induced nausea and vomiting (Molassiotis et al. 2002), sleep quality and fatigue (Demiralp et al. 2010), and anxiety and quality of life (Cheung et al. 2003) among adults with cancer. Research suggests the strongest benefits of PMRT in reducing or delaying the onset of distress from chemotherapy if taught prior to the initiation of cancer treatment (Burish and Tope 1992).

### 7.2.3.5 Feldenkrais Method®

The *Feldenkrais Method*® of somatic education is a movement therapy that uses two complementary styles of teaching, Awareness Through Movement® (ATM) and Functional Integration® (FI), to enhance physical coordination and movement. Using verbal guidance and touch, therapists encourage enhanced body awareness and perception with the aim to improve motor development and physical functioning. Though limited research has been conducted on the intervention, *Feldenkrais Method*® has become increasingly popular in a variety of clinical settings (Buchanan and Ulrich 2001).

### 7.2.3.6 Pilates

A movement therapy that mixes elements of gymnastics, martial arts, yoga, and dance, *Pilates* coordinates movement with the breath while strengthening and building control of muscles to improve flexibility, strength, and posture (Latey 2002). One study among women who completed cancer treatment reported that Pilates improved

functional capacity, physical function, and depression (Eyigor et al. 2010). Additionally, in the only randomized controlled study of Pilates among children, Jago et al. (2006) reported girls (10–12 years of age) who participated in a 4-week Pilates intervention had a significantly lowered BMI percentile. This study suggests the potential feasibility of Pilates as an intervention for young girls with cancer and cancer survivors who need to find ways to increase their physical activity and improve their body composition.

## 7.2.4 Sensory Therapies

### 7.2.4.1 Aromatherapy

*Aromatherapy* is the use of essential oils from plants (flowers, herbs, or trees) as therapy to improve physical, emotional, and spiritual well-being (National Cancer Institute 2011). Essential oils (EO) are not chemical fragrances or perfumes, but consist of naturally derived steam-distilled or cold-pressed material expressed from aromatic plants, thereby retaining their healing properties. Essential oils are most commonly inhaled directly from the bottle, dispensed into the air through the use of a diffuser, or diluted in a carrier oil (1–5 %) and massaged into the skin or added to the bath. The aerosolized volatile odor molecules are absorbed through the nasal mucosa, where they send signals along the nervous system to the olfactory bulb and then on to the amygdala and hippocampus of the limbic system, seats of emotion and memory (Lis-Balchin 1997). The limbic system also controls heart rate, blood pressure, breathing, stress levels, and hormone balance, all of which have been shown to respond uniquely to different oils. EOs enter the bloodstream by lung inhalation or by olfactory, skin, or gastrointestinal absorption and are excreted through respiration, kidneys, and insensate loss (Halcon 2010).

Aromatherapy is most often used for calming or stimulating effects, to reduce symptoms or to enhance sleep (Table 7.2). Lavender (*Lavandula angustifolia*) has sedative effects (increased sleep time, greater drowsiness and relaxation, reduced alpha waves) without toxicity (Buchbauer et al.

**Table 7.2** Essential oils and select uses for children

Essential oil	Botanical name	Use
Bergamot	<i>Citrus bergamia</i>	Anorexia, anxiety, stress, depression, acne, abscesses, cold sores, psoriasis, itching
Chamomile, Roman	<i>Anthemis nobilis</i>	Insomnia, nausea, headache, dermatitis, cuts, wounds, sprains
Eucalyptus	<i>Eucalyptus globulus</i>	Bronchitis, cold sores, colds, coughing, fever, flu, arthritis, sinusitis
Frankincense	<i>Boswellia carterii</i>	Anxiety, asthma, bronchitis, extreme coughing, scars, stress
Ginger	<i>Zingiber officinale</i>	Nausea, aching muscles, arthritis, poor circulation
Lavender	<i>Lavandula angustifolia</i>	Anxiety, depression, stress, asthma, migraine, bruises, burns, cuts, dermatitis, itching, scars, sprains, strains, chicken pox, colic, earache, headache, insect bites/repellant, acne, allergies
Lemon	<i>Citrus limon</i>	Colds, flu, oily skin, spots, warts, athlete's foot
Orange, sweet	<i>Citrus aurantium var. sinensis</i>	Constipation, slow digestion, flatulence, colds, flu, gums, mouth, stress
Peppermint (>age 6)	<i>Mentha piperita</i>	Nausea, colic, flatulence, sinusitis, asthma, exhaustion, fever, headache, vertigo
Sandalwood	<i>Santalum album</i>	Bronchitis, laryngitis, stress, chapped/dry/sensitive skin, oily skin, depression, scars
Spearmint	<i>Mentha spicata</i>	Nausea, vertigo, flatulence, asthma, exhaustion, fever, headache
Tea tree	<i>Melaleuca alternifolia</i>	Acne, athlete's foot, candida, chicken pox, cold sores, colds, flu, cuts, insect bites, itching, oily skin, ringworm, migraine, sinusitis, warts
Ylang ylang	<i>Cananga odorata</i>	Anxiety, depression, frigidity, hypertension, palpitations, stress

Adapted from content from Lawless (1995), McNeilly (2004)

1991; Dunn et al. 1995; Hardy et al. 1995; Lis-Balchin and Hart 1999; Masago et al. 2000). EOs are often added to massage (McNeilly 2004; Molassiotis and Cubbin 2004), with the addition of lavender, orange, or chamomile, reducing anxiety and increasing well-being (Cooke and Ernst 2000). Citrus oils and peppermint oil are often contraindicated in epilepsy because of their stimulating effect (Buckle 2003). Ginger, spearmint, and peppermint have antiemetic and antispasmodic effects on the gastric lining and colon (Asao et al. 2001; Leicester and Hunt 1982), although most antiemetic studies show efficacy with ingested botanicals, rather than inhaled essential oils. Some studies in adults show the efficacy of peppermint EO to reduce postoperative nausea and vomiting (Tate 1997), while other studies show no effect (Anderson and Gross 2004). One study of QueaseEase essential oil (ginger, spearmint, peppermint, lavender) showed

some effectiveness in adults and children for motion sickness related to boat travel (Post-White and Nichols 2007). Tea tree oil and peppermint have antibacterial, antiviral, or antifungal properties and can be used full strength directly onto minor wounds and burns (Halcon 2010).

Aromatherapy is often used with children and adolescents (Simpson and Roman 2001) and has been used in pediatric oncology to manage fatigue and nausea (Frank 2008). EOs are noninvasive and low risk, they can be used as often as desired, and they empower the child with some control over his or her symptoms. Children have specific essential oil preferences, with gender and ethnicity potentially influencing these preferences (Fitzgerald et al. 2007).

Essential oils have few adverse effects, although deaths from accidental ingestion by children have been reported (Tisserand and Balacs 1995). Skin irritations and allergic skin

reactions also can occur (Crawford et al. 2004), and sun sensitivity is enhanced with citrus-based oils. Lavender and tea tree oils have been found to have some estrogen-like effects (Henley et al. 2007). There is little guidance on the safety of use of EOs in children, although caution is advised in children under the age of two or in children with seizure disorders (McNeilly 2004). A license is not required to practice aromatherapy, although several organizations offer certification programs to train aromatherapists on the specific uses of individual oils.

Although aromatherapy is often used in practice, particularly in Europe (Crawford et al. 2006; Molassiotis and Cubbin 2004), few clinical trials have investigated its efficacy. Challenges to conducting research with EO include the difficulty in blinding subjects and bias toward personal preferences and individualized responses to odors. Aromatherapy research with cancer patients has mainly studied its effect on cancer-related symptoms, such as nausea and pain, and on stress and anxiety, including the physiological effects of lower blood pressure, heart rate, and respiratory rates.

In the first published study testing aromatherapy in children with cancer, Ndao and colleagues (2010) tested the effectiveness of bergamot EO to reduce anxiety, nausea, and pain in 37 children and adolescents undergoing infusion of stem cells for the treatment of malignant and nonmalignant disorders. Using an aromatherapy diffuser, patients were randomized and exposed to bergamot EO (*Citrus × bergamia*) or placebo (a nonessential oil-based scented shampoo) just prior to and following the infusion of stem or bone marrow cells. Instead of reducing anxiety, as hypothesized, children receiving bergamot had greater anxiety than the placebo group, which was partly explained by the children's monitoring coping style. Although nausea and pain subsided in both groups, nausea remained significantly greater in the group receiving the bergamot EO.

A small unpublished pilot study of 13 children established the feasibility of using aromatherapy for chemotherapy-induced nausea and vomiting in children receiving inpatient highly emetogenic chemotherapy. Children self-administered by inhalation their choice of either ginger, spearmint,

or peppermint EO an average of 11–19 times per day over 3 days. Although the sample size was too small to draw conclusions, mean scores of self-reported nausea, reported throughout the day, were lower during the intervention with the essential oil than during the crossover control cycle of the same chemotherapy (Post-White 2006). One other known study of aromatherapy for nausea and vomiting in children with cancer is in progress (Karen Moody, personal communication 2009).

Several studies in children with other conditions found varying effects. Nord and Belew (2009) found that lavender and ginger EOs were more effective than placebo (jojoba oil) in reducing observed distress pre- and postoperatively in 94 children undergoing primarily orthopedic surgery, although the difference was not quite significant. Holm and Fitzmaurice (2008) found that music reduced parent anxiety, but not Neroli aromatherapy, when alternatively diffused through a pediatric emergency room over a 28-day period. In children receiving massage or EO with massage for eczema, there was no additional benefit with the EO added (choice of sweet marjoram, frankincense, German chamomile, myrrh, thyme, benzoin, spike lavender, *Litsea cubeba*) (Anderson et al. 2000).

Although aromatherapy is often used in clinical practice, there are few studies to support its efficacy. Lavender (*Lavandula angustifolia*) appears to have the greatest evidence in adults, but is not recommended in prepubertal children because of potential estrogenic effects. Additional studies are needed in children to determine efficacy of ginger, peppermint, and spearmint EO for nausea and vomiting, other EO potentially useful for insomnia and calming effects (chamomile, frankincense, ylang ylang) and citrus-based EO for mood-enhancing effects (bergamot, sweet orange, lemon).

#### 7.2.4.2 Massage

*Massage therapy (MT)* is the manual manipulation of soft tissue to promote health and wellness. Massage is one of the most often used integrative therapies for adults and children with cancer (Boon et al. 2007; Hughes et al. 2008;

Myers et al. 2008, Post-White et al. 2009b) and is one of the most frequently used strategies for pain management among children during the first year after a cancer diagnosis (Van Cleve et al. 2004). During stressful times, touch can be comforting, healing, and nurturing and can counter the negative touch encountered during invasive procedures. Massage therapies studied in patients with cancer include Swedish massage, aromatherapy massage, reflexology (trigger point foot massage), acupressure, and manual lymphatic drainage.

Massage is thought to downregulate the sympathetic stress response through tissue receptors, thereby reducing cortisol, increasing blood and lymph flow to provide oxygen and nutrients to cells and tissues, and generating positive emotional responses to release tension and promote relaxation. Positive mood states and beliefs, perceived and processed through the amygdala in the hypothalamus, then release dopamine, endogenous opiates, and oxytocin, which activate the vagus nerve and parasympathetic nervous system (Kolcaba et al. 2004; Lund et al. 2002) and decrease salivary and urinary cortisol (Field et al. 2005; Hernandez-Reif et al. 2004).

Despite beliefs about this bidirectional mechanism, evidence for effects of massage on biological outcomes is inconsistent, showing either no evidence for reductions of stress hormones (Billhult et al. 2008, 2009; Moyer 2008, Moyer et al. 2011, Post-White et al. 2009b) or some evidence for decreased cortisol and increased neurohormones related to positive mood states (Field et al. 2005; Listing et al. 2010; Rapaport et al. 2010; Stringer et al. 2008). Effects on immune function are equally variable, with some comparative increases in natural killer cell number and cytotoxicity reported (Billhult et al. 2009; Hernandez-Reif et al. 2004, 2005) and other studies showing no effects (Billhult et al. 2008; Goodfellow 2003). More recently, upregulation of Th1 cytokine immune responses, with lower proinflammatory cytokines, has been measured after massage, indicating either no effect (Krohn et al. 2010) or a greater Th1/Th2 (greater cytotoxic to humoral) immune response to massage (Rapaport et al. 2010). Neurohormone and

cytokine responses are often fleeting and have intricate feedback systems, and NK cells and oxytocin are known to be both downregulated and upregulated in response to stress, making these effects difficult to capture and to interpret their clinical effects. Massage effects are likely complex and mediated by diverse central, peripheral, and local tissue responses (Sagar et al. 2007).

Although there is no conclusive evidence explaining how massage works, several systematic reviews evaluating the efficacy of massage research for children and adults with cancer show that massage consistently reduces cancer-related symptoms of pain and anxiety and has some effect on reducing perceived stress, anger, depression, fatigue, sleep disturbances, nausea, and blood pressure (Ernst 2009a; Hughes et al. 2008; Jane et al. 2008; Myers et al. 2008; Russell et al. 2008; Wilkinson et al. 2008). At this time, there are few recommendations for dose and frequency of massage for specific outcomes. Most studies measure only immediate effects, and little is known about long-term effects or clinical relevance of ongoing massage. More than one session may be needed to observe expected benefits, with most studies showing the strongest effects when a series of massage is given.

Massage has a very favorable risk-benefit ratio and very low risk of adverse side effects (Wesa and Cassileth 2009). Serious adverse events are rare and massage is generally safe when given by credentialed and experienced practitioners (Corbin 2009; Deng et al. 2009). More than 60 trials provide evidence for the feasibility and safety of massage for children and adults at every phase of the cancer experience, although some modifications are recommended for patients at the end of life (Smith et al. 2009). In a systematic review of 10 studies involving 386 patients with cancer, one case report of a skin rash was the only adverse event reported (Wilkinson et al. 2008).

Adverse effects can often be prevented with modification of touch and changes to positioning. Massage should be avoided near or above tumor sites, surgical areas, radiation fields, or intravenous lines (Deng et al. 2009). Only light touch is appropriate when patients have bleeding



tendencies, are in postoperative recovery, or are nauseous or cachexic. Long, slow, light touch triggers a parasympathetic or relaxing response, whereas vigorous deep massage may stimulate the sympathetic nervous system, increasing heart rate and blood pressure. To provide safe and effective massage, MacDonald (2007) recommends reducing the pressure, slowing the strokes, shortening the session length, and working gently. Children may be particularly sensitive to changes in body image and being unclothed. Asking permission and proceeding gently when touching even a well-healed scar, amputated limb stump, or bald head conveys compassion and respect. Some younger children respond favorably to having a parent receive massage first or having the parent provide the massage. In one study, children declined therapeutic massage if they were nauseous, in pain, or feeling ill, but responded to their parent's light and comforting caress of their arm or leg (Post-White et al. 2009b). Several studies provide evidence that parents themselves benefit from providing massage to their ill child (Ghazavi et al. 2010).

Six studies have tested the effectiveness of massage for children with cancer. Consistent with adult studies, decreased anxiety was the most commonly observed effect in children receiving massage for a variety of conditions, including cancer (Beider et al. 2007; Beider and Moyer 2007). Other findings included improved mood (Field et al. 2001; Haun et al. 2009), less general discomfort (Haun et al. 2009; Phipps et al. 2005), and decreased heart rate (Post-White et al. 2009b) and respiratory rate (Haun et al. 2009). In these small studies, massage did not lower blood pressure (Haun et al. 2009; Post-White et al. 2009b); lessen symptoms of pain, nausea, or fatigue; or reduce cortisol levels (Post-White et al. 2009b). Phipps et al. (2004) found massage reduced the time to engraftment after bone marrow transplant, but had no effects on mood or symptoms. In a follow-up multisite trial of 178 children undergoing transplant, Phipps and colleagues (2010) found no differences in somatic distress, mood disturbance, or medical outcomes among children receiving massage plus humor, children and parents receiving massage plus humor or

imagery intervention, or standard care control. Children and parents each received a mean of eight to nine massages over the 4-week period. Two other studies provided massage to parents of children with cancer, with parents reporting less anxiety (Post-White et al. 2009b) and less fatigue and greater vigor (Iwasaki 2005). Importantly, these studies support the feasibility and safety of therapist (Haun et al. 2009; Phipps et al. 2004, 2005; Post-White et al. 2009b) or parent provided massage (Field et al. 2001; Phipps et al. 2004, 2005) for children with cancer.

### 7.2.4.3 Reflexology

*Reflexology* uses a specific technique to massage reflex points on the feet or hands that correspond to parts and organs of the body. The left foot/hand represents the left side of the body and the right foot/hand represents the right side of the body. Reflexology is often combined with other massage techniques and is considered both a touch and an energy therapy. Applying pressure to specific points on the foot is proposed to invoke a healing response by redirecting areas of deficient and excess energy, thereby balancing energy flow to that corresponding part of the body (Kunz and Kunz 2003). Patients who are more frail or nearing the end of life may tolerate reflexology better than full body massage (Wesa and Cassileth 2009).

Although there is little research testing its effects, several small studies of adults with cancer have reported short-term effects of less anxiety and pain (Stephenson et al. 2000, 2003, 2007) and greater relaxation (Ross et al. 2002) and quality of life (Hodgson 2000). Ross and colleagues (2002) found no differences in anxiety and depression when comparing six sessions of reflexology to simple foot massage in 26 patients with cancer. Two of the three small studies of reflexology for cancer showed some evidence for decreased anxiety and increased quality of life (Ernst 2009b). Other studies and anecdotal reports suggest that reflexology can reduce pain and distress in other conditions (Ernst 2009b; Gunnarsdottir 2010), but there are no published reports of the effectiveness of reflexology for children or for children with cancer.



### 7.2.5 Biofield Therapies (Energy, Circulation, Environment)

Biofield energy therapies (Reiki, Qigong, therapeutic touch, healing touch, polarity therapy) facilitate the flow of energy through the body's chakras and meridians. Chakras are seven circular vortex centers of energy along the spine, starting from the tail bone and ending at the crown of the head. In ayurvedic medicine, chakras are considered the center of life force (*prana*) affecting physical and emotional energies when weak. Qigong is the Mandarin Chinese term for the chakra system, in which qi energy flows through energy channels known as meridians. According to Traditional Chinese Medicine, meridian lines carry energy (qi) throughout the body and are associated with the functioning of the body's internal organs. Under healthy conditions, the energy will flow freely through the meridians and chakras. If the internal organs function abnormally, or if external stimulation disrupts flow, the energy will stagnate in the meridians and chakras and cause illness or changes in physiology and mood.

The goal of biofield energy therapies is to release the blockage and reestablish energy flow. Practitioners of energy therapies use an intention of healing and specific hand placement to unblock and promote energy flow, sometimes hovering above the body, as with Therapeutic Touch (TT), and sometimes placing hands on the body, as in the Japanese Reiki therapy, polarity therapy (PT), or healing touch (HT). Energy imbalances are felt as changes in temperature, texture, or vibration (Hover-Kramer 2002). National certification for TT, HT, PT, Qigong, and Reiki requires varying levels of training, practice, and supervised treatment sessions. Self-practices of visualization, meditation, and the breathing and stretching of yoga also can help unblock chakra centers and promote the flow of energy throughout the body.

Energy therapies are considered safe, with no known risks, and are often used clinically to promote relaxation and a sense of well-being. There is limited but growing evidence for the effectiveness of TT, HT, and Reiki to reduce pain and other symptoms related to cancer and its treatment (Jain and Mills 2010). Despite theories,

there is no scientific evidence for the mechanism of action. Instruments to detect and measure these magnetic biofields are inconsistent, which incite skepticism of energy therapies. In addition, most biofield studies tend to have small sample sizes.

Clinical studies testing energy therapies in cancer primarily focus on managing pain, anxiety, and stress (Wardell and Engebretson 2001). In the only known published study of energy therapies in children with cancer, nine children on continuation or consolidation treatment (mostly for leukemia), who received one 20-min session of healing touch, nested within a 40-min rest session, had less reported stress, negative mood states, and lower heart rate variability parameters, compared to a 40-min rest time in a crossover design of the same subjects (Kemper et al. 2009). Heart rate variability, a measure of autonomic function that reflected lower sympathetic activation, was physiologically consistent with the decrease in reported stress by the children and parents. More studies are required to evaluate the effect of energy therapies on children.

In adults, several systematic reviews support the efficacy of HT, TT, and Reiki to reduce pain related to cancer and other conditions (Jain and Mills 2010; Monroe 2010; So et al. 2008). In eight studies specific to cancer, Mills and Jain (2010) found moderate evidence of HT, TT, or Reiki to reduce acute pain in cancer and conflicting evidence for reducing fatigue and quality of life in patients with cancer. In contrast, Lee and colleagues (2007a) found no evidence for improvement in cancer symptoms or outcomes in response to Qigong, although most subjects had late stages of cancer and the methodological quality of the nine studies was poor (Lee et al. 2007a). Several other reviews make recommendations for future research in biofield therapies (Hintz et al. 2003; Miles and True 2003; Wardell and Weymouth 2004). Despite emerging evidence, there is little consistency in doses received or the timing of administration of biofield therapies.

Individual studies of Reiki demonstrate feasibility and preliminary evidence for reductions of anxiety in 54 men with prostate cancer receiving biweekly Reiki over 8 weeks of external beam

radiation (Beard et al. 2011), less fatigue and improved quality of life in 16 patients with cancer receiving five daily Reiki sessions (Tsang et al. 2007), and increased comfort and well-being in 189 participants receiving either Reiki or sham Reiki (but not placebo) in a chemotherapy infusion center (Catlin and Taylor-Ford 2011). In a pilot study of 45 women undergoing radiation therapy for breast cancer, polarity therapy, an energy therapy that includes gentle stretching, rocking, and light touch, resulted in positive trends toward less fatigue and better quality of life, but the differences were not significantly better than massage or usual care control (Mustian et al. 2011). In a feasibility study of HT, 12 adults with leukemia had less fatigue and nausea immediately after the sessions, but no changes over the 5 weeks of treatment (Danhauer et al. 2008). Two larger studies of TT and HT found greater stress reduction and pain relief with TT and HT (Wilkinson et al. 2002) and reduced fatigue, negative mood states, and pain in 230 patients receiving HT during cancer therapy (Post-White et al. 2003).

Few studies have tested biological effects of biofield therapies. Lutgendorf and colleagues (2010) determined that HT preserved levels of natural killer cell cytotoxicity (NKCC) in 60 women being treated for cervical cancer, compared to relaxation therapy or usual care control. Women receiving HT also had less depression, but mood states did not mediate NKCC results. Future models of cellular signaling pathways may help explain biological mechanisms of biofield therapies (Mills and Jain 2010).

### 7.3 Practice/Application

Acute toxicities and long-term effects are expected consequences of cancer therapy. Nausea and vomiting, pain, anxiety, fatigue, loss of appetite, and constipation/diarrhea are symptoms that fluctuate over time and span the course of the disease, from diagnosis to end-of-life care. Mind-body therapies have gained acceptance for supportive care of adults with cancer. Studies in adults support the efficacy of hypnosis and imagery/relaxation for controlling pain and anxiety

and meditation for reducing stress and improving mood, quality of life, and sleep problems (Carlson and Bultz 2008). There is growing evidence that yoga can improve quality of life, sleep, and mood and that dance, music, and art may help patients express their feelings and cope with the demands of the cancer experience. Less evidence is available for children, although imagery, hypnosis, and relaxation have consistently been shown to reduce anxiety, nausea, and acute pain in children with cancer (Table 7.3) (see Box 7.1).

#### Box 7.1: Massage and Yoga for Constipation

During the early months of consolidation therapy, Julian, a 17-year-old male with acute lymphoblastic leukemia, was experiencing unbearable constipation and bloating. After receiving approval from his doctor, Julian visited with a massage therapist twice a week. The massage therapist primarily used Swedish massage techniques and foot and hand reflexology, targeting the small and large intestine, lumbar and sacrum, and colon areas. Julian's massage therapist also instructed Julian on how to conduct self-care abdominal massage using petrissage (kneading) strokes and on using both backbending and twisting yoga postures to tone the abdominal muscles between visits. Within a week of using this regimen, Julian began to experience more regular, smooth bowel movements.

Most studies are conducted with patients on treatment, although mind-body therapies are often used at the end of life for supportive care (see Box 7.2). Energy and touch therapies, music, and aromatherapy provide comfort, facilitate relaxation and sleep, and assist with chronic pain management. Hypnosis helps to reframe the diagnosis as an opportunity to enjoy and appreciate the time that is left, manage anxiety, dissociate from pain, and process emotions and feelings (Marcus et al. 2003). Parents and siblings can benefit from these same mind-body

**Table 7.3** Suggested application of mind-body therapies by treatment phase

Phase	Need/symptom	Recommended mind-body therapies
Treatment	Anxiety, fear, distress, negative mood states	Drawing, writing, storytelling, humor <sup>a,b</sup> Massage <sup>a,b</sup> Imagery/hypnosis/CBT <sup>a,b</sup> MBSR, meditation <sup>b</sup> Healing touch <sup>a</sup> Music <sup>a</sup> Yoga <sup>a</sup> Foot reflexology <sup>b</sup> HT, TT, Reiki <sup>b</sup> Relaxation/PMR <sup>b</sup> Aromatherapy: lavender <sup>b</sup> Bach flower remedies
	Depression	Massage <sup>a</sup> Music <sup>a</sup> Imagery/hypnosis <sup>b</sup> Narrative/expressive writing <sup>b</sup> Yoga – slow and calming
	Fatigue	Massage <sup>a,b</sup> Healing touch, Reiki, TT <sup>b</sup> Relaxation, PMR <sup>b</sup> Imagery <sup>b</sup> Aromatherapy: citrus – bergamot, sweet orange, lemon Tai chi chuan Yoga
	Nausea/vomiting	Imagery/hypnosis <sup>a,b</sup> Aromatherapy: ginger, spearmint, peppermint <sup>a</sup> Healing touch <sup>b</sup> Relaxation, PMR <sup>b</sup> Deep breathing Foot reflexology
	Procedural/acute pain	Imagery/hypnosis, cognitive-behavioral therapy (CBT) <sup>a,b</sup> Art therapy, drawing <sup>a</sup> Massage <sup>a</sup> Relaxation, distraction <sup>a</sup> Music <sup>a</sup> HT, TT, Reiki <sup>b</sup>
	Sleep disturbances, insomnia	Massage <sup>b</sup> Imagery/hypnosis <sup>b</sup> PMR <sup>b</sup> Meditation <sup>b</sup> Aromatherapy – lavender <sup>b</sup> Yoga <sup>b</sup> Music

(continued)

**Table 7.3** (continued)

Phase	Need/symptom	Recommended mind-body therapies
Survivorship	Emotional stress, depression	Pilates <sup>b</sup> Tai chi chuan <sup>b</sup>
	Self-esteem	Tai chi chuan <sup>b</sup> Art therapy Imagery/hypnosis Yoga
	Body image, self-awareness, posture	Art therapy Dance/movement therapy Feldenkrais <sup>®</sup> Imagery/hypnosis Meditation/MBSR Pilates
	Energy/fatigue	Tai chi chuan Qigong Yoga
	Physical fitness, balance, cardiorespiratory health	Dance/movement therapy <sup>b</sup> Pilates <sup>b</sup> Tai chi chuan <sup>b</sup> Yoga
	Weight management	Pilates <sup>a</sup> Dance, yoga, tai chi chuan
Palliative care	Comfort	Reiki/HT/TT <sup>b</sup> Massage
	Constipation	Biofeedback <sup>a</sup> Aromatherapy: sweet orange Massage
	Insomnia	Massage <sup>b</sup> Aromatherapy – chamomile, frankincense, ylang ylang, sandalwood Music
	Pain	Massage <sup>a,b</sup> Foot reflexology <sup>a</sup> Music <sup>a</sup> Reiki/HT/TT <sup>b</sup> Visualization/imagery
	Shortness of breath	Reflexology, imagery Reiki/HT/TT Aromatherapy: eucalyptus

HT healing touch, TT therapeutic touch, PMR progressive muscle relaxation

<sup>a</sup>Research evidence in pediatrics

<sup>b</sup>Research evidence in adults

therapies to reduce their own fatigue, depression, insomnia, and headache or musculoskeletal pain. Therapies that address multiple symptoms and focus on the child as a whole human being are likely to be most effective (Angelescu et al. 2006).

#### **Box 7.2: Massage and Touch for Comfort**

A school-aged child was admitted to the hospital for palliative care. Ally had received massage therapy at the hospital

for several years and had often expressed how much it helped her to cope with the treatments. When the therapist entered the room, her family smiled and brightly announced, “The massage therapist is here!” Though Ally appeared lethargic and was unable to sustain eye contact, she indicated her consent for massage with a slight nod of her head. Aware that the little girl might die within the week, Karen invited her parents and sister to assist with the massage. Ally’s Mom held her face and one shoulder, Dad stood next to the bed and lightly touched her other shoulder and hand, and the sister and therapist each held a foot. They quietly held their positions as Ally fell into a deep sleep, and the room became very quiet and peaceful. She died two days later.

Some survivors of childhood cancer continue to have symptoms of fatigue, anxiety, and pain, and most survivors face late effects such as obesity, infertility, osteopenia, reduced cardiac function, chronic fatigue, impaired cognitive processing, and a higher risk of second malignancies (Hudson 2008; Oeffinger and Hudson 2004). Although mind-body therapies have limited known efficacy in addressing survivorship issues, some evidence in adults supports the use of spiritual practices, massage, and meditation to reduce stress (Bell 2010) and physical therapies to increase physical fitness and balance (Birdee et al. 2009; Mansky et al. 2006).

Physical therapies, such as yoga, dance, and tai chi chuan, may be particularly helpful in addressing issues of self-esteem, body image, and weight management in children and adolescents. Mind-body therapies such as MBSR and other forms of meditation, Qigong, hypnosis, and art and music therapy may reduce stress and improve coping of survivors by promoting emotional self-regulation (Monti et al. 2008). Of great interest is the potential for mind-body therapies to foster healthy lifestyle behaviors, which ultimately may have an effect on the incidence of

late effects and the risk of cancer recurrence (Chlebowski 2003).

Most mind-body therapies carry little risk, are noninvasive, and capitalize on children’s naturally active imagination. Selecting and individualizing therapies to the developmental age and motivation of the child or adolescent may require a trial approach, with exposure to a variety of therapies to determine the best fit for the individual patient (see Boxes 7.3 and 7.4). Consideration should be given toward patient preferences and

#### **Box 7.3: Healing Touch for Nausea**

Jay found no relief from standard antiemetics, administered with his first round of chemotherapy, and he had not been able to eat or sleep for more than 24 h. He recoiled in response to the suggested massage but accepted healing touch, an energy modality that did not require touch. After getting permission from Jay and his father, the massage therapist, also trained in healing touch, used energy clearing, brushing her hands 6–12 in. above Jay’s body from head to toe, for approximately 25 passes. Jay fell asleep after 10 min. His father was astonished at how quickly and deeply his child was able to rest.

#### **Box 7.4: Aromatherapy for Nausea**

Though receiving anti-nausea medications, Daniel, a 12-year-old with a low-grade glioma, experienced both acute and delayed nausea when receiving his carboplatin treatments. After researching different complementary medicine therapies, Daniel’s father decided to first see if aromatherapy could help alleviate Daniel’s discomfort. Reading that lemon, ginger, and peppermint essential oils were all potentially therapeutic for nausea, Daniel’s father gave Daniel a “smell test.” Choosing peppermint, Daniel carried a small dram bottle of the essential oil with

him on his way to the outpatient clinic. Using the direct inhalation method, Daniel would wave the dram bottle approximately 1 centimeter from his nostril and breathe deeply for a few minutes at a time. On the days Daniel would receive carboplatin, Daniel's father would also utilize the topical application of peppermint essential oil using a compress over Daniel's stomach a few hours before bedtime to prevent the onset of delayed nausea in the middle of the night. Although Daniel still experienced periods of nausea, the severity became less frequent and more manageable.

interests, in addition to the level of evidence available in the literature. Children and adolescents who are fearful or hesitant to try new therapies may benefit from watching a parent or sibling or stuffed animal first receiving the therapy. There is no known "dose" or recommended frequency for mind-body therapies, although some studies found greater benefit with more practice of imagery and MBSR (Lengacher et al. 2009; Van Kuiken 2004).

Mind-body therapies can be adapted to any setting. Massage and energy therapies have been used in the intensive care unit (see Box 7.5), yoga and tai chi have been adapted to inpatient units, and meditative and hypnotic therapies can be practiced anywhere. Most hospitals require accreditation for massage therapists; other mind-body therapies are often used within nursing and psychology practices. Finding healing practitioners with expertise in pediatric care can be difficult in some geographic areas or smaller cities. Although experience with children is ideal, primary criteria should be educational and experiential qualifications, including licensure and certification if relevant. Families and practitioners should participate as shared decision makers in selecting therapies, with consideration for benefits over risks and use of therapies as adjunctive to conventional care (Cohen 2006).

#### **Box 7.5: Reiki for Stress**

Following her surgical resection, Zoe, an 8-month-old female with rhabdomyosarcoma of the tongue, required careful monitoring in the pediatric intensive care unit. Zoe was experiencing slightly elevated blood pressure and exhibited agitation and restlessness confined to her crib. Certified in Reiki, Zoe's mother began administering Reiki by placing her hands on Zoe's head and torso for 15–20 min. After just a few sessions during her first day in the pediatric intensive unit, Zoe's mother noticed a significant drop in Zoe's systolic blood pressure. Not only was Zoe notably calmer over the next few days as her mother continued to practice Reiki with her, but Zoe's mother also noted feeling less stressed herself.

## **7.4 Open Questions**

The goal of integrative care is to reduce distress, manage symptoms, and maintain functional family, social, and developmental roles. Evidence has emerged for the safe and effective use of hypnosis, relaxation, distraction, meditation, massage, yoga, and expressive art therapies to reduce distress and symptoms, although further investigation with larger randomized clinical trials is warranted for each of these promising therapies (Carlson and Bultz 2008; Myers et al. 2005). There is scant research on the use of mind-body therapies for supporting family, social, and developmental roles.

Gaps in research remain for interventions effective for reducing chronic pain, controlling symptoms in palliative care, and preventing long-term effects. Determining efficacy of mind-body therapies in preventing illness and maintaining health in survivors carries potential promise for long-term outcomes. For example, obesity and metabolic syndrome compound the survivor's risk for diabetes and cardiovascular disease. Interventions that promote mindful eating, exercise, and healthy



lifestyle choices may reduce these increasingly observed late effects of survivors.

Additional studies are needed to determine optimal timing and dose of mind-body interventions, as well as characteristics that increase performance, compliance, and clinical effectiveness. Further effort is needed to standardize interventions and determine treatment efficacy according to the child's development and individual characteristics, as well as the clinical indications for use. More research is needed on the specific conditions that each mind-body therapy is effective for and the testing of therapies for conditions that are not responsive to standard treatment options.

Research on biological effects of mind-body therapies remains inconclusive. Testing theories to tease out potential mechanisms may illuminate relevant biological outcomes. However, individual mind-body therapies likely work through varied mechanisms, such as expressing and interpreting feelings, finding meaning, or releasing physiological tension. It is unlikely that all interventions work by reducing stress or inflammation, particularly in children. Research specific to children is especially indicated, as findings from adult studies cannot be generalized to children, particularly in the area of mind-body medicine where children's perceptions and interpretations influence outcomes.

