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The complementary medicine: The promotors, the prescriptors and the users in different countries

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Unproven Methods in Cancer: A World-wide Problem

Unproven methods include questionable diagnostic tests and treatments such as drugs, vitamins, homeopathy, diets, herbs, faith healing, "psychologic‰ treatmentsΣ

The frequency of unproven methods in cancer is not easy to evaluate because some are being used as a complementary treatment to conventional ones (and often not mentioned by patients), others are being used as curative treatment (alternative treatment) and also hidden by some patients. Both alternative and complementary unproven methods are prescribed either according to classical concepts of cancer treatment or according to a new concept in the world and life systems. Alternative and complementary methods can be found worldwide.

In Europe, data concerning unproven methods are available for Scandinavian countries, Switzerland, Germany, Austria, United Kingdom, Netherlands, France and Italy. The highest frequency of use is observed in German-speaking countries (up to 65%). In North America, the percentage of cancer patients who use unproven methods varies between 7 to 54%. In Mexico, the frequency is 50%, higher than in Argentina (17%). In Australia, 22% have use complementary medicines. In Asia, there are some data from India, Taiwan and Japan. Very few data from African countries is available. Some unproven methods are country-specific (Moerman diet in the Netherlands), others are used world-wide (mistletoe, vitamins$Sigma;). Some traditional medicines are also country-specific (Chinese medicine, aryuvedic medicine in India). Few data are published on the personal characteristics of the promotor or the subscriber. The goal of the UICC committee on alternative and complementary methods is to provide oncologists with informations and data concerning these methods.

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The use of complementary medicine in the German speaking countries

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Alternative methods against cancer are very popular in the german-speaking countries. They suggest or even promise to offer another, better, easier way to reach the same target. In fact some unconventional methods are propagated by their inventors to be a real alternative to mainstream medicine. Most of them however are recommended as additives, complementary to scientific cancer therapy. They are claimed to strengthen the natural immune defence and prevent recurrence, enhance the anti-tumor activity of other treatment modalities and to improve the tolerance of chemo- or/and radiotherapy. The following methods are most popular in CH/D/A:

(1) Dietetics; Vollwertkost in several variations, antioxidants, enzymes
(2) Plant-products: Mistletoe, Apotheke Gottes, Hildegard-Medizin, Jomol
(3) Immunotherapeutics, Autologous Tumor vaccines, Active Specific Immunotherapy, Ney-Tumorin, AF-2, Polyerga
(4) Psychological methods, Neue Medizin, Energy therapies
(5) Oxygen, Krebsmehrschritt-Therapie.

Why are patients using alternative methods? Most are not or not fully satisfied by mainstream medicine and tend towards something complementary, more natural, holistic, psychological and less toxic. Herewith real subjective needs (the so-called "therapeutische Lücke") can hopefully be filled and patients may contribute themselves to cure. Massmedia, trend for natural, irrational, mystic methods intensify this. Disappointment by the "Schulmedizin" is only rarely the decisive motif. Almost all these methods have not been investigated properly and have therefore to be classified as unproven concerning antitumor activity, tolerance/toxicity and symptom control. To satisfy better the needs of informed cancer patients, they should be accepted if there is a clue for beneficial effects, if they are proven harmless, not too expensive and when a regular follow-up in full consent with the physicians responsible is guaranteed. They have to be tested according to established criteria.

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Why do people affected by cancer use complementary therapies and how can their efficacy be evaluated?

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National surveys indicate that complementary therapies are popular throughout the industrialised world, and the use of such therapies has increased considerably over recent years. One in eight Britons and one in two Americans now use complementary therapies (Eisenberg, Davis, Ettner et al 1998). Patients with cancer seek and use complementary therapies in conjunction with cancer treatments to enhance their quality of life. Studies have investigated patients' attitudes to complementary therapies and the extent to which patients with cancer use them, but their effectiveness has not been established. These therapies have significant resource implications. Aromatherapy massage is one complementary therapy currently being provided by many hospitals and hospices in the UK; while its positive effect on quality of life has been demonstrated in the short term, there is no evidence of its long term efficacy. To address this issue a multi-centred randomised controlled trial to evaluate the use of aromatherapy massage in reducing psychological distress and enhancing quality of life in patients with advanced cancer is being conducted. Drawing on this study the issues of conducting trials involving complementary therapies will be highlighted and the reasons for why people use complementary therapies will be reviewed.

