

## Ten Years of Medical Oncology as Medical Specialty

Tanja Čufer and Cvetka Grašič Kuhar

Back in 1972, due to an increasing complexity of systemic treatment of cancer patients, there was a felt need in the USA for implementing a separate specialization in medical oncology. The beginnings of medical oncology in Europe reach back to 1980, while the specialization in medical oncology itself was not implemented until 1997, when it was introduced as one of the measures aimed at improving the survival ratio in Europe, which was at that time significantly lower than in the USA. Medical oncology is recognized as a self-dependant specialization in Slovenia from the year 2000 onwards. It is conducted in the frame of a specialization in internal medicine, sharing the first two years of the core curriculum. In the following four years, the resident acquires basic as well as in-depth knowledge in the field of medical oncology and research work. The medical oncology network estimates that, by the year 2020, there will be approxima-

tely 27 medical oncologists working at the comprehensive cancer center, Institute of Oncology Ljubljana and additional 23 in at least five secondary (regional) oncology centers. Due to an ever-increasing number of cancer patients as well as indications for systemic therapy all over the world, we are faced with a huge problem of how to secure an adequate number of medical oncologists. Slovenia needs to keep improving its network of medical oncologists by increasing the number of medical oncologists in training and by ensuring that the network functions at its best. An optimal way to reach these goals is to motivate medical doctors who have just graduated, to select medical oncology as their specialization of choice and, at the same time, to motivate the leaderships of healthcare institutions to follow the goals and requirements set by the national cancer plan, for performing medical oncology in various oncology centers.

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## The Role of Interferon in the Treatment of Cutaneous T-Cell Lymphoma

Mateja Dolenc-Voljč

IFN-alpha has been used successfully for the treatment of cutaneous T-cell lymphoma for many years and it remains an indispensable drug for this condition. Its antiproliferative and immunomodulatory properties are used in the treatment of this disease. According to the current guidelines for the treatment of cutaneous T-cell lymphoma, it is considered as the first-line drug for stages IIB and III, where it is often administered concomitantly with systemic PUVA and retinoids. As monotherapy, it is recommended in stages IA and IIA, if skin

directed therapies are not effective. As a maintenance therapy with low dosages, it is associated with prolongation of the duration of remissions. Optimal treatment regimen is adjusted individually, according to the stage of disease, dissemination of skin lesions and the patient's tolerance for IFN. Several acute and chronic side effects can occur during the treatment with IFN-alpha, which are dose-related, predictable and often reversible.

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## Nasopharyngeal carcinoma: review of treatment results at the Institute of Oncology Ljubljana

Janka Čarman and Primož Strojani

Nasopharyngeal carcinoma is a very rare type of malignant tumor which appears sporadically in the district of Slovenia and most parts of the Western world. Factors important for its development are infection with Epstein-Barr virus, genetic susceptibility and some environmental factors. The main modality of treatment is radiotherapy. Chemotherapy has an important role in the treatment of advanced

stages of the disease, including distant metastases. In the article, etiology, pathology, symptoms, diagnostics and treatment of nasopharyngeal carcinoma as well as retrospective analysis of treatment results and value of prognostic factors in the patients with nasopharyngeal carcinoma treated at the Institute of Oncology Ljubljana between 1990–2003 are described.

## Rescreening of Cervical Smears as a Method of Internal Quality Control

Ana Pogačnik, Margareta Strojan Fležar, Brenda Smith and Janja Zalar

Efficient quality control is essential in a well-organized screening program for early detection of cervical precancerous lesions. Various Pap smear review procedures are used to improve the detection of high-grade lesions. In the Department of Cytopathology at the Institute of Oncology Ljubljana, Slovenia we re-screened 6,813 (12.6%) conventional Pap smears out of a total of 54,000 slides screened in 2006, 2007 and 2008. Random re-screening of the slides (both negative and atypical) was conducted as a component of the educational program for screeners. False negative rate (FNR) was calculated according to the formula: false negative cases / (false negative cases + true positive cases) X 100. Of 6,813 re-screened Pap smears, 302