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Elena J. Ladas

## Contents

<b>8.1</b>	<b>Introduction</b> .....	109
<b>8.2</b>	<b>Integrative Nutrition Counseling for the Child with Cancer</b> .....	110
<b>8.3</b>	<b>Nutrition Management for the Child with Cancer</b> .....	110
<b>8.4</b>	<b>Integrative Dietary Approaches in Supportive Care</b> .....	113
8.4.1	Loss of Appetite.....	113
8.4.2	Nausea and Vomiting .....	114
8.4.3	Constipation.....	114
8.4.4	Diarrhea .....	114
8.4.5	Mucositis.....	116
<b>8.5</b>	<b>Specialized Diets: Research Overview</b> ...	117
8.5.1	Neutropenic Diet/Low Microbial Diet.....	117
8.5.2	Ketogenic Diet .....	118
8.5.3	Macrobiotics .....	119
8.5.4	Gerson Diet.....	120
<b>8.6</b>	<b>Nutrition and Survivorship</b> .....	120
<b>References</b>	.....	121

## 8.1 Introduction

Nutrition is a component of supportive care that expands throughout the spectrum of cancer care. Practitioners must balance the delivery of the necessary medications for cancer treatment while maintaining growth and development. This can be challenging especially during times of malnutrition. The prevalence of malnutrition is common among children with cancer with surveys reporting that nearly 25 % of patients present with malnutrition in developed countries. This figure increases to over 50 % when developing countries are considered (Ladas et al. 2012). Malnutrition often develops over the course of therapy and is related to the intensity of therapy and diagnosis. It was not until the late 1970s that the role of nutrition status began to be described among children with cancer. Initial studies reported increased toxicity and adverse outcomes in children who were malnourished compared to nourished children. Recent studies have confirmed some of these initial findings and have reported that poor nutrition status, either over- or undernutrition, was associated with increased therapy-related side effects and poor survival (Brinksma et al. 2012). Patients with acute myeloid leukemia who presented with either over- or undernutrition had poorer survival when compared to well-nourished patients (Lange et al. 2005). In children with osteosarcoma, malnutrition was associated with a trend toward increased slough and wound infections and arterial thrombosis (Hingorani et al. 2011). Most recently, a retrospective study exploring the effect

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of nutrition status at diagnosis and throughout therapy in children with high-risk ALL reported that patients who were malnourished experienced increased toxicity and reduced survival (Orgel et al. 2011). When evaluated as a whole, these studies underscore the importance of timely and effective nutrition interventions.

It is important to recognize that nutrition interventions often require a multidisciplinary approach in the delivery of nutrition therapy and may include the collaboration of physicians, nutritionists, psychologists, social workers, and nurses. The role of the family must also be considered as caregivers often view nutrition as an aspect of supportive care in which they can take an active role and deliver care. Nutrition allows medical providers to partner with parents and family members and develop nutrition plans for the child. Maintaining adequate dietary intake as indicated by dietary reference intakes (DRIs) will reduce the risk of the development of malnutrition. A complete table of the DRIs may be found at [www.nap.edu](http://www.nap.edu). Preventing the development of malnutrition can be challenging especially in young children, children undergoing treatment for extended periods of time, children receiving intensified therapies, and children undergoing stem cell transplant and may require partnering with the parent to ensure nutrition needs are being met. Ideally, nutrition therapy should be embedded in the institution's standard of care, and proactive intervention should be implemented to avoid nutrition depletion. Provision of nutrition therapy should consider the intensity of upcoming therapy and anticipated side effects that may impact nutrition status.

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## 8.2 Integrative Nutrition Counseling for the Child with Cancer

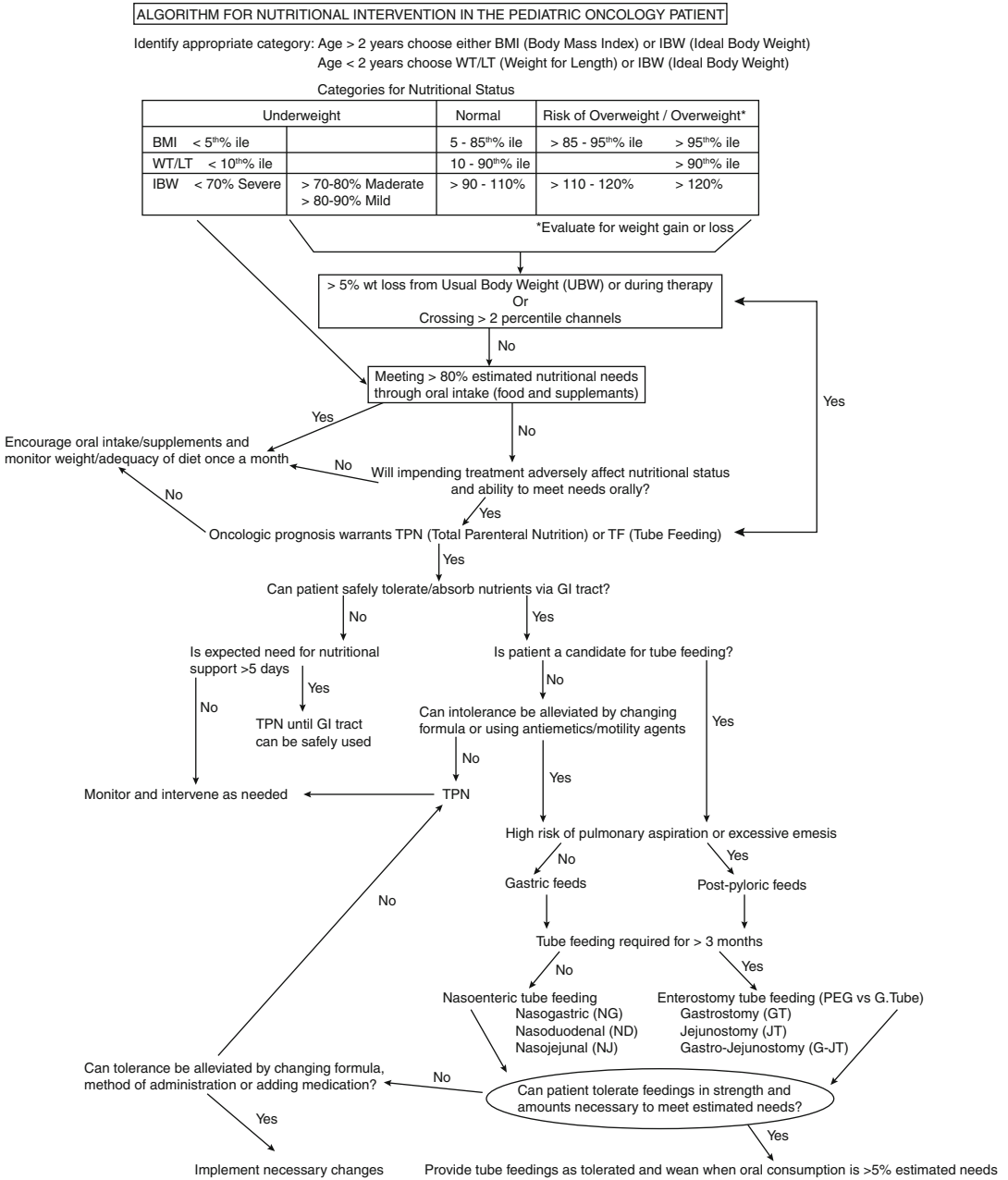
It has been well documented that a significant number of parents of children with cancer turn to the use of complementary/alternative medicine (CAM) to either manage side effects of cancer therapy or for a cure (Bishop et al. 2010). This

has fostered the development of integrative nutrition counseling in which both conventional and CAM therapies are part of an individualized nutrition plan. Integrative nutrition may be defined as nutrition counseling in which Western dietetics form the backbone of dietary recommendations but often incorporate nutrition prescriptions from traditional food knowledge and complementary/alternative whole medical systems. Integrative nutrition relies upon the use of nutrient-dense foods and dietary counseling theories that may be based in other medical frameworks as well as varied cuisines. Nutrition recommendations are often modified to create individualized nutrition prescriptions. Terms such as “strengthening,” “supportive,” “prevention,” and “immune enhancing” are often part of the matrix of creating the personalized nutrition recommendations. In some cases, genetic consultation may be included into dietary counseling. Integrative nutrition is often more theoretical in nature as dietary prescriptions often are derived from whole system theories and place emphasis on the importance of a whole-foods-based diet as a component of a healthy lifestyle.

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## 8.3 Nutrition Management for the Child with Cancer

For the child with cancer, nutrition therapy is composed of assessment, intervention, and evaluation. Each of these domains may be complemented with integrative dietary counseling. Nutrition assessment is the first level of nutrition therapy and should be completed at diagnosis and throughout cancer therapy. Nutrition assessment at the initiation of cancer therapy allows for the collection of baseline anthropometric, biochemical, or dietary intake data which may be used as comparison values to subsequent assessments. Categorization of nutrition status can be beneficial to guide the timing of subsequent nutrition interventions. The nutrition committee of Children's Oncology Group has developed guidelines that provide recommendations on the nutrition assessment and intervention of the child with cancer (Fig. 8.1). A standard nutrition



**Fig. 8.1** Algorithm for nutritional intervention in the pediatric oncology patient

assessment follows the ABCD format and often includes assessment of (1) anthropometric data, (2) biochemical data, (3) clinical presentation, and (4) dietary intake. Assessment of dietary intake may emphasize the quality and quantity of

the diet. A thorough discussion of each of these indices has been published elsewhere (Mosby et al. 2009).

Children and adolescents who are underweight, at risk for overweight, overweight, or have been

**Table 8.1** Childhood cancers associated with a high nutritional risk

Wilm's tumor
Neuroblastoma
Rhabdomyosarcoma
Nasopharyngeal sarcoma
Ewing's sarcoma
Acute myelogenous leukemia
Acute nonlymphocytic leukemia
High-risk acute lymphocytic leukemia
Medullablastoma, ependymoma, and low-grade glioma
Stem cell transplantation

diagnosed with a malignancy associated with nutrition depletion (Table 8.1) should be evaluated for advanced forms of medical nutrition therapy. Nutrition intervention includes dietary counseling, oral supplements, and evaluation for placement of enteral or total parenteral nutrition (TPN). If the patient is unable to meet recommended intakes orally, consideration for the placement of enteral tube feeding should be recommended (Bakish et al. 2003; den Broeder et al. 1998; Deswarte-Wallace et al. 2001; Mathew et al. 1996). Advantages for using enteral feeding for nutritional support include lower costs, decreased risk of infections and liver abnormalities, and maintenance of the gut mucosa (Ladas et al. 2005; Han-Markey 2000; Mathew et al. 1996). Moreover, enteral tube feeding may reduce both parent and patient anxiety related to achieving daily calorie and micronutrient recommended intakes (den Broeder et al. 1998; Deswarte-Wallace et al. 2001; Mauer et al. 1990).

Dietary substitutions may be recommended including adherence to a whole-foods diet abundant in vitamins, minerals, and phytonutrients. A whole-foods approach to common nutrition issues encountered by children with cancer may focus on enhancing calories and protein, managing steroid-related effects and electrolytes. During periods of immunosuppression, special attention should be placed on foods that support the immune system while limiting processed foods that may compromise the immune system. Integrative dietary counseling should include a discussion of food

**Table 8.2** Integrative approaches to dietary counseling

Nutrition indication	Integrative recommendation
Increase caloric intake	Fruit topped with nut butter Nuts and seeds Dried fruit Homemade smoothies made with full fat yogurt and protein powder Unsaturated fats (olive oil, avocados) Omega-3-rich fish (sardines, sea bass, monk fish, salmon) Vegetables combined with calorie-rich dressings (hummus, guacamole, or yogurt-based dip) Coconut milk (added into food preparation)
Increase protein	Whey protein powder added to any food or liquid, as palatable Mediterranean or Greek yogurt (full fat variety) Lean meats such as chicken and turkey Protein-rich soups such as congee with chicken or turkey Quinoa, kashi, or brown rice Tofu, tempeh, or seitan
Maintain electrolytes	Coconut water
Steroid-related nutrition management	Low glycemic foods: oats, barley, bran, whole grain breads, whole fruit, vegetables including leafy greens, basmati or brown rice, quinoa, whole-wheat pasta, legumes, nuts/seeds

safety especially during periods associated with neutropenia. Examples of an integrative dietary approach to nutrition counseling are described in Table 8.2.

In many cases, integrative dietary counseling will also include a discussion of dietary supplements. A discussion of the risks and benefits may be incorporated into the dietary assessment along with documentation in the patient's medical record. Documentation should include the intended purpose of supplementation, evidence for effectiveness, and possible interactions associated with its administration. In some cases, supplementation may be replaced with specified foods. The DRIs may provide



guidance for supplementation so as to ensure oral intakes do not exceed the upper tolerable intakes. An evidence-based approach should guide counseling on dietary supplements when a DRI is not available. In some circumstances, supplements with less support for efficacy may be replaced with supplements supported by evidence (Ladas et al. 2006).

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## 8.4 Integrative Dietary Approaches in Supportive Care

### 8.4.1 Loss of Appetite

Loss of appetite is encountered by approximately 60 % of children undergoing therapy for cancer (Ladas et al. 2005). Temporary loss of appetite can affect a child's quality of life and often leads to frustration on behalf of the patient and parent. Appetite stimulants may be frequently prescribed but are limited in their efficacy to promote appetite. Dietary counseling emphasizes nutrient-dense whole foods such as avocados, nuts and nut butters, coconut milk, and fish. However, oral dietary interventions often fail to overcome the effects of cancer therapy. In many clinical conditions advanced forms of nutrition intervention are indicated. Dietary supplementation may be considered as an adjunct to advanced nutrition interventions. In some cases, evidence for effectiveness is available to guide clinical practice.

There are a few nutrition supplements that have been explored for the management of cancer-related cachexia. Among these, essential fatty acids (EFAs) are the most thoroughly researched. Clinical studies were driven by the observation that adults with advanced cancer with cachexia have lower plasma EFAs (Brown et al. 2003; Pratt et al. 2002). The biological plausibility of EFAs was supported with the finding that EFAs reduce inflammatory cytokine production, a process associated with development of cachexia, in patients with pancreatic cancer (Falconer et al. 1994). Several clinical trials of EFAs with various scientific rigor (case series, Phase 1 trials, and randomized, controlled trials) have been conducted among adults with

cancer (Barber et al. 2000; Barber et al. 2001; Bruera et al. 2003; Burns et al. 1999; Falconer et al. 1994; Fearon et al. 2003; Gogos et al. 1998; Wigmore et al. 2000). A Phase 1 trial in adults with cancer found the maximum tolerated dose of EFAs to be 0.3 grams/kg/day (Burns et al. 1999). Benefits from EFAs were observed in small trials; however, in a large, randomized, placebo-controlled trial involving 200 adults with pancreatic cancer, supplementation with an EFA-enriched nutrition supplement was not associated with the prevention of weight loss. The variable doses and duration of supplementation may have contributed to conflicting results. More recently, investigators have suggested that increased dosages of EFAs are necessary to stimulate appetite. Clinical trials have not confirmed these initial hypotheses.

Melatonin is a hormone secreted from the pineal gland and has been associated with the promotion of appetite. Although the mechanism at which melatonin exerts its stimulant effects is largely unknown, its mediating effects on cytokine release associated with the promotion of cachexia have been postulated. One randomized, open label, pilot study administered melatonin, fish oil, or a combination for an 8-week period to 24 adults with advanced gastrointestinal cancer and a documented history of weight loss (Persson et al. 2005). The study suggested a weight-stabilizing effect of both interventions and improvement in quality of life in patients in the melatonin arm. Currently, a melatonin Phase I study is underway among children with cancer.

More recently, the role of whey protein has been promoted as an appetite stimulant (Ladas et al. 2006). Whey protein is a complete protein with an elevated amount of branched-chain amino acids and a variety of other proteins that include alpha-lactalbumin, beta-lactoglobulin, lactoferrin, serum albumin, lysozyme, and immunoglobulins A, G, and M. Supplementation with whey protein in patients with other life-threatening illnesses including HIV reported no adverse effects, promotion of appetite, and increased muscle tone (Micke et al. 2001; Micke et al. 2002; Micke et al. 2001). A small pilot study in children with cancer also found improvements in

weight gain (Melnick et al. 2005). Subsequent trials are needed to confirm these preliminary findings.

#### 8.4.2 Nausea and Vomiting

Nausea and vomiting is an aspect of supportive care that impacts the majority of patients with cancer at some point in their therapy. Integrative dietary approaches to nausea and vomiting rely on the use of congee, clear broth soups, high-protein fruit and vegetable drinks or shakes, fruit ice pops, and ginger candies to aid in relieving the sensation of nausea. Coconut water may be suggested to replenish electrolytes in individuals with persistent vomiting. Herbal teas such as citrus flavors or peppermint may also be beneficial.

Oral intake of food and fluids is limited during periods of nausea and vomiting. Dietary supplements may be considered as an adjunct to the prescribed antiemetic protocol. The most thoroughly researched supplement is ginger as clinical trials have been conducted in both adults and children with cancer. A double-blind, placebo-controlled, randomized trial among 32 children and young adults with newly diagnosed bone sarcomas evaluated the efficacy of ginger as an adjunct to the standard of care (Pillai et al. 2011). Children and young adults between the ages of 8–21 were randomized to receive ginger powder (1,000–2,000 mg/day) or placebo for five days at the beginning of a chemotherapy cycle and for 2 days post in addition to the standard of care. The authors' reported a reduction in the incidence of moderate to severe acute nausea in the experimental (55.6 % of cycles) compared to the placebo arm (93.3 % of cycles) ( $P=0.003$ ). Decreased incidence of moderate-severe vomiting was also found in the experimental arm (33.3 %) compared to the placebo arm (76.7 %) ( $P=0.002$ ), and decreased incidence of moderate to severe delayed nausea ( $P<0.001$ ) and vomiting ( $P=0.022$ ) was reported in the experimental arm compared to placebo. No adverse events were reported. However, the study is limited by a

small sample size, lack of stratification by antiemetic regimen, and no intra- or interindividual reporting.

#### 8.4.3 Constipation

Constipation is frequently reported in children being treated with cancer and is associated with certain classes of chemotherapy agents or the tumor itself. In severe cases, constipation may also be accompanied by severe bowel pain. An integrative dietary approach to constipation will begin with nutrition education on foods high in insoluble fiber. A diet high in insoluble fiber is recommended for decreased gut movement, whereas diets high in soluble fiber act as a stool softener. Whole foods high in insoluble fiber may be found in Table 8.3. The recommended grams of the daily intake of fiber is “age+5” up to the 18 years old. After 18, 25–30 grams per day is recommended. The introduction of fiber should be in 3–5 gram increments and be accompanied with adequate intake of fluids. Incorporating fiber into small meals throughout the day may be more feasible rather than in a single serving. Dietary supplements such as blond or black psyllium and senna may provide additional relief. Evidence for effectiveness is available for psyllium although no trials have been conducted within the context of cancer therapy. Psyllium has been found to be safe in children when accompanied by adequate fluid intake. Psyllium increases the volume of the stool through exerting a laxative effect and acts as a stool softener by increasing stool water content. The combination of blond psyllium with senna has been found to increase its effectiveness (Marlett et al. 1987).

#### 8.4.4 Diarrhea

Diarrhea is a common side effect of cancer therapy, yet most of the published research investigating diet or dietary supplement for the treatment of diarrhea in children has been in newborns, malnourished children, or children with HIV/

**Table 8.3** Foods high in soluble versus insoluble fiber

Food	Serving size	Total fiber (g)	Soluble fiber (g)	Insoluble fiber (g)
<i>Fruit</i>				
Figs, dried	3 medium	10.5	4.9	5.6
Raspberries	1 cup	8	2.1	5.9
Blackberries	1 cup	7.6	1.9	5.7
Pear with skin	1 medium	5.1	1.9	3.2
Tangerine	2 medium	5	4.4	0.6
Cranberries	1 cup	5	1.7	3.3
Orange	1 large	4	2.5	1.5
Apricot, whole	5	4	2.1	1.9
Red apple with skin	1 medium	4	1.4	2.6
<i>Vegetables</i>				
Cooked spinach	1 cup	7	2.2	4.8
Cooked Brussels sprouts	1 cup	6.4	3.4	3
Red cabbage, cooked	2 cups	6	0.3	5.7
Acorn squash, baked	1 cup	6	0.7	5.3
Butternut squash, baked	1 cup	5.7	2.3	3.4
Parsnips	1 cup	5.4	2.7	2.7
Collard greens, cooked	1 cup	5.3	2.4	2.9
Okra	1 cup	5.2	1.3	3.9
Cooked broccoli	1 cup	5	2.5	2.5
Cooked turnip greens	1 cup	5	1.6	3.4
Cauliflower	1 cup	4.9	2	2.9
Sweet potato with skin	1 medium	4.8	1.8	3
Cooked carrots	1 cup	4.7	2.6	2.1
Artichoke hearts, canned/jar	4 small	4.5	3.3	1.2
Green peas	½ cup	4.4	1.3	3.1
Cooked beets	1 cup	4	1.8	2.2
Cooked green beans	1 cup	4	1.6	2.4
<i>Beans/legumes</i>				
Navy beans, cooked	½ cup	9.6	3.2	6.4
Split peas, cooked	½ cup	8	2.5	5.5
Lentils, cooked	½ cup	7.8	0.9	6.9
Pinto beans, cooked	½ cup	7.7	1.8	5.9
Black beans, cooked	½ cup	7.5	3	4.5
Kidney beans, cooked	½ cup	6.9	2	4.9
Lima (butter) beans	½ cup	6.6	1.7	4.9
Chickpeas, cooked	½ cup	6.3	1.9	4.4
<i>Bread/cereals/grains</i>				
Fiber One cereal	½ cup	11.9	0.8	11.1
All-Bran cereal	½ cup	8.8	1.4	7.4
Raisin Bran cereal	1 cup	6.8	1.2	4.6
Pearl barley, cooked	1 cup	6	1.6	4.4
Grape nuts cereal	½ cup	5	1.6	3.4
Bulgur, cooked	½ cup	4.1	0.7	3.4
Whole-wheat bread	2 slices	4	0.8	3.2
Shredded wheat, spoon size	½ cup	4	0.5	3.5
Oatmeal, cooked	1 cup	4	2.1	1.9

(continued)

**Table 8.3** (continued)

Food	Serving size	Total fiber (g)	Soluble fiber (g)	Insoluble fiber (g)
<i>Seeds/nuts</i>				
Sunflower seed kernels (dry roasted, w/salt added)	½ cup	6	2.4	3.6
Peanuts, dry roasted	¼ cup	4.6	1.5	3.1
Almonds, sliced	¼ cup	3.5	0.6	2.9

AIDS. It is plausible that these strategies may be applicable to children undergoing treatment for cancer as these studies have been conducted in populations with compromised immune systems or to manage side effects due to conventional treatment.

Diet may be modified to manage the severity of diarrhea. Advising patients to avoid food or drinks high in sugar, dairy, greasy foods, and gas-forming foods may provide some relief of diarrhea. Extreme temperatures of food or liquid may also promote diarrhea. Increasing dietary intake of soluble fiber (up to 10 grams/day) may also reduce the severity of diarrhea. Table 8.3 lists foods high in soluble fiber. In adults, clinical studies have found that a diet high in blond psyllium (18 grams/day in divided doses, taken with fluid) may be effective in reducing diarrhea. Diarrhea induced by enteral feeds may also be relieved by supplementation with psyllium. Administration of 30 grams/day with fluids in patients with enteral feeding reduced the frequency of bowel movements (Belknap et al. 1997; Heather et al. 1991).

Probiotics are one of the most frequently used biologic CAM therapies used in children. Probiotics have been evaluated in premature infants, adults and children with HIV, adults receiving organ transplantation, and adults with cancer. Among adults and children with HIV, administration of probiotics appears to be well tolerated and safe (Cunningham-Rundles et al. 2000; Trois et al. 2008; Cunningham-Rundles et al. 2000). *L. rhamnosus* was found to decrease the severity of diarrhea and increase CD4 counts among adults with HIV/AIDS (Anukam et al. 2008). Cunningham-Rundles et al. found that administration of *L. plantarum* 299 and 299v effectively colonized the gastrointestinal tract and promoted growth and development among children with

HIV (Cunningham-Rundles et al. 2000). In a double-blind, randomized controlled trial, 450 adults with cancer who were receiving radiation to the pelvic region were randomized to receive the blend probiotic product, VSL #3, or placebo during radiation therapy. The authors reported a decrease in the incidence and severity of diarrhea. No adverse events were reported (Delia et al. 2007). Because the use of probiotics contains live active organisms, there has been hesitation in prescribing their use among patients with compromised immune systems. A small pilot study is ongoing among children undergoing stem cell transplant using *L. plantarum* 299 and 299v.

Colostrum is the milk secreted by mammals within the first few days after giving birth and contains high concentrations of antibodies (IgG, IgM, and IgA), cytokines (interleukin-1 beta, interleukin-6, tumor necrosis factor-alpha, and interferon-gamma), growth factors (insulin-like growth factor I and II, transforming growth factor-beta, epidermal growth factor), lactoperoxidase, and lactoferrin (Inoue et al. 1998). A small case series describes the use of colostrums obtained from humans in children undergoing bone marrow transplantation (Inoue et al. 1998); however the safety of its use is unclear in children with cancer. Colostrum has been administered to infants for the management of diarrhea (Sarker et al. 1998; Szajewska and Mrukowicz 2001; Tawfeek et al. 2003). No adverse events were reported.

### 8.4.5 Mucositis

In children cancer and undergoing bone marrow transplantation, mucositis can be debilitating and

severely painful. Dietary changes are often not effective at maintaining nutrition status in children with moderate to severe mucositis due to the child's inability to swallow. Under these circumstances, short-term use of TPN is often necessary to provide the necessary nutrients. Dietary supplements may be beneficial in the prevention of mouth sores; less benefit may be observed when dietary supplements are used for the treatment of mucositis. Glutamine, an amino acid, is often used in the setting of stem cell transplantation for the prevention of mouth sores. In a review, administration of glutamine (2 grams/m<sup>2</sup>, BID) was suggested to be effective in preventing the duration and severity of mucositis in children undergoing bone marrow transplantation (Worthington et al. 2011); however, others did not report a benefit of glutamine in children undergoing stem cell transplantation. The large amount of liquid required for glutamine administration can be prohibitive in children with severe mucositis and may affect compliance.

TRAUMEEL S<sup>®</sup> is a homeopathic dietary supplement that has been found to be effective in reducing the stomatitis in children undergoing bone marrow transplantation. In a randomized, placebo-controlled, double-blind clinical trial, TRAUMEEL S<sup>®</sup> was administered to 32 pediatric patients undergoing a bone marrow transplant and was associated with significant reductions in the severity and duration of stomatitis ( $P < 0.01$ ) (Oberbaum et al. 2001). No adverse events were reported. In larger double-blind, randomized trial conducted through Children's Oncology Group, patients between the ages of 3–25 years who were undergoing myeloablative stem cell transplantation were administered TRAUMEEL S<sup>®</sup> or placebo (Sencer 2012). The study found no statistical difference in incidence or severity of mucositis in the TRAUMEEL S<sup>®</sup> group compared to placebo. Full data were obtained on 106 (56 %) of the eligible patients. Adherence to 100 % of the days was poor, 37 and 35 % in the TRAUMEEL S<sup>®</sup> and placebo groups, respectively. There was no difference between groups in narcotic use, days of parenteral feeding, or days of nasogastric feeding. However, there was a trend toward less narcotic usage in the

TRAUMEEL S<sup>®</sup>-treated group of patients. It is unknown if concentrated doses and fewer administrations would improve adherence.

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## 8.5 Specialized Diets: Research Overview

The role of specialized diets as an aspect of supportive care for the treatment of cancer has been promoted in both adults and children with cancer. Little evidence is available to support the efficacy of any single diet. When counseling patients on comprehensive dietary plans, consideration to the dietary regimen along with the required effort to adopt the diet should be discussed. Additionally, the risks and benefits should be considered particularly in cases with limited data guiding implementation. The cost of the diet and the impact on family structure and quality of life should be weighed from the perspective of a child undergoing cancer therapy. In some cases, dietary change empowers children and adolescents to take an active role in the medical plan. However, in some circumstances, dietary change may lead to increased stress and anxiety related to food, increase family conflicts, and to meet the DRIs. Most of the diet studies have been conducted among adults with cancer or among survivors of adult cancer. Very few studies have explored dietary changes among children and adolescents undergoing treatment for cancer.

### 8.5.1 Neutropenic Diet/Low Microbial Diet

Treatment for cancer often results in neutropenia (low white blood cell counts) which increases the risk of developing an infection. The duration and severity of neutropenia can be predicted by the dose and class of chemotherapy agent, dose and field of radiation, and the cancer. Food is an established vector of infections, and it is presumed that neutropenia increases the risk of a food-borne illness especially in the setting of severe neutropenia (ANC < 500 cells/mm<sup>3</sup>). The

neutropenic diet or low microbial diet is frequently prescribed to minimize the risk of an infection through bacterial translocation by eliminating foods susceptible to infectious organisms.

While the scientific support for the neutropenic diet is largely empirical, the foundation of the diet dates back to the 1960s when sterile diets were a component of cancer supportive care. Evidence supporting the neutropenic diet was largely based on animal studies that found that neutropenic animals who resided in a sterilized environment responded better to chemotherapy and had lower toxicities compared to animals in non-sterilized environments (Berg 1995). Studies also reported isolated germ-free rodents could withstand higher doses of chemotherapy and radiation without succumbing to toxic death. As these studies were applied to clinical practice, sterilization of the gastrointestinal tract was necessary prior to the patient beginning the anticancer regimen that may render them neutropenic.

In one of the earliest studies exploring the role of the neutropenic diet on cancer outcomes, subjects with acute leukemia ( $n=21$ ) were randomized to either a fixed or rotating antibiotic regimen and administered a cooked or sterile diet (Preisler et al. 1970). Historical patients were used as controls. All patients began on the sterile diet and then were randomized to the cooked foods diet or continued with the sterile diet. Patients randomized to the sterile diet complained of unpalatability, whereas patients on the cooked food diet had few comments. No significant differences in incidence of aerobic, anaerobic, or fungal infections were observed between the groups, although higher levels of bacterially sterile stool cultures were observed in subjects receiving the sterile diet and rotating antibiotic regimen. Upon discharge, a subsequent analysis on the same group of patients found the rotating antibiotic regimen maintained bacterial suppression regardless of diet, suggesting that a sterile may not be necessary. This initial finding has been supported in subsequent randomized trials. One recent clinical study explored the neutropenic diet in a small pilot study ( $N=19$ ) among children with cancer

(Moody et al. 2006). Participants were randomized to the neutropenic diet or to the Food and Drug Administration (FDA)-approved food safety guidelines for one chemotherapy cycle. The primary outcome was febrile neutropenia, and secondary outcomes included adherence and diet tolerability. The adherence rate was 94 % for the neutropenic diet and 100 % for the food safety guidelines. Four patients on each diet arm developed febrile neutropenia. Infection rates for patients on the neutropenic diet were similar to those following food safety guidelines. The results of this study suggest that food safety guidelines are as effective as the neutropenic diet in minimizing the risk of food-borne infection. A larger trial conducted in adults also found no beneficial effect of the neutropenic diet (Gardner et al. 2008).

Historically, all uncooked fruits and vegetables without peels, unpasteurized juice and dairy products, cheeses with molds, salad bars, dried fruits, delicatessens, raw fish, and certain spices should be avoided on a neutropenic diet. However, as the evidence supporting these restrictions is limited, the recommendations have been slightly relieved. At the very minimum, *food safety guidelines should always be followed by any patient undergoing anticancer therapy*. These guidelines will minimize the risk and extent at which a patient is exposed to food contamination. A comprehensive review of these guidelines can be found at the Food Safety Working Group website ([www.foodsafety.gov](http://www.foodsafety.gov)).

### 8.5.2 Ketogenic Diet

The relationship between carbohydrates and cancer has been supported by preclinical experimental studies, prospective observational studies, and small pilot studies. The role of sugar in cancer growth is embedded early work of Otto Warburg who discovered that cancer cells preferentially underwent glycolysis for energy production, even in the presence of oxygen (Klement and Kammerer 2011). Now termed the Warburg effect, this observation has become one of the most consistent hallmarks of cancer (Hanahan and Weinberg



2011). While initially this pathway seems counterintuitive due to the inefficiency of ATP production, aerobic glycolysis allows tumor cells to bypass cell death pathways linked to mitochondria, reduces the amount of harmful reactive oxidation species, employs other pathways to increase nucleic acid and lipid production, and enhances tumor aggressiveness through lactate and hydrogen ion production (Walenta et al. 2000). However, use of aerobic glycolysis ensures that tumor cells become dependent on glucose as an energy substrate for growth.

The theory behind the ketogenic diet is rooted in limiting the tumor's glucose supply, therefore limiting growth, invasion, and metastases. Hyperglycemia has been linked to poor survival in cancer patients (Krone and Ely 2005; Maestu et al. 1997; McGirt et al. 2008; Weiser et al. 2004; Derr et al. 2009; Hudson et al. 2003) and correlated with increased risk of some cancers (Stattin et al. 2007; Ikeda et al. 2009; Jee et al. 2005). Cancer cells often lack the mitochondrial enzymes to convert other substrates, including ketones, to energy. However, peripheral cells including myocytes and brain cells can employ ketones for energy. Therefore, by limiting blood glucose availability in a cancer patient, cancer growth can be limited while maintaining the overall health of the patient.

The efficacy of the ketogenic diet among patients receiving cancer treatment has not been tested in a randomized trial. The available studies are limited to case reports in 27 adults with tumors of the gastrointestinal tract and a case series among children with a brain tumor (Rossi-Fanelli et al. 1991; Nebeling 1995). In adults, patients were assigned to glucose- or lipid-based TPN or an oral diet similar in nutrient content delivered by TPN for 14 days. Tumor proliferation was measured by thymidine labeling index at the beginning and end of the dietary intervention. No difference in tumor proliferation was observed between the groups suggesting that diet composition does not have an impact on tumor cell growth. Among children with cancer, a case series describes the administration of a ketogenic diet (60 % medium-chain triglycerides, 20 % protein, 10 % carbohydrate, and 10 % dietary fat) for a

period of 8 weeks to two children with astrocytoma (Nebeling et al. 1995). The authors described the effects of the diet on nutrition status, tumor metabolism (measured by [fluorine-18] 2-deoxy-2-fluoro-D-glucose-PET), and quality of life. The ketogenic diet promoted weight gain and improved quality of life. A 21.8 % average reduction in glucose uptake was observed. While these studies did not report adverse events associated with the ketogenic diet, they provide little evidence for efficacy. It is plausible that the ketogenic diet may provide benefit to select tumor diagnosis. It is also plausible that a longer duration that monitors the development and duration of ketosis may produce beneficial results. However, the ability of patients to adhere to a diet that is significantly different than typical dietary regimens may be difficult to test in a randomized study.

### 8.5.3 Macrobiotics

The word "macrobiotic" comes from Ancient Greek and means "long life," reflecting the view toward long-term health and spirituality embodied by the macrobiotic philosophy. The macrobiotic philosophy and diet were developed by George Ohsawa, a Japanese philosopher, who sought to integrate Zen Buddhism, Asian medicine, Christian teachings, and some aspects of Western medicine. Mr. Ohsawa believed simplicity in diet was the key to good health and that abstaining from certain foods could cure cancer and other serious illnesses. In the 1930s, he began advocating his philosophy of health and healing through proper diet and natural medicine. In the 1960s, these ideas were brought to the United States by an early disciple, Michio Kushi, who adopted and expanded Mr. Ohsawa's ideas and became a leader of the macrobiotic lifestyle.

The standard macrobiotic diet of today consists of 50–60% organically grown whole grains, 20–25 % locally and organically grown fruits and vegetables, and 5–10 % soups made with vegetables, seaweed, grains, beans, and miso. Other elements may include occasional helpings of fresh

white fish, nuts, seeds, pickles, Asian condiments, and decaffeinated and nonaromatic teas. Early versions of the diet excluded all animal products. Proponents discourage dairy products, eggs, coffee, sugar, stimulant and aromatic herbs, red meat, poultry, and processed foods. Some vegetables, such as potatoes, tomatoes, eggplant, peppers, asparagus, spinach, beets, zucchini, and avocados were also discouraged. The diet advocates for locally grown food. Macrobiotics is considered a way of life, not just a dietary regimen.