[1] Eisenberg, Davis, Ettner et al Trends in Alternative Medicine Use in the United States 1990-1997 JAMA 1998, 280 (18): 1569-1575

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Oncology nurses' attitudes towards alternative medicine

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The purpose of this study was to describe attitudes towards alternative medicine among nurses working on oncology wards in three university and one central hospital in Finland. The response rate was 68.1% (n = 92).

The data were collected with a self-developed questionnaire. The analysis was based on percentage distributions, cross-tabulation and analysis of variance. Levels of significance were tested with the Chi-squared test.

The nurses did not believe that alternative medicine provided safe and natural treatments in cancer care and the nurses' attitudes towards alternative medicine turned out to be mostly negative. Attitudes were most sceptical towards vitamin and trace element therapies. Half of the nurses believed that alternative therapies are offered by quack doctors for financial gain. However, the nurses concidered it important for the patients to be able to discuss their use of alternative medicine both with nurses and doctors and half of the nurses showed some interest in alternative medical training in case it was arranged.

An interesting question in future is whether this attitude is reflected in nursing practice? In addition, we need more research about the use of alternative medicine by cancer patients and what are cancer patients attitudes towards alternative medicine.

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The interaction of patient selection, surgical expertise and intensive care competence in esophageal cancer

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Treatment of carcinoma of the esophagus and gastroesophageal junction has changed substantially over the last two decades.

Better staging methods including barium swallow, endoscopy, CT, echography, EUS and more recent PET scan are resulting in an increasing accuracy in selecting candidates for treatment modalities with curative options.

Lowered postoperative mortality rate and increased radicality at the time of resection are believed to be the main factors responsible for better survival rates varying between 25% and 40% in recent reports.

In this respect surgical expertise seems to be of paramount importance. Indeed data from literature suggest a beneficial correlation between increasing patient volume and the resulting surgical experience and both the oncologic outcome as well as hospital mortality and morbidity. Close cooperation between the surgical and anesthesiological team is a crucial factor in the succesful management of major complications and the possibly resulting mortality.

In experienced centres hospital mortality is well below 5% despite the increased radicality of the surgery and the increasing presence of preop-

erative risk factors in many patients. As many patients present themselves with an advanced stage of carcinoma at the time of diagnosis, multimodality regimens mainly induction chemotherapy and/or chemoradiotherapy increasingly become part of the therapeutic strategy. This results in more complex decision making algorithms and more complex surgery with higher surgical risk requiring interdisciplinary team approach on a regular base with an ever more demanding expertise from all involved disciplines.

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Quality of surgery and outcome in gastric cancer surgery

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The main aspects, being responsible for a high *quality* of gastric cancer surgery, are the surgical expertise, a high number of operations and an efficient intensive care medicine. There centers of excellence in gastric cancer surgery demonstrate a low postoperative morbidity with a total complication rate below 20%, a rate of anastomotic insufficiencies of less than 3%, a 30-day mortality below 3% and a 90-day mortality of 25%, which should be the future standard for all centers doing gastric cancer surgery. The postoperative outcome is closely related to the type of reconstruction. With regard to quality of life after total gastrectomy, the best reconstruction type in curatively operative patients is the interposition of a jejunum pouch with preservation of the duodenal passage. These patients demonstrate a better food intake with a larger quantity of meals, a low frequency of reflux esophagitis (1–5%), rare dumping symptoms (<5%) and a significantly higher body weight (8% higher) at 6 months postoperatively in comparison to Rouxen-Y reconstruction.

From the oncological point of view, however, long term *outcome* of gastric cancer surgery is still unsatisfactory. The prognosis is poor in stages III and IV (2-year survival 62% and 8%, respectively; 5-year survival 34% and 6%, respectively). The risk of local recurrency at 5 years postoperatively ranges between 37 and 43% in curatively operated patients. The positive impact of lymphadenectomy on prognosis is generally accepted. Future studies have to find out whether multimodal therapy approaches using neoadjuvant chemotherapy are able to improve prognosis decisively in advanced stages of gastric cancer.

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Liver tumor surgery: Quality of surgery and outcome on the basis of a large interdisciplinary treatment unit

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Liver tumour surgery is the distillation of several types of expertise: high technology surgery, close familiarity with the complexity of liver disease, modern techniques of functional investigation, advanced oncologic practice.