(4.4%) were reclassified into different categories: 221 (3.2%) smears were reclassified from negative to reactive, 73 (1.1%) from normal to LGSIL, 7 (0.1%) from LGSIL to HGSIL and one case (0.015%) was reclassified from negative to HGSIL (true false negative). Of 8 cases reclassified as HGSIL, 7 were histologically confirmed as CIN2 and CIN3, one was designated as CIN 1. In this study, FNR was 2.4% for LG atypias in squamous cells and 1.3% for HGSIL. In our laboratory, small number of personnel limits the potential for rapid re-screening of all negative smears. Therefore, random re-screening of smears during the screeners' educational program is an adequate policy for quality control.

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## Advances in Systemic Treatment of Stomach Cancer

Janja Ocvirk

In a great deal of patients operated on for gastric and gastroesophageal junction cancer, the disease is likely to recur as local recurrence, distant metastases or the combination of both. In the treatment of certain types of solid tumors, adjuvant chemotherapy can prolong the overall survival by reducing residual micrometastases. The effect of adjuvant chemotherapy in the treatment of gastric and gastroesophageal junction cancer is not very clear, whereas adjuvant radiochemotherapy significantly prolongs the relapse-free interval as well as the overall survival. Perioperative treatment with ECF-based chemotherapy also prolongs significantly the disease-free and overall survival. ECF-based chemotherapy and the analogue regimens, such as EOF, ECX and EOX, are considered to be the standard treatment for ad-

vanced gastric and gastroesophageal junction cancer. The treatment with taxanes applied in combination with 5-FU and cisplatin (TCF regimen) is also very efficient. New combinations of cytostatics and application of new cytostatics in the treatment of patients with gastric and gastroesophageal junction cancer have significantly improved the median survival of these patients. Recently, also target drugs are being introduced in the treatment of gastric and gastroesophageal junction cancer. With the measurement of biomarkers and application of target drugs, a new era in the patient-adjusted treatment is opening, also in the treatment of patients with advanced gastric and gastroesophageal junction cancer.

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## Perioperative Management of Patients with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) - An Anesthesiologist's Point of View

Barbka Novak Supe

The diagnosis of peritoneal carcinomatosis is often associated with poor prognosis and a median survival of a few months, depending on the primary tumor. Hyperthermic intraperitoneal chemotherapy (HIPEC) after complete surgical resection is currently accepted as a therapeutic option for peritoneal carcinomatosis and it considerably

prolongs the survival in several tumor types with peritoneal spread. Perioperative anaesthetic management of the patients undergoing such procedure is described and characteristics of the first 11 HIPEC procedures, performed at the Institute of Oncology Ljubljana in 2009, are presented.

### **Anemia in Cancer Patients**

Breda Škrbinc and Tanja Južnič Šetina

Anemia is defined as a significant reduction of the red cell mass and a corresponding decrease of the oxygen-carrying capacity of the blood. The etiology of anemia can be due to decreased red blood cell (RBC) production, increased RBC destruction and blood loss. Anemia is prevalent in 30-90 % of cancer patients with a number of factors that may contribute to its development, most often overexpression of inflammatory cytokines accompanying malignant disease and myelosuppressive cancer treatment. Anemia in cancer patients should

be identified by standard diagnostic procedures. Decision about treatment of cancer related anemia depends on the patient's symptoms, degree of anemia and the rate at which it has evolved, patient's comorbidities and the goal of cancer treatment in a certain patient. Management of anemia in cancer patients includes the transfusion of packed red blood cells and / or the administration of recombinant erythropoietin

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### **Thrombocytopenia in Cancer Patients**