Since the 1960s, the diet has been promoted as a treatment for cancer. Interest in the diet evolved as various individuals claimed that the macrobiotic lifestyle had cured their cancer. There have been no randomized clinical studies published in the available medical literature to support the efficacy of macrobiotics for the prevention or cure for cancer. A low-fat, high-fiber diet is promoted to reduce the risk of cardiovascular disease and some forms of cancer. However, it is unknown if the extreme approach of the macrobiotic lifestyle further reduces these risks significantly more than a low-fat, healthy diet.

#### 8.5.4 Gerson Diet

The Gerson therapy, developed by physician Max Gerson, was initially designed to treat migraine headaches but was later expanded to treat other conditions such as arthritis, tuberculosis, and cancer. The Gerson therapy is considered a metabolic therapy and is based on the theory that disease is caused by the accumulation of toxic substances. Practitioners of the Gerson therapy believe that fertilizers, insecticides, herbicides, and other chemicals “contaminate” food by lowering the potassium and increasing sodium, a process further enhanced by food processing and preparation. These changes alter the metabolism of cells and foster the development of cancer. According to the Gerson therapy, individuals with cancer have too much sodium and not enough potassium in their cells. This imbalance is corrected by a fruit and vegetable diet which revitalizes the liver thereby exerting anticancer

effects. Coffee enemas are a component of the therapy and used to relieve pain, eliminate liver toxins, and promote detoxification. The Gerson therapy recommends a strict low-salt, low-fat, vegetarian diet. Juicing is an integral component of therapy; one glass of juice is recommended each hour, 13 times a day. Supplementation with potassium, vitamin B12, pancreatic enzymes, thyroid hormone, and liver extracts are used to stimulate organ function, particularly the liver and thyroid. The therapy may also include therapies such as laetrile.

There have been no well-controlled studies published in the medical literature supporting the efficacy of Gerson therapy. Papers describing patients’ experiences with Gerson therapy may be found, but these are not available in peer-reviewed medical literature. A review of 153 adult patients with melanoma seeking treatment in Mexico reported a survival advantage with the Gerson approach (Hildenbrand, et al. 1995). However, no randomized clinical trial have confirmed these findings. Molassiotis et al. reported a case review of six patients with advanced cancer (Molassiotis and Peat 2007). The authors reported prolonged survival; however, confounding variables preclude the study from supporting further research. Moreover, the Gerson therapy is associated with many toxicities of which some have resulted in death. The rigorous nature of the diet also questions its application in the clinical setting, especially in children and adolescents undergoing treatment for cancer.

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## 8.6 Nutrition and Survivorship

Significant advances in survival of children with cancer have led to nearly 70% of children and adolescents surviving the diagnosis of cancer (National Cancer Institute, 2002). Improved survival has promoted increased awareness on the prevention of secondary cancers and late effects. The increased use of corticosteroids in the treatment of many childhood malignancies presents new challenges to the clinician as an increasing number of patients are becoming obese. Survivors of acute lymphoblastic leukemia are at increased

risk for obesity and heart disease; females appear to be especially vulnerable (Veringa et al. 2012). Survivors of Hodgkin's disease are at increased risk for heart disease (Hancock et al. 1993). Other nutrition-related late effects encountered by survivors include reduced bone density and metabolic syndrome.

Much of our current understanding of the role of nutrition among survivors of childhood cancer is extrapolated from large epidemiologic studies conducted among adults. Currently, it is unknown if the increased risk of nutrition-related side effects among survivors is related to poor dietary patterns, reduced physical activity, metabolic aberrations, or the cancer therapy itself. Reviews have suggested that cancer therapy may also impact the appetite-regulating network and could be one of the factors contributing to the increase in obesity (Hagan and Niswender 2012). An increased understanding of the conditions leading to nutrition-related late effects will identify areas for future research and interventions. It is likely a combination of factors result in increased obesity. Thus, effective nutrition interventions must consider the lifestyle of the patient rather than diet alone.

As patients enter survivorship, the priorities of nutrition therapy shift to prevention-based counseling with an emphasis placed on nutrition education. Educating families and practitioners on diets associated with cancer prevention directs dietary counseling. Dietary supplementation may complement diet counseling to reduce the risk of late effects. Limited data is available and much of integrative clinical practice is extrapolated from other disease conditions. Ideally, dietary counseling should include lifestyle interventions that emphasize diet and exercise education. Clinical studies have found lifestyle counseling to be effective among survivors of adult malignancies. Lifestyle counseling may be especially effective when goals are personalized and are modified based upon sociodemographic variables. Lifestyle counseling may be delivered through new forums such as smartphone technology, social support networks, and email correspondence. Delivery of nutrition education utilizing these methods has been found to be effective in adults who are survi-

vors of breast, prostate, and colon cancer (Chlebowski 2003; Demark-Wahnefried et al. 2007; Morey et al. 2009).

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## Contents

<b>9.1</b>	<b>Background</b> .....	125
9.1.1	TCM Treatment Modalities .....	126
9.1.2	TCM and Cancer.....	126
<b>9.2</b>	<b>Research Overview</b> .....	127
9.2.1	Clinical Research on TCM in Cancer and Cancer-Related Disorders .....	127
9.2.2	Chinese Herbal Medicine.....	127
9.2.3	Acupuncture.....	129
<b>9.3</b>	<b>Pediatric Oncology in TCM</b> .....	131
<b>9.4</b>	<b>Practical Recommendations for Pediatric Oncology</b> .....	131
9.4.1	TCM Treatment Based on Syndrome Differentiation.....	131
<b>9.5</b>	<b>Common TCM Treatment Methods for Pediatric Oncology</b> .....	132
9.5.1	Herbal Medicine .....	132
9.5.2	Acupuncture.....	133

<b>9.6</b>	<b>Advantages of Integrating Chinese and Western Medicine in Treating Cancer ..</b>	133
<b>References</b> .....		134

## 9.1 Background

Traditional Chinese medicine (TCM) has been practiced for at least 2000 years in China. It is based on two fundamental theories, *yin-yang* and five elements (*wu xing*), which together explain all change as well as all natural phenomena in the universe, including human beings (Li and Cheng 1987). Yin-yang theory posits that the universe is a whole composed of two opposites, yin and yang, which are interdependent and can transform into each other. Their equilibrium ensures that harmony, including the harmony of the body, is maintained.

Five element theory, also known as five phase theory, developed from an ancient Chinese philosophical system in which the universe was held to consist of five basic elements: wood, fire, earth, metal, and water. Five element theory describes the relationships between the human body and the external environment and the physiological and pathological interactions among the internal organs within the body (Lao 1999).

According to the principles of TCM, human physiological functions are maintained by *Qi*; the *zang-fu*, or internal organs; blood; bodily fluids; and *jing-luo*, or meridians and collaterals. *Qi*, pronounced *chi*, denotes vital energy and is an essential substance for maintaining the activities of life. *Zang-fu* theory explains

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the physiological functions and pathological changes of the internal organs, which are determined by observing the outward manifestations of the body. The five *zang* are the heart, liver, spleen, lung, and kidney; the six *fu* are the gallbladder, stomach, small intestine, large intestine, urinary bladder, and *sanjiao* (triple warmer). Blood originates from food essence developed in two of the *zang-fu* organs, the spleen and the stomach. It is controlled by the heart, stored in the liver, and held in the vessels by the spleen; it nourishes the organs and tissues of the body. The vital energy known as *Qi* flows through the channels, or meridians, of the body and participates in the homeostatic regulation of bodily functions.

When illness occurs and a patient's symptoms manifest, a TCM practitioner analyzes them using the four diagnostic methods of TCM: inspection; auscultation, or listening; inquiring; and palpation. With these, a TCM differentiation such as *Qi* stagnation, blood stasis, or kidney deficiency, for example, can be made that will often correspond to the manifestations of a Western medical condition.

### 9.1.1 TCM Treatment Modalities

TCM modalities include Chinese herbal medicine, acupuncture, Chinese massage (*tui na*), mind/body exercise, and dietary therapy. Of these, Chinese herbal medicine and acupuncture are the most commonly used.

Chinese herbal medicine (*zhong yao*) is an integral part of traditional Chinese culture and medical practice. The Chinese *materia medica* includes plants, minerals, and animal parts. These are categorized by nature, flavor, and function. There are four natures, cold, cool, hot, and warm, and five flavors, pungent, sweet, sour, bitter, and salty. Functions include heat-clearing, expectoration and antitussive action, dampness elimination, and interior warming. Typically, an herbal practitioner will prescribe a formula containing ten or more herbs with differing functions, natures, and flavors, which are selected based on the syndrome to be treated. In these carefully constructed formulas, the herbs are believed to act synergistically to harmonize their

effects and to neutralize or minimize any toxicity of the individual constituents (Bensky and Barolet 1990; Bensky and Gamble 1993).

Acupuncture has been used for thousands of years in China to treat various diseases and symptoms, including those such as the pain, nausea, vomiting, and weakness that are common among cancer sufferers. According to TCM, there are 12 primary and 8 additional meridians through which *Qi* flows; each follows a given directional course through the body. Some 360 points distributed along the meridians serve as both pathognomonic signs of disorder and loci for acupuncture treatment (Cheng 1999; Stux and Pomeranz 1987).

It is presumed that when the normal flow of energy through a meridian is obstructed, for example, in the case of a tumor, symptoms occur. Acupuncture treatment aims to reopen the meridians and restore the flow of the *Qi*, thereby reducing pain or other symptoms from tumors and blood and tissue problems. It also is used to control the side effects of conventional drug treatments, including chemotherapy for cancer (Ezzo et al. 2006a). Side effects from acupuncture are rare and tend to be associated with violations of sterile procedure or negligence on the part of the acupuncturist (Lao et al. 2003).

### 9.1.2 TCM and Cancer

In recent years, cancer has become a common disease, not only among adults, but also in children. Treatment options in Western medicine include surgery, radiotherapy, chemotherapy, targeted therapy, and biological therapy. However, the overall survival rate of these treatments is still low, particularly in patients with late-stage cancer, and patient quality of life is often poor. In many Asian countries including China, TCM is commonly used as an adjunct in cancer patient care to improve the quality of life by alleviating symptoms and side effects of those undergoing conventional therapies and sometimes to treat the primary disease itself.

The pathogenesis and treatment of cancer and cancer-like diseases have been discussed in various

classical TCM texts and can be summarized as follows (Zhou 2006; Zhang 1955).

1. *Disharmony of Internal Organs*. In the Eastern Han Dynasty classic, *Shang Han Lun*, or *Treatise on Cold Damage*, Zhang Zhong Jing (150–219 A.D.) says, “For the treatment of *Ye Ge* (difficulty in swallowing), one should regulate the Spleen and Kidney by keeping the Spleen warm and the Kidney nourished.” In his Ming Dynasty classic, Dr. Jingyue Zhang (1563–1640) says, “Syndromes involving masses are usually due to insufficiency, weakness, and disorders of the internal Spleen and Stomach,” and “For the treatment of *Ye Ge* (difficulty in swallowing), one should regulate the Spleen and Kidney by keeping the Spleen warm and the Kidney nourished.”
2. *Qi Stagnation and Blood Stasis*. In the Qing Dynasty classic, *Yi Lin Gai Cuo*, or *Correcting the Errors in the Forest of Medicine*, Wang Qing Ren (1768–1831) says, “Blood stasis is often secondary to *Qi* stagnation, and prolonged *Qi* or Blood stasis can give rise to a mass.” He suggested that promoting the circulation of blood and removing stagnation should be the main principal of treatment for such tumors.
3. *Retention of Phlegm and Dampness*. Because the spleen is responsible for the transportation of body fluids, spleen deficiency can disturb that function, causing water retention. This dampness can become concentrated into phlegm. In the Sui Dynasty classic, *Zhu Bing Yuan Hou Lun*, or *General Treatise on the Cause and Symptoms of Diseases*, Chao Yuan Fang (550–630 A.D.) says, “Phlegm causes a pathology in the human body that manifests as subcutaneous masses. The treatment should be reduction of the phlegm and elimination of the accumulated Dampness.”
4. *Internal Accumulation of Toxic Heat* (Intrinsic Heat Toxin). The prolonged accumulation of heat and fire caused by the invasion of exogenous pathogens can “burn” the internal organs (the zang-fu) and lead to a tumor. The treatment principle for this type of tumor is to clear heat and toxic material and nourish yin in order to induce fire to descend.
5. *Weakness of Vital Qi* (Immune System Deficiency). A deficient constitution may be

vulnerable to the invasion of pathogenic factors that will lead to *Qi* stagnation and blood stasis or the formation of a pathogenic mass.

Overall, TCM treatment strategy for tumors and cancer is to strengthen the body’s resistance in order to restore normal function, while removing phlegm and blood stasis is a secondary strategy.

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## 9.2 Research Overview

### 9.2.1 Clinical Research on TCM in Cancer and Cancer-Related Disorders

Several survey studies on the use of alternative medicine, including Chinese medicine, in children with cancer have been reported. Yeh et al. (2000) conducted a survey in Taiwan and found that 73% of child patients received one or more alternative therapies; 20% were given TCM and 13%, “secret herbal recipes.” In a cross-sectional survey performed by Hamidah et al. (2009) at a pediatric oncology center in Kuala Lumpur, Malaysia, 84.5% of the respondents had used complementary and alternative medicine (CAM); 12% had used TCM. Quimby (2007) reviewed the effect of CAM for treating syndromes associated with tumors and the side effects of chemotherapy, reporting that herbal therapies in the pediatric oncology population are usually initiated and managed by parents, for example, ginger for nausea and vomiting, St. John’s wort for depression and anxiety, and echinacea for immunostimulation.

### 9.2.2 Chinese Herbal Medicine

A literature search of English and Chinese language databases produced a few randomized clinical trials on Chinese herbal medicine in combination with conventional treatment for pediatric cancer. See Table 9.1 for a summary of the herbal trials, all of which were conducted in China. In two of these, the researchers studied the effects on cancer itself, specifically remission and survival time. The other five concern alleviation of symptoms and side effects.

**Table 9.1** Clinical trials on Chinese herbal medicine for pediatric cancer disorders

Reference citation(s)	Type of study	Type of cancer	No. of patients	Administration methods	Benefit reported
Gai (2002)	RCT	Leukemia	N=53 Tx n=30 Control n=23	Tx: A TCM herbal formula, p.o. Control: Chemotherapy	The groups were equivalent in effect
Su (2002)	RCT	Acute leukemia	N=60 Tx n=30 Control n=30	Tx: Chemotherapy + Chinese formula, p.o. Control: Chemotherapy only	Tx group had fewer side effects from chemotherapy, and symptoms were alleviated sooner than in the control group
Xu et al. (2005)	RCT	Leukemia	N=30 Tx n=15 Control n=15	Tx: Chemotherapy + Chinese herbal medicine, p.o. Control: Chemotherapy only	During a 3-month follow-up, the tx group had a quicker recovery time than did the control group in WBC count, Hgb, and fever
Wang (2007)	RCT	Non-Hodgkin's lymphoma phases III and IV	N=30 Tx n=16 Control n=14	Tx: Chemotherapy + Chinese herbal medicine (shenqi fuzheng), i.v. Control: Chemotherapy only	Side effects observed: Tx group had less decrease of WBC and Hgb compared to the control group $p < 0.05$
Shi et al. (2007)	RCT	Solid tumors	N=60 Tx n=30 Control n=30	Tx: Chemotherapy + Chinese herbal medicine Control: Chemotherapy only	Tx group: Both WBC and Hgb increased compared to baseline ( $p < 0.05$ ) Control group: No significant changes compared to baseline Symptom score: Tx group decreased; control group, no change
Shi (2009)	RCT	Solid tumors	N=76 Tx n=35 Control n=41	Tx group: Chemotherapy + Chinese herbal medicine, p.o. Control group: Chemotherapy only	Average survival time: Tx group: $31 \pm 2$ months (95%CI 27–34 months) Control group: $21 \pm 2$ month (95%CI 16–25 months) $p < 0.01$
Wang (2010)	RCT	Cancer (various)	N=57 Tx n=29 Control n=28	Tx group: Chemotherapy + Chinese herbal extract matrine, i.v. injection; Control group: Chemotherapy only	Tx group: Fewer cases of toxicity than control; faster restoration of normal neutrophil count and platelet levels than control

Gai (2002) randomly assigned 53 children with leukemia into a treatment group in which traditional Chinese herbal medicine, a decoction of a number of herbs, was used in combination with chemotherapy ( $n=30$ ) and a control of chemotherapy alone ( $n=23$ ). The herbal formula contained rhizome *Rehmannia dride* (shengdi), *Taraxacum sinicum Kitag.* (dandelion; pugongying), herba *Cirsii japonici* (daji), and rhizome *Phragmites communis Trin.* (lugen). According to TCM theory, this formula is designed to nourish yin, clear heat, and cool the blood. The decoction was given orally (p.o.), 50–100 ml per dose according to the age of the children, two or three times a day during a course of 30 days, for up to six courses. Outcome assessments were based on the 1998 *Standard Diagnosis and Efficacy of Hematological Disease*, published in China (Zhang 1998). The authors reported that 23 of the 30 patients in the treatment group showed complete remission, and 3 showed partial remission; 12 of the 23 patients in the control group had complete remission, and 5 had partial remissions. The authors concluded that Chinese herbal medicine in addition to conventional chemotherapy seems superior to chemotherapy alone in treating children with leukemia. Similar results were reported by other research groups in three randomized clinical trials (Su 2002; Xu et al. 2005; Wang 2007) showing that a TCM herbal formula combined with chemotherapy significantly reduced such symptoms as fever, bleeding, nausea, and vomiting compared to chemotherapy alone. See Table 9.1.

Research on Chinese herbal medicine in children with solid tumors was also reported. Shi et al. (Shi et al. 2007; Shi 2009). investigated the effect of concurrent use of a traditional Chinese herbal formula with chemotherapy on relief of clinical symptoms and survival in children with solid tumors. See Table 9.1. The average survival period was  $31 \pm 2$  months (95% CI; 27–34 months) in the treatment group, significantly longer than the  $21 \pm 2$  months of the chemotherapy-only control group (95% CI; 16–25 months;  $p < 0.01$ ). Furthermore, improvement of symptoms in the treatment group was superior to that in the control group. Wang (2010) reported a

randomized clinical trial ( $n=57$ ) investigating the effect of a Chinese remedy, compound matrine injection, in combination with chemotherapy in the treatment of children with advanced solid tumors. Their data show that the rate of toxicity in the digestive and hematologic systems was significantly less in the treatment group ( $n=29$ ) than in a chemotherapy-alone control group ( $n=28$ ). The treatment group also had shorter recovery times for absolute neutrophil count and platelets (11.3 and 12.6 days, respectively) than did the control group (13.9 and 15.7 days). Chen et al. (2008) observed 44 children with advanced neuroblastoma treated with concurrent use of chemotherapy and a Chinese herbal formula containing ginseng and astragalus. Three-year survival rate was 51.3%, 5-year survival rate was 41.0%, and 10-year survival rate was 30.8%.

In two uncontrolled clinical observational studies, Xie (1999; Chen and Wu 2004) reported that the use of Chinese herbs reduced the side effects of chemotherapy and improved quality of life in children with leukemia.

### 9.2.3 Acupuncture

Our literature search turned up very few acupuncture trials on pediatric cancer treatment, possibly because children tend to fear needles. Acupuncture use in pediatrics is, however, becoming more widespread for pain and the other symptoms commonly experienced by children suffering from cancer. Jindal and Mansky (2008), in a National Center for Complementary Medicine, National Institutes of Health review of complementary and alternative medicine use in pediatrics in the United States, found evidence that acupuncture is efficacious in children, particularly for management of postoperative and chemotherapy-induced nausea and vomiting.

In a 2006 systematic review of eleven RCTs on acustimulation for chemotherapy-induced nausea and vomiting, Ezzo et al. (2006b) found that, overall, the incidence of acute vomiting was reduced ( $p=0.04$ ) but, compared to control, acute and delayed nausea was not. Dune and Shiao (2006), in an analysis of several RCTs on

acustimulation effects on postoperative vomiting in children, reviewed two acupressure and six acupuncture RCTs ( $p < 0.005$ ) that showed these modalities to be effective for reducing vomiting in children. They reviewed three trials comparing acustimulation techniques to medications that showed acustimulation to be as effective as antiemetics in children ( $p = 0.6025$ ). Interestingly, two trials on electrostimulation showed no significant reduction of vomiting ( $p = 0.118$ ).

In an RTC by Wang and Kain (2002) on the effect of an acupoint injection (a 0.2-mL glucose solution introduced to a depth of between 5 and 7 mm) at P6 (Neiguan) versus that of droperidol, 187 children aged 7–16 years, given outpatient surgery under general anesthesia, were randomized into four groups: (1) i.v. saline plus bilateral P6 point injection ( $n = 50$ ), (2) i.v. droperidol plus sham P6 injection ( $n = 49$ ), (3) i.v. saline plus sham point injection, and (4) i.v. saline plus sham P6 injection. Bouts of nausea and vomiting were evaluated postanesthesia and 24 h after surgery. Group 1, P6 injection plus i.v. saline, showed significantly fewer bouts of postoperative nausea and vomiting compared to group 3, sham point injection, (nausea, 32% vs. 64%,  $p = 0.002$ ; vomiting, 12% vs. 31%,  $p = 0.029$ ) and group 4, sham P6 injection, (nausea, 32% vs. 56%,  $p = 0.029$ ; vomiting, 12% vs. 33%,  $p = 0.026$ ). Postoperative differences were not significant between group 1 and group 2, i.v. droperidol with sham acupoint injection (nausea, 32% vs. 46%, respectively; vomiting, 12% vs. 18%; combined, 42% vs. 51%,  $p =$  insignificant). The researchers concluded that P6 injections and droperidol were equally effective in controlling early postoperative nausea and vomiting (42% in the acupoint group vs. 51% for droperidol,  $p =$  insignificant). They also found that significantly fewer subjects in the acupoint group required intravenous ondansetron as an initial rescue therapy ( $p = 0.024$ ).

Acupuncture for pediatric pain is less well studied, but according to a 2005 survey of 43 accredited pediatric anesthesia training programs in major American universities, almost a third (33%) offered acupuncture (Lin et al. 2005). And in a Harvard Medical School Department of Pediatric phone survey of forty-seven families

with a child whose chronic pain, from such conditions as migraine, endometriosis, and reflex sympathetic dystrophy, was being treated with acupuncture at Children's Hospital, Boston, 70% believed that the treatment had improved symptoms (Kemper et al. 2000). Because there is resistance to the use of narcotics in children for fear of addiction and the increase in respiratory depression and because pain can result from a variety of causes, including tumor invasion, chemotherapy, other therapies and procedures, and sources unrelated to the cancer and its treatment, management of cancer pain in children is challenging and requires a multidisciplinary approach (Suresh 2004) in which acupuncture and Chinese herbs may play an important role.

RCTs specifically on acupuncture for pediatric cancer and cancer-related symptoms and side effects are rare. Two RCTs, an interim and a pilot trial, both part of a randomized, multicentered crossover study of acupuncture for nausea and vomiting in children aged six to eighteen, who were undergoing highly emetogenic chemotherapy for the treatment of solid malignant tumors, have been reported by a group of researchers from pediatric oncology centers across Germany. In the pilot study ( $n = 23$ ), Gottschling et al. (2008) compared 46 courses of chemotherapy with and without acupuncture. They found that the need for rescue antiemetics was significantly lower when patients received acupuncture and that patient acceptance was high. In the earlier study, Reindl et al. (2006) reported interim results of the project. In this smaller trial, children ( $n = 11$ ) taking highly emetic chemotherapy for malignant solid tumors received 22 courses randomized as chemotherapy with acupuncture or chemotherapy alone. Baseline antiemetic amounts were recorded and daily bouts of nausea and vomiting were charted. The published interim results showed no differences in episodes of vomiting ( $p = 0.374$ ), and baseline medication requests were not statistically significant between courses ( $p = 0.074$ ). However, the need for additional antiemetic medication was decreased in courses with acupuncture ( $p = 0.024$ ). The researchers observed that children receiving acupuncture were more alert and their nausea and vomiting were reduced.



Other documentation of clinical acupuncture studies for pediatric cancer is slight, although Ladas et al. (2006) reviewed several small clinical trials that provided evidence of a role for acupuncture in symptom management, finding them to be of “varying quality.”

These herbal and acupuncture studies indicate that Chinese medicine, combined with chemotherapy, may prolong survival time and improve patient quality of life, control pain, and reduce nausea and vomiting and other symptoms. However, due to the low quality of the research methods and small sample sizes in most of the existing studies, larger, more rigorously designed clinical trials are warranted to confirm this.

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### 9.3 Pediatric Oncology in TCM

According to TCM theory, the key organs of a child’s development are the “kidney” and “spleen.” The kidney is the congenital base of life, and the spleen supports that base after birth. Many aspects of the development of infants, including growth, formation of the immune system, and normal development and functioning of bones, brain, hair, hearing, and dentition, are attributed to kidney *Qi*. Furthermore, a proper diet with sufficient nutrition is important for maintaining functioning of a child’s spleen and stomach. Pathologically, infantile viscera are considered delicate, and the body’s immunity is held to be weak. Given this organ and immune system deficiency, children are vulnerable to pathological factors. With insufficiently developed spleens and less efficient transformation and transportation of nutrients, they are more likely than adults to be affected by poor nutrition. If timely and proper treatment is not given, disease can become serious.

In TCM theory, the main causes of infantile tumors are prolonged insufficiency of the spleen, kidney essence, *Qi*, and blood. Thus, the principal treatment is to strengthen the internal organs in order to bolster immune resistance to pathological factors. Since treatment should be based on syndrome differentiation, methods should correspond to the different phases of disease and

the particular organs found to be deficient. For example, in a complicated syndrome when deficient antipathogenic *Qi* manifests, the treatment should mainly consist of replenishing methods combined with mild elimination. The combination of TCM and chemotherapy is believed to strengthen vital *Qi* and harmonize the spleen and stomach while reducing the side effects of the conventional drugs.

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## 9.4 Practical Recommendations for Pediatric Oncology

Because the practice of acupuncture and TCM requires extensive knowledge and training, it is strongly recommended that a physician/oncologist refer to, or work closely with, a licensed TCM practitioner when treating a child with cancer. In the United States, many schools and colleges provide 3- or 4-year acupuncture and Oriental medicine/TCM training. Most offer master’s degrees; some confer doctoral degrees. About sixty of these schools are accredited by the Accreditation Commission for Acupuncture and Oriental Medicine (ACAOM), an agency that ensures the quality of the training (Ladas et al. 2006). At least forty-four states and District of Columbia require non-MD acupuncturists to be licensed. Most also require certification, and thus a passing grade on the national examination administered by the National Commission for Certification of Acupuncture and Oriental Medicine (NCCAOM) is usually a licensing requirement. The following are principles of TCM treatment for pediatric oncology that a trained TCM practitioner should employ.

### 9.4.1 TCM Treatment Based on Syndrome Differentiation

Cancer treatment requires strengthening immune resistance and eliminating pathogenic factors. Based on the different phases of development of the disease and the relationship between the patient’s healthy *Qi* and the pathogens, these corresponding treatment principles should be

followed: on the one hand, eliminate the masses; on the other, protect the ability of the antipathogens of the human body and mobilize the patient's capacity to fight against the cancer.

According to the patient's constitution and the clinical development of the cancer, its loci, malignancy, and metastatic condition, TCM treatment may be divided into three phases:

- (a) Early Stage. In this stage, although cancer has been detected, the patient is symptom-free or experiences mild symptoms, normal daily activity, and an unremarkable tongue and pulse. The patient still has sufficient antipathogenic *Qi*. The TCM differentiation is "active healthy (正*zheng*) *Qi* and incipient pathogenic (邪*xie*) factors." The treatment is to eliminate pathogenic factors and protect the healthy *Qi*.
- (b) Intermediate Stage. In this stage, patient has a noticeably enlarged mass, feels fatigue and weakness, and appears emaciated. The TCM differentiation is "excessive *xie* factors and deficiency of *zheng Qi*." At this stage, the TCM treatment principle is simultaneously to expel the pathogenic factors and strengthen the antipathogenic *Qi*.
- (c) Advanced Stage. In this late stage of the disease, the tumor becomes hard, and the cancer may have metastasized to distant regions. The patient has a yellowish complexion and is emaciated. The TCM treatment focuses on strengthening the patient's healthy *zheng Qi* and on managing symptoms, for example, alleviating pain and the side effects of chemotherapy.

## 9.5 Common TCM Treatment Methods for Pediatric Oncology

### 9.5.1 Herbal Medicine

The following treatment methods and remedies can be used in accordance with the particular stage of the cancer. It should be noted that they may be used in one or more stages of cancer based on the patient's individual condition as determined by TCM differentiation (Gao and Wang 2003).

1. Strengthen Antipathogenic *Zheng Qi*. This method is used to restore organ function and the balance of *yin* and *yang*, *Qi*, and blood in order to strengthen the body's immune resistance to cancer. Chinese remedies for nourishing *yin* include *Radix Asparagi* (asparagus), *Radix Trichosanthes*, *Radix Polygonatum*, *Bulbus Lili*, *Carapax trionycis* (turtle shell), *Colla Corii Asini* (donkey-hide gelatin), *Caulis milletiae*, and *Radix Angelicae sinensis*. Herbs that invigorate the kidney include *astragalus*, *ginseng root*, *Ganoderma lucidum*, *Smilax glabra*, and *mahonia leaves*. Herbs commonly used to strengthen the spleen and harmonize the stomach include *Atractylodes*, *Rhizoma Dioscoreae* (Chinese yam), *Semen coicis* (coix seed), white beans, figs, and *Radix zanthoxyli* (Bensky and Gamble 1993).
2. Remove Blood Stasis and Promote Blood Circulation. Blood stasis is one cause of tumors and is often the result of *Qi* stagnation. Common clinical symptoms and signs of blood stasis include internal or superficial masses, dark purple tongue with petechia, ecchymosis, and varicose veins. In addition, fixed pain with aggravation at night is typical. The commonly used Chinese herbs are red peony root, Szechuan lovage root, safflower, red sage root, turmeric, corydalis rhizome, frankincense, myrrh, angelica, bur reed rhizome, and peach kernel (Bensky and Gamble 1993). Their functions are to invigorate blood circulation, reduce or remove blood stasis and masses, and alleviate the cancer pain.
3. Clear Heat and Toxins. According to TCM theory, toxic heat is one of the major pathologies of pediatric cancer. It may manifest as fever, headache, dry and sore throat, brown urine, constipation, reddish eyes and face, burning pain of local tumors, and red tongue with thin yellow tongue coating. The herbs commonly selected for treating heat and toxins are honeysuckle, forsythia, hedyotis, barbata, lobelia, black nightshade, *Paris polyphylla*, *Radix Sophora subprostata*, *Radix Isatis indigotica* (banlangen), *Polygonum cuspidatum*, *Lithospermum*, viola, dandelion, *Houttuynia*, *Prunella vulgaris*, *Andrographis*

*paniculata*, *Coptis*, *Scutellaria*, *Phellodendron*, gentian, wild buckwheat, *Solanum lyratum*, *Selaginella*, *Smilax glabra*, *Cortex Lycium chinensis*, *Anemarrhenae*, *Scrophulariaceae*, *Duchesnea indica*, purslane, and pulsatilla (Bensky and Gamble 1993).

4. Soften Hard Masses. According to TCM differentiation, phlegm accumulation is often a cause of cancer masses. It is closely related to fluid metabolism and dysfunction of lung, spleen, and kidney. It manifests as fullness and distending pain in the epigastric area, poor appetite, chest pain and shortness of breath, abdominal distension, lower extremity edema, neck and joint pain, reddish or yellowish urine, diarrhea, and hard masses. Commonly used Chinese remedies for resolving phlegm and softening hard mass include *Pinellia*, *Trichosanthes*, fritillaria, silkworm, white mustard seed, *Fructus citri aurantii*, *Arisaema*, oysters, *Prunella*, *Cremastra*, kelp, seaweed, *Dioscorea bulbifera*, *Smilax glabra*, bamboo shavings, and pumice (Bensky and Gamble 1993).

It should be noted that although these remedies have been widely used in China, Japan, Korea, and other Asian countries for cancer patients including pediatric cancer treatment, evidence from well-designed clinical research is limited. Therefore, although no significant adverse effects or negative drug interactions from their use have been reported in the literature, further rigorous scientific research on their efficacy and safety in pediatric cancer patients is urgently needed.

### 9.5.2 Acupuncture

Because children may fear needles, small-gauge needles such as gauge 36, few points, and shorter needle retention time should be employed. Acupuncture points often used for pediatric oncologic include Hegu (LI 4) and Taichong (Liv 3) for pain, Zhusanli (ST 36) and Qihai (CV 6) for fatigue, Baihui (GV 20) and Neiguan (PC 6) for sleep disorders, Neiguan and Zhusanli for nausea and vomiting, Taishu (ST 25) and Shangjuxu (ST 37) for diarrhea or constipation, and Quchi (LI 11) and Hegu for fever.

## 9.6 Advantages of Integrating Chinese and Western Medicine in Treating Cancer

Nowadays, due to the rapid development of modern medical technologies, malignant tumors are mainly treated with conventional Western medicine. This includes surgical removal of the cancer, chemotherapy, radiation therapy, and biological therapy. Despite advances, which have saved numerous lives, the management of cancer and cancer treatment-related symptoms remains problematic. In many Asian countries, TCM is widely used in cancer treatment. Particularly in China, almost every cancer patient requests TCM treatment, which is well integrated with conventional cancer treatment in most hospitals. In the United States, acupuncture in particular is becoming more common in oncology settings (Capodice 2010; Lu and Rosenthal 2010a).

After many years of clinical observation, at least two major advantages of integrating TCM into Western medical treatment for cancer patients have emerged.

1. TCM can attenuate the side effects of chemotherapy and radiation therapy and minimize postoperative complications. Commonly seen adverse effects of cancer therapies include nausea and vomiting, fatigue, peripheral neuropathy, hair loss, low white blood cell (WBC) count, anemia, postoperative pain, and constipation. These symptoms can be minimized and eliminated by the use of TCM. For example, acupuncture has been reported to alleviate such conditions as chemotherapy-induced nausea and vomiting (Dundee et al. 1989), chemotherapy-induced neuropathy (Wong and Sagar 2006), and radiation therapy-induced xerostomia (dry mouth) and dysphagia (O'Sullivan and Higginson 2010; Weidong et al. 2010; Lu and Rosenthal 2010b). The Chinese remedies donkey-hide gelatin and jujube are often used to increase WBC count and prevent infection. The Chinese herbs roasted astragalus, Chinese angelica root, moutan, honeysuckle flower, *Codonopsis* root, forsythia fruit, and bletilla rhizome have been used to promote postoperative healing. The Chinese formula “minor

purgative decoction” has been used for constipation. Chinese remedies such as notoginseng root, cattail pollen, and charred human hair have been used in combination with anticoagulants to improve blood circulation without causing the side effect of excessive bleeding (Bensky and Gamble 1993).

- TCM can improve the quality of life during prolonged survival periods. When modern medical technologies enhance survival rate among cancer patients, quality of life becomes critically important. TCM is widely used to enhance quality of life. Acupuncture, Chinese herbs, and qigong (a type of meditation) can be used to treat debilitating cancer pain, cancer-related insomnia, hot flashes, loss of appetite, weight loss, fatigue, and the other cancer and cancer therapy-related symptoms that afflict survivors.