The Centre Hépatobiliaire was established on this multidisciplinary concept in 1993, with all of the specialised medical and support staff needed for acute and elective surgical and non-surgical management of liver disease. Caseload, notably for liver tumour surgery and associated chemotherapy, is increasing by >10% per year. For hepatocellular carcinoma (HCC – 778 new cases since 1993) our multimodal approach involves combinations of resection, liver transplantation, transarterial chemoembolization (TACE), chemotherapy, and percutaneous in-situ tumour destruction by cryosurgery, thermal coagulation, or ethanol injection. Operative mortalities for HCC are 1% without cirrhosis, 7% if Child A/B, and <4% for transplantation. For hepatic colorectal metastases (574 new cases since 1993), resection can be curative, and we use techniques to increase the proportion of resectable patients. Tumour size is reduced with neoadjuvant chemo-therapy or percutaneous destruction. Remnant liver volume is increased by preoperative portal vein embolization. Two-stage hepatectomies may be performed. Early repeat resection has outcomes similar to primary resection. Operative mortality for all hepatectomies is 1%.

Chronomodulation has allowed higher chemotherapy dose intensity without added side-effects. For each surgical procedure, reference scales for quality – mortality, morbidity, and survivals – are determined by comparison with our historical performance data and with the literature. The multidisciplinary structure and multimodal approaches in the CHB seem to achieve the two objectives of liver tumour surgery: to increase the quality of the surgical outcome, and to increase the number of operable patients.

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Abstract not received.

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Surgical Oncology – The volume-outcome impact. Breast cancer

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The relationship between caseload (volume) and outcome remains controversial. Complication rates and 30 day mortality are less for surgeons specialising in oesophageal and pancreatic cancer resections but the situation in colorectal cancer is less clear.

For patients with breast cancer there are now a number of studies showing that specialisation, however measured, improves survival. Gillies (1) showed that patients looked after by a surgeon with an interest in the disease had a lower relative risk (0.63) of death at 5 years. We have shown widespread differences in the utilisation of adjunctive therapies across Yorkshire (2) and that these translate into survival differences (3). Significant factors for delivery of improved breast cancer survival included use of chemotherapy and workload. Had appropriate levels of chemotherapy been used then the 5 year survival rates would have approached those seen elsewhere in Europe at that time.

An additional Scottish study has shown that area of residence and workload were significant factors for both survival and local recurrence.

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Eps8 and E3b1 mediate transduction of signals from Ras to Rac

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The small guanine nucleotide-binding protein, Rac, regulates mitogen-reduced cytoskeletal changes, c-jun aminoterminal kinase and its activity is required for Ras-mediated cell transformation. Epistatic analysis, using actin reorganization as a readout, placed Rac as the key downstream target in Ras signaling, however the biochemical mechanism regulating the crosstalk among these small GTP-binding proteins is not completely understood. In this study we report the positioning of Eps8 in the mitogenic network. Our results indicate that Eps8 is indispensable for the transfer of signals between Ras and Rac, by regulating the action of Rac-specific GEFs. By combining genetic and biochemical approaches we showed that: i) overexpression of Eps8 led to the potentiation of Ras-dependent signaling, in particular affecting the branch of the Ras pathway leading to JNK activation; ii) genetically-engineered removal of *eps*8 from cells resulted in the impairment of signal transduction from Ras to Rac; iii) Eps8 is in a genetic epistatic relationships with Ras/phosphatidylinositol 3-phosphate Kinase, upstream, and Rac, downstream; iv) Eps8 seems to be exclusively involved in the Ras-dependent activation of Rac, since stimuli able to bypass Ras and to converge on the pathway downstream (such as TPA-induced activation of Rac or UV light-induced activation of JNK) are unaffected; v) Eps8 dependent regulation of a Rac-GEF, likely by regulating the activity of Sos-1 via E3b1, an Eps8-associated protein Based on these results, we would like to propose a model in which Eps8 is a functional activator of a Rac-specific GEF and is regulated by the activity of PI3K. Ras downstream regulatory molecules, like Eps8, are likely necessary to elicit full transforming and oncogenic responses. However they appear to be dispensable for a variety of other Ras-dependent functions. This property could make them ideal target for therapeutic strategy aimed at specifically blocking the oncogenic potential of Ras proteins.