Barbara Jezeršek Novaković

Thrombocytopenia is a decrease in number of platelets in the peripheral blood below normal range defined for population. There is no clear-cut definition for mild, moderate and severe thrombocytopenia. However, the thrombocytopenia grades are described in cancer patients receiving systemic treatment. Thrombocytopenia causes predominately skin and mucosal hemorrhage as well as, though rarely, central nervous system (CNS) hemorrhage. Thrombocytopenia is a consequence of low production of platelets or of their increased decay and consumption, as well as of delayed release of platelets by the spleen. The main causes of thrombocytopenia in cancer patients are inhibited proliferation and maturation of megakaryocytes induced by cytostatic therapy and also, though rarely, by radiotherapy. There are also other causes, e.g. excessive infiltration of bone marrow with tumor cells, hypersplenism linked to spleen enlargement, increased decay of platelets due to the use of certain drugs (heparin), in the course of chronic leukemia and lymphoma, or in association with disseminated intravascular coagulation and sepsis. In case of severe

thrombocytopenia ( $< 10 \times 10^9/l$ ) the risk of spontaneous skin, mucosal and intracranial hemorrhage is significantly increased. These patients are also at risk of excessive postsurgical hemorrhage. Thrombocytopenia is diagnosed on the basis of complete blood count from which the grade of thrombocytopenia is also determined. In order to define the precise cause of thrombocytopenia, a detailed medical history should be collected, as well as specifically oriented clinical examination and additional laboratory tests should be performed. In some cases, aspiration biopsy of the bone marrow is required. The thrombocytopenia-related hemorrhages are treated or can be prevented by platelet replacement. The platelet count at which the replacement is required depends upon the cause of the thrombocytopenia and presence or absence of hemorrhage. The platelet transfusion is recommended when the thrombocyte count is below  $10 \times 10^9/l$  in order to avoid the risk of spontaneous hemorrhages, particularly CNS hemorrhage.

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### **Role of tumor markers in the treatment of solid tumors and lymphomas**

Simona Borštnar, Tanja Ovčariček and Branko Zakotnik

Tumor markers may be produced by tumor cells or by the body as a response to the tumor. A diagnosis of cancer cannot be based only on the presence of higher level of tumor markers in the blood or body fluids because tumor markers can be elevated in the patients who don't have cancer or can be normal in the patients with cancer, and because no tumor marker is entirely specific to a particular type of

cancer. One of the most important uses of tumor marker testing is to evaluate the efficacy of cancer treatment in the patients on treatment, especially in cases of advanced cancer. Tumor marker testing is also used in the follow-up of patients after the completed treatment of some cancers in order to detect early relapse.

### **Follow-Up of Cancer Patients**

Cvetka Grašič Kuhar, Maja Ravnik, Danica Rotar-Pavlič and Tanja Čufer

Cancer is a disease with nearly the highest incidence and also the most frequent cause of death in humans today. Cancer burden is getting higher every year. However, due to early detection of cancer, more efficient and less harmful treatment, the survival of cancer patients is improving. Consequently, also the percentage of cancer survivors is significantly on the rise and, in the developed world, this percentage amounts to 3% of total population there. Cancer survivors require careful follow-up also after completed cancer treatment. These patients are not followed up only because of recurrence risk (locoregional or distant recurrence) but also because of late sequelae and undesired effect of treatment (physical, psychological and social) as well as of increased risk for developing secondary cancers.

There is an urgent need to make people aware of the importance of healthy lifestyle and of early detection of secondary malignancies as well as of late sequelae of cancer treatment. The patients and their relatives should be informed that, for hereditary cancers, genetic testing is available, while for the detection of other cancers, screening methods (mammography, coloscopy) are used. Cancer survivors more frequently develop other non-malignant diseases. With the increasing number of cancer survivors and considering that cancer is becoming a chronic disease, it is indispensable that the team who is in charge of comprehensive care of cancer survivors includes, in addition to an oncologist and family doctor, also experts of other disciplines, such as nurses specialized in oncology nursing and psychologists.