Bringing the strengths of Chinese and Western medicine together into an integrative medicine is the best patient care for children suffering from cancer. Due to its lack of adverse effects, TCM should be promoted and incorporated into Western pediatric oncology. Concomitantly, more scientific research should be funded and encouraged in order advance our knowledge regarding TCM’s efficacy, effectiveness, and mechanisms of action in its role as an integral part of pediatric cancer care.

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# Botanicals in Pediatric Oncology and the Issue of Botanical/ Drug Interactions

# 10

Patrick J. Mansky

## Contents

10.1	<b>Introduction</b> .....	137
10.1.1	CAM Biologics and Botanicals Used for Cancer Symptom Management.....	137
10.2	<b>Chemotherapy and Cancer Related Side Effects</b> .....	138
10.2.1	Hepatotoxicity: Milk Thistle.....	138
10.2.2	Mucositis: Traumeel .....	138
10.2.3	Chemotherapy-Induced Febrile Neutropenia: MSC .....	138
10.2.4	Nausea and Vomiting: Ginger.....	139
10.2.5	Chinese Herbal Medicines.....	139
10.2.6	Pain .....	139
10.2.7	Fatigue: Chinese Herbal Medicine and Ginseng .....	140
10.2.8	Insomnia: Valerian Root and St. John's Wort .....	140
10.3	<b>Botanicals Used for Cancer Treatment</b> ....	139
10.3.1	Garlic .....	140
10.3.2	Green Tea .....	141
10.3.3	Turmeric ( <i>Curcuma longa</i> L.), Curcumin, and Related Compounds .....	141
10.3.4	Mushroom and Immune Stimulators in Cancer.....	142
10.4	<b>Botanical-Drug Interactions</b> .....	143
10.5	<b>Product Quality and Safety</b> .....	143
	<b>References</b> .....	144

## 10.1 Introduction

### 10.1.1 CAM Biologics and Botanicals Used for Cancer Symptom Management

Cancer patients frequently explore complementary and alternative medicine (CAM) modalities to alleviate symptoms related to disease and treatment. Patients are increasingly turning to botanical and herbal medicines to replace or supplement conventional treatments in order to provide relief.

A number of plants have been the primary source for the development and production of some of the most commonly used approved anticancer agents. Taxanes such as taxol and docetaxel were developed from extracts of the bark of the Pacific yew tree *Taxus brevifolia*. Vinca alkaloids isolated from the periwinkle plant *Catharanthus roseus* gave rise to the drugs vincristine, vinblastine, and vinorelbine. *Podophyllum peltatum*, the mayapple, was the source for podophyllotoxin, which was used in the development of such semisynthetic drugs as etoposide and teniposide. Camptothecins such as topotecan were produced from the Chinese plant *Camptotheca acuminata*. Some of these drugs are among the most widely used chemotherapeutic agents in pediatric oncology.

A study by Richardson et al. surveyed 493 cancer patients, revealing that 83.3 % had tried at least one CAM therapy. While 88.1 % of the survey population had generally heard of the use of vitamins and herbs, 38 % had actually used herbs at one time or another (Richardson et al. 2000). Bishop

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et al. recently conducted a systematic review of CAM use in pediatric cancer based on a review of 28 studies with survey data (collected from 1975–2005) from 3,526 children. In 20 studies with 2,871 participants, the prevalence of any CAM use (since cancer diagnosis) ranged from 6 to 91 %; considerable heterogeneity across studies precluded meta-analysis. Herbal remedies were the most popular CAM modality, followed by diets/nutrition and faith-healing (Bishop and Prescott 2010).

Herbs and botanicals are predominantly used in a supportive role for symptom relief and improvement of quality of life. As children may react and respond differently to medications than adults, there is a need for well-designed clinical trials to evaluate and support the use of botanicals and herbs in pediatric cancer. Most children with cancer are treated with complex multiagent chemotherapy regimens, often over months and frequently as part of a clinical trial. There is therefore a particular concern about potential of botanical/drug interactions, which could give rise to different additional symptoms and affect the response of the patient to the prescribed cancer therapy.

There are only a few published clinical trials evaluating the use of botanical preparations for symptom management in children with cancer.

## 10.2 Chemotherapy and Cancer Related Side Effects

### 10.2.1 Hepatotoxicity: Milk Thistle

The herbal plant milk thistle (*Silybum marianum*) has been used for the treatment of liver toxicity in hepatitis and cirrhosis. It is available as a nutritional supplement in the USA. In clinical trials, protective effects against hepatic and renal toxicity have been observed (Tamayo and Diamond 2007). A recent randomized, placebo-controlled pilot study explored the effects of milk thistle on hepatotoxicity in children undergoing treatment for ALL (Ladas and Kroll 2010). Fifty children were enrolled. At day 56, the milk thistle group had a significantly lower AST and a trend toward a lower ALT. Milk thistle did not affect the

efficacy of the administered chemotherapeutic agents, and the authors concluded that future studies of dosing, duration of treatment, and the impact on hepatotoxicity and leukemia survival were warranted.

### 10.2.2 Mucositis: Traumeel

Traumeel-S R is a homeopathic complex preparation used in Europe for the past 50 years for the treatment of mucositis as an over-the-counter remedy. A randomized, placebo-controlled, double-blind clinical trial of 32 patients ages 3–25 years who had undergone allogeneic or autologous stem cell transplantation observed lack of stomatitis in five patients (33 %) in the TRAUMEEL S treatment group compared to one patient (7 %) in the placebo group. Stomatitis worsened in only 7 patients (47 %) in the TRAUMEEL S treatment group compared with 14 patients (93 %) in the placebo group. The mean area under the curve stomatitis scores were 10.4 in the TRAUMEEL S treatment group and 24.3 in the placebo group. This difference was statistically significant ( $P < 0.01$ ) (Oberbaum et al. 2001).

Subsequently, the Children's Oncology Group conducted a larger, randomized, controlled clinical trial. Results of this study have not been published.

### 10.2.3 Chemotherapy-Induced Febrile Neutropenia: MSC

There is limited information on the reduction of the risk of febrile neutropenia in pediatric cancer patients. Garami et al. conducted an open-label, matched-pair pilot clinical trial in children with pediatric solid cancers to test whether the combined administration of the medical nutriment MSC (Avenmar) with cytotoxic drugs and the continued administration of MSC on its own might help to reduce the incidence of treatment-related febrile neutropenia compared with the same treatments without MSC. Twenty-two patients (11 pairs) were enrolled in this study. Thirty febrile neutropenic episodes (24.8 %) were observed in the MSC group versus 46 (43.4 %) in the control

group (Wilcoxon signed rank test,  $P < 0.05$ ). The authors concluded that “the continuous supplementation of anticancer therapies with the medical nutriment MSC helps to reduce the incidence of treatment-related febrile neutropenia in children with solid cancers” (Garami et al. 2004).

#### 10.2.4 Nausea and Vomiting: Ginger

Nausea and vomiting are two distressing side effects associated with chemotherapy treatment for cancer. Two RCTs concluded that cancer patients suffering from nausea and vomiting may find some relief in the antiemetic properties of ginger. A systematic review by Ernst and Pittler identified an RCT in 41 leukemia patients. The trial studied the effects of ginger capsules versus placebo on the severity and duration of chemotherapy-induced nausea. Results showed a statistically significant decrease in severity and duration of nausea in the ginger group. Unfortunately, this trial was only published as an abstract, and therefore further details are unavailable (Ernst and Pittler 2000).

A second RCT by Sontakke and Thawani compared the effects of ginger root powder to metoclopramide and ondansetron in 50 cancer patients. Results showed that 62 % of the patients given ginger had complete control of nausea. Similarly, 58 % of those given metoclopramide had control of nausea. However, ondansetron was the most effective given that 86 % of these patients had complete control of nausea. Results for control of vomiting were similar; 68 % of the ginger group, 64 % of the metoclopramide group, and 86 % of the ondansetron group achieved complete control of vomiting. Results show that ondansetron is a superior antiemetic drug, and the difference in ginger and metoclopramide is not statistically significant (Sontakke et al. 2003).

#### 10.2.5 Chinese Herbal Medicines

Chinese herbal medicines (CHM), such as Huangqi decoctions, have demonstrated efficacy in reducing chemotherapy-induced nausea and

vomiting (Mansky and Wallerstedt 2006). Seven randomized, controlled studies of variable quality are worth discussing in support of CHM. However, studies specifically evaluating the benefit of botanical preparations for the treatment of nausea in pediatric cancer patients are lacking.

#### 10.2.6 Pain

Pain associated with cancer and cancer treatment can be debilitating and reduces patient’s QOL. Conventional analgesics such as anti-inflammatory medications and opioids have distinct adverse effect profiles.

Chinese herbal medicine may be beneficial in the treatment of cancer pain. A comprehensive study by Xu et al. reviewed 115 trials from both Chinese and English databases, which compared the effects of CHM to conventional analgesics or placebo. Although 41 of the studies reviewed were randomized, controlled trials, most were not of high-quality design and had many limitations such as lack of randomization process or control group, small sample size, or deficiencies in the masking process. Furthermore, due to inadequate follow-up, it cannot be determined whether CHM has comparable long-term effects to conventional medicine. Another technical limitation is the use of established analgesic as control, as ethical concerns prevented the Chinese studies from using a placebo.

Despite these limitations, it is possible to draw some significant findings from these studies. Most importantly, the review concludes that CHM may be effective for short-term cancer-related pain, having similar outcomes to those of conventional western medicine. Additionally, CHM may produce fewer side effects than conventional treatments and helps to enhance overall quality of life. Furthermore, there were no serious adverse events associated with the CHM regimens. Finally, the review found that CHM is effective through multiple modes of application, such as oral, topical, and intravenous (Xu et al. 2007). Although pain is mostly treated externally, these studies show some promise in using botanicals as an analgesic and call for larger and more

rigorous clinical trials of botanicals in the treatment of cancer pain. However, the review did not specifically address the role of CHM in pediatric cancer pain.

### 10.2.7 Fatigue: Chinese Herbal Medicine and Ginseng

Research shows that 80–90 % of cancer patients often have prolonged fatigue, categorized as a disturbance in circadian patterns. This type of fatigue is not relieved by rest and relaxation and has distressing effects on quality of life. Chinese herbal medicine (CHM) may be effective in relieving cancer-related fatigue (Zhang et al. 2007; Taixiang et al. 2005). These studies convey that CHM may be effective for reducing fatigue; however, larger, controlled clinical trials are necessary in order to safely advocate its use, and data specifically reporting on the benefit in pediatric patients are not available.

Ginseng has been known to increase energy and physical stamina. A study by Elam et al. evaluated the efficacy of ginseng in reducing fatigue and improving sleep quality in cancer patients. This randomized, double-blinded, placebo-controlled study used American ginseng. A number of unforeseen problems prevented the completion of the study, such as the inability to mask the potent taste and smell of the ginseng to secure adequate blinding. Additionally, the measurement devices used to measure sleep and wake activity were inaccurate, and recruitment was challenging due to rigorous inclusion and exclusion criteria; this was especially related to contraindications between ginseng and current medications (Elam et al. 2006).

### 10.2.8 Insomnia: Valerian Root and St. John's Wort

Insomnia can be a detrimental side effect of cancer. Research shows that patients who had seriously disturbed circadian rhythms had a shorter survival time (Block et al. 2004). Primarily treated with hypnotic drugs (benzodiazepines), there is little research regarding herbals and botanicals for reduction of insomnia.

Some literature shows that valerian (*Valeriana officinalis* L.) and St. John's wort (*Hypericum perforatum* L.) may improve sleep; however, warnings about contraindications are serious. Other studies have explored the effects of botanicals such as chamomile, hops, passionflower, lavender, and lemon balm and found the results to be encouraging. Many of these botanicals showed beneficial effect in controlled clinical trials; however, the patient populations varied in disease, and data on pediatric patients are limited. The need remains for these trials to be conducted in pediatric cancer populations, therefore verifying whether or not the botanicals are effective for cancer-related insomnia, specifically (Block et al. 2004).

## 10.3 Botanicals Used for Cancer Treatment

### 10.3.1 Garlic

Numerous animal and in vitro studies provided evidence for a relation between garlic intake and cancer risk reduction. Several studies also reported an inverse association in humans. However, no claims have been made about garlic intake and cancer risk reduction with respect to food labeling. With the use of the US Food and Drug Administration's evidence-based review system for the scientific evaluation of health claims, 19 human studies were identified and reviewed to evaluate the strength of the evidence that supports a relation between garlic intake and reduced risk of different cancers with respect to food intake. There was no credible evidence to support a Correlation between garlic intake and a reduced risk of gastric, breast, lung, or endometrial cancer. Very limited evidence supported a Correlation between garlic consumption and reduced risk of colon, prostate, esophageal, larynx, oral, ovary, or renal cell cancers (Kim and Kwon 2009).

There are some recent reports suggesting that garlic-derived OSCs cause cell cycle arrest, generate reactive oxygen species (ROS), activate stress kinases, and also stimulate the mitochondrial pathway for apoptosis in malignant neuroblastoma (Karmakar and Choudhury 2011).

### 10.3.2 Green Tea

An expanding body of preclinical evidence suggests that EGCG, the major catechin found in green tea (*Camellia sinensis*), has the potential to impact a variety of human diseases. EGCG may have antioxidant properties, thus preventing oxidative damage in healthy cells, but also exert anti-angiogenic and antitumor effects. EGCG induces apoptosis and promotes cell growth arrest by altering the expression of cell cycle regulatory proteins, activating killer caspases, and suppressing oncogenic transcription factors and pluripotency maintain factors. In vitro EGCG blocks carcinogenesis by affecting a wide array of signal transduction pathways including JAK/STAT, MAPK, PI3K/AKT, Wnt, and Notch (Singh and Shankar 2011).

Consumption of green tea (*Camellia sinensis*) may provide protection against chronic diseases, including cancer. Green tea polyphenols can be direct antioxidants by scavenging reactive oxygen species or chelating transition metals as has been demonstrated in vitro. Alternatively, they may act indirectly by upregulating phase II antioxidant enzymes. Evidence of this latter effect has been observed in vivo, yet more work is required to determine under which conditions these mechanisms occur. Green tea polyphenols can also be potent pro-oxidants, both in vitro and in vivo, leading to the formation of hydrogen peroxide, the hydroxyl radical, and superoxide anion. The potential role of these pro-oxidant effects in the cancer preventive activity of green tea is not well understood (Forester and Lambert 2011).

Experimental studies have consistently shown the inhibitory activities of tea extracts on tumorigenesis in multiple model systems. Epidemiological studies, however, have produced inconclusive results in humans. A comprehensive review was conducted to assess the current knowledge on tea consumption and risk of cancers in humans. High intake of green tea has been associated with reduced risk of upper gastrointestinal tract cancers. Limited data support a protective effect of green tea on lung and hepatocellular carcinogenesis. Phase II clinical trials have demonstrated an inhibitory effect of green tea extract against the progression of

prostate premalignant lesions. Green tea may exert beneficial effects against mammary carcinogenesis in premenopausal women and recurrence of breast cancer. There is no sufficient evidence that supports a protective role of tea intake on the development of cancers of the colorectum, pancreas, urinary tract, glioma, lymphoma, and leukemia (Yuan and Sun 2011).

Evidence for pediatric cancer-specific anticancer effects is lacking.

### 10.3.3 Turmeric (*Curcuma longa* L.), Curcumin, and Related Compounds

There is a substantial body of preclinical evidence that curcumin targets multiple molecules in the biochemical pathway of carcinogenesis, particularly in blocking transformation, proliferation, and invasion of tumor cells (Aggarwal and Kumar 2003; Shishodia et al. 2007).

Turmeric and its active constituent, curcumin, have been found to have direct anti-inflammatory effects, inhibiting TNF- $\alpha$ , IL-8, monocyte inflammatory protein-1, IL-1B, and monocyte chemotactic protein-1 (Abe et al. 1999). It significantly inhibits lipoxygenase enzymes and COX-2 activity (Rao et al. 1993), potentially through suppression of NF- $\kappa$ B (Plummer et al. 1999). Curcumin downregulates the expression of cyclin D1 at the transcriptional and posttranscriptional levels (Mukhopadhyay et al. 2002) and downregulates specific protein kinases, including EGFR and Her2neu (Korutla and Kumar 1994; Korutla et al. 1995), as well as numerous protein kinases (as reviewed in (Shishodia et al. 2007)).

Evidence of curcumin's effects on apoptosis includes the finding that it suppresses activation of the NF- $\kappa$ B-regulated genes, including Bcl-2 (Bharti et al. 2003, 2004a, b). It appears to have direct antiangiogenic properties as well, suppressing proliferation of human vascular endothelial cells in vitro (Singh et al. 1996; Thaloor et al. 1998) and inhibiting angiogenesis in LNCaP prostate cancer cells in vivo (Dorai et al. 2001).

While preclinical evidence supports curcumin's potential to interrupt carcinogenesis at multiple

target sites, several preliminary clinical studies have demonstrated its tolerability. In a phase I study, Cheng et al. found that a cohort of 25 patients with high-risk or premalignant lesions tolerated up to 8 g/day of curcumin with no observed treatment-related toxicities (Cheng and Hsu 2001). In another phase I study conducted by Sharma et al. (2004), 15 patients with advanced refractory CRC tolerated up to 3.6 g/daily for 4 months with no dose-limiting toxicity. Although curcumin was well-tolerated in these phase I studies, it appears to have poor bioavailability with oral dosing; however, detectable levels of curcumin have been measured in the urine (Sharma et al. 2004). Dhillon and colleagues recently published a study of patients with advanced pancreatic cancer who tolerated a dose of curcumin at 8 g/day without toxicities (Dhillon et al. 2008). Of the 11 patients who were evaluable for response, 4 had stable disease at 2–7 months posttreatment, and 1 had a brief partial remission for 1 month. In summary, curcumin has demonstrated anti-inflammatory, antioxidant, antiangiogenesis, and pro-apoptotic effects in preclinical studies and has been well-tolerated in several clinical trials. Thus, it has potential benefits in cancer chemoprevention studies as well (Sharma et al. 2007), which is currently being investigated in a number of ongoing phase II–III clinical trials in the USA and internationally, as reviewed recently by Goel and colleagues (2008).

Other curcuminoids such as demethoxycurcumin and bisdemethoxycurcumin have not been as widely studied as curcumin. Recent studies in vitro suggest an inhibitory effect on cancer cell invasion via downregulation of matrix metalloproteinases, warranting further investigation (Yodkeeree and Chaiwangyen 2008).

Several turmerones derived from turmeric have shown anti-inflammatory and antiproliferative properties in vitro, although these compounds have not entered clinical trials (Sandur et al. 2007).

### 10.3.4 Mushroom and Immune Stimulators in Cancer

TCM and other Asian native medical traditions that evolved from TCM document the use of well

over 270 species of mushroom for a wide range of ailments (Ying et al. 1987). Several mushroom-derived medicinal products are produced by Japanese, Korean, and Chinese pharmaceutical companies and have been used as standard cancer therapy for over 30 years as adjuncts to surgery, chemotherapy, and radiation for the treatment of gastrointestinal and lung cancer (Smith et al. 2002). Current data do point to improved survival trends that are incremental but significant. Polysaccharide-K (PSK), from the mushroom *Trametes versicolor*, is an example of an approved mushroom product used for cancer treatment in Japan and has been approved as an adjunctive cancer treatment since the mid-1970s with use in thousands of patients. The safety record for PSK is well established in Japan, and there are notably few adverse events reported. Subfraction analysis of PSK showed a 50-kd polysaccharide-rich fraction was principally responsible for the anticancer effect (Mizutani et al. 1992). Clinical studies of PSK in colorectal and gastric cancer treatment have shown reduced recurrence and improvement in overall survival with adjuvant use.

A meta-analysis of gastric cancer and PSK studies included 8,009 patients from eight randomized, controlled trials after central randomization. The overall hazard ratio for patients who received PSK was 0.88 (95 % confidence interval, 0.79–0.98;  $P=0.018$ ) (Oba et al. 2007).

In China, a similar product to PSK called polysaccharide peptide (PSP) is used for cancer treatment and is derived from the same mushroom. It is used in esophageal, gastric, and lung cancer (Ng 1998). Clinical investigation has focused on the role of medicinal mushrooms as biological response modifiers (BRM), defined as agents boosting or restoring the ability of the immune system to fight infections, cancer, and other diseases (2007).

The principal medicinal mushrooms used in cancer treatment in Asian countries are lentinan (*L. edodes*), schizophyllan (*S. commune*), PSK and PSP (*T. versicolor*), and Grifron-D (*G. frondosa*). PSK, PSP, and Grifron-D are taken orally, while lentinan and schizophyllan are purified beta-D-glucans and are administered by the intraperitoneal route (Sullivan et al. 2006).



The active components in medicinal mushrooms are thought to be principally biologically active polysaccharides in the form of beta-D-glucans with various protein linkages forming proteoglycans (Sullivan et al. 2006). There are preliminary studies ongoing with some of these agents with cancer patients in the USA as well as beta-glucans derived from baker's yeast. Medicinal mushrooms have not been studied in pediatric cancer.

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## 10.4 Botanical-Drug Interactions

While the concern of potential adverse botanical-drug interactions has been raised ever since Piscitelli et al. reported the decrease of indinavir serum concentrations after use of St. John's wort by patients with HIV (Piscitelli et al. 2000), the topic gained relevance for cancer treatment when Mathijssen et al. demonstrated that the ingestion of St. John's wort reduced the serum concentration of irinotecan in patients on treatment for colorectal cancer (Mathijssen et al. 2002), thus rendering the chemotherapy regimen potentially ineffective. St. John's wort induces several enzymes of the hepatic p450 complex. One of the various p450 complex enzymes affected by St. John's wort is CYP3A4, which is involved in the metabolism of 35 % of all oncology drugs. Increased enzyme complex activity may accelerate drug metabolism and result in lower, potentially ineffective plasma drug concentrations, while decreased enzyme activity may lead to increased drug toxicity. Some of the properties of St. John's wort to affect drug metabolism are shared by several other commonly used herbs including Echinacea, Ginkgo, Valerian, and Grape seed. Sparreboom et al. provide a detailed review of the mechanistic understanding of the hepatic metabolism of chemotherapeutic agents and the impact of botanicals on these processes (Sparreboom and Baker 2009).

Hepatically metabolized chemotherapeutic agents commonly used in pediatric oncology include:

- Busulfan
- Cisplatin
- Cyclophosphamide

- Dacarbazine
- Anthracyclines
- Taxanes
- Etoposide
- Ifosfamide
- Imatinib
- Irinotecan
- Methotrexate
- Teniposide
- Topotecan
- Vinca alkaloids

St. John's wort also affects the p-glycoprotein pathway, which could result in resistance to drugs such as anthracyclines, epipodophyllotoxins, taxanes, and vinca alkaloids (Mansky and Straus 2002).

Concern has been raised about induction of CYP3A4 by milk thistle. However, clinically achievable concentrations of silymarin, one of the main active constituents, did not inhibit this enzyme pathway to an extent that would justify a clinical concern (van Erp et al. 2005).

Another potential adverse effect of botanicals is the interaction with the metabolism of warfarin. While the incidence of deep vein thrombosis (DVT) in pediatric patients is much lower than in adults, cancer and cancer treatment may increase the risk for DVT, making this a valid concern in childhood cancer as well. Commonly used botanicals such as *Allium sativum* (garlic), *Ginkgo biloba* (Ginkgo), and *Panax ginseng* (ginseng) affect the metabolism of warfarin (Mansky and Straus 2002; van Erp et al. 2005).

An informative source for botanical drug interactions is the Natural Standards Database (<http://www.naturalstandard.com/databases/>).

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## 10.5 Product Quality and Safety

There has been ongoing concern about the product quality and safety of botanical products, both with respect to the quantity and quality of the desired active ingredients as well as the potential for contamination with chemicals and heavy metals as well as adulteration with prescription drugs. Guidance and oversight regarding manufacturing and quality control in the USA are provided through the FDA. However, as most



botanical products currently are approved and marketed in the USA as dietary supplements, content standardization and verification are limited to the requirement for dietary supplements and are not held to the same standards as FDA-approved drugs. The National Center for Complementary and Alternative Medicine (NCCAM, [www.nccam.nih.gov](http://www.nccam.nih.gov)) and the Office of Dietary Supplements (ODS, <http://ods.od.nih.gov/healthinformation>) at the National Institutes of Health (NIH), as well as the FDA (<http://www.fda.gov/Food/DietarySupplements/>), among others provide information about botanical safety and quality.

Equivalent to the FDA for the USA, there is the European Medicines Agency (EMA) for the European Union ([http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000208.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800240cf](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000208.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800240cf), accessed: 16.11.2011). The EMA is a decentralized agency located in London. Its main task field is the evaluation and supervision of medicines for both human and veterinary use. The process of licensing and marketing of herbal products in the EU is regulated in a European Parliament and Council Directive from 2004 (*Directive 2004/24/EC*). It also implies general definitions for herbal medicinal products, herbal preparations, and substances. The aim of the Directive is to bring the process of licensing and information on herbal substances and preparation into accordance within the EU, while most of the herbal products are licensed nationally by Member States. For example, in Germany, it is the Federal Institute for Drugs and Medical Devices (in German BfArM) (<http://www.bfarm.de/DE/BfArM/BfArM-node.html>, accessed: 16.11.2011). Especially for herbal products, the Commission E Monographs hold information on the evaluation of safety and efficacy of herbal medicine products in Germany ([http://www.bfarm.de/DE/Arzneimittel/2\\_zulassung/zulArten/besTherap/amPflanz/ampflanz-inhalt.html?nn=1013980](http://www.bfarm.de/DE/Arzneimittel/2_zulassung/zulArten/besTherap/amPflanz/ampflanz-inhalt.html?nn=1013980), accessed: 16.11.2011). As a result of the aforementioned European Directive, the Committee on Herbal Medicinal Products (HMPC) was founded in 2004 ([http://www.ema.europa.eu/ema/index.jsp?curl=pages/about\\_us/](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/)

[general/general\\_content\\_000122.jsp&murl=menus/about\\_us/about\\_us.jsp&mid=WC0b01ac0580028e7d](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/about_us.jsp&mid=WC0b01ac0580028e7d), accessed: 16.11.2011). The main task of the Committee is the establishment of herbal monographs that include information on therapeutic use and safety of herbal medicine products in the EU. Quality conditions for herbal products are defined in the European Pharmacopoeia Monographs developed by a Committee of the European Directorate for the Quality of Medicines (*EDQM*) (<http://www.edqm.eu/en/Background-Legal-Framework-50.html>, accessed: 16.11.2011).

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# Potential Role of Complementary and Alternative Medicine in Pediatric Oncology: The Future of CAM Research – Addressing the “Effectiveness Gaps”

Sagar Chokshi and Kara Kelly

## Contents

11.1	<b>Theory and Background</b> .....	147
11.1.1	Background .....	147
11.1.2	Research Methodology in CAM .....	148
11.1.3	Exploring Measures of Effectiveness .....	149
11.2	<b>Research Overview</b> .....	150
11.2.1	A Framework for CAM Studies in Cancer ..	150
11.2.2	Comparative Effectiveness Research .....	151
11.2.3	Natural Products Research .....	151
11.2.4	CAM for Supportive Care Indications .....	152
11.3	<b>Pediatric Oncology</b> .....	152
11.3.1	Where Standard Therapy Fails .....	152
11.3.2	Challenges Specific to Pediatric Oncology Research .....	153
11.4	<b>Open Questions</b> .....	154
11.4.1	The Need for CAM Research and Collaborations .....	154
	<b>References</b> .....	155

There is paucity of convincing scientific evidence to support practice of complementary and alternative medicine (CAM) therapies in pediatric cancer patients even though their use is well documented. However, certain CAM therapies have been proven effective for symptoms that conventional therapies fail to treat, such as nausea, pain, and psychosocial well-being. Rigorous research methods in pediatric oncology need to be followed to build the evidence base in CAM and bridge these effectiveness gaps. A strategy that combines qualitative and quantitative studies to assess CAM therapies in the context they are being used in, with awareness of the unique challenges in pediatric oncology research, will guide future clinical practice. Finally, national and international collaborations among researchers, policy makers, and clinicians will facilitate the regulated use of effective CAM therapies in pediatric oncology.

## 11.1 Theory and Background

### 11.1.1 Background

A systematic review of survey data published between 1977 and 2007 estimates the prevalence of any CAM (complementary and alternative medicine) use since diagnosis to range from 6 to 91 % in pediatric patients with cancer (Bishop et al. 2010). Despite the well-researched and documented prevalence of CAM, the quality of evidence for the use of these products and practices is unclear.

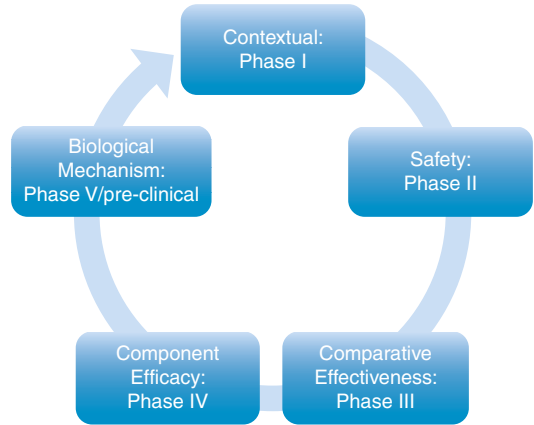
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In 2008, more than 7,500 CAM trials were indexed in MEDLINE, with more than 1,600 involving children aged 18 years or younger (Chan 2008). Moreover, less than half of the 207 randomized clinical trials (RCTs) used for systematic reviews of homeopathy, acupuncture, and herbal extracts were in English or indexed in MEDLINE, and most had significant flaws in design or analysis, such as the failure to describe how the randomization sequence was generated, inadequate concealment of the allocation sequence, lack of cataloging the number and reasons for post-randomization attrition, or they did not use intent-to-treat data analysis (Linde et al. 2001). A review of RCTs in pediatric CAM suggested that the quality of RCTs of CAM is inferior to RCTs of conventional medicine (Klassen et al. 2005). However, the quality of systematic reviews of CAM exceeds that of systematic reviews of conventional medicine (Lawson et al. 2005).

Despite the inconsistent evidence in CAM, there exists a gap between the strong experimental results showing safety and evidence of effectiveness and the widespread nonuse of these CAM treatments. This deficiency in health services not covered by conventional interventions is the “effectiveness gap.” Examples include the predominance of fatigue in cancer patients as well as the high incidence of nausea and vomiting despite antiemetic drugs and reports of pain despite the use of conventional medications. By focusing our attention on a research strategy that stretches from contextual to randomized controlled trials, we can best evaluate the effectiveness of popular and promising CAM modalities. This will guide future clinical practice to include the safest and the most effective complementary or alternative therapies in the pediatric oncology setting.

### 11.1.2 Research Methodology in CAM

Much of the initial literature on CAM in pediatric oncology relies upon surveys to determine prevalence of CAM use. Surveys are useful to identify a population’s current behaviors and beliefs associated with frequency of use. Survey studies doc-



**Fig. 11.1** A strategy for CAM research. Challenges specific to CAM research can be addressed with a strategy that emphasizes both qualitative and quantitative research methods at different phases during study (Dhillon 2011; Fonnebo et al. 2007)

ument disclosure of use, factors associated with it, and types of CAM therapies in use, usually in conjunction with conventional chemotherapy and radiation therapy. This guides healthcare providers in addressing the dangers or benefits of CAM use and researchers of the nonharmful complementary therapies that may have a supportive role during cancer therapy (Kelly 2004).

CAM research cannot adopt the conventional, pharmacological research strategy; it is commonly expected to follow. Fonnebo et al. point to the absence of a statutory body, or gatekeeper, to ensure the quality, safety, efficacy, and effectiveness of CAM therapies before they appear in the marketplace. The inherently individualized nature of CAM treatment modalities and the absence of “gatekeepers” makes CAM research especially challenging (Fonnebo et al. 2007). The lack of regulation of many commonly used practices increases heterogeneity, making treatment effect difficult to measure and standardize for research purposes. Our conventional research methodology must be tailored to account for these challenges. A revised strategy is proposed for CAM therapies already in use (Fig. 11.1). These guidelines offer a way to address the growing need for rigorous effectiveness studies in CAM to bridge the effectiveness gap in clinical care:

- *Phase I – Contextual research:* Qualitative research, including observational retrospective and prospective studies, survey studies, and case reports explore the context of CAM use and factors associated with it.
- *Phase II – Safety assessment:* Risks of well-defined CAM treatments guide large-scale clinical studies and current practices.
- *Phase III – Comparative effectiveness research:* Randomized controlled trials comparing treatment intervention to placebo and/or standard practice best assess the effectiveness of CAM, especially when evaluated in a system that is allowed to function as it is clinically practiced.
- *Phase IV – Assessment of component efficacy:* Among many components within a CAM treatment approach, those that can be eliminated and at the same time retain or improve overall treatment effectiveness are assessed. Randomized controlled trials evaluate this. It is, however, important to recognize that results from such research cannot be used to document or disprove the effectiveness of a “whole-system” treatment.
- *Phase V/preclinical – Exploration of biological mechanisms:* Phase V research may shed light on the mechanisms of action for a specific CAM therapy and guide future work in determining its efficacy or refine future trials’ outcome and safety measures. Mechanistic studies can, however, precede clinical trials in a research model where a physiologic theory for a particular CAM therapy is being developed and tested. Preclinical data can aid in theory development and testing, especially in biologically based therapies.

### 11.1.3 Exploring Measures of Effectiveness

There is a difference between efficacy and effectiveness. The former uses a reductionist scientific method to examine specific effects of an intervention on a defined health outcome, one that is usually evaluable physiologically. Effectiveness research studies the effect of the intervention in

the real-world clinical setting and is measured by examining all aspects of the treatment’s effect, specific and nonspecific, on a patient (Sagar 2006). In light of the multidimensional nature of clinical care and nature of CAM therapies, effectiveness research is necessary. Many therapies emphasize patient-clinician interaction, which can synergistically influence outcome.

Rigorous, well-designed clinical trials for many CAM therapies are often lacking. Thus, the safety and effectiveness of many CAM therapies already in use are uncertain. The gold standard for conventional medicine is the RCT. CAM therapies must be tested with the same rigor; therefore, RCTs are an important and essential way to evaluate effectiveness.

The RCT is methodologically superior because it has the capacity to preclude several forms of confounding factors. Randomization of patients to treatments and single or double blinding enhance the internal validity such that observed differences at the end of the trial can be attributed with more confidence to the intervention. However, RCTs should not compromise the external validity of a study, which is its applicability into the “real world.” Randomization, blinding, and homogeneity of the patients are crucial to establish the efficacy of a therapy. But, the “effectiveness” seeks to maximize external validity and obtain information about actual effects in broad practice. This is important to CAM research in the oncology setting where the treatment is complex, sometimes requiring multiple modalities to treat a milieu of conditions that may be receptive to nonspecific effects, like the patient-clinician interaction so many CAM therapies emphasize (Walach et al. 2003).

For this reason, RCTs should be complemented with qualitative studies. Qualitative methods may be used before starting an RCT to assist in the development of appropriate outcome measures or they may be embedded in the trial to assist in understanding the measuring context and process of the intervention. Also, qualitative methods can be used after the trial is completed to explain the trial results (Verhoef et al. 2002). This is especially important when assessing therapies based on different cultural concepts of what causes or constitutes disease and health.



Challenges in clinical research are especially exacerbated when performing research in children. Lack of evidence does not mean there is absence of effect. The small clinical studies, lack of standardization of the interventions, and lack of control over the many factors influencing responses, all reduce the quality of the trials that have been conducted to date. Pediatric-specific research studies are particularly important, as results from studies in adults cannot always be extrapolated to a pediatric population because of the unique developmental, social, and metabolic aspects of children (Sencer and Kelly 2007).

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## 11.2 Research Overview

### 11.2.1 A Framework for CAM Studies in Cancer

Lack of “theory development and testing” is a major challenge to research on CAM practices. Theory development and testing is critical to the success of CAM research (Wayne 2005). Acupuncture is a good example of the development of a theory, in biomedicine and physiology, and testing. The theory of endogenous opioid production with acupuncture offered a more testable theory for Western science and opened up doors to research in acupuncture and pain. The psychoneuroimmune (PNI) framework is another theory that builds on the way in which stress influences the neurophysiologic response and results in immune suppression and illness. PNI offered researchers a way to test and evaluate CAM therapies, especially mind-body interventions and massage therapy. Both are examples of theory and development used in intervention trials to strengthen the research methodology of CAM.

While the mechanisms of acupuncture are still being understood, clinical trials investigating the effects of acupuncture treatment are most commonly based in a theory involving neurochemical responses. The release of endogenous opioids or serotonin is used to explain the physiologic effects of acupuncture on analgesia, nausea/vomiting, immune function, and sleep quality, to name a few. Such a rationale helps investigators

to develop and test a causal hypothesis, choose an appropriate control to account for the nonspecific effects CAM is notoriously criticized to exert, and produce reproducible results. Additionally, these rationales can guide investigators to use appropriate biomedical diagnostic inclusion criteria and outcome measures (Moffet 2006).

Even with this physiologic theory guiding clinical trials to test the efficacy of acupuncture, the practice of acupuncture is more complex in children than in adults. Children may have a fear of needles, and practitioners stress the importance of reducing anxiety and establishing a friendly and trusting environment before the administration of acupuncture (Jindal et al. 2008). Some children are accepting of acupuncture (Rooney et al. 2006). A review of 23 RCTs and 8 meta-analysis/systemic reviews conducted by the National Institutes of Health (NIH) found that there is evidence for the efficacy and low risk associated with acupuncture in pediatrics (Jindal et al. 2008). Acupuncture’s therapeutic role in managing postoperative and chemotherapy-induced nausea/vomiting and pain has yielded the most evidence-based results on acupuncture efficacy. However, manifestations of cancer-related pain are different in children than in adults, and thus, the data cannot be extrapolated from adult research.

Mind-body CAM intervention research is often developed from a PNI framework. Mind-body and stress-reducing CAM therapies, such as yoga, meditation, and hypnosis, are among the most commonly used CAM therapies for anxiety/stress, insomnia, and nausea/vomiting in children with cancer in the year 2007 in the United States (Birdee et al. 2010). The PNI framework can aid investigators attempting to evaluate the effectiveness of select CAM therapies in reducing symptom and emotional distress and improving physical and emotional outcomes. For example, an RCT conducted at Children’s Hospital in Minneapolis and St. Paul studied the use of massage therapy to reduce symptoms and distress in children with cancer and their parents. The PNI framework guided their choice of salivary cortisol to measure physiological relaxation and suppression of the hypothalamic-pituitary-adrenal axis response in addition to qualitative measures.

Heart and respiratory rates, systolic and diastolic blood pressures, and scales to assess fatigue and anxiety were used in this short, limited RCT. The results warrant larger, multisite clinical trials to determine if reducing stress affects immune measures and its influence on clinical outcomes as well as family functioning and distress (Post-White and Hawks 2005). Others propose that massage may be helpful in reducing pain because it inhibits pain signals from reaching the brain, inhibits substance P production by increasing the amount of time spend in deep sleep, increases serotonin levels, or reduces stress and/or psychological symptoms as per the PNI rationale (Buttle et al. 2011). While none of these theories have evidence in pediatric cancer patients, their rationale is commonly used to guide investigators in various methodological choices.

### 11.2.2 Comparative Effectiveness Research

In addition to the theory-guided clinical trials, comparative effectiveness research may prove to be a promising strategy for CAM research. The Institute of Medicine (IOM) emphasizes two key elements to this research design: the direct comparison of effective interventions and their study in patients who are typical of day-to-day clinical care (Sox and Greenfield 2009). Comparing the effectiveness of already researched CAM therapies may prove more fruitful than RCTs alone. Using observational data obtained from large clinical trials in CAM is essential to compare the outcomes of using several effective interventions in a population that is representative of daily care. The great numbers of patients in these data sets also make it possible to study subgroups with precision and perhaps identify key predictors of response to an intervention, both of which would facilitate decision making at the individual and population level (Sox and Greenfield 2009).

Moreover, observational research methods increase external validity by including speed, real-world decisions, large numbers of decisions and outcomes, and low cost (Sox and Greenfield 2009; Walach et al. 2003). However, the heterogeneity

of the patients who drive real-life clinical decisions may also influence clinical outcomes, confounding the effectiveness of the intervention if it is administered alone. We have too often used the conceptual elegance of randomization to answer the wrong questions. We ask, “Does this work?” when our patients and colleagues want to know, “Is this better than that?” (Walach et al. 2003). Randomized trials that are designed to create ideal circumstances to see whether the intervention can work must be complemented with the “real-life” information about actual effects in broad practice collected from large, methodologically strong observational studies (Walach et al. 2003).

### 11.2.3 Natural Products Research

Botanical and natural products’ research is common in cancer patients. There is an abundance of pre-clinical and clinical data on specific herbs and natural products and their bioactive constituents that demonstrate potential in cancer therapeutics. However, these studies are limited to adult cancer and laboratory studies. Turmeric, mistletoe, green tea, ginseng, mushrooms, and micronutrients are representatives of compounds that exert their effects through mechanisms attributed to specific chemical classes relevant to cancer biology (Melnick 2006).

There is paucity in clinical research of biologically based CAM therapies for anticancer therapy in pediatric oncology. The focus is not as strong in pediatric oncology because relapses are rare, and such therapies would not impact the care children with cancer receive. A recent review found no prospective randomized clinical trials and only two preliminary studies of biologically based CAM therapies in the pediatric oncology population between 1994 and 2004 (Myers et al. 2005).

However, given the high rate of use of biologically based CAM therapies in children with cancer, research is warranted. The major concern among pediatric oncologists is the potential for interactions among biologically based therapies and conventional treatments, especially chemotherapy and radiation therapy. Few actual herb-drug interactions have been reported in humans undergoing cancer treatment, and so the potential

for interaction must be regarded as theoretical. However, concomitant administration may affect chemotherapy levels or increase toxicity that may ultimately impact outcome (Kelly 2004). The data remains insufficient to guide clinical practice on the concurrent use of antioxidants and chemotherapy or radiotherapy. There are too few RCTs to conclude benefit of high-dose supplementation. On the contrary, limited evidence suggests potential harm. The benefit and risks need to be explored with large-scale clinical trials that are properly controlled, powered, and equipped to measure tumor growth (Lawenda et al. 2008). Recent preclinical studies have shown interactions of antioxidant supplements, including vitamin C, at orally achievable concentrations (equivalent to 1 g/day, a dose frequently used by patients), with the proteasome inhibitor bortezomib, an agent that is currently being evaluated for the treatment of pediatric acute myeloid leukemia (Perrone et al. 2009). Further research in biologically based therapies is needed to establish clinical practice guidelines during cancer therapy.

#### **11.2.4 CAM for Supportive Care Indications**

Complementary and alternative therapies for symptom management related to cancer or its conventional treatment include a plethora of treatments including acupuncture, massage therapy, aromatherapy, energy healing, imagery, prayer, and herbal and nutritional supplements. Parallel to the increasing prevalence of CAM use in cancer patients is the number of qualitative and quantitative clinical trials on CAM. Some therapies have more evidence for effectiveness (e.g., hypnosis and acupuncture) than others (e.g., herbal therapies and homeopathy), and clinical trials in children lag behind CAM trials in adults (Ladas 2006).

Integrative oncology, or the use of CAM in conjunction with conventional cancer treatment, seeks to improve the supportive care available to patients and to determine the safety, effectiveness, and compatibility of adjunctive CAM thera-

pies with standard chemotherapy and radiation (Post-White and Hawks 2005). Integrative oncology emphasizes awareness of and sensitivity to the mental, emotional, and spiritual needs of a patient. To this effect, the clinician combines the best of evidence-based, complementary therapies and mainstream care to deliver a multidisciplinary approach to evaluate and treat the whole person (Abrams et al. 2009). The challenge to pediatric oncology research is to improve survival rates, and also reduce late effects, and improve overall health and well-being of patients and their families. A consistent component of CAM use in pediatrics is the intention to comfort, to reduce pain and symptoms, and to promote an environment conducive to healing, one in which the child feels empowered to manage his/her own responses to the painful or unpleasant situation (Post-White and Hawks 2005).

There is evidence supporting the effectiveness of CAM therapies for pediatric oncology patients. Nausea and vomiting, pain, anxiety, fatigue, loss of appetite, and constipation/diarrhea are symptoms that fluctuate over time and span the course of the disease, from diagnosis to end-of-life care. Moreover, there is evidence of CAM therapies for symptom management in pediatric oncology, as outlined by Ladas et al. (2006).

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### **11.3 Pediatric Oncology**

#### **11.3.1 Where Standard Therapy Fails**

As Ladas et al. have emphasized, research in CAM has provided pediatric cancer patients with a variety of evidence-based, adjunctive therapies to manage some of the most commonly reported cancer-related symptoms and late effects. Conventional therapies sometimes fail to provide patients with relief. CAM interventions that are safe and effective may bridge this gap in clinical practice (Table 11.1). The ideal protocol for symptom management uses a combination of drugs and procedures in an individualized fashion, based on the patient's disease history, symptom etiology, developmental stage, and social issues.

**Table 11.1** Effective CAM therapies in children with cancer

Symptomatology	Effective treatment as per RCTs
Nausea/vomiting	Cognitive distraction, hypnosis, music therapy
Mucositis	Glutamine
Procedural pain	Hypnosis
Cachexia	Fish oil supplements
Anxiety/insomnia	Hypnosis, massage
Hepatotoxicity	Milk thistle

Conventional medicines sometimes fail to manage the side effects of cancer therapy. Here is a list of common CAM therapies that have been proven effective by RCTs in the management of these symptoms in children.

The effective management of symptomatology in pediatric oncology is a unique challenge for many reasons. Procedure-related symptoms have been studied extensively. Bone marrow aspiration or biopsy, lumbar puncture, venipuncture, and percutaneous vascular access are common invasive procedures that have potential to cause pain, anxiety, and/or distress in children and adolescents undergoing cancer therapy. An integrative review shows distraction, hypnosis, and imagery emerged as the three most commonly studied mind-body modalities for management of procedural pain, anxiety, and distress in pediatric oncology (Landier and Tse 2010). Clinical trials of hypnosis have demonstrated effectiveness in relieving procedure-related symptoms. Self-hypnosis appears to be effective in reducing anticipatory anxiety in certain children (Landier and Tse 2010; Rheingans 2007). Among other approaches that have been found to be efficacious are cognitive behavioral therapy and distraction, particularly for procedural anxiety, distress, and pain (Rheingans 2007). There is also promising evidence for massage, music, and ingested peppermint oil in the treatment of acute, chronic, and procedural pain (Ladas et al. 2006).

Acute and delayed nausea and emesis have been shown to remain significant problems among children who receive emetogenic chemotherapy. Even with “usual care” antiemetic prophylaxis, chemotherapy regimens that contained either cisplatin or higher doses of alkylating

agents, methotrexate, or cytarabine had low rates of complete protection in either the acute phase and/or the delayed phase (Holdsworth et al. 2006). CAM therapies may be of potential use in the management of these problematic symptoms. Acupuncture has been shown to be effective in significantly reducing the number of as needed antiemetics administered, although no change in nausea scores was seen. Hypnosis was also effective in reducing anticipatory nausea and the number of antiemetics (Rheingans 2007). Distraction, relaxation, and self-hypnosis were successful in reducing nausea and vomiting (Rheingans 2007).

### 11.3.2 Challenges Specific to Pediatric Oncology Research

Addressing the effectiveness gaps in pediatric oncology research poses many challenges. Children and adolescents, as a single population to study, represent developmental, disease state, and psychological heterogeneity that makes RCTs and observational studies especially difficult.

Tumors are less likely to have been caused by an environmental factor that can be easily modified for research purposes. Rather, cancer in children and adolescents are more embryonal in nature and development. There is no clear lifestyle or environmental factor in the pathogenesis of such cancers, when compared to common adult carcinomas.

Cognitive developments limit the use of certain therapies, such as acupuncture, which may cause fear in the child. Ayurvedic medicines that have been cited to have metal compounds, such as lead, may pose a risk to the child’s developing brain. The developmental status of the child also influences the availability of appropriate instruments for assessment of patient-reported outcomes, particularly for assessment of interventions geared toward alleviating symptoms. An elusive cancer history coupled with the developing nature of children’s psyche and body makes any type of research challenging in pediatric oncology.

While research in adults has focused on individualized CAM treatments, research in pediatric oncology must be cognizant of the complex familial network a child is surrounded by. This network is intricately involved in the child's cancer journey. Families experiencing childhood chronic illness must adapt to caregiving burdens, stress, and anxiety demands, all of which have the potential to exert effects on research outcome measures. A meta-analysis found a statistically significant and negative effect for having a sibling with a chronic illness and parents' reports to be more negative than child self-reports (Sharpe and Rossiter 2002). Another study concluded that parents view both physical and psychosocial side effects of cancer therapy to be bothersome to their children. For example, parents identified disappointment at missing activities with friends or peers, mood swings, nausea, and fatigue as the most prevalent symptoms affecting their children (Dupuis et al. 2010). Future CAM research and effective interventions can focus on both the patients and families.

## 11.4 Open Questions

### 11.4.1 The Need for CAM Research and Collaborations

While there is growing evidence in the effectiveness and efficacy of many CAM therapies in the adult cancer population, trials that address the specific challenges in the pediatric cancer patients are still lacking.

One of the first steps in addressing the effectiveness gaps would be to identify clinical areas that pediatric oncologists experience as difficult to treat with available treatments and identify CAM treatments that may be effective in bridging this gap. Effectiveness gaps, for which there are effective CAM treatments, do exist and have been identified in a pilot study by general practitioners through a survey (Fisher et al. 2004). Such work can guide clinical service to incorporate effective treatments, or research to explore deficiencies in clinical care that cannot be addressed with existing evidence.

**Table 11.2** Strong recommendations for use after diagnosis

Modality	Indication	Quality of evidence
<i>Natural products</i>		
Dietary supplements	Do not take for prevention	High
Supplement counseling	Prevent side effects and interactions	Moderate
<i>Mind-body</i>		
Mind-body techniques	Anxiety, pain, QOL	Moderate
Support groups	Anxiety, pain, QOL	High
<i>Body-based</i>		
Massage	Anxiety, pain	Low
Acupuncture	Pain, side effects	High
	Radiation xerostomia	Moderate
<i>Energy therapies</i>		
Reiki, healing touch	Anxiety	Moderate
	Pain, fatigue, symptoms	Low

Guidelines ranking the quality of evidence for heavily researched CAM modalities and their indications can guide practice in integrative oncology (Deng GE et al. 2009)

Additionally, we need to facilitate the collaborations between clinicians of conventional and CAM modalities, educators, patient advocates, and policy makers. The Society for Integrative Oncology (SIO) is exemplary in the dissemination of evidence of CAM and recommendations for clinicians. The Society has put together guidelines that rank the effectiveness and quality of evidence for the practice of integrative oncology (Table 11.2). Mind-body modalities can reduce anxiety, mood disturbance, and pain and improve quality of life (QOL). Massage therapy may also have a role in treating anxiety or pain (Hughes et al. 2008). Physical activity and energy therapies may help promote basic health and improve QOL. Also, the risk of harm is insignificant, so long as the therapy is provided by a qualified and trained professional.

Government also needs to have a role in the funding of and support for CAM research. The National Center for Complementary and Alternative Medicine (NCCAM) of the US National Institute



of Health (NIH) grew out of the mission of the US Office of Alternative Medicine to fund research into CAM practices, to train CAM researchers, and to disseminate CAM-related information to professionals and the public. Since its creation, the NCCAM annual budget has grown from US\$2 million in 1991 to nearly US\$130 million in 2010 (Ernst et al. 2012). In the United States, total funding by all institutes and centers of the NIH for research and training on CAM and the training of investigators to study CAM exceeded \$225 million in 2006. However, of the approximately 360 NCCAM funded research projects in 2006, fewer than 5 % were related to pediatrics (Kemper et al. 2008). For this reason, the work ahead of us lies in the hands of clinicians and researchers.

Organizations like the Children's Oncology Group (COG) and the International Society of Pediatric Oncology (SIOP) are essential to the execution of well-designed scientifically sound clinical trials in pediatric oncology. A National Cancer Institute (NCI) supported clinical trials group, COG, has a committee on CAM cochaired by two pediatric oncologists with expertise in the field of CAM. Committee membership is drawn from the disciplines of pediatric oncology, nursing, nutrition, psychology, and biostatistics. In formulating strategy, the committee has reviewed results of preliminary research in CAM conducted at COG member institutions and elsewhere.

The first randomized, double-blind, placebo-controlled clinical trial initiated in 2004 by the COG assessed the efficacy of Traumeel-S® (Heel, Inc, Albuquerque, NM), a homeopathic remedy prepared from plant extracts for the prevention and treatment of mucositis in children undergoing stem cell transplantation (Sencer et al. 2012). While this clinical trial did not support the use of Traumeel in preventing or treating mucositis associated with stem cell transplant in children, it did show that it is possible to conduct a large-scale, multisite clinical CAM trial within the rigorous paradigm of conventional RCTs.

For integrative oncology to flourish and provide solutions to our current health care crises will take systemic change. It will require a commitment to focus on prevention and health promotion and to embrace new providers and new provider models

(Maizes 2009). For this to occur, we must recognize the challenges inherent to CAM research and build a stronger evidence base that will translate into effective integrative medicine in the pediatric oncology setting and bridge the effectiveness gaps in clinical practice that patients, families, and healthcare providers identify.

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# Medical Education in Complementary and Alternative Medicine (CAM): A European Perspective

# 12

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## Contents

<b>12.1</b>	<b>Introduction</b> .....	157
<b>12.2</b>	<b>Why Should CAM Be Taught at Medical Schools?</b> .....	158
12.2.1	The Usage of CAM in Pediatric Oncology.....	158
12.2.2	Communication About CAM.....	158
12.2.3	The Physicians' Wish for CAM Education .....	159
<b>12.3</b>	<b>Integration of CAM Courses into Medical Curricula in Europe:</b>	
	<b>The Status Quo</b> .....	160
12.3.1	Opinions on CAM.....	160
12.3.2	The Status Quo.....	160
<b>12.4</b>	<b>What Should Be Taught in CAM Courses?</b> .....	161
12.4.1	Communication Skills.....	161
12.4.2	Teaching of Basics .....	162
12.4.3	Development of Attitudes .....	162
<b>12.5</b>	<b>How Should Complementary and Alternative Medicine Be Taught?</b> .....	162
<b>12.6</b>	<b>The Integrated Curriculum for Anthroposophic Medicine</b> .....	163
12.6.1	Integration into the Main Medical Curriculum.....	163
12.6.2	Experience from the ICURAM Program.....	165
	<b>References</b> .....	165

## 12.1 Introduction

As use of complementary and alternative medicine (CAM) is becoming increasingly popular among patients, we need to take a new look at how we are educating our future doctors. Opinions on integration of CAM courses into the main curriculum at medical faculties differ. In this chapter, we would like to discuss various aspects of this issue. Starting with the question of why CAM should be taught at medical schools, in the first section, we briefly outline the current usage of CAM among patients and then look at CAM from the physician's point of view. How do physicians view the increasing popularity of CAM among patients and how do they deal with it? Do physicians integrate CAM into their regular practice? Do they wish for more training on CAM topics? We then go on to describe the current situation of CAM education in Europe. This section includes reports on how CAM is viewed at universities or medical faculties as well as a paragraph about possible reasons for the slow progress in integrating CAM into medical curricula in Europe. In the next section, we look at the content that should be taught and possible ways of integrating it into the

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medical curriculum. The final section describes the “Integrated Curriculum for Anthroposophic Medicine” (ICURAM) at the University of Witten/Herdecke in Germany as an example of successful integration of CAM into the medical education of students at a German university.

## 12.2 Why Should CAM Be Taught at Medical Schools?

### 12.2.1 The Usage of CAM in Pediatric Oncology

Complementary and alternative medicine (CAM) is gaining in popularity worldwide (Eisenberg et al. 1993; Fisher and Ward 1994; MacLennan et al. 1996; Abbot et al. 1996; Astin 1998). Use of CAM therapies is common in the treatment of cancer patients, especially in pediatric oncology (McLean and Kemper 2006). According to figures published by the World Health Organization (WHO), 90 % of the population in France, 75 % in Germany, and 60 % in Great Britain have tried CAM at least once in their lives (World Health Organization 2002).

Studies evaluating the overall frequency of CAM use worldwide among pediatric cancer patients show figures from 12 to 85 % (Clerici et al. 2009; Hamidah et al. 2009). For Europe, the reported percentages on the usage of CAM among children suffering from cancer vary less widely. A study of a small nonrepresentative group of 97 pediatric cancer patients from Italy reported that 12 % used CAM (Clerici et al. 2009). A nationwide representative study from Germany reported CAM usage of about 35 % among a group of 1,063 pediatric cancer patients (Längler et al. 2008). (For further details, see Chap. 3.)

Societal changes in the direction of increasing acceptance and usage of CAM methods call for changes in medical education (Wetzel et al. 1999). In 2007, American authors put forward several arguments for the development of CAM educational programs as part of conventional medical education (Gaylord and Mann 2007):

- I. The increasing usage of CAM treatments
- II. The need to improve the safety aspect of CAM methods

- III. The need to improve communication between physicians, CAM therapists, and patients
- IV. The potential to enhance health-care coordination
- V. The enhancement of quality of care
- VI. The impact on increasing the quality of CAM research
- VII. Education in CAM broadens core competencies for conventional medicine professionals

### 12.2.2 Communication About CAM

Studies like the above-mentioned show that in pediatric oncology CAM treatments play an important role in addition to the conventional cancer therapies. Nevertheless, patients suffering from cancer or their parents often do not inform their treating physicians about the use of CAM (Clerici et al. 2009; Martel et al. 2005). The worldwide communication situation between pediatric cancer patients, or rather their parents, and the treating physicians about the use of CAM therapies in addition to the conventional cancer treatments is bad (Hamidah et al. 2009; Weyl Ben Arush et al. 2006; Gomez-Martinez et al. 2007; Gözümlü et al. 2007). A study conducted in the United States in 2009 tried to find out the reasons for this poor rate of communication (Roth et al. 2009). Ninety pediatric oncologists practicing in the United States were asked to answer a questionnaire about their views on the use of CAM in children suffering from cancer. Ninety-nine percent of them believed that it was important to know what complementing therapies their patients used. In contrast, only 11 % of the pediatric oncologists stated that they routinely asked their patients about additional CAM usage. Forty-three percent reported that they occasionally asked their patients about the use of CAM. More than half of the physicians believed that some kind of CAM such as massage therapy, prayer, or guided imagery might improve their patients' quality of life. Almost all of the physicians asked, that is, 99 % believed that knowledge about CAM was important to prevent drug interactions and 84 % thought it was essential to improve the trust between patient and physician. Therefore, it seems strange that only so few asked their patients

about these complementing CAM treatments. A similar study from Germany revealed that more than half of the responding 175 pediatric hemato-oncologists, that is, 58 %, never or rarely asked their patients about the use of CAM (Länger et al. 2012). Similar to the findings mentioned above, only 41 % of the respondents stated that they often or always brought up the topic of CAM at the first consultation.

It is important for the doctor-patient relationship that patients can ask all their questions relating to their health (House of Lords 2000). A lack of knowledge on CAM methods makes it impossible to answer questions related to this subject. This may compromise the patient's trust in his treating physician. The aforementioned American study reports major reasons for the low rate of communication (Roth et al. 2009). Ninety-three percent of the 90 pediatric oncologists asked cited lack of knowledge on the subject and 56 % of the physicians reported concerns over potential adverse reactions that may be associated with the CAM therapy. The German study among 175 pediatric hemato-oncologists revealed that a large number of the respondents, that is, 76 %, were concerned about possible interactions with the conventional cancer treatment while 66 % of them feared possible side effects (Länger et al. 2012). Another 65 % of the respondents reported lack of competence in guiding the patients in CAM. Interestingly, two further concerns about CAM treatments were mentioned: 75 % of the responding pediatric oncologists were afraid of the additional costs for the patient and 68 % of the 175 pediatric hemato-oncologists feared that effective conventional treatments might be prevented or delayed.

It is crucial for effective communication that physicians should know which questions to ask about CAM and be able to answer the patients' questions. Therefore, physicians must be trained in CAM topics to enable them to be competent communication partners for their patients. Effective communication about CAM topics requires not only a reasonable knowledge base in this area but also the willingness to discuss these topics with the patient and to admit a lack of knowledge (Kligler et al. 1999). (For further details on CAM communication, see Chap. 15.)

### 12.2.3 The Physicians' Wish for CAM Education

The aforementioned study from America asking 90 pediatric oncologists for their views and attitudes concerning CAM therapies revealed that more than 50 % of the responding physicians would like to learn more about CAM treatments (Roth et al. 2009). Physicians who had already acquired knowledge about CAM had done so on their own initiative. They reported using the Internet, colleagues, or medical journals to gather information on the subject.

These findings are supported by another study published in 2007 (Sawni and Thomas 2007). Thirty percent of a cohort of 348 American pediatricians surveyed in 2004 reported using CAM therapies on their patients. In contrast, only 18 % stated that they had formal training in CAM. In 55 % of the cases, the pediatricians reported that their knowledge was self-taught or gained by CME.<sup>1</sup> The majority of pediatricians, that is, 84 %, expressed the wish for more CME courses on CAM. Eighty percent of the respondents would prefer CAM to be taught within the conventional medical curriculum in medical school. These findings are in line with results of an exploration among 17 German general practitioners (GPs) published in 2008 (Joos et al. 2008). Most of the responding GPs considered that CAM should be integrated into the regular undergraduate curriculum in medical school. The GPs asked stated that they would prefer the postgraduate curriculum to contain sections on CAM and sections on conventional medicine in order to provide a broader perspective. Most of the responding GPs were dissatisfied with the existing possibilities for learning about CAM. The courses seemed to be too expensive and were not very well structured, and both content and presentation seemed to be poor. The responding GPs proposed that CAM courses should be evidence-based, independent, and practice-orientated.

Among 175 surveyed German pediatric oncologists, 85 % thought that there should be more CME courses available on the subject of CAM

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<sup>1</sup> Continuing medical education

(Länger et al. 2012). Another 70 % considered it important to integrate CAM topics into postgraduate training.

Not only physicians but also medical students would like to learn more about CAM methods. As seen in a recently published study from Germany in 2011, most of the 217 German students responding thought that integrating CAM into the regular undergraduate curriculum at medical school was necessary (Münstedt et al. 2011). Most students said they would like more education in CAM topics and would welcome a critical confrontation with the subject during their studies.

## 12.3 Integration of CAM Courses into Medical Curricula in Europe: The Status Quo

Both the increasing usage of CAM among patients and the growing interest in CAM among medical students and doctors have led to a controversial discussion about the integration of CAM into the medical curricula (Barker et al. 2000). In contrast to the situation in Europe, the development of training in CAM in American medical schools is more advanced (Jobst and Musselmann 2003). Discussions about CAM courses in Europe often focus on whether CAM should be integrated in the medical curriculum or not (Witt et al. 2010).

### 12.3.1 Opinions on CAM

A representative cross-sectional study performed in three European countries investigated the current situation of CAM in medical schools including opinions on CAM (Brinkhaus et al. 2011). Several departments ( $n=1,017$ ) at 42 medical schools in Germany, Austria, and Switzerland were contacted. Of the 487 respondents, 40 % stated that they had a positive opinion on CAM therapies. However, 28 % reported a neutral opinion on CAM, while 29 % claimed to have a negative opinion. Interestingly, in 88 % of the cases, the negative opinion was based on scientific

research whereas a positive attitude toward CAM was based on personal experience in 82 % of the cases. Seventy-four percent of the respondents reported that they saw CAM methods as a supplement to conventional medicine, while 34 % believed CAM methods were an alternative to conventional treatment. The CAM methods viewed most positively by the respondents of this study were acupuncture, osteopathy, naturopathy, and herbal medicine.

### 12.3.2 The Status Quo

Few studies evaluating the current situation of CAM at European medical schools exist. Whereas in the United States 64 % of medical schools are providing CAM education, the percentage for European medical faculties is lower (Barberis et al. 2001). The percentage of European medical schools offering CAM education is about 40–42 % in the former EU (fEU) countries and about 20 % in the recent EU (rEU) countries (Barberis et al. 2001; Vargaa et al. 2006). We reviewed three studies concerning this question and will address them in detail now:

The authors of a study published in 2006 contacted 265 medical faculties in different European countries (Vargaa et al. 2006). Replies were received from 90 medical faculties in fEU countries and 15 faculties in rEU countries. In 42 % of the fEU countries, training in CAM is possible, whereas figures for rEU countries show that education in CAM is available in 20 % of the faculties.

These findings match the results of a study published in 2001 addressing the same question in order to document the incidence of educational courses in CAM for the European Union (Barberis et al. 2001). Five hundred and fifty universities in the EU listed by the Confederation of European Union Rectors' Conference were contacted. Of these 550 universities, 326 replied. Not all of the responding universities had a faculty of medicine; some had a faculty of health sciences instead. Replies were received from 107 universities with a faculty of medicine, 29 universities with a faculty of health sciences, and 190 other

miscellaneous universities. Educational courses on CAM were offered by 43 (40 %) medical schools, 21 (72 %) health sciences faculties, and by 15 (8 %) other miscellaneous faculties.

A recently published study from 2011 investigated the integration of CAM into the regular curriculum at universities in Austria, Switzerland, and Germany (Brinkhaus et al. 2011). Of the 487 respondents from these three EU countries, 162 (34 %) indicated that CAM therapies had already been integrated into the regular curriculum. These figures are difficult to compare with those mentioned in the two surveys above because in this survey the respondents were not medical schools in their entirety but different department or institute directors of a total of 42 medical schools in Austria, Switzerland, and Germany. Interestingly, this study revealed that the majority of respondents, that is, 73 %, were in favor of integrating CAM into the medical curriculum. Eighty-five percent of the respondents willing to integrate CAM approved of its usage in research, 83 % in teaching, and 60 % in treating patients. The implementation of CAM in those medical schools which had already integrated it into their curriculum showed that their main focus lay on patient treatment (25 %), followed by research (19 %) and student education (18 %).

According to the CAMDOC Alliance,<sup>2</sup> chairs in CAM and/or integrative medicine exist in Germany (Berlin, Duisburg/Essen, Rostock, Munich, Witten/Herdecke), France (Nantes), Hungary (Pécs), Italy (Florence and Bologna), Norway (Tromsø), Sweden (Stockholm), Switzerland (Bern, Zürich), and the United Kingdom (Exeter, Sheffield, Southampton, Thames Valley) (CAMDOC Alliance). All these chairs in CAM at medical faculties are endowed chairs (Witt et al. 2010).

<sup>2</sup> The CAMDOC Alliance is an affiliation of the European Committee for Homeopathy (ECH), the European Council of Doctors for Plurality in Medicine (ECPM), the International Council of Medical Acupuncture and Related Techniques (ICMART), and the International Federation of Anthroposophic Medical Associations (IVAA). It represents 132 European associations of medical doctors practicing CAM.

Despite the aforementioned high and increasing public interest in CAM and its related topics, integration of CAM into medical school curricula remains a slow process (Wetzel et al. 2003). German authors published a study in 2011 where they stated several reasons for the slow integration of CAM (Münstedt et al. 2011):

- I. Dislike of CAM and its related topics, possibly a fear that including CAM education in the curriculum might be judged as a sign of acceptance of CAM
- II. Lack of knowledge
- III. Lack of practical experience
- IV. Inexperience concerning education in CAM
- V. Lack of qualified, objective teachers
- VI. Uncertainty as to whether CAM should be integrated in other disciplines or should be regarded independently
- VII. Uncertainty as to the extent to which treatment of patients with CAM should be integrated

## 12.4 What Should Be Taught in CAM Courses?

The question of whether the approach should be to teach content, critical analysis, or theory or rather personal experience and practical skills in different CAM methods remains unclear. Is the aim to train mentors who can guide the patient through the diverse and complex CAM market? Or should the objective of educational CAM courses be the practically trained physician?

### 12.4.1 Communication Skills

Some authors suggest that it is important to equip the students to communicate about the present CAM methods in a proper and well-informed manner. Therefore, students should be trained in communication skills to enable them to communicate with patients about the usage of CAM or its avoidance. Students should also be able to integrate CAM treatments into a medical treatment plan (Wetzel et al. 2003). Communication about CAM is important not only between



physicians and patients but also between allopathic physicians and CAM providers (Caspi et al. 2000).

### 12.4.2 Teaching of Basics

Authors also suggest that students should not be trained as CAM practitioners but should rather know the fundamental basics and principles of different CAM approaches (Oberbaum et al. 2005). That should enable them in guiding patients who may be considering usage of CAM. A recent article by German authors published in 2010 considers two aspects important: First of all, medical education in CAM should provide an introduction to the most commonly used unconventional treatments, and secondly it should address aspects such as efficacy, effectiveness, current evidence, and safety issues regarding CAM treatments (Witt et al. 2010).

Students should know the common clinical applications and also the possible indications for specific CAM treatments (Kligler et al. 1999). Furthermore, future medical doctors should be aware of the current research evidence concerning efficacy and effectiveness, the potential for adverse reactions, and finally they should know reputable references for in-depth information on certain CAM treatments (Kligler et al. 1999).

### 12.4.3 Development of Attitudes

A curriculum in CAM should impart not only knowledge but also specific attitudes regarding unconventional medical treatments (Kligler et al. 1999). These attitudes include openness toward different cultural influences on health beliefs and respect of the potential of certain CAM treatments.

Integrating CAM courses into the normal medical education curriculum may broaden medical core competencies such as an increase in self-awareness or personal growth (Elder et al. 2007). The learning of mind-body techniques, for example, may encourage the students to use these skills for their own management of stress and well-being.

Another attitude that may be fostered by CAM educational courses is the understanding that development of self-reflection, personal growth, and self-care by future medical doctors is important in order to enable them to make authentic recommendations to their patients (Kligler et al. 1999). A British survey among 47 third-year medical students attending CAM courses revealed that students valued the opportunity for personal development and self-reflection (Murdoch-Eaton and Crombie 2002). The development of self-awareness may include the application of previously trained skills for stress-management, nutrition awareness, or mind-body skills, for example (Kligler et al. 2004).

The experience related from medical schools in the US shows that qualities like critical analysis, empathy, and compassion, which can be understood as classical aims of conventional medical education, are promoted by CAM courses (Oberbaum et al. 2005).

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## 12.5 How Should Complementary and Alternative Medicine Be Taught?

Scientific discussion in the USA tends to focus on questions of practical transposition of CAM-related content into the existing curriculum, especially on the factors time and money, while in Europe, the debate still concentrates on the question of whether to integrate CAM into universities at all (Witt et al. 2010; Brinkhaus et al. 2011). However, irrespective of these differences, the didactic difficulties and challenges have rarely been addressed.

Whether courses on CAM should be optional or obligatory remains an open question. On the one hand, it is argued that such courses widen the personal perspective of all students and should therefore be integrated into the main curriculum (Caspi et al. 2000). Regarding the need for competent advisers in a confusing CAM market (Witt et al. 2010), a minimum of knowledge about the most common CAM therapies would be helpful for all students. An elective course carries the risk of marginalizing CAM as a side issue and of

lack of funding if it is not in line with the overall objectives of the medical school (Wetzel et al. 2003). On the other hand, an integrated curriculum would have to be reduced to a minimum and no therapy could be taught in depth (Murdoch-Eaton and Crombie 2002).