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### **Family Doctor and His Role in Palliative Care of Cancer Patients**

Jožica Červek

Cancer may intrude deeply into the lives of cancer patients and their families. Palliative care is the care for patients which aims to optimize the comfort, function and social support of the patient and their family when cure is not possible. The efficiency of palliative care is based on knowledge and teamwork of the experts of several disciplines. Palliative care principally aims at assuring quality of life to the patient. Indicators of high quality of life are only a few hospitalizations in the terminal period of life and palliative care at home. Possibilities to assure high quality home care depend primarily on family doctor and his partners in the team who should be skilled enough to recognize and alleviate efficiently in time every early symptom as well as to

make sure that all the needs and wants of the patient are fulfilled. In palliative care, the role of the patient's family is vital, and the qualities that are indispensable in palliative care are time, team work respect, patience, sincerity, and awareness and respect of approaching death. Palliative care will be recognized as a human right only after it is acknowledged as a part of compulsory health insurance and also after it is included in the curriculum of compulsory education of health care professionals. Without fulfilling the above conditions the status of palliative care will be as it is now – a discipline, dependant on the endeavors and aspirations of few individuals and accessible to a few number of patients.

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### **Case Report on a Patient with Invasive Lobular Carcinoma of the Breast and Indications for Breast MRI**

Maja Marolt Mušič, Kristijana Hertl and Marta Zebič

Invasive lobular carcinoma (ILC) is the second most common histologic type of breast carcinoma and represents 5-15 % of all breast cancers. Due to specific growth pattern, it is frequently missed on mammography. It is known that mammography and US underestimate the size of the tumor. Contrast-enhanced breast MRI is widely

accepted method to assess preoperatively the disease extent in patients with ILC and, in 28.3% of patients, it has an effect on the change of surgical treatment plan. In our article we present a case of 74-year-old patient with ILC, in whom breast MRI showed an infiltration in the pectoralis muscle.

## Wound Management by Using Negative Pressure Wound Therapy

Helena Uršič and Marko Novak

Negative pressure wound therapy (NPWT) enhances wound healing and helps to prepare the wound for closure by reducing oedema and increasing perfusion, by removing exudate from the wound and by enhancing granulation tissue formation. The duration of treatment has no limitations and depends on the goal of therapy, wound size and pathology, and comorbidities. NPWT should be stopped when

the wound is closed or ready to be closed surgically or shows no progress for one to two consecutive weeks. NPWT helps to optimize patients care and can be used in hospital or in outpatient care. There are no detailed recommendations for NPWT in oncology, decision is made individually. At the Institute of Oncology Ljubljana NPWT is used since 2007 and since then 62 wounds have been treated.

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## Physical Activity in Cancer Patients

Nada Rotovnik-Kozjek

Cachexia-induced metabolic changes stimulate an enhanced loss of functional tissue in human body, particularly muscles. Inadequate physical activity and undernourishment further increase the loss of tissue. In cancer patients as well as in chronic patients, physical activity inhibits straightforwardly the negative effect of the disease on the body organs. Regular aerobic exercise enhances functional capacity

of blood circulation, heart, muscles and metabolic processes, which help to sustain better physical condition. The strength training exercises help to maintain the muscles in good condition, thereby inhibiting their weakening. Physical exercises should be regularly performed, at least 3 to 5 times per week. A patient with derailed metabolism or severely impaired immune system is not advised to perform exercises.

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## A Case of Late Death after Treatment for Medulloblastoma

Jože Balažic, Andrej Vogrin and Berta Jereb

A 27-year-old male was treated for medulloblastoma with complete removal of tumor, postoperative RT to CNA with 36 Gy and boost to the posterior fossa 16 Gy. Nine years later, a suprasellar recurrence was treated with Carboplatin and Vepezid and 33 Gy to the tumor bed. Three years later he complained about headaches, periodic loss of consciousness and progressively showed bizarre behavior. He was

referred to psychiatrist. No recurrence was found. He did not appear on the day of follow-up appointment. He died at home, at the age of 43 years, 16 years after the first treatment. The cause of death determined by forensic autopsy : anemic subacute infarction in the left cerebellum.