The medical curriculum at this stage is rather overloaded, so time is a restricting factor for scheduling an additional CAM curriculum (Jobst and Musselmann 2003; Waldstein et al. 2001). The experience from US medical schools shows that CAM content can be integrated into existing medical courses instead of providing a separate curriculum (Wetzel et al. 2003). The authors reported on “Anatomy of Acupuncture,” which is part of the regular anatomy course at Georgetown faculty. Another approach in this direction would be to implement communication about CAM therapies into current courses on the doctor-patient relationship (Kligler et al. 2004).

Nevertheless, the main challenge in implementing CAM courses is not the lack of time or money but rather the difficulty of integrating humanistic aspects related to these lessons. Studying CAM means more than just accumulating knowledge and certain techniques but also developing a different way of viewing the interaction between physician and patient (Kligler et al. 2004) as well as a personal model of health and illness (Wetzel et al. 2003). This means that it is necessary to integrate philosophical questions into education. If we want to recover humanist values in medicine and understand health as an emergent property of the individual patient (Bell et al. 2002), we have to investigate how we can promote the personal growth of medical students. The finding that empathy decreases during medical education (Newton et al. 2008; Neumann et al. 2008) implies an additional task in the design of CAM curricula. How can empathy be taught within CAM courses? How can we convey the process of comprehending the patient as partner in the development of the appropriate therapy combining the best from conventional and complementary medicine (Gaudet 1998)? How can we teach the integration of different disciplines in mutual respect at a time when medical disciplines are becoming increasingly specialized and

dialogue is becoming more and more difficult? The development of a common language among different disciplines and health systems is a challenge for CAM education (Caspi et al. 2000).

Medicine requires the work of heart and soul, values that can be learned by education, not by training (Remen 2001).

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## 12.6 The Integrated Curriculum for Anthroposophic Medicine

In the following, we want to report experience with an integrative curriculum at a German university. The Integrated Curriculum for Anthroposophic Medicine (ICURAM) started in 2004 at the University of Witten/Herdecke. It consists of seminars, experiential workshops, and clinical training offered optionally throughout the main medical curriculum. Beside theoretical and practical lessons in Anthroposophic Medicine (AM), this program also focuses on Integrative Medicine in a broader context and tries to develop a holistic view of the patient.

The University of Witten/Herdecke was founded in 1982 as the first nongovernmental University in Germany. The founders sought a different way of education and research in an open-minded and pluralistic atmosphere (Wiedersheim 1989). Since some of the founders of the university were anthroposophic physicians, AM has been enrooted from the beginning. Accordingly, there was candidness toward different medical therapies and room for reflection on current concepts of illness and healing.

### 12.6.1 Integration into the Main Medical Curriculum

The first 2 years of the medical course in Germany are for the most part theoretical, providing a biomedical base. Throughout this part of the study the ICURAM offers two weekly seminars:

“Integrative physiology” teaches a more macroscopic and holistic view of disease, based on Goethe’s phenomenological approach in natural sciences (Bortoft 1996). A course on cardiac

arrhythmias, for example, can deal with the dynamic adjustment of different rhythmic processes in the organism (Cysarz et al. 2008) and the impact of mind-body therapies on these rhythms (Seifert et al. 2009).

“Anthroposophic anthropology” deals with the philosophical construct underlying AM and guides students to reflect on their own beliefs about individuality and the relation of body and mind. Furthermore, a course in reflective observation has been developed for first-year students. Weekend workshops and weekly courses continuing over one semester complete the curriculum. These cover topics such as different health concepts, salutogenesis, or homeopathic remedies.

The following 3 years are comprised of clinical rotations. Students are taught at academic hospitals in different medical departments, staying there for usually 4 weeks. Clinical rotations in integrative medicine are offered for most clinical specialties including pediatrics. They are usually offered by the local academic hospital, the anthroposophic “Gemeinschaftskrankenhaus Herdecke.” In addition to the contents of the main medical curriculum, students learn to develop a holistic view of the individual patient and to understand the possible psychosomatic history of a disease. Furthermore, they are taught the application of natural remedies and specific therapies such as art therapy and eurhythmy therapy.

The regular internship in pediatrics during these clinical rotations takes place within the fourth year of studies. It lasts for 4 weeks and is offered several times during the semester, for four students at a time. The internship consists of a strictly structured sequence with daily patient contact. Each day, every student is assigned one patient and is asked to examine the patient. During the whole internship, every student has a mentor who is at least a senior physician so that every student works and learns under the close supervision of an experienced pediatrician. Every day, the students have the opportunity to participate in complementing CAM treatments, for example, eurhythmy therapy. Additionally, the students also process their patients from an extended perspective: What does the disease mean for the patient? Why does this patient suffer

from this specific illness? Are there biographical reasons for the patient’s suffering? What complementing therapies could support the patient’s recovery, for example, herbal therapies, art therapy, massage therapy, or eurhythmy therapy?

A specialty during the clinical part of the course is the “integrative medicine case conference.” This workshop has been developed together with students and is placed between the clinical rotations. Experts of different medical approaches are invited to develop treatment plans for a particular patient and to enter into dialogue. For example, a conventional physician, an anthroposophic doctor, a homeopath, and a physician working with traditional Chinese medicine come together and investigate and diagnose the same patient on the basis of their medical approach. Finally, they present their different therapeutic options for this patient. Evaluation of this course among students shows an increasing interest in different medical systems and a positive appraisal of the opportunity to discuss different health concepts with professionals.

Year six of the medical curriculum consists of an internship including three rotations. In order to introduce students to their responsibility as physicians without overstraining them, a special program has been developed in teamwork with students. In the “Clinical Education Ward for Integrative Medicine” (CEWIM), they treat one to four patients on their own under close supervision. Treatment begins with the history and includes conventional and naturopathic drugs as well as the prescription of different additional therapies. In a peer group facilitated by a supervisor, the students reflect on their experiences, questions, and conflicts. The patients were shown to be very satisfied with this guided participation of students (Scheffer et al. 2009). Students report that they were able to acquire competencies in different fields of CAM.

Since 2011, this clinical education ward has also existed for integrative pediatrics at the Gemeinschaftskrankenhaus Herdecke. One final-year student treats one to three pediatric patients on his own. He looks after them from their arrival in the emergency room or the outpatient department to their discharge. He organizes the entire

diagnostic work-up and prescribes the relevant therapy. All of these steps are performed under the close supervision of a senior pediatrician. Especially in the field of therapy, the student is also able to prescribe complementary therapies to accompany the conventional treatment.

The students and physicians carefully evaluate all the clinical internships. During a 4-week internship, at least two feedback discussions are obligatory. The students' feedback is essential and is taken into account for the further development of the internship.

### 12.6.2 Experience from the ICURAM Program

During the first years, students are taught analytic thinking and given a detailed grounding in bio-medical correlations. Questions about the patient as an individual and about meaning and sense of illness decrease progressively. But students obviously bear these questions in mind and seek answers. The ICURAM courses offer encounters with patients from the beginning as well as room for reflection and developing personal questions and interests. ICURAM courses give a different meaning to "learning by heart." The focus is not on being able to reproduce factual content, but the students are encouraged to develop their own opinions about different medical approaches and to have the courage to put forward their own views. Personal growth and increasing self-awareness are the result of this learning process.

During the clinical phase, the students' encounters with patients and self-experience of different therapies together with reflection on their own behavior can enhance empathy. The "case conferences" and the close supervision during the CEWIM train responsibility and self-confidence.

The integration of complementary medical approaches into the main curriculum and the inclusion of students in the development of the ICURAM program should not be underestimated. The students' intrinsic motivation and questions are important reference points for the improvement of the ICURAM curriculum. The personal engagement of students in the curriculum results

in a high level of identification and commitment for projects such as the "case conference," for example.

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# Communicating CAM: How to Talk to Children and Parents About CAM in Pediatric Oncology

# 13

Tycho J. Zuzak and Genn Kameda

## Contents

<b>13.1</b>	<b>Communication Between Physician and Patient</b> .....	169
13.1.1	Communication Model of Schultz von Thun .....	170
<b>13.2</b>	<b>Achieving Patient-Centered Communication in Cancer Care</b> .....	171
13.2.1	Foster a Healing Relationship.....	171
13.2.2	Exchange Information.....	171
13.2.3	Respond to Emotions .....	171
13.2.4	Manage Uncertainty.....	172
13.2.5	Make Decisions.....	172
13.2.6	Enable Patient Self-Management.....	172
<b>13.3</b>	<b>Recommendations for Effectively Discussing CAM During Consultations</b> ...	172
13.3.1	Example of Patient Noninvolvement at Diagnosis .....	174
<b>13.4</b>	<b>Communication in Everyday Life in Pediatric Oncology</b> .....	174
<b>13.5</b>	<b>Conversations About CAM Today: The “Don’t Ask, Don’t Tell” Approach</b> ...	177
13.5.1	Patient’s Reasons for Nondisclosure of CAM Use.....	178
13.5.2	Oncologists Refuse to Speak About CAM .....	179
<b>13.6</b>	<b>Objectives of Discussions About CAM in Pediatric Oncology</b> .....	179
13.6.1	Increase Safety of CAM Use and Conventional Treatment .....	179
13.6.2	Elucidate the Patients’ and Their Families’ Approach to Health and Illness.....	180
13.6.3	Enhance Relationship-Building Between the Patient and the Oncologist .....	180
13.6.4	Clarify Potential Patient Misconceptions ....	180
13.6.5	Positively Influence Patient Outcome.....	181
13.6.6	Decrease the Risk of Physician Burnout and Malpractice .....	181
<b>13.7</b>	<b>Communication and Treatment Refusal</b> .....	181
<b>13.8</b>	<b>The Role of Media in Conversations on CAM</b> .....	182
<b>13.9</b>	<b>Communication Around the Language Barrier</b> .....	183
	<b>References</b> .....	184

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## 13.1 Communication Between Physician and Patient

Communication between physicians and patients plays a central role in patient care. It is essential for a beneficial physician-patient relationship and important for therapeutic success (Baile and

Aaron 2005). The application of patient-centered communication instead of the commonplace disease-centered communication leads to improved medical treatment. Communication should be focused to the patients' psychosocial and medical needs, holistically integrated in daily life, especially in complementary cancer care (Stewart et al. 2000). Communication is essential to establish verbal and nonverbal alliance between the physician and the patient, establish trust, exchange information, and decide on the best type of medical and psychological treatment. Patient care is always an interactive process requiring time and emotionally involved physicians (Stewart and Donner 2000). Even though physicians are aware of this, their daily workload often prevents them from reaching the ideal, since the quality of communication not only involves the ability to communicate with patients in an appropriate way but also must function within the structured logistic approach to time management in daily patient care. Physicians should be careful not to allow stressful time management to prevent cultivating the physician-patient relationship, and learning the appropriate communication skills can help achieve this even within a busy schedule. Although the need for good communication skills is well documented, training physician-patient communication is not a part of standard medical training (Walker 1998). Impaired communication skills can also lead to burnout symptoms in the physician, since physical constitution can be exhausted by the permanent psychological burdens of patient care, including experiencing feelings of failure or insecurity, expectations of the families, or physician's self-doubts (Ramirez et al. 1995). All of these factors point to communication playing a central role in healthcare, and therefore, support giving more attention to physician-patient communication in the daily life and training of physicians.

### 13.1.1 Communication Model of Schultz von Thun

A good model presenting the essential components of communication was described by

Friedemann Schulz von Thun in 1981. He developed the model "square of communication" (Thun 1981) to describe a multilayered content of communication. Besides the transfer of actual data and facts in the factual level, he presented three further levels of communication: (1) the self-disclosure level, (2) the interpersonal level, and (3) the appeal level. The sender communicates both advertent and inadvertent motives, values, and emotions in the self-disclosure level. In the interpersonal level, the sender expresses the relationship to the recipient. Wishes, advice and/or orders, and instructions are transferred in the appeal level.

Communicating about CAM is an additional challenge for physicians beyond the medical competence in CAM techniques. Physicians are always recipients of all four levels of conversation from patients but must maintain high awareness to detect and distinguish these components. This type of competence may help prevent misunderstandings and interpersonal complications in the physician-patient relationship. This is even true for communication about CAM itself with patients and their families, because parents addressing CAM may be trying to satisfy other needs, such as gaining more attention. Physicians have to analyze patients' statements and have to focus on one communication level on which to respond. In this way, they have to formulate the most appropriate answer that will satisfy patients and parents.

Physicians act as senders too. Most physicians focus only on transmitting the factual level in their communication. They must inform patients and parents about diagnoses, new findings, or appropriate therapies. Parents tend to perceive only the self-disclosure and/or interpersonal levels of what the physician says when they are anxious about their child's life but not the factual and appeal levels. This makes it difficult for the physician to communicate his advice and wishes to the parents. Misunderstandings are inevitable and lead to the next problem, namely that the conflicts can only be solved on the level of communication which they occur. Thus, physicians should listen carefully to discern the content and level communicated by the patients and their families and

**Table 13.1** The six core functions of physician-patient communication centered to improve health outcome (Epstein and Street 2007)

1. Foster a healing relationship
2. Exchange information
3. Respond to emotions
4. Manage uncertainty
5. Make decisions
6. Enable patient self-management

be able to switch between the appropriate communication levels to transmit everything the patient and their families need within the physician-patient conversation.

## 13.2 Achieving Patient-Centered Communication in Cancer Care

A framework for patient-centered communication in cancer care has been outlined by the National Cancer Institute (Epstein and Street 2007) with the aim to optimize communication with cancer patients. This framework includes six core functions (explained in detail in Sects. 13.2.1–13.2.6) that can be adapted to a pediatric oncology setting (Table 13.1).

### 13.2.1 Foster a Healing Relationship

Mutual trust must be established between the physician and patient to foster a healing relationship. This requires expressing, feeling, and showing honest commitment in addition to obtaining and sharing basic information. Communication should take into account all facets of the patient, including ideology, education, race, friends, and family. This helps to establish a healing relationship and may improve the whole healing process. For example, parents consumed by fear and anxiety about their child's death cannot build a trusting relationship with their child's physician. Negative coping strategies result in low compliance and in a withdrawal of parental involvement from the healing process. Parental fear and anxiety can only be relieved if the physician adapts communication to foster a healing relationship by

including all the facets of the parents' ideas of life from the beginning (Grootenhuis and Last 1997).

### 13.2.2 Exchange Information

The physician needs to both sufficiently obtain information from and share information with his patients. The full exchange of information arms the physician with complete medical and psychological facts about his patient enabling him/her to give significant therapeutic advice. The physician should include the following information:

- Conventional treatments that have been tried, failed, or rejected because of concerns for safety or quality of life, cost, or other issues
- Patient and parent understanding of prognostic factors associated with disease stages and potential risks and benefits of conventional therapy
- Spiritual and religious values and beliefs of the patient and their family, including how these views impact quality of life or palliative issues and resulting healthcare choices
- Levels of support provided by the family, community, faith, and friends that the patient relies on
- Patient beliefs, fears, hopes, expectations, and experiences with CAM
- Patient concerns about integrating CAM into his or her care

### 13.2.3 Respond to Emotions

Emotional reactions of patients and their families to a cancer diagnosis commonly include anxiety, depression, or fear (Mao et al. 2008). These emotions can also affect response to chemotherapy and modulate how sensitive the patient perceives pain (Watson et al. 1999). The emotional status of an unsatisfied patient often indicates unmet needs, and these patients tend to utilize CAM therapies more than satisfied patients (Herth 1989). Therefore, a CAM physician may act as a rescue boat for an emotionally unsatisfied patient. But such a relationship tends to be fragile and may burst if the expectations of the patients and their families are not considered (Ben-Arye et al. 2011).

### 13.2.4 Manage Uncertainty

Uncertainty has a significant negative effect on pediatric cancer care. A degree of uncertainty accompanies most situations following diagnosis of cancer and during therapy, the most extreme of which being the central question of patient survival. But there are many other questions that remain open besides patient's outcome. Many parents focus on trying to find a reason why their child got this life-threatening disease. Since this question cannot be answered in most cases, a long-standing uncertainty accompanied by fear and anxiety may develop in the patients' families that remains years after therapy is completed due to the fear of a possible relapse. Furthermore, therapeutic guidelines or protocols often do not exist for cases of relapse or palliative situations, so parents become more involved in therapeutic decisions, and there often is no reliable clinical data to answer their questions. Physicians cannot resolve the uncertainty in many cases, but they must handle it and help the patient and their families to handle it. Patient-centered communication should try to reduce uncertainty where possible and assist the patient and their families in dealing with the uncertainties that cannot be reduced. In many situations, patients appreciate it when the physician acknowledges that uncertainty is unavoidable and can supply information in terms of what is known and what is unknown. Helping the patients and their families to handle uncertainty can improve quality of life and facilitate further communication. Uncertainty also includes the potential for hope and allows space for new ideas, personal initiatives, and efforts. Emphasizing and utilizing this positive side of uncertainty can help families affected by cancer to adjust to the illness, enhance their psychosocial well-being, and improve their quality of life (Felder 2004; Mao et al. 2008).

### 13.2.5 Make Decisions

It is necessary to analyze, discuss, and obtain information carefully before sharing it with patients and their families or making decisions. The quality of the decision should depend on the accomplishment of four tasks:

- Physician and patient/family perspectives are voiced and understood
- Differences are reconciled satisfactorily
- Mutual agreement is achieved regarding the best course of action
- Decision is supported by current clinical evidence

Interestingly, a "shared decision" will not lead inherently to a satisfying decision-making process. Instead, the quality of the physician-patient interaction, and not the patient's role per se, is the most important factor affecting the quality of the decision-making process (Bluebond-Langner 1978; Miyata et al. 2005).

### 13.2.6 Enable Patient Self-Management

Enabling patient self-management is of major importance in cancer therapy. It is very fascinating to listen to families describe how individually they manage their lives with a cancer patient and what factors are the most important in influencing and encouraging them (Tautz 1990). It is always important for families to have influence in decisions for their child's therapy and daily routine, especially for families of palliative patients. But at diagnosis, most families underestimate the importance of a good self-management because they do not know that it will raise quality of life. Therefore, self-management has to be established and reinforced by physicians. In a good physician-patient relationship, the physician should guide and assist families in their self-management, including advising them medically and protecting them from untrustworthy treatments.

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## 13.3 Recommendations for Effectively Discussing CAM During Consultations

Communication in pediatric oncology presents a special situation, since it includes a triangle formed by the patient, the parents, and the physician. It is important that physicians talk with both the parents and the patient about the diagnosis, diagnostic procedures, and therapy, since many

of the routine tests are invasive procedures such as bone marrow biopsy or lumbar puncture. Children are often traumatized by these procedures for many years. Lack of communication reduces the fundamental trust between physician and child, resulting in a loss of compliance and increased chance of traumatization. If the child is able to communicate and understands the situation, the physician should take the time to sit next to the patient and start a child-orientated conversation and ask questions adapted to the patient's age and mental status. During the conversation with the children, the parents should only listen and not be allowed to interrupt. Parents often tend to interrupt such conversations, because they fear that the physician will overstrain the patient's emotional balance. Besides that, parents often try to protect their children by hiding important information or bad news (Bluebond-Langner 1978; Slavin et al. 1982). However, children often understand the emotional impact of their diagnosis better than their parents expect, because they observe how their parents and the physicians communicate. Therefore, it is important to include the patient in the discussions as well, even if it looks like the patient is too young or of an impaired mental status to understand this diagnosis and prognosis.

Many parents need the support of the physician when speaking with their child about diagnosis and therapy. If this is the case, parents and physician should discuss important topics alone first, and then involve children in a second conversation conducted in a child-orientated setting. The number of parents opting to include children at the initial conversation about their disease is increasing. Many older children and adolescents consider it important that the physician talks directly to them and directs questions toward them and not their parents. The physician needs to adapt the conversation to the level of the patient, speak in his or her language, and not overstrain his imagination with complex thoughts. The factual level of conversation is not in the foreground, but the emotional content, so it is essential to give the children enough time to respond and to formulate its emotions. It can be beneficial to ask an open question, such as "Do you have questions today? If not, maybe tomorrow, I will wait".

All children eventually have questions, but these develop at different paces. These questions must be answered when they occur to prevent uncertainty and traumatization.

Interestingly, pediatric patients are often not involved in decisions to include CAM therapies in their treatment, but these decisions are usually made in discussions by their parents with grandparents or friends. In some cases, the reason why the child is excluded from the meeting with the CAM therapist may be because the patient is physically unable to attend (i.e., weakened from chemotherapy, requiring hospitalization, or staying at home) or the meeting concerns some topics best not discussed in the patient's presence. Furthermore, distant relatives often try to play an active role and help the patient and parents. However, in most cases, it demonstrates that a symmetric physician-patient-parent communication triangle was not established. It is crucial that the CAM therapist makes treatment decisions with the primary focus on the patient and not the parents, although their opinion must be considered. Physicians must try to preserve the autonomy of the patient and protect children from overwhelming or unserious therapies. The CAM therapist should encourage the parents to try to see the situation from their child's perspective to determine the wishes and needs of their child. This is especially true in palliative situations when parents often visit several CAM therapists to ask for a curative treatment with the aim of preserving hope. This is exhausting for both the patient and parents and is a step in the wrong direction, since parents busy themselves with finding and organizing new solutions instead of developing a personal and child-orientated palliative life with their child. In some situations, this bears the risk that more focus is put on the parents than on the child, although it is the child that must take the medication or participate in therapies such as healing touch and acupuncture. The patients often know about the life-threatening situation they are in, try to protect the parents from bad news, and are worried about their emotional status. Therefore, a responsible CAM therapist should always treat and protect the children and advise parents toward taking a child-orientated approach. Sometimes, the role

of the physician is to reject any treatment, especially if no scientific data on the CAM therapy in question exists (Bluebond-Langner 1978). This is one of the biggest challenges for pediatric oncologists, and it requires excellent communication skills to avoid that parents get the feeling that they are being left alone and their child has been renounced.

### 13.3.1 Example of Patient Noninvolvement at Diagnosis

A 9-year-old depressed girl with osteosarcoma never asked something about her disease or told the physician about her symptoms and problems. One day, 3 months after starting chemotherapy, she was asked by the physician what she knows about her tumor. She responded: “I don’t know, because nobody has asked and spoken to me about my disease, not even my parents.” To initiate communication with the girl, the physician did not give information about her disease, but he asked her to try to draw her situation with the disease. Every day from there on, the girl told or asked the physician something about her tumor and about the time after chemotherapy. Although she did not show her drawings, for the first time, she was involved in the healing process and started to think about how treatment with chemotherapy and surgery works. Her depression disappeared quickly. This example illustrates the necessity of patient-centered communication, especially in pediatric oncology. It is essential to talk and listen to the patients and not only to their parents (Tables 13.2 and 13.3).

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## 13.4 Communication in Everyday Life in Pediatric Oncology

In the busy, everyday life of a pediatric oncology ward, it is difficult to fulfill all needs of the patients and patient-centered communication is often neglected. Especially at the time of diagnosis, the emotional burden and the quantity of information about the disease and treatment can cause the patient not to be at ease enough and results in

fragmental communication. Pediatric oncology centers often treat more than 100 newly diagnosed children per year, almost two new families per week. The high workload in these centers makes it difficult to talk with the families for more than 30–60 min. In addition, there is a tendency to split one long conversation (e.g., to inform about time schedule, results, and procedures for patients) by many shorter ones. This form of unstructured or unplanned and “unprotected” communication puts the family and the physicians under emotional pressure, especially when discussing difficult topics like diagnosis and/or prognosis. Continuous care by a single physician is neither realistic nor possible in a ward because nurses and physicians work in shifts to provide constant 24-h care that also bridges weekends and holidays and because medical treatment has been increasingly shifted toward outpatient clinics to reduce costs. Information that patients and their families have gleaned from internet or television also influences communication, since most families are well informed by internet. Specialized chat rooms give families advice and information about diseases, physicians, and conventional or CAM therapies. However, while the internet can provide serious sources of information, these are complicated by many doubtful sources that can confuse patients and their families and undermine the physician-patient relationship. Physicians must often spend communication time to assess and correct this information. All these circumstances can lead to misunderstandings and complicate physician-patient/family communication. In some cases, high expectations of the patient’s family coupled with inadequate physician-patient/family communication can even result in refusal of conventional treatment. Many pediatric oncology departments have moved toward assigning a single physician to oversee treatment and communicate with the patient and family during the period of intensive therapy to combat this problem.

In the period surrounding the first conversation with the parents relating the cancer diagnosis, parents often want to discuss more than the medical information with the physician. Parents often want to know why, of all children, their child got cancer. They can feel unsatisfied if the



**Table 13.2** Recommendations for effectively discussing CAM in oncological consultations

<p>1. <i>Clarify the patient's and parent's understanding of their situation and their preferences for information and decision-making before asking about CAM use:</i> Ask open questions to determine how much the patient understands about their disease and any prior treatments. Ask open questions with a psychological/existential focus to determine their concerns and goals.</p> <p>What is your understanding of things at this point?</p> <p>What concerns you most about your illness?</p> <p>Would you prefer decisions about treatment to be made by you, you and me together, or by me alone?</p>
<p>2. <i>Respect cultural and linguistic diversity and different religious diversity:</i> Be aware of attitudes and information needs of different cultural groups, especially in relation to models of illness and treatment. Remember that individuals can step outside their cultural circle.</p> <p>What do you believe might have caused your illness?</p>
<p>3. <i>Ask questions about CAM use at critical points in the illness trajectory:</i> Crucial points in the illness trajectory include the initial consultation when talking about the patient's medical history, points such as which treatment is decided on, significant changes in the condition (e.g., the first diagnosis of metastatic disease), and experiences of severe side effects or unexpected reactions to conventional treatment.</p> <p>Are you currently doing/considering doing anything else for this condition/these side effects or your overall health or well-being?</p> <p>Are you taking any other medications or treatments?</p>
<p>4. <i>Explore details of CAM use and actively listen:</i> Inquire about the patient's reasons for using or considering using the specific CAM treatment chosen. Ask what benefits the patient is expecting from using CAM in addition to conventional treatment. Ask who will provide the CAM treatment or medication and how CAM use will be monitored by whom. Provide balanced evidence-based advice about the CAM treatment the patient proposes to use/uses. If necessary, describe the western medical approach to evidence-based research and case-controlled testing and explain that not many CAM treatments have been tested in this way. Help the patient to understand, respond to, and integrate advice from family and friends from a knowledge-based perspective.</p> <p>Can you please tell me more about this CAM treatment? What does it involve? How often do you use it? Have you used it before? Who is conducting or overseeing this treatment?</p>
<p>5. <i>Respond to the patient's emotional state and encourage the patient to express his or her feelings:</i> Express empathy and support the patient's desire for hope and control over the situation. Address the issues they seek to influence by using CAM, such as whether they seek to control symptoms of the disease or believe it will help them to live longer.</p> <p>How are you feeling emotionally?</p> <p>How are you coping with all of this?</p> <p>I can understand you want to do everything possible. It sounds like you have been having a pretty tough time. It is natural that you feel the need to explore all possible options to help you survive this disease, and I fully support you in that.</p>
<p>6. <i>Discuss relevant concerns about the CAM treatment the patient has chosen, while respecting the patient's belief systems:</i> Topics of discussion could include the need for caution about taking substances of unknown quality or with unknown effect and high financial or time costs and potential adverse psychological effects. Discuss what might be a reasonable trial period, after which an assessment can be made regarding benefits and efficacy. Discuss how to make an assessment in line with the patient's expectations and existing medical background about what could be problematic.</p>

(continued)

**Table 13.2** (continued)

<p>At this time, there is little evidence about benefits or harm associated with this CAM treatment. So I think that we should be cautious. It may be beneficial but may also be harmful.</p>	
<p>How long do you think it will take to see a benefit from this CAM treatment?</p>	
<p>What do you expect to experience that would be evidence the treatment is beneficial?</p>	
<p>What do you plan to keep track of as potential harmful effects and how?</p>	
<p>7. <i>Provide balanced, evidence-based advice:</i> Encourage CAM use that may be beneficial. Consider making a referral to a qualified CAM practitioner. Accept use of CAM treatments for which there is no evidence of physical harm or benefit. Support the patient's decisions, even if they conflict with your personal views. Discourage the use of CAM where there is good evidence that it will be unsafe or harmful (either directly or in combination with conventional treatment). You may need to consider suspending or withdrawing conventional treatment if there are specific contraindications. Particularly discourage the patient from using unproven CAM treatments if it is to be used in place of a potentially beneficial or curative treatment. If the patient insists on replacing conventional treatment with an unproven CAM treatment, consider documenting this decision in writing (signed by physician, patient, and parents), including a brief outline of the treatment options that were advised and the alternative therapy that the patient chose. Balance advice with the patient's right for self-determination and autonomy.</p>	
<p>I would encourage you to use to this CAM treatment, since the evidence suggests it could really help you.</p>	
<p>We do not know much about this CAM, but it does not seem to be harmful and may even be helpful. I respect that you wish to try it and will help you monitor both possible good and bad effects.</p>	
<p>I have to be honest with you. I am concerned that this CAM may do more harm than good.</p>	
<p>I respect and support your right to make this decision. However, as we have discussed, I firmly believe that you have a better chance of benefitting from the conventional treatment plan I explained. Would you be willing to document our discussion today and your decision?</p>	
<p>8. <i>Summarize main points of the discussion and check the patient's understanding:</i> If necessary, offer to talk to the CAM provider, general practitioner, or family members about CAM use. Provide websites and information/resources from respected authorities about the CAM treatment the patient has elected to use/is using. Ask if there is anything else the patient or their family wants to ask or discuss.</p>	
<p>We have covered a lot today. Just so I can check that I have explained things properly, can you summarize what we have discussed?</p>	
<p>If you like, I would be happy to discuss this with your CAM provider.</p>	
<p>9. <i>Document the discussion:</i> Inform the other members of the treatment team and the patient's general practitioner about what was discussed, especially if the CAM treatment is potentially harmful. Include your perception of the patient's understanding. Document the discussion in the medical records.</p>	
<p>10. <i>Monitor and follow-up:</i> Follow up on what was previously discussed about the CAM treatment at the next consultation. Ask if any further questions or concerns have arisen for the patient or their family or been posed by members of the treatment team, the CAM practitioner, or the general practitioner.</p>	

Extracted and adapted from a systematic review (Schofield et al. 2010)

**Table 13.3** Guidelines for a child-centered conversation

1. Before talking with the child, start the meeting by talking to the parents alone to give them the information and to plan with them how best to talk with their child.
2. Ways that the meeting might then proceed:
  - Invite the child to join the conversation with the parents/primary caregivers.
  - Meet with the child without the parents. This is sometimes the preference of adolescent patients who sometimes prefer another support person such as a friend or partner to be present.
  - Allow the parents to talk to their child before meeting with the child and the parents.
3. Ensure that the setting is private, child-friendly, and safe. Arrange to have everyone seated, especially if the child is confined to bed, so that everyone is at the same level.
4. Ask the child what they know about their illness and prior treatments.
5. Ask the child how much they want to know. Some children may not want to know details about their cancer or treatments or may not want to know more than the immediate plans.
6. Explain things using language that the child can understand.
7. Make sure the child has understood the previous discussion and ask if he/she has any questions.
8. Ask the child how he/she is feeling, and if he/she has any specific worries.

Extracted and adapted from Skeen et al. (Skeen 2004)

physician cannot answer this question and mistrust the other information the physician presents or be too distracted to listen, understand, and discuss their other questions. Although modern medicine usually cannot answer why a child develops cancer, it is essential to discuss all questions that the families have on their emotional level to reinforce trust. Cancer treatment requires a holistic approach that includes empathy for the patient and their family and skill in communicating and explaining the patient's situation. These skills are integral to the CAM approach, which is geared toward holistically coping with a situation (Kaplan et al. 1989). Many families contact CAM therapists because they provide these skills better than their treating physician.

### 13.5 Conversations About CAM Today: The “Don’t Ask, Don’t Tell” Approach

Discussions about CAM are often avoided by physicians and patients. This has been summarized as the “don’t ask, don’t tell” approach (Sidora-Arcoleo et al. 2008; Shelley et al. 2009). Nondisclosure rates of CAM usage have been investigated in three surveys: Oh et al. reported that 55 % of adult respondents using biologically based CAM therapies and 80 % of those using nonbiologically based CAM therapies since the diagnosis

of cancer did not disclose their CAM use to their physician (Oh et al. 2010). Adler and Fosket found that only 54 % of patients disclosed their CAM use to their physicians (Adler and Fosket 1999). Baker et al. reported that CAM discussions are rare and most likely to be initiated by the patient. Taken together, more than half of adult CAM users do not disclose their CAM use to their physicians.

Nondisclosure of CAM use is very common in general pediatrics as well. A large survey with 1,143 respondents revealed that half the respondents had never discussed using CAM with their pediatricians and that 62 % of CAM use was self-medication recommended from family members or friends, not even involving a CAM therapist for advice (Zuzak et al. 2009). Other investigators found that 36 % of the pediatric subjects who reported using CAM in the past month failed to disclose this to their pediatricians (Sibinga et al. 2004). In contrast, 53 % of the parents expressed the desire to discuss CAM therapies with their pediatricians. This desire was expressed by 75 % of parents, if only those who used CAM themselves were included, and 81 % if only parents who used CAM for their child were included. Parental disclosure of CAM use was correlated with younger child's age and lack of parental CAM use. CAM therapies were used in children as young as 1 month without parent-pediatrician discussion, raising significant concerns about the potential for harmful effects and the pediatrician's

understanding of what general health beliefs and practices the families they were treating had (Sleath et al. 2001). These reports describe a current situation in pediatrics where parental nondisclosure of CAM usage is universal, even when very young children are concerned.

CAM nondisclosure rates reported for adult cancer patients and from general pediatrics are similar to those for pediatric patients with cancer. In a German survey of pediatric cancer patients, 29 % of CAM users had not disclosed their CAM use to their treating physician (Längler et al. 2008). In another survey, only 37 % of parents reported being asked about CAM use by their pediatric oncologist during the cancer care for their child and 60 % of the patients replied that their oncologist was unaware of their CAM use (Paisley et al. 2011). Vitamin supplements, special diets, dietary supplements, herbal medicine, and antioxidants were the CAM therapies most discussed by pediatric cancer patients with their oncologists (Roth et al. 2009). Surveys of both adult and pediatric cancer patients show that CAM use increases with unfavorable prognosis. This may explain why discussions about CAM use with early-stage breast cancer patients only took place in 24 % of the initial consultations (Juraskova et al. 2010). Patients diagnosed with advanced stages of cancer use CAM more frequently and also discuss it more frequently with the physician. Of the pediatric respondents, 52 % reported increasing their CAM use, 35 % reported no alterations in CAM use, and 13 % reported decreasing CAM use when frontline therapy failed. Interestingly, 80 % of pediatric oncologists were as likely to discuss CAM use with patients with poor prognosis as with those with good prognosis (Roth et al. 2009). However, it would be more useful if physicians would use the occasion at initial consultations to discuss CAM with the patients.

### 13.5.1 Patient's Reasons for Nondisclosure of CAM Use

Patients have various reasons for nondisclosure of their CAM use to their physician (Table 13.4).

**Table 13.4** Reasons why CAM use is not discussed

*Patient statements:*

- Fear of a negative response from oncologists to the idea of using CAM
- Oncologists show disinterest in patients' CAM use
- Patient assumes that the physician is unfamiliar with CAM
- Physician fails to ask about CAM use
- Patient believes that CAM use is irrelevant for conventional treatment
- Patient is unaware that the treatment or medication they are using is considered CAM
- Patient is unable to articulate their concerns or questions regarding CAM

*Physician statements:*

- Skepticism regarding the efficacy of CAM
- Insufficiently informed about CAM treatments, so that the physician does not know how to respond to questions about CAM
- Apprehension about initiating a time-consuming discussion
- Assumption that the patient will disclose CAM use without being asked

The most important factor reducing patient openness to discuss CAM use with the physician was fear of negative response (Adler and Fosket 1999; Tasaki et al. 2002). Other reasons include the physicians' disinterest in their patients' CAM use (Adler and Fosket 1999; Yates et al. 2005), physicians' unfamiliarity with CAM treatments, the patients' belief that their CAM use is irrelevant for his/her conventional treatment, the patients' unawareness of what treatments or medications count as CAM causing them not mention their use, and the patients' inability to articulate their concerns or questions regarding CAM (Lerman et al. 1993; Saxe et al. 2008). Some patients mentioned previous experiences, during which they felt rebuked by the physician for using CAM, which prevents subsequent disclosure of CAM use to any physician. Interestingly, patients did not expect physicians to be experts on CAM therapies, only to have a broad awareness of most types of CAM (Zuzak et al. 2009). This indicates that disclosure of CAM use could be improved by the physician accepting the patient's attitude toward CAM without being judgmental.

### 13.5.2 Oncologists Refuse to Speak About CAM

Many pediatric oncologists do not routinely ask their patients a general, open-ended question about their use of CAM. A study by Längler revealed that 43 % of pediatric oncologists only occasionally ask their patients an open-ended question about CAM use and that 7 % of pediatric oncologists never ask (Längler 2012). The frequency at which pediatric oncologists ask patients about the use of specific CAM therapies varies greatly and depends on the CAM therapy. More than one third of the pediatric oncologists surveyed reported asking more than half of their patients specifically about their use of dietary supplements, herbal medicines, special diets, and vitamins. However, more than half of these pediatric oncologists also reported never asking patients about their use of aromatherapy, enzymes, acupuncture, homeopathy, magnets, prayer, chiropractics, craniosacral therapy, massage therapy, guided imagery, martial arts, meditation, and yoga. In a study of 291 oncology healthcare professionals in the United States, most agreed that good communication enhances patient satisfaction (76 %) and treatment compliance (88 %). However, only 34 % of these physicians felt comfortable discussing CAM, and approximately half of all respondents felt they lacked the skills needed to communicate and help patients maintain hope (Roberts et al. 2005a).

Many of the reasons given by physicians for refusing to discuss CAM treatments or use with their patients recur in various studies (Table 13.4) (Richardson et al. 2000). Physicians often avoided initiating discussions about CAM use because they reported being skeptical of the efficacy of any CAM treatments. Often physicians perceived themselves as not being able to respond to questions concerning CAM because of being un- or underinformed and, therefore, refrained from broaching the subject. Time constraints often caused the physician not to ask about CAM use because they were apprehensive about initiating a time-consuming discussion. When physicians are faced with providing information about unfamiliar CAM therapies, they may feel forced outside

their zone of competence (Adler and Fosket 1999; Tasaki et al. 2002). This situation can lead to a defensive response by the physician, causing a breakdown in communication with the patient. Only 34 % of physicians felt comfortable providing information about CAM, and approximately half of all respondents felt they lacked the skills needed to communicate and help patients maintain hope (Roberts et al. 2005a). The situation portrayed by these surveys implies that physicians should be educated about at least those CAM therapies that are most often used by the patients in their fields as well as about communication skills. Including these topics in the general curricula at medical schools will eventually eliminate this deficiency, but to solve this problem more quickly, field-appropriate training programs should be integrated for practicing physicians.

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## 13.6 Objectives of Discussions About CAM in Pediatric Oncology

CAM use in conjunction with conventional cancer treatment can challenge and frustrate the pediatric oncologist as well as the patient. The physician can become frustrated if his or her knowledge about the CAM therapy being used is limited, and it can become frustrating for the patient if they cannot discuss their CAM use with their physician. Insufficient disclosure of CAM use to the treating physician represents a serious challenge in medical communication. The importance of discussing CAM use has been elaborated in multiple investigations and is summarized in the following paragraphs (Table 13.5) (Tasaki et al. 2002).

### 13.6.1 Increase Safety of CAM Use and Conventional Treatment

Potentially dangerous side effects of CAM therapies or interactions with conventional therapies can pose serious health risks. The danger is heightened if the oncologist is unaware of the patient's CAM use, since he or she will not be looking for occurrence of specific symptoms. One



**Table 13.5** Advantages of including discussions about CAM in oncologist-patient communication in pediatric oncology

Increases the safety of both CAM and conventional treatments
Elucidates individual needs of the patient and their family
Enhances relationship-building between the patient and the physician
Clarifies any potential patient misconceptions
Positively influences patient outcomes
Decreases the risk of physician burnout and malpractice

commonly used type of CAM is St. John's wort, a cytochrome P450a inducer. Taking St. John's wort has been shown to dramatically affect the pharmacokinetics of imatinib and reduce the level of the active metabolite of irinotecan in the plasma from patients during therapy by 42 % (Seely et al. 2007; Hardy 2008). Most of the adverse events reported for CAM therapies have been observed in adult cancer patients, and St. John's wort is used rarely in pediatric oncology patients, but caution is advised as it may similarly affect pediatric cancer patients. The pediatric oncologist should be aware of all CAM therapies that their patient is using during conventional cancer therapy and know what the potential adverse effects and risk of interactions between the conventional and CAM therapies are. The only way to achieve this is if physicians ask their patients about their CAM use, making communication about CAM use between physicians and patients crucial to ensuring patient safety (Paisley et al. 2011).

### 13.6.2 Elucidate the Patients' and Their Families' Approach to Health and Illness

The individual approach of the patients and their families to health and illness is important for the self-healing response. Psychological, social, and spiritual dimensions of care are often not taken into account. Providing care adapted to the individual needs of the patient requires communication about previous visits and involvement of the family, caregiver, and possibly other healthcare

providers. Family, employment, emotions, desires and wants, hidden wishes and concerns, health beliefs, and social, religious, and spiritual issues influence the patient's approach to health, illness, and treatment, including both conventional and CAM therapies (Adler and Fosket 1999; Pappas and Perlman 2002; Ladas and Kelly 2010). Inquiring about these topics is necessary. A physician who is receptive to patient inquiries and aware of subtle, nonverbal communication can create an environment in which the patient feels protected and the healing process is fostered. Discussions about CAM can be a good starting point for such a process.

### 13.6.3 Enhance Relationship-Building Between the Patient and the Oncologist

The failure of physicians to communicate effectively with patients about CAM topics may result in a loss of trust within the therapeutic relationship. Furthermore, patients may select harmful, useless, ineffective, or costly unconventional therapies although affordable and more effective CAM therapies exist. Poor communication may also diminish patient autonomy and self-determination, and thereby, interfere with the self-healing response (Tasaki et al. 2002). Patients who feel that they are being listened to and that their oncologists are interested in their personal situation are more satisfied with the consultation. The quality of communication in cancer care has been shown to affect not only patient satisfaction but also decision-making, patient distress, compliance, and even malpractice litigation (Roberts et al. 2005a, b; Oh et al. 2010). This fits in well with the finding that discussions about CAM usually enhance the physician-patient relationship (Baker et al. 2005).

### 13.6.4 Clarify Potential Patient Misconceptions

People hold diverse perceptions of health, illness, body, and risk, which influence attitudes and



behavior (Agdal 2005) and can interfere with the physician-patient relationship. There is a difference between experiencing an illness and the medical model describing the disease. This must be borne in mind when studying communication between patients and physicians to allow patients' perspectives to be taken into account. An integrative model of medicine must take qualitative differences in body perception and the communicative challenges that arise due to difference in perceptions by the patients and their families into account. Discussing CAM use can clarify any potential patient misconception about its safety, evidence base, and efficacy and also enhance relationship-building between the oncologist and the patient and their family (Adler and Showen 1999; Roberts et al. 2005b) by building rapport and fostering confidence and trust (Saxe et al. 2008).

### 13.6.5 Positively Influence Patient Outcome

Cancer patients who get involved in treatment decisions have better health outcomes and less psychological distress than patients who do not (Adler and Page 2007). Effective communication by healthcare professionals improves patient health by positively influencing emotional health, symptom resolution, behavior, and pain control (Boon and Kelner 2004; Pincus and Patel 2009). This could be shown for the involvement of discussing CAM in the decision-making process as well: Schofield et al. (2010) found an association between CAM discussion and higher levels of "fighting spirit," "anxious preoccupation" with having cancer and lower levels of "fatalism" about the disease.

### 13.6.6 Decrease the Risk of Physician Burnout and Malpractice

In a study including 291 healthcare professionals working in the field of oncology in the United States, most agreed that good communication enhances patient satisfaction (76 %) and improves treatment compliance (88 %). However, only

34 % of respondents felt comfortable discussing CAM, and approximately half of all respondents felt they lacked the skills needed to communicate and help their patients maintain hope (Crocetti et al. 1998). Communication positively influences patient outcome as well as the efficiency of the healthcare professional. Encouraging patients to discuss their concerns has been shown to decrease the risk of malpractice (Crocetti et al. 1998). Open communication about CAM options, therapies, and use may also benefit the oncologist by reducing the likelihood of litigation. Oncologists who feel inadequately trained to respond to patients' emotional needs have also been shown to be at increased risk of burnout (Ramirez et al. 1995, 1996). Discussions on CAM may be a good way for these physicians not only to start fostering a healing relationship with their patients but as well as to decrease their own risk of break down.

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## 13.7 Communication and Treatment Refusal

The possibility that parents could refuse conventional medical treatment of their child is a permanent worry of pediatric oncologists. Fortunately, less than 1 % of all pediatric cancer patients or their parents refuse conventional therapy at diagnosis or during intensive treatment (Längler et al. 2012). When the child can be cured by conventional treatment, physicians must treat the patient, even against the will of patients or their parents. Treating patients with potentially toxic forms of treatment against the parents' will is an extreme situation for the patient, parents, and physician. According to the authors' experience, withdrawing legal custody from the parents is not the best solution because it is hardly conceivable to subject a child to such intensive medical treatment without the support of his or her family or another closely connected person, such as a grandparent. Communication between the treating oncologists and the family should always be maintained, yet it is likely to be greatly strained or at risk of complete disruption in a case of legally enforced custody withdrawal. A compilation of cases demonstrates (Tautz 1995) that decisions in this

regard should always be taken into consideration of the physician-parent dialogue because the child's treatment ultimately proceeds according to what the parents want. Good communication skills are needed to solve such situations, and communication on CAM themes should be made as well-considered as possible.

Refusing treatment can be a coping strategy. Sometimes parents prefer an uncertain or untested therapy to conventional treatment even after being completely informed about the disease prognosis without conventional treatment. This response can be understood from a psychological point of view within the framework of coping strategies. Parents of children with cancer can adopt various coping strategies, one of which is a form of emotional coping that includes responses, such as trusting in their religion for healing, uncritical acceptance of all proposals, or denial to the point of noncompliance. Despite marked increase in survival rates of pediatric oncology patients, most parents associate "cancer" with death (Grootenhuis and Last 1997). Many recommendations have been published in recent years for supporting parents with the day-to-day coping with fears and anxieties (Bonilla et al. 2009). These emphasize communication as the core issue to prevent an emotional coping strategy that makes parents abandon conventional therapy. Recurring efforts are necessary with such families to gain their compliance because isolation of a family should be avoided under all circumstances. In this way, treatment refusal can be avoided by good communication skills.

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### 13.8 The Role of Media in Conversations on CAM

The emergence of web-based media, such as the Internet and social networks, has greatly influenced discussions between the physician and the patient. The presence of a multitude of websites devoted to health and lifestyle in the Internet is changing the way people experience health and illness. A survey nationally representative of the USA reported that eight in ten Internet users proactively search for health-related information.

The UK reports estimate that 37 % of the general population will use the Internet to search for health-related information by 2020 (Foundation 2009). Apart from using health-related information from the Internet for self-diagnosis of medical problems (Foundation 2009), almost half of the people searching for health-related information in the Internet report doing so on behalf of someone else (Clark and Gomez 2001; Edgar et al. 2002). The importance of the Internet as an information resource should not be ignored in pediatric oncology. Dictionaries, social networks, online forums, and message boards are increasingly being used by young people to obtain health information and share health experiences.

Written media also influence how the patient deals with CAM. Magazines with a focus on general health are studded with advertisements about established and new CAM therapies. Many of them have not been evaluated but are costly, and often the advertisement promises improved health without explaining through which action this is supposed to occur. Parents are also often confused by advertisements that are potentially dangerous because the therapies are not appropriate for pediatric patients, often costly, and from unreliable sources. Especially, pediatric cancer patients need to be protected from unserious offers since they are more susceptible to hope-giving offers and have difficulty rejecting them. Most patients and their families expect their oncologists to know something about the use of CAM therapies in the context of their disease and conventional treatment and want to be able to obtain educated advice from their oncologist and work with them to select the best regimen of CAM and conservative treatment (Crocetti et al. 1998; Eliason et al. 1999). Thus, an important job of oncologist is to evaluate the CAM offers brought up by the patient and protect the patient from the unserious offers by discussing their drawbacks. If the physician is not responsive to the questions about CAM from the patients and their families or is perceived as being an unreliable source of information, patients and their families may turn to other resources, such as friends, relatives, nonprofessional literature, magazines, newspapers, the Internet, advertisements, and health food stores for information

about CAM. The information gathered from these resources can often be inaccurate and, occasionally, can direct the patient toward using therapies that are dangerous or may interact with conventional therapy (Rees et al. 2000; Kinnane and Milne 2010). Discussions between the oncologist and the patient about CAM therapies and CAM use are greatly influenced by the resources the patients and their families have used to gather information, and the goal of such discussions should be to irradiate uncertainty in the patients and their families and make them feel fully informed.

A new phenomenon influencing physician-patient communication is the use of e-mail communication. E-mail can be used as a means to build and maintain relationships with healthcare professionals (Monnier et al. 2002; Cornwall et al. 2008). Having access to healthcare professionals via e-mail is considered desirable and preferable to many patients (Monnier et al. 2002). Often, e-mail is the most convenient method of contacting healthcare professionals, since they have constraints on their available time that limit appointment availability or may be located geographically distant to the patient or hospital (Eysenbach 2003; Cornwall et al. 2008). A small percentage of parents use e-mail for non-urgent contact with healthcare professionals, such as clarifying details and asking questions. The patients and their parents view this type of communication as an intermediate measure that is not intended to replace a face-to-face conversation. E-mail communication is inappropriate to discuss the diagnosis or provide second opinions and can never replace a face-to-face conversation in these cases. Hospitals planning to use e-mail communication as a resource should set up clear policies about privacy and consent in addition to scope and nature of communications conducted via e-mail before involving patients in e-mail correspondence (Bovi 2003). The time involved in replying to e-mail requests may or may not be cost-effective from the perspective of a healthcare professional (Eysenbach 2003). Therefore, its future role in communication remains unclear. Taken together, media influence communication about CAM a lot and should not be ignored. They

may increase the need to discuss CAM and may support the patient's self-determination by making reliable information about conventional as well as CAM therapy more accessible.

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### 13.9 Communication Around the Language Barrier

In the USA, the number of individuals with limited English proficiency has more than doubled over the last two decades and over four million households have been termed "linguistically isolated" (Shin and Bruno 2000). In Europe, characterized by over 50 countries with a mix of different languages, cultures, and religions, the percentage of linguistically isolated families may well be even higher. This trend is coupled with a far slower increase in the number of bilingual or multilingual healthcare providers, including providers of pediatric care (Stoddard et al. 2000). Language barriers between the physician and patients and their family have been associated with misdiagnoses and inappropriate treatment, patient and family dissatisfaction in the quality of care, the need for repeat visits, and other time-consuming and costly outcomes (Elderkin-Thompson et al. 2001; Flores et al. 2003). Oncologists increasingly face the challenge of communicating with nonnative speaking parents of children with cancer. Oncologists, interpreters, and parents expressed considerable concern over the process of communicating across a language barrier (Abbe et al. 2006). Some of these concerns could be minimized by the oncologist employing communication using simpler phrasing and language (Table 13.6). Questions that include examples are often helpful in enhancing disclosure. Rather than asking whether a patient is using any "alternative therapies," the pediatric oncologist might ask whether the patient is taking any "vitamins, herbs, dietary supplements, special teas, or home remedies or receiving back rubs, chiropractic treatments, acupuncture, or other services to enhance health." It is also often useful to ask how the patient manages stress. Examples here may include exercise, prayer, music, or talking to friends or trusted adults.

**Table 13.6** Recommendations for communication with patients with a different sociocultural background

Recognize cultural or educational differences.
Respect families' perspectives, values, and cultural beliefs.
Demonstrate respect for families and their values.
Work together with the parents as a team to consider and evaluate all appropriate treatments. This may require discussing an array of treatment options.
Use simple language.
Use examples of specific types of medicines or treatments (homeopathic remedies, vitamins, back rubs, etc.) and avoid complicated catch-all terms (complementary and alternative medicine, etc.)
Try to become important allies in examining all potential treatment options for children by actively listening to families and patients.

Sometimes including art therapy can facilitate communication, especially for children of different languages or of young ages. Use of simple, figurative language and knowledge of the patient's cultural background have a positive impact on patient outcome by improving communication and increasing safety of applied therapies.

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# Establishing a Comprehensive Pediatric Integrative Oncology Program

# 14

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and Sunita Vohra

## Contents

<b>14.1 Introduction</b> .....	187	14.3.4 Practices.....	193
<b>14.2 Developing Academic Integrative Medicine Programs: Lessons Learned</b> .....	188	14.3.5 Practical Advice: How to Choose a CAM Provider.....	194
14.2.1 Clinical Care.....	188	<b>14.4 Creating a Pediatric Integrative Oncology Practice: A Case Study</b> .....	194
14.2.2 Research.....	189	14.4.1 Research.....	197
14.2.3 Education.....	190	<b>References</b> .....	198
<b>14.3 Special Considerations When Integrating CAM Products and Practices Together with Conventional Care: Focus on Patient Safety</b> .....	191		
14.3.1 Natural Health Products.....	191		
14.3.2 NHP Interactions.....	192		
14.3.3 Practical Advice: How to Choose Natural Health Products.....	193		

## 14.1 Introduction

The use of complementary and alternative medicine (CAM) by adult and pediatric oncology patients is highly prevalent around the world. Surveys in Europe, Japan, Singapore, and the United States have demonstrated substantial use, with 40–91 % of adult cancer patients choosing CAM as part of their treatment (Molassiotis et al. 2006; Hyodo et al. 2005; Shih et al. 2008; Yates et al. 2005). Pediatric CAM use is also high, as confirmed by a recent systematic review of 28 studies of pediatric cancer patients from 14 countries (Yates et al. 2005). The prevalence of pediatric CAM use ranged from 6 to 91 %, with the most popular therapies being herbal remedies, nutritional interventions, and faith healing (Bishop et al. 2010). This increased use of CAM has been associated with a concurrent rise in adult and pediatric academic integrative medicine centers, where CAM research and education complement clinical initiatives with a common mission to provide high-quality, evidence-based care.

“Integrative” medicine is a relatively new term and describes the coming together of CAM with

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conventional medical care. As defined by the Consortium for Academic Health Centers in Integrative Medicine (CAHCIM), integrative medicine can be defined as “the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals and disciplines to achieve optimal health and healing” (Consortium of Academic Health Centers for Integrative Medicine 2010). The Consortium consists of 48 academic institutions all over North America and plays a key role in the advancement of academic integrative medicine throughout the United States and Canada (Consortium of Academic Health Centers for Integrative Medicine 2010). Its mandate emphasizes the synthesis of complementary and conventional therapeutic approaches, by focusing on advancing integrative healthcare education, research, and clinical practice among academic leaders, faculty, and students within academic centers (Consortium of Academic Health Centers for Integrative Medicine 2010).

Integrative oncology centers are more established for adults than for children. Adult integrative oncology centers such as those established by the Memorial Sloan-Kettering Cancer Center (MSKCC), the Mayo Clinic, and Cancer Clinics of North America provide care for both inpatients and outpatients, conduct research, and provide education for medical staff, students, and the community (Memorial Sloan-Kettering Cancer Center 2010). In contrast, pediatric integrative oncology is still an emerging field.

The growing popularity of CAM use by pediatric oncology patients has led to questions as to how academic integrative medical programs can be adapted for pediatric oncology patients. In this chapter, we review lessons learned from adult and pediatric academic integrative medicine programs in general and consider how these may be adapted to integrative pediatric oncology. We will examine specific issues raised when integrating CAM products and practices into conventional care and conclude the chapter with an in-depth look at one of North America’s leading pediatric integrative oncology programs.

## 14.2 Developing Academic Integrative Medicine Programs: Lessons Learned

There are many important lessons to be learned from existing academic integrative medical programs, both adult and pediatric. In this section, we will explore clinical, research, and educational initiatives undertaken by pioneering North American academic integrative programs over the last decade.

### 14.2.1 Clinical Care

Integrative medicine focuses on healing the “whole person” rather than the individual’s specific health condition, and as a result there is greater consideration for the emotional, social, and environmental factors contributing to the illness or its treatment. Integrative medicine programs complement conventional medical services with CAM therapies, with specific emphasis on optimizing individual care in a way that respects patients’ health-related preferences, values, and beliefs. CAM service choices are based on regulatory status, patient demand, and the ability to find competent individuals to provide the service. Although there is a plethora of CAM services offered to patients at integrative centers, there is considerable variation between centers due to (i) differences in terms of licensing and credentialing of CAM providers; (ii) issues regarding the safety, efficacy, and product quality of natural health products (NHPs); and (iii) lack of insurance coverage for CAM services. Each of these is discussed in detail in Sect. 14.3.

The most commonly seen patients at adult integrative centers are those with chronic conditions, such as fibromyalgia, depression, irritable bowel syndrome, or cancer. The main on-site CAM services offered include: traditional Chinese medicine, acupuncture, chiropractic, massage, aromatherapy, homeopathy, herbal medicine, mind-body, and biofeedback (Vohra and Feldman 2005). Similar to the adult centers, pediatric integrative medicine programs most often see infants, children, or youth with cancer,

chronic pain, gastrointestinal problems, or mental health concerns. Approximately 75 % of pediatric integrative medicine programs offer inpatient and outpatient care, often including acupuncture/acupressure, mind-body, and energy therapy (unpublished).

Given the frequent gaps in evidence with respect to CAM, there is substantial variation regarding NHP administration/use in both adult and pediatric integrative centers. Although NHPs are generally regarded as safe, significant heterogeneity in product quality is known to exist. Just as hospitals develop formularies to guide product use, hospitals are now developing policies regarding NHP use, including guidelines for choosing products and obtaining informed consent for their use.

Another common barrier faced by integrative centers in the CAM services they provide is that CAM is not covered by most private or public insurers. Because integrative medicine programs share a goal to provide services broadly (i.e., to as many individuals as possible), programs have had to create strategies to achieve this. Many centers provide sessions on a fee-for-service basis, and in order to make services accessible to those who are unable to afford the care, subsidies or reduced fees are often offered (Vohra and Feldman 2005).

Evidence-based care is the model of modern healthcare, and as such many more academically inclined integrative medicine centers have established a research component to their programs to contribute new knowledge to this growing field.

### 14.2.2 Research

There are more than 200 pediatric oncology centers, and the vast majority of children with cancer are cared for at these institutions. Most are members of the Children's Oncology Group (COG), and more than 7,500 of the 12,500 children with cancer diagnosed yearly participate in the COG registry. Commitment to clinical as well as translational research is a hallmark of pediatric cancer care. Pediatric oncologists have very strongly held beliefs that the best treatment for children with cancer is within a pediatric setting participating in cooperative group trials. Similarly, the

best place to answer the important questions about cancer in children is within that same cooperative group structure. There are relatively few children diagnosed each year with cancer, making it difficult to obtain significant findings within any one institution. Integrative pediatric oncology research requires the similar collaborative approach either within COG or smaller consortiums such as the Pediatric Integrative Research Consortium developed to design and implement IM research studies particularly with brain tumor patients.

Research is an integral part of a successful academic integrative medical center. Given the diverse array of CAM practices and products, integrative medicine research spans a broad domain from basic science research at the cellular level to outcomes research at a population-based level. Some programs were established around a foundation of research. Often, utilization studies have been done as a way to assess the relevance/importance of initiating a program locally and to establish support for it.

An important component of integrative medicine research has been the mixed-methods approach, whereby qualitative research complements quantitative findings helping to explain not only if integrative therapy is effective but for which patients and why. The most common research method in pediatric academic integrative medicine centers includes randomized controlled trials (RCTs), with cancer being among the most commonly researched conditions (unpublished). CAM use among pediatric oncology patients has been well documented and is among the highest as compared to other pediatric populations (Sencer and Kelly 2007). CAM among these patients is most often used to alleviate cancer-related symptoms (due to treatment or the cancer itself), with mind-body therapies, nutritional and herbal supplements, vitamins, and message therapy being the most frequently used (Kelly et al. 2000; Mottonen and Uhari 1997; Fernandez et al. 1998a; Grootenhuis et al. 1998). As a result, several small clinical trials have been conducted over the past 20 years, evaluating the effectiveness and safety of these CAM

therapies in pediatric oncology; however, further investigation with larger, high-quality RCTs is still needed. One such initiative includes a large scale cooperative group trial through the COG to evaluate the use of the homeopathic remedy Traumeel in the prevention and treatment of the mucositis associated with stem cell transplantation (Children's Oncology Group 2010).

Lack of funding and resources are major barriers to research. Many pediatric integrative medicine programs describe inactive research components due to these problems, and as such, pediatric integrative centers have demonstrated significantly less research undertakings as compared to their adult counterparts. By combining resources, funds, and expertise, an opportunity exists for pediatric integrative oncology programs to create a research network and develop evidence collaboratively.

Evidence-based practice is the central aim of clinical care in both adult and pediatric programs. CAM research, however, particularly in pediatric populations, suffers from issues common to other pediatric researchers, i.e., that pediatric disease is relatively rare, making large sample sizes hard to achieve. In addition, CAM is often individualized, making parallel group research more challenging. A potential solution is an N-of-1 trial. An N-of-1 trial is a prospective, multiple, crossover trial in a single subject (Johnston and Mills 2004). In an N-of-1 trial, each participant is assured of getting both the active medication and placebo and therefore learns whether the treatment works specifically for them or not. This method of clinical research is particularly advantageous, as it not only refines the clinical care offered to patients but also may provide research evidence on the efficacy of a certain product/service and thus may potentially accelerate the rate of accumulation of high-grade evidence to support therapies used in clinical practice. While not yet commonly used at academic integrative medicine programs, N-of-1 trials are starting to emerge to help overcome the evidence-practice gap so commonly encountered in pediatric CAM (Johnston and Mills 2004) (see Table 14.1). While the N-of-1 trial is well suited to studies in symptom control such as nausea or fatigue, it is

**Table 14.1** Key characteristics of N-of-1 trials

Chronic stable condition
Intervention with quick onset and offset action <sup>a</sup>
Intervention with quick onset/offset
Enthusiastic participant
Multiple crossovers
Randomized treatment pairs <sup>b</sup>
Double blinded <sup>b</sup>
Tailored outcome measures

<sup>a</sup>If offset is delayed, sufficient washout period must be included

<sup>b</sup>Possible to do formal N-of-1 evaluation even if these must be compromised

inefficient when evaluating a product or modality whose primary outcome would be treatment of a malignancy.

### 14.2.3 Education

Although the integration of research is essential to a strong academic program, efforts would be futile without the translation of this knowledge to healthcare providers, patients, and the community; a robust education program must also be implemented. Because there is not yet any standardized or mandatory training in integrative medicine in conventional medical curricula, academic integrative medicine programs have had to develop their own content and methods of promoting educational opportunities and outreach initiatives for medical students, residents, fellows, physicians, patients, and the community. Offering opportunities to learn about CAM services and natural health products is essential for the growth of an integrative program; therefore, CAM must be integrated at all levels of medical training as well as across disciplines.

Although over 60 % of medical schools have incorporated some education regarding CAM, few initiatives have been adopted as part of the required curriculum or training (Wetzel et al. 1998). Only 19 % of pediatric programs have mandatory CAM training at the undergraduate level and only 25 % at the residency level. Though much of the training is not mandatory, diverse educational opportunities have been implemented

at various centers for different training levels. One adult program holds an annual continuing CAM education event and prepares online cases for credit while another recruits 25 CAM providers to run various workshops (Vohra and Feldman 2005). Another adult program offers student exchanges to CAM training institutions (Vohra and Feldman 2005). In 2008, eight US Family Medicine Residency programs launched the “Integrative Medicine in Residency” project, which combined integrative medicine and family medicine through online curriculum support (Guerrera et al. 2008). Preliminary results of this pilot project have shown a greater “openness and acceptance” of integrative approaches among residents and faculty (Kligler et al. 2009). Training at the fellowship level has also been emphasized. For example, the Arizona Center for Integrative Medicine offers a fellowship in integrative medicine designed for physicians, nurses, and physician assistants. Of note, initially this program was specifically for pediatrics, receiving an NCCAM center grant. The program focuses on nutritional health, botanical and dietary supplements, mind-body medicine, complementary and alternative practices, as well as integrative approaches (Education. Arizona Center for Integrative Medicine 2010). The goal of the program is to allow trainees to develop an understanding in these areas, as well as how to guide patients into successfully integrating these practices into their lives. The Memorial Sloan-Kettering Cancer Center (MSKCC) also has an Integrative Oncology Research Training program, which is designed to train postdoctoral fellows in the clinical and research aspects of integrative oncology. The trainees are not only expected to conduct scientific research in CAM therapies for oncology but to be able to implement evidence into mainstream practice (Integrative oncology research training program 2010). MSKCC also offers training in integrative oncology for physicians and nursing staff.

Pediatric programs offer more opportunity and variety in their educational initiatives compared to the adult programs. Integrative training is offered for medical students (56 %), residents (91 %), fellows (56 %), faculty/physicians

(56 %), and nurses (33 %) (unpublished). Diverse opportunities were reported from lectures and conferences to online resources and magazine articles (unpublished). The Complementary and Alternative Research and Education (CARE) program, at the University of Alberta, introduced a Pediatric Integrative Medicine (PIM) fellowship in 2004, which focuses on integrating the skills and concepts of both conventional and CAM care. The primary goal of the fellowship is to create healthcare professionals who have established an integrated approach to healthcare and can assess as well as guide CAM therapy specifically for children and their families.

Though most programs are interested in developing more training opportunities, lack of funding continues to be a major barrier. Presence of funding may potentially aid in the development of a core integrative curriculum which all programs can share among their trainees.

Of note, nursing schools have often been more forward looking than medical schools in incorporating CAM theory and practice. Holistic nursing is now officially recognized by the American Nurses Association as a specialty practice with certification. Holistic nursing is theory based and incorporates strategies to address and integrate the concepts of technology, body, mind, and spirit into nursing practice and provide models of care that guide healing (Dossey et al. 2000). Nurses are being trained in guided imagery, massage, breathing, music, distractions, art projects, acupuncture, and relaxation techniques. Concepts such as intention, presence, and compassionate caring are increasingly taught in nursing school.

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## **14.3 Special Considerations When Integrating CAM Products and Practices Together with Conventional Care: Focus on Patient Safety**

### **14.3.1 Natural Health Products**

To have effect, natural health products (NHPs) must be pharmacologically active. Lessons learned from clinical pharmacology are therefore



particularly important as it relates to patient safety and polypharmacy. It has been reported that there are approximately 100,000 deaths each year as a result of medical errors, 75 % of which are drug related (Kohn et al. 2000). These statistics have also been found to extend to children, particularly those with chronic conditions (Kozar et al. 2002; Ball et al. 2005; Gardiner et al. 2004). While NHPs have generally enjoyed a good reputation for safety, one must be careful to differentiate between data confirming safety and lack of data demonstrating harm. Serious harms with NHPs appear to be rare, but this must be balanced against emerging evidence that NHP-related harms are grossly underreported (Goldman et al. 2008). Particular caution should be applied when planning concurrent use of NHPs with conventional pharmaceuticals.

### 14.3.2 NHP Interactions

Despite the popular assumption that “natural=safe,” recent studies have reported adverse events associated with NHP use. NHPs have the potential to interact with other NHPs as well as with prescribed and over-the-counter (OTC) drugs that could result in pharmacodynamic or pharmacokinetic interactions resulting in adverse events (Goldman et al. 2009). Although interactions of NHPs with prescribed and OTC pharmaceuticals have been previously reported in adults (Goldman et al. 2009), the adverse events associated with these interactions continue to be underreported and often overlooked. In a study looking at the potential adverse events that can arise from NHP-NHP and NHP-OTC/prescribed drugs in children, it was found that concurrent NHP-drug use was reported in 20 % ( $n=355$ ) of the patients, with 15 % ( $n=269$ ) of the patients taking multiple NHPs (Goldman et al. 2008). Similarly, despite the potential for harmful interactions, only 62 % of parents reported pediatric vitamin use to their family physicians (Rogovik et al. 2010). This low reporting rate can be attributed to (i) parents believing the use of vitamins is safe, (ii) parents believing vitamin use is irrelevant to their child’s presenting complaint, (iii) parents being afraid of discouragement, and/or (iv) lack of inquiry by the

**Table 14.2** Important considerations when using NHPs in combination with other therapies

What documented interactions have occurred clinical, if any?
What interactions have been posited on theoretical grounds, based on mechanism of action?
What contributory information does animal or in vitro/ in vivo data provide?
Are there any potential contradictions based on patient’s underlying health state (e.g., compromised renal/hepatic functioning, immune status)?
What monitoring should be put in place based on potential risks?

physician. It has been found that many physicians fail to include CAM use in history taking, most likely due to general lack of CAM knowledge in terms of safety and efficacy, resulting in an inability to know how to deal with the large number of potential risks associated with these products. Though our current understanding of NHP-drug and NHP-NHP interactions is quite limited given the small amount of research available, their simultaneous use is quite high and needs to be appropriately managed (see figure 1, <http://www.cpjournal.ca/doi/pdf/10.3821/1913-701X-142.5.224a>; see Table 14.2).

Currently, worldwide, there is limited government regulation of dietary supplements and relatively few high-quality pediatric reports on efficacy and outcomes of NHPs used. Moreover, consumers often lack knowledge concerning appropriate use, dose, and/or frequency (Goldman et al. 2008). Only recently have Health Canada (HC) and the US Federal Drug Administration (FDA) introduced regulatory guidelines for NHPs. In the United States, the FDA recently published comprehensive guidelines for those who manufacture, package, and hold dietary supplements. The regulations focus on practices that ensure the identity, purity, quality, strength, and composition of dietary supplements (Industry Information and Regulations 2010). Health Canada introduced their natural health product regulations in 2004, which assure that all Canadians have ready access to NHPs that are safe, effective, and of high quality, while respecting freedom of choice and philosophical and cultural diversity (Natural Health Products 2010).



Although the Natural Health Products Directorate (NHPD) was formed by Health Canada to address issues of dosing, upper intake limits, and potential toxicities, the relative lack of pediatric evidence regarding effectiveness and safety continues to be a problem (Natural Health Products 2010). Because children, predominantly those with chronic conditions, are frequent consumers of NHPs, further research needs to explore basic pharmacology in children regarding absorption, distribution, metabolism, and excretion of NHPs. Furthermore, specific information about which NHPs may be safely combined with which drugs, and in which populations, is urgently needed.

Simultaneous use of CAM therapies with conventional treatments continues to be prevalent, particularly in oncology patients (Fernandez et al. 1998b; Bold and Leis 2001). NHPs are often used to help overcome the side effects of conventional therapy; however, it is important to ensure that taking these NHPs does not reduce the effectiveness of the conventional treatments or inadvertently promote the disease. Many studies have looked at antioxidant supplementation in oncology patients. Because cancer is associated with increased levels of oxidative stress due to the cancer itself (Senturker et al. 1997), as well as chemotherapy (Kennedy et al. 2005; Mazor et al. 2008), proponents hold that antioxidants may enhance the anticancer effects of chemotherapy as well as reduce or prevent side effects related to chemotherapy (Conklin 2000). In contrast, other studies have shown that because antioxidants work to reduce reactive oxygen species (ROS), supplementation may actually interfere with the action of chemotherapeutic agents, which rely on ROS production for their action (Michaud et al. 2007). This example serves to illustrate the need for further research to establish a clear role for the use of NHPs as adjuncts to chemotherapy.

### 14.3.3 Practical Advice: How to Choose Natural Health Products

Large variation in the standards of quality and quantity of active ingredients results in heterogeneity of NHPs; therefore guidelines on choosing

the appropriate product and its use must be set in place. Because there are no national guidelines, it is up to each integrative center to set up policies on choosing appropriate CAM therapies for their patients. For example, at the Stollery Children's Hospital (Edmonton, Alberta, Canada), the CARE program has helped to develop a patient care policy, which provides direction for choosing CAM products. The policy encourages open dialogue between the patient and clinician regarding the use of CAM and requires that primary healthcare providers be aware of the evidence which is currently available regarding the safety and efficacy of different CAM therapies. A stratified approach to product selection is recommended as follows: (i) products that had favorable evaluations in peer-reviewed published clinical research (i.e., the brand/dose that was studied); if this is not available, then (ii) products that have had independent third-party testing for quality assurance; if this is not available, then (iii) expert clinical opinion; if this is not available, then (iv) patient/legal guardian choice.

### 14.3.4 Practices

A common barrier among both adult and pediatric programs is the large heterogeneity across North America in terms of licensing and credentialing of CAM providers. This lack of standardization compounds heterogeneity in care provided by the different academic centers. Though they share a desire to offer access to a range of safe and effective CAM services to the public, most CAM professions have not yet developed the formal consistency and uniformity of licensing and credentialing processes of regulated healthcare professionals. When an external credentialing body does not exist, the academic integrative programs have needed to develop their own internal credentialing process (see Table 14.3).

As CAM use increases in popularity, the amount of referrals and shared care by conventional care providers will also increase. Liability of referrals and shared care varies between jurisdictions, and as such it is important for primary healthcare providers to be aware of the appropriate

**Table 14.3** Things to consider when credentialing a CAM provider

Reviewing state or national standards set by the profession for education/training requirements
Reviewing the defined scope of practice of the CAM provider as determined by the state (e.g., primary caregiver, authority to prescribe)
Mechanism used by state to regulate CAM providers (i.e., mandatory licensure, title licensure, registration)
Reviewing continuing education requirements set out by the state
Certification of CAM provider by professional organization (independent of state)
Proof of professional liability insurance
Documentation of satisfactory completion of required training and respective certification examination
Rigorous interview process with the academic health center

Sources: Eisenberg et al. (2002); Credentialing CAM Providers (2010)

laws surrounding these issues. In certain cases, a physician can be held liable for negligence in referring (Cohen and Eisenberg 2002). It is therefore the responsibility of the referring physician to determine whether or not the CAM therapy will be effective and safe (based on existing evidence) and be aware that the referred practitioner has the appropriate training and credentials to offer the respective services to his/her patient (Cohen and Eisenberg 2002). The physician should also be transparent about the risks and benefits of using CAM with the patients.

### 14.3.5 Practical Advice: How to Choose a CAM Provider

Since many CAM providers are not yet regulated in most jurisdictions, it is important that primary healthcare providers be aware of licensing standards for CAM providers in their jurisdiction and be prepared to offer advice and recommendations to those patients seeking it. Basic information on the referred CAM provider should also be provided, including education and training (accredited or not), pediatric experience, standards of practice, as well as any pediatric certifications they may have. Prior to treatment, CAM providers should discuss therapeutic goals, potential

adverse effects, time commitments, and cost of treatments with their patients. A time frame should be established a priori, in which the CAM therapy can be evaluated for its effectiveness (i.e., how many treatments, at what frequency, does the provider suggest before a treatment effect may be apparent?).

## 14.4 Creating a Pediatric Integrative Oncology Practice: A Case Study

Pediatric oncologists as a group have historically had reason to be particularly fearful of CAM. The success rates for most types of children's cancers are remarkably high compared to those for adults, and there is an understandable reluctance on the part of providers to encourage any therapies which might compromise care. Cancer patients and their families are particularly vulnerable to high-profile CAM therapies and are at risk of abandoning potentially curative conventional treatments in pursuit of a more "natural" approach.

As the prevalence of CAM use among pediatric cancer patients has increased, the oncology programs caring for these patients have struggled to meet the integrative oncology needs of the patients and their families. The design, implementation, and ongoing evaluation of the integrative medicine program at Children's Hospitals and Clinics of Minnesota are illustrative. This is a large urban hospital system with two campuses, one in Minneapolis and one in St. Paul, and is the seventh largest pediatric healthcare organization in the United States. The oncology program sees close to 200 new patients a year and is one of the larger programs within COG. Their patients speak 40 different languages. The metropolitan area of the Twin Cities has the largest Somali and Hmong communities in the United States. Each new immigrant group has brought with them their own healing cultures; Hmong patients are particularly wary of Western medicine, especially cancer care.

Children's Hospitals and Clinics of Minnesota began discussions about developing an integrative medical program in 1997. As in many institutions,

the impetus came initially from the oncology department. Oncology patients are frequent users of CAM and quite often the families of patients who used CAM at end of life are strong supporters of program development. Understandably, parents wish to “leave no stone unturned” in their search for a cure for their children and often turn to CAM, particularly at relapse. Our initial philanthropic donors were parents who wished to memorialize their children by helping develop an integrative oncology program.

Most pediatric oncologists who completed their fellowships in the twentieth century were trained to dissuade families away from any CAM therapy. The party line was that any parent who wanted to discuss alternative approaches was a potential threat to the successful treatment of their child, even if the prognosis was particularly grim. Increasingly, however, many parents have obviously investigated different therapies in-depth and want to rationally discuss pros and cons, not content with a rote negative response. As the internet became more widely available, the opportunity for parents to become more knowledgeable increased; pediatric oncologists with an interest in CAM began to emerge. In 1997, Dr. Sencer was able to obtain a sabbatical grant to study integrative therapy in children with cancer, trying to collect as much disparate data as existed at the time. Clear gaps in the collective knowledge became apparent, which have then been used to drive the research agenda for this fledgling program.

Physician and nurse champions are core components for successful implementation of any CAM program. Physicians are helpful at enlisting key supporters in administration and professional staff. A vociferous “quack-buster” can set a program back years. Nurses tend to be the master implementers—developing policies and determining scope of practice for CAM providers. Nurses who are cross trained in CAM modalities such as healing touch or massage can speed up the acceptance of new ideas by patients and staff, as can cross trained physicians, such as an anesthesiologist with acupuncture training.

Philanthropic support is essential. CAM therapies are rarely covered by insurance, although

that is slowly changing. As a group, pediatric oncology programs are relatively socialistic in that it is terribly uncomfortable to imagine that one child would get certain treatments based upon ability to pay while another would be denied. Therefore, the fee-for-service approach is not widely accepted. Philanthropic dollars initially were used to supply services, but changes in the rules governing inducements further proscribed delivery of any care without compensation. We now offer extensive inpatient CAM services, including massage, acupuncture, aromatherapy, as well as many mind-body approaches. The cost of delivering inpatient services is “bundled” into the inpatient charges. Outpatient services are available but are more rarely utilized because of the fee-for-service model. Mind-body techniques such as biofeedback and self-hypnosis can often be covered under psychological services.

We have attempted to use available research data, our own or published by others, to direct IM program development. For instance, an early survey identified which modalities parents desired for their children (Post-White et al. 2009). Results indicated integrative therapies were used most often in children with life-threatening and chronic conditions such as epilepsy, cancer, asthma, and sickle cell disease (Post-White et al. 2009). Children most often used prayer, massage, vitamins, and supplements. Decisions about adding subsequent modalities have been determined by (1) evidence for efficacy, (2) patient/parental desire, and (3) availability of pediatric trained practitioner. We are selective, rather than inclusive, based upon the above factors as well as cost, controversy, and personal provider interest. For instance, we do not include chiropractic medicine in our program because (1) it is widely available in the community, (2) primarily an outpatient modality, and (3) little evidence exists that it is of value to oncology patients in particular.

As mentioned above, there are few RCTs evaluating pediatric integrative oncology therapies. Therefore, other methods of evaluating new ideas must be utilized. Within the oncology practice group, there has been an effort to use a systematic process for answering clinical questions which is particularly useful for CAM or other “not fully

tested” modalities. “Evidence-based practice” begins with asking a clinical question. The process involves asking the question in a specific way that will yield relevant literature. The next step is to assemble relevant research and form a group to evaluate the evidence. If there is sufficient evidence, pilot the change in practice. If there is not sufficient evidence, consider doing research. If there is sufficient evidence, the process for evidence synthesis should include (i) grading according to a hierarchy of levels of evidence, (ii) summarizing the evidence, and (iii) making a recommendation for change (Titler et al. 2001). For example, a teenaged female patient read an article in the newspaper about “cold caps” to prevent chemotherapy-induced hair loss. One of the clinical nurse specialists did a literature review, graded, and summarized the evidence with the following results: (i) there were no pediatric studies, (ii) cost and convenience would be a factor to consider, (iii) demonstrated effectiveness was limited to single agent chemotherapy, (iv) treatments were time consuming, and (v) treatments are uncomfortable. It was therefore concluded that “cold caps” are unlikely to be appropriate for all but adolescent girls who strongly want to avoid hair loss (M. C. Hooke, November 20, 2010, personal communication). Using a systematic process for clinical inquiry is a way for CAM research to be integrated into practice in a timely manner.

One primary role of the integrative oncologist is to discuss NHPs with families. Most patients/parents now have at least a passing acquaintance with NHPs and are often bombarded with suggestions by family, friends, and online “support groups.” All of our IM providers are skilled at helping families to sift through the information available on the Internet, teaching them to avoid testimonials and advertisements in favor of published research articles where available. The integrative oncologist is familiar with the NHPs which are currently being used in the area, or with a particular disease type; there is clearly a wavelike fad aspect to many products. All patients are queried about their medications, including NHPs, and are given a medication carry-all to bring all medications with them at each visit. A

dedicated oncology pharmacist checks drug interactions for all medications, including over-the-counter and NHPs. Our philosophy is not to discourage use of any individual product but rather to encourage disclosure so that appropriate discussions can take place.

While most CAM modalities used by pediatric cancer patients are purportedly for treatment of symptoms or to increase wellness, in reality many NHPs are used with at least a hope that they will help to cure the underlying disease or its recurrence. Although many agents show promise as anticancer agents, there is still little published evidence to suggest that any one supplement has significant efficacy to warrant widespread adoption by the pediatric oncology population. However, vitamin D, which is deficient in many pediatric oncology patients (Helou et al. 2008), is being increasingly linked to both the treatment and prevention of cancer. It can therefore be considered for use in the majority of patients. Similarly, fish oil, with both anti-inflammatory and immunomodulating qualities can be helpful in broad categories of patients; care should be taken with patients with thrombocytopenia requiring surgery, however, because of its anticoagulant properties.

Nurses have continued to be the backbone of the pediatric integrative oncology program.

Complementary and alternative therapies utilized by nurses are gaining recognition and acceptance in many areas of nursing, including pediatric oncology. Nurses are engaging in practice aimed at providing comforting, holistic care and creating healing environments. In many ways, this represents a back to the basics approach to patient-centered care that addresses all aspects of human needs. In the age of electronic medical records, high-tech equipment, and endless documentation, many nurses are seeking to incorporate the theoretical foundations for the art of caring nursing practice. This practice can then be blended with evidence-based nursing interventions that include complementary and alternative therapies. In pediatric oncology, especially, nurses often feel frustrated and helpless caring for suffering children, many with poor prognoses. Failure of conventional therapies to alleviate

distressing symptoms is leading more and more nurses to seek other effective interventions, including CAM, and to approach their nursing practice from a more holistic perspective.

The nurses in the inpatient and outpatient departments of the CHCM oncology program are deeply committed, with little turnover and an average experience of 7 years in the program. Increasingly, the nurses became interested in incorporating CAM into their daily practices. In conjunction with the affiliated adult hospital's integrative medicine program, a Transformative Nurse Training 5-day course was created and has been offered to nurses on a rotating basis. Content includes healing touch, Chinese medicine, massage therapy, relaxation techniques, holistic nursing theory, and aromatherapy, with pediatric-specific content. The majority of the nurses who have completed the program are now comfortable utilizing CAM interventions in their practice. The nurses believe these interventions and therapies have been the most effective for nausea, anxiety, and pain. Sixty-five percent of nurses have requested additional education.

Nurses who completed the program also helped develop another key component of the integrative oncology program at CHCM, the "CAM Cart." One of the frustrations expressed by inpatient nurses was the lack of access to CAM therapy supplies especially at night and on weekends. A grant was obtained to develop and implement wheeled CAM Carts which can be brought to the bedside of the patient, inpatient or outpatient. Nurses and providers can choose appropriate therapies and individualize their interventions to match their patients concerns or complaints. On the carts there are bubbles, acupressure bands, pinwheels, massage pens, stress balls, aromatherapy, biofeedback devices, and children's books on CAM therapies.

Many state Nursing Boards have published guidelines for CAM therapies in nursing practice. It is the individual nurse's responsibility to know what the nurse practice guidelines include. For example, in Minnesota nurses who employ integrative therapies are required to ensure patient safety, acquire specialized knowledge and maintain competence by staying current with research

and pertinent literature, utilize practices consistent with a recognized nursing body of knowledge, and provide patients with education including risks and benefits of the therapy. The Minnesota Board of Nursing's Statement of Accountability for Utilization of Integrative Therapies in Nursing Practice also recommends collaboration with other healthcare providers and practice within the limits of the nurse's education and competence (Minnesota Board of Nursing 2010). Nurses must document the use and effectiveness of such therapies within the context of standard nursing diagnosis, care plans, and outcomes.

Each institution is responsible for safe and efficacious practice of integrative medical and nursing practices. This can be facilitated by incorporating evidence-based CAM therapies and interventions into the electronic medical record. Automatic prompts can be built into nursing care plans and provider order sets. For example, if a child is documented to have pain, massage, distraction, holding, and touch are all offered as nursing intervention options on the electronic medical record. A prompt to order probiotics is displayed when the provider uses gastroenteritis or antibiotic therapy admission order sets. All children, newly diagnosed with cancer are automatically referred for an integrative medicine consult as well as massage therapy through inclusion of these items on the computerized admission order sets.

#### 14.4.1 Research

Research is an important component of our integrative oncology practice. Many CAM research studies have been conducted at Children's Hospitals and Clinics of Minnesota either alone or in collaboration with other institutions. One recent study evaluated the feasibility of yoga as an inpatient intervention to increase the patient's sense of well-being and reduce anxiety levels of patients and their parents. The results indicated that yoga is a beneficial and feasible intervention for adolescents and their parents. (Thygeson et al. 2010). The results have inspired nursing researchers to



conduct another yoga study aimed at evaluating the feasibility and benefits of a 6-week yoga intervention for pediatric cancer survivors who completed therapy in the past 2 years. Another current study is evaluating an activity intervention for decreasing fatigue for children and adolescents in maintenance ALL treatment (M. C. Hooke, November 20, 2010, personal communication).

Earlier studies have evaluated the effect of gender and ethnicity on children's attitudes and preferences for essential oils (Fitzgerald et al. 2007). The results were utilized in practice for maintaining supplies of essential oils in the Integrative Medicine Department and more recently, for stocking the CAM Carts. Another pilot study was conducted in collaboration with the University of Minnesota School of Nursing to determine the feasibility of providing massage therapy to children with cancer and their parents while hospitalized and receiving chemotherapy. Anxiety and symptoms were the outcome variables. Relaxation was measured with vitals signs and salivary cortisol levels. Anxiety and fatigue were measured in parents. The results indicated that massage in children with cancer is feasible and appears to decrease anxiety in parents and younger children (Post-White et al. 2009).

The Integrative Oncology program has been embraced by patients, staff, and the community. Our patients report great satisfaction with the services provided and the opportunity to discuss NHPs with knowledgeable, open-minded providers. The rapid adaptation of new modalities, through evidence-based evaluation, has been a satisfier to staff members at all levels. In particular, dual-trained practitioners, such as bedside nurses giving massage or oncologists performing hypnosis or shiatsu, are themselves gratified by the opportunity to expand upon their compassionate skill sets.

There has been a recent worldwide increase in the use of complementary and alternative medicine, particularly in oncology patients. As a result, there has been a concurrent rise in adult and pediatric academic integrative medicine centers, where CAM research and education complement clinical initiatives with a common mission to provide high-quality, evidence-based care. There are many

important lessons to be learned from existing academic integrative medical programs, both adult and pediatric. We have taken an in-depth look of the integrative medical program at the Children's Hospitals and Clinics of Minnesota, assessing its design, implementation, and ongoing evaluation. It is evident that a strong academic integrative program should include clinical, research, and educational initiatives to ensure its continued progress and ultimate goal of providing optimum care.

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# Index

## A

Accreditation Commission for Acupuncture and Oriental Medicine (ACAOM), 131  
Aconitum, 64, 71, 73  
Active imagery, 83  
Acupoint injection, 130  
Acupressure, 93, 189  
Acupuncture, 10, 21–24, 65, 126, 129, 148, 150, 152, 153, 160, 173, 188, 189, 195  
  points, 133  
Acustimulation, 130  
*Allium sativum* (garlic), 143  
*Andrographis paniculata*, 132–133  
*Anemarrhenae*, 133  
Animal substances, 34, 60  
Animal therapy, 86  
Anthroposophic anthropology, 164  
Anthroposophic lifestyle, 39  
Anthroposophic medicine, 23, 24, 29, 65, 163  
Anthroposophic pharmacy, 33, 34  
Antimonium tartaricum, 74  
Antioxidant, 152, 178  
  supplementation, 193  
Antonovsky, 80  
*Apis*, 34  
Arab treatments, 9  
Argentum, 41  
*Arisaema*, 133  
Arizona Center for Integrative Medicine, 191  
Arnica, 73  
Aromatherapy, 90, 188, 195, 197  
Arsenicum album, 69, 71, 72, 74  
Art therapy, 23, 36, 45, 164, 184  
*Astragalus*, 129, 132  
Astral body, 31  
*Attractylodes*, 132  
Aurum/Prunus, 40  
Aurum valeriana, 41  
Avenar, 138  
Ayurvedic medicine, 95, 153

## B

Bach flower therapy, 13  
Bamboo shavings, 133  
Bar-bata, 132

Belladonna, 61, 66, 71, 73  
Bergamot, 91  
Bioenergies, 12  
Biofeedback, 80, 188, 195  
Biofield therapies, 81  
Biologically based CAM therapies, 151  
Black nightshade, 132  
Borax, 71  
Bossinger, Wolfgang, 49  
Botanical and herbal medicines, 137  
Botanical/drug interactions, 138, 143  
Bridge drawing, 47  
Bryophyllum, 41  
*Bulbus Lillii*, 132  
Bur reed rhi-zome, 132

## C

Cadmium sulfuratum, 70  
CAHCIM. *See* Consortium for Academic Health Centers in Integrative Medicine (CAHCIM)  
Calendula, 41, 71  
CAM. *See* Complementary and alternative medicine (CAM)  
CAMDOC alliance, 161  
*Camptotheca acuminata*, 137  
Cancer Clinics of North America, 188  
*Carapax trionycis*, 132  
Carbo vegetabilis, 74  
Carcinosinum, 65  
*Catharanthus roseus*, 137  
*Caulis millettiae*, 132  
Causticum, 72  
CEWIM. *See* Clinical education ward for integrative medicine (CEWIM)  
Chakras, 95  
Chamomilla, 73, 91  
Children's Hospital in Minneapolis, 150  
Children's Hospitals and Clinics of Minnesota, 194  
Children's oncology group (COG), 155, 189  
Chinese herbal medicine (CHM), 126, 127, 139, 140  
Chinese herbs, 22  
Chinese massage, 126  
Chininum arsenicosum, 72  
Chininum sulfuricum, 72  
Chiropractic medicine, 11, 21, 24, 188, 195

- CHM. *See* Chinese herbal medicine (CHM)  
*Cichorium*, 40  
 Cinchona bark, 60  
*Cirsii japonici*, 129  
 Cisplatinum, 62  
 Clinical education ward for integrative medicine (CEWIM), 164  
 Coconut water, 114  
 Coffee enemas, 120  
 COG. *See* Children's oncology group (COG)  
 Cognitive-behavioral therapy, 80  
 Cognitive distraction, 153  
 Cognitive mind-body therapies, 81  
 Cold caps, 196  
*Colla Corii Asini*, 132  
 Colostrum, 116  
 Columbia University Medical Center, 81  
 Committee on Herbal Medicinal Products (HMPC), 144  
 Communication, 16, 158, 169  
   about CAM, 20  
   behavior, 21  
   skills, 161, 179  
 Comparative effectiveness research, 149, 151  
 Complementary and alternative medicine (CAM), 197  
   education, 160  
   research, 148  
 Complementary and alternative research and education (CARE) program, 191  
 Complex remedy homeopathy, 62  
 Compresses, 35  
 Concerns, 24  
 Congee, 114  
 Conium, 65  
 Consortium for Academic Health Centers in Integrative Medicine (CAHCIM), 188  
 Constitutional treatment, 60, 62, 67  
 Contextual research, 149  
*Coptis*, 133  
*Cortex Lycium chinensis*, 133  
 Corydalis rhizome, 132  
*Cremastra*, 133  
 Cullen, 60  
 Cultural factors, 22  
 Curcumin, 141  
 Custody, 181
- D**  
 Dance movement therapy (DMT), 45, 80, 86, 88, 89  
 Dandelion, 132  
 Dietary reference intakes (DRI), 110  
 Dietary supplements, 9, 21, 23, 24, 112, 178, 192  
*Dioscorea bulbifera*, 133  
 DMT. *See* Dance movement therapy (DMT)  
 Donkey-hide gelatin, 133  
 Drama, 45, 80, 86  
 Drawing, 48, 80, 86  
 DRI. *See* Dietary reference intakes (DRI)  
*Duchesnea indica*, 133
- E**  
 Echinacea, 127, 143  
 EFA. *See* Essential fatty acids (EFA)  
 Effectiveness gaps, 147, 153, 154  
 Ego organization, 31  
 Electrostimulation, 130  
 EMA. *See* European medicines agency (EMA)  
 Empathy, 163, 165, 177  
 Energy fields, 12  
 Energy therapy, 154, 189  
 Essential fatty acids (EFA), 113  
 Essential oils, 198  
 Essiac tea, 9  
 Etheric body, 31  
 Ethnicity, 81, 198  
 Eucalyptus, 91  
 Euphorbia peplus, 71  
 Eurhythmy therapy, 36, 164  
 European Medicines Agency (EMA), 144  
 Ewing sarcoma, 67  
 Expressive arts therapy, 45, 86  
 Expressive writing, 86  
 External applications, 23  
 External treatments, 24, 35
- F**  
 Federal Institute for Drugs and Medical Devices (BfArM), 144  
 Feldenkrais method®, 88, 90  
 Ferrum phosphoricum, 71, 72  
 Fish oil, 113, 196  
   supplements, 153  
*Formica*, 34  
 Forsythia, 132  
 Frankincense, 91, 132  
 Free write, 87  
 Fritillaria, 133  
*Fructus citri aurantii*, 133  
 Functional threefoldness, 32
- G**  
 Gameboy advance®, 83  
*Ganoderma lucidum*, 132  
 Garlic, 140  
 Gemeinschaftskrankenhaus Herdecke, 39, 40, 164  
 Gentiana, 133  
 Gerson therapy, 120  
 Ginger, 91, 114, 127, 139  
*Ginkgo biloba*, 143  
 Ginseng, 129, 132, 140, 143, 151  
 Glutamine, 117, 153  
 Grape seed, 143  
 Green tea (*Camellia sinensis*), 141, 151  
 Griessmaier, Barbara, 49  
 Grifron-D, 142  
 Grounded theory approach, 48  
 Guided imagery, 10, 24, 158

**H**

Hahnemann, C.F. Samuel, 59  
 Hamer method, 13  
 Harvard Medical School Department of Pediatrics, 130  
 Hatha yoga, 88  
 Healing touch, 24, 95, 173, 195, 197  
 Health Canada, 192  
 Heat processes, 35  
 Hedyotis, 132  
 Herbal drugs, 24  
 Herbal extracts, 148  
 Herbal medicine, 21, 160, 178, 188  
 Herbal supplements, 8, 14, 189  
 Herbal teas, 9, 114  
 Herbal therapies, 152, 164  
 Hey, Alder, 51  
 Hippocrates, 60  
 HMPC. *See* Committee on herbal medicinal products (HMPC)  
 Holistic nursing practice, 191  
 Holistic nursing theory, 197  
 Holistic patient care, 48  
 Homeopathic remedy provings, 64  
 Homeopathy, 21–24, 59, 148, 152, 188  
 Honeysuckle, 132  
*Houttuynia*, 132  
 Huangqi decoctions, 139  
*Hypericum perforatum* L., 73, 140  
 Hypnosis, 80–83, 150, 152, 153, 195

**I**

ICURAM. *See* Integrated Curriculum for Anthroposophic Medicine (ICURAM)  
 Ignatia, 72  
 Imagery, 81, 83  
 Imagination, 31  
 Integrated Curriculum for Anthroposophic Medicine (ICURAM), 158, 163  
 Integrative care, 100  
 Integrative dietary approach to nutrition, 112  
 Integrative medicine, 4, 40, 134, 164, 187, v  
 Integrative medicine case conference, 164  
 Integrative Medicine in Residency, 191  
 Integrative nutrition counseling, 110  
 Integrative physiology, 163  
 Integrative Therapies Program for Children with Cancer (ITPCC), 81  
 Interactions, 24, 179  
 International Society of Pediatric Oncology (SIOP), 155  
 Intuition, 31  
 Ipecacuanha, 70  
 ITPCC. *See* Integrative Therapies Program for Children with Cancer (ITPCC)

**J**

Jacobson, Edmund, 90  
 Jing-luo, 125

Journaling, 80  
 Jujube, 133

**K**

Kabat-Zinn, Jon, 85  
 Kelp, 133  
 Ketogenic diet, 119  
 Kushi, Michio, 119  
 Kuttner, Leora, 79

**L**

Lachesis, 41, 71, 74  
*Lactobacillus*, 9  
 Laetrile, 120  
 Lavender, 90–92  
 Law of similars, 60  
 Lebed method, 89  
 Ledum palustre, 62  
 Legacy work, 54  
 Lemon, 91  
 Lentinan, 142  
 Light therapy, 12  
*Lithospermum*, 132  
 Lobelia, 132  
 Low microbial diet, 118

**M**

Macrobiotic diet, 10, 119  
 Magnets, 12  
*Mahonia* leaves, 132  
 Manual lymphatic drainage, 93  
 Massage therapy (MT), 11, 21–24, 80, 92, 96, 150, 153, 158, 164, 188, 189, 195, 197, 198  
 Materia medica, 126  
 Mayo clinic, 188  
 MBSR. *See* Mindfulness based stress reduction (MBSR)  
 Medical play, 48  
 Medicas, 61  
 Meditation, 10, 24, 80, 81, 84, 88, 96, 150  
 Melatonin, 113  
 Memorial Sloan-Kettering Cancer Center (MSKCC), 188, 191  
 Mercurius solubilis, 71  
 Meridians, 95, 126  
 Metabolic-limb system, 32  
 Metal processes, 35  
 Meteoreisen, 41  
 Miasms, 62  
 Micronutrients, 151  
 Milk thistle, 138, 153  
 Mind-body medicine, 10, 21, 22, 79, 97, 150, 154, 162, 188, 189, 195  
 Mindfulness based stress reduction (MBSR), 84, 89  
 Mineral medicines, 34  
 Mineral remedies, 61  
 Minerals, 60

- Mineral supplements, 9  
Mistletoe therapy, 23, 24, 37, 39, 151  
Mixed-methods approach, 189  
Movement-based mind-body therapies, 88  
Movement therapies, 12  
MSKCC. *See* Memorial Sloan-Kettering Cancer Center (MSKCC)  
MT. *See* Massage therapy (MT)  
Mushroom, 142, 151  
Music improvisation, 51  
Music therapy, 23, 24, 48, 86, 153  
Musique et santé, 51  
Myrrh, 132
- N**  
Narrative family therapy, 80  
National Center for Complementary and Alternative Medicine (NCCAM), 144, 154  
National Commission for Certification of Acupuncture and Oriental Medicine (NCCAOM), 131  
National Institute of Health (NIH), 154–155  
Natural health products (NHP), 191  
Natural Health Products Directorate (NHPD), 193  
Natural products, 8, 151, 154  
Naturopathy, 13, 160  
NCCAM. *See* National Center for Complementary and Alternative Medicine (NCCAM)  
Nerve-sense system, 32  
Neutropenic diet, 118  
NHP. *See* Natural health products (NHP)  
NHPD. *See* Natural Health Products Directorate (NHPD)  
NIH. *See* National Institute of Health (NIH)  
Nitric acidum, 71, 72  
N-of-1 trial, 190  
Nondisclosure, 177, 178  
Norwegian National Hospital, 50, 51  
Nutrition, 109, 189  
Nutritional intervention in the pediatric oncology patient, 111  
Nux vomica, 40, 41, 70–73
- O**  
Ohsawa, George, 119  
Okoubaka, 70, 72  
Opium, 71, 74  
Orange, 91  
Organon of medicine, 61  
Osteopathy, 24, 160  
Outcome or end-state-oriented imagery, 83  
Oxalis, 40, 41  
Oysters, 133  
Ozone, 12
- P**  
Palliative care, 52, 100  
Palliative homeopathic treatment, 73  
Paper-trees, 48  
*Paris polyphylla*, 132  
Patient-centered communication, 171, 174  
Patient self-management, 172  
Peach kernel, 132  
Pediatric Integrative Research Consortium, 189  
Peppermint, 91  
Peter MacCallum Cancer Centre (Peter Mac), 50  
*Phellodendron*, 133  
Phosphorus, 40, 68–72, 74  
*Phragmites communis Trin*, 129  
Physical body, 30  
Physician-patient relationship, 169, 172, 180  
Phytolacca, 65  
Phytotherapy, 34  
Pictures, 47  
Pilates, 88, 90  
*Pinellia*, 133  
Placebo action, 24  
PMR. *See* Progressive muscle relaxation (PMR)  
PMRT. *See* Progressive muscle relaxation training (PMRT)  
*Podophyllum peltatum*, 137  
Poetry, 45  
Polarity therapy, 95  
Polychrests, 61  
*Polygonum cuspidatum*, 132  
Polysaccharide-K (PSK), 142  
Postoperative nausea, 91  
Posttraumatic stress disorder, 47  
Potentization, 60  
Potentized medicines, 34  
Prana, 95  
Prayer, 24, 80, 158  
Probiotics, 116, 197  
Process-oriented imagery, 83  
Progressive muscle relaxation (PMR), 82  
Progressive muscle relaxation training (PMRT), 88, 89  
*Prunella*, 133  
*Prunella vulgaris*, 132  
PSK. *See* Polysaccharide-K (PSK)  
Psora, 62  
Psychoneuroimmune model, 80  
Psyllium, 114, 116  
Pulsatilla, 72, 133  
Pumice, 133  
Puppetry, 48  
Purslane, 133  
Pyrogenium, 71
- Q**  
Qi, 125, 126, 131  
Qigong, 95, 134
- R**  
Radium bromatum, 72  
*Radix Angelicae sinensis*, 132  
*Radix Asparagi*, 132  
*Radix Isatis indigotica* (banlangen), 132

*Radix Polygonatum*, 132  
*Radix Sophora subprostata*, 132  
*Radix Trichosanthes*, 132  
*Radix zanthoxyli*, 132  
 Ratanhia, 40  
 Red peony root, 132  
 Red sage root, 132  
 Reflexology, 93, 94  
*Rehmannia dride*, 129  
 Reiki, 12, 95  
 Relaxation techniques, 11, 82, 153, 197, 198  
 Religion, 81  
 Remedy proving, 60  
 Resilience, 49, 50  
*Rhizoma Dioscoreae*, 132  
 Rhus toxicodendron, 74  
 Rhythmic massage, 35  
 Rhythmic pharmaceutical processes, 35  
 Rhythmic system, 32

**S**

Safety assessment, 149  
 Safflower, 132  
 Salutogenesis, 2, 30, 33, 164  
 Sandalwood, 91  
 Sanjiao, 126  
 Schizophyllan, 142  
 Schulz von Thun, Friedemann, 170  
*Scrophulariaceae*, 133  
*Scutellaria*, 133  
 Seaweed, 133  
*Selaginella*, 133  
 Self-awareness, 47, 162  
*Semen coicis*, 132  
 Sense of coherence (SOC), 3  
 Sepia, 70  
 Shark cartilage, 9  
 Silica, 72  
 Silkworm, 133  
*Silybum marianum*, 138  
 Silymarin, 143  
 Similimum, 62  
 Singing, 49  
 Single remedy, 62  
 SIO. *See* Society for Integrative Oncology (SIO)  
 SIOP. *See* International Society of Pediatric Oncology (SIOP)  
*Smilax glabra*, 132, 133  
 SOC. *See* Sense of coherence (SOC)  
 Society for Integrative Oncology (SIO), 154  
*Solanum lyratum*, 132, 133  
 Solum, 41  
 Solum uliginosum, 35  
 Song writing, 51  
 Soul, 33  
 Spearmint, 91  
 Special diets, 21, 24  
 Spinal manipulation, 11  
 Spiritual healers, 24  
 Spirituality, 81

Spring water, 9  
 Staphysagria, 73  
 Steiner, Rudolf, 29  
 St. John's wort, 127, 140, 143, 180  
 Stollery Children's Hospital, 193  
 Storytelling, 48  
 Stramonium, 72  
 Stress-related responses, 79  
 Succussion, 61  
 Sugar, 118  
 Sulfur, 69, 70  
 Swedish massage, 93  
 Sycosis, 62  
 Syphilis, 62  
 Szechuan lovage root, 132

**T**

Tabacum, 70  
 Tai chi chuan (TCC), 88, 89  
*Taraxacum sinicum Kitag*, 129  
*Tarentula cubensis*, 74  
*Taxus brevifolia*, 137  
 TCC. *See* Tai chi chuan (TCC)  
 TCM. *See* Traditional Chinese medicine (TCM)  
 Tea tree, 91  
 Telling stories, 80  
 Theory-guided clinical trials, 151  
 Therapeutic touch therapy, 12, 95  
 Thuja, 65  
 Traditional Chinese medicine (TCM), 95, 125, 188  
 Traditional healers, 12  
 Traditional medicine, 2  
 Traumeel S<sup>®</sup>, 66, 155, 190  
 Treatment refusal, 181  
*Trichosanthes*, 133  
 Turmeric, 132, 141, 151

**U**

University of Witten/Herdecke, 158  
 US Federal Drug Administration (FDA), 192

**V**

Valerian (*Valeriana officinalis L.*), 140, 143  
 Vincristinum, 62  
 Viola, 132  
 Visual art therapies, 47  
 Visual imagery, 10  
 Visual imagination, 48  
 Vitamin C, 152  
 Vitamin D, 196  
 Vitamins, 24, 189  
 Vitamin supplements, 9, 178

**W**

Warburg effect, 118  
 Wegman, Ita, 29, 35  
 Whey protein, 113



White mustard seed, 133  
Whole medical systems, 12, 13, 80, 110  
Wild buckwheat, 133  
Withdrawal, 181  
Wraps, 35  
Writing, 86  
Wu xing, 125

**X**

X-ray, 72

**Y**

Yin-yang, 81, 125  
Ylang ylang, 91  
Yoga, 10, 24, 80, 85, 88, 95, 96, 150, 197

**Z**

Zang-fu, 125  
*Zheng Qi*, 132