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Oncology Pharmacy Practice

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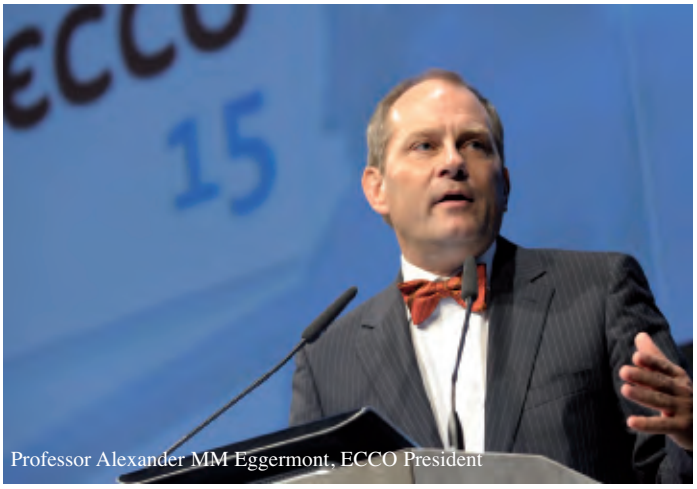
Conference Report



Professor Alexander MM Eggermont, ECCO President

Meeting Report

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Everything changes, nothing stays the same

Klaus Meier
Editor-in-Chief
President of ESOP

EJOP

Panta rhei - everything flows. Nothing is now as it has been before. You can find many such phrases in literature since the times of Heraclitus, Plato and Shakespeare. For the last 2,000 years change has been inevitable and common for everyone, but each person has to learn this for themselves. Human nature seems to learn fast, but also to forget just as quickly. This is mostly when the results of such thoughts and actions will only be seen decades in the future. Copenhagen, Denmark, in 2009, has shown that mankind finds it very difficult to change its behaviour; especially when this involves giving something up when the results will only be realised for future generations.

I remember the discussions in 2000, in Prague, Czech Republic, about the needs of oncology pharmacy.

Most European delegates in the International Society of Oncology Pharmacy Practitioners (ISOPP) declared the necessity for regional chapters in order to support new colleagues throughout the world implement oncology pharmacy in hospitals everywhere. However, the discussion was not effective enough. The situation of one common language, one common law and one country with several states compared to the European situation with more than 27 languages, more than 27 different countries and laws was not comprehensively respected. At that time it was not possible to bring these different experiences together and build an understanding of the needs in Asia, South America, Africa and finally Europe. Therefore, in order to foster regional collaboration and development, the EU delegates formed a new society, the European Society of Oncology Pharmacy (ESOP). Today, after ten years, ESOP is a full member of the European CanCer Organisation (ECCO), in close collaboration with more then 45,000 physicians and nurses, a society of 33 countries and more then 2,100 oncology pharmacists.

The reports of the different countries in this issue present highlights of the improvements which have been achieved in the last ten years. I see them as a strong base for more progress towards a better service for cancer patients in the future.

The nations of Europe have still to learn how to talk with one voice and with the motto 'Unity in diversity' this goal has still to be reached. The aim of ESOP is to support optimal treatment for cancer patients. Our constitution shows us how to act on this. Collaboration with all people and societies which have the same purpose is evident. We have the chance and the obligation to be active in our home countries, in Europe, as well as in the whole world. We will have a second chance to share our growing understanding at the next ISOPP meeting in May 2010, in Prague, Czech Republic.

Third masterclass in oncology pharmacy

The 3rd Masterclass in Oncology Pharmacy was held in Athens, Greece, 23–26 November 2009. The meeting was the latest in a series of successful events and both participants and instructors agreed that the lectures and workshops had so far achieved the Masterclass's aim of offering high-calibre knowledge to pharmacists from across Europe.

This year the Masterclass attracted 40 pharmacists from as far away as Brazil! Of course most participants came from Europe, notably Portugal, which had the highest representation in the Masterclass, as well as Belgium, Bosnia, Cyprus, Denmark, Estonia, Greece, Germany, Hungary, Latvia, Slovenia, Spain, Sweden and Turkey. So there was a multinational aspect to the meeting, in which ideas and experiences were exchanged from a wide range of different countries.

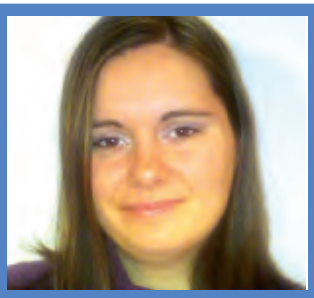
Participants also had the opportunity to enjoy the balmy Athens weather and the social events that went with the meeting, particularly the visit to the New Acropolis Museum, which better acquainted them with the world of Ancient Greece.

Ioanna Saratsiotou, PharmD
ESOP Delegate

Quality Standards for the Oncology Pharmacy Service

ESOP quality standards are the basis for a new Slovenian quality manual. They were much appreciated by hospital and independent pharmacists.

On 13–14 November 2009, a two-day meeting on quality standards for the oncology pharmacy service took place in Kranjska Gora, Slovenia. The main purpose of the meeting was the presentation of the book of the same name, accompanied by lectures on the preparation of cytotoxic drugs. As pharmacists active in this field, ESOP (European Society of Oncology Pharmacy), seeks to standardise and harmonise approaches. The Slovenian manual based on QuapoS (Quality Standards for Pharmaceutical Oncology Service) presents a significant contribution to the oncology pharmacy service in Slovenia. The book is divided into five parts: personnel, rooms and equipment, production of cytotoxic drug solutions, the pharmacy as coordination centre in treatment with cytotoxic drugs, and pharmaceutical care of the patient. It is hoped the manual will be of great assistance to pharmacists handling and administering cytotoxic drugs, organising work and rooms, and providing advice to patients, relatives and medical personnel.



Andreja Eberl
MPharm

As well as presenting the book, the guest speakers lectured on the first day on various aspects of handling cytotoxic drugs. Professor Per Hartvig-Honoré, Lecturer in Pharmacokinetics at the University of Copenhagen, Denmark, graphically illustrated the benefits and drawbacks of production practice. Presenting the preparation of cytotoxic drugs for individual patients in hospitals 'GMP in Small Scale Sterile Production' he focused on ways to ensure quality throughout the process. The quality manual is a significant element, which should be recommended for planning all processes and tests. In his lecture 'Health hazards to personnel handling cytotoxic drugs' Professor Hartvig stressed again the significance of quality personal protection equipment, such as double gloving, and presented research on the risk to personnel of disease.

Safety in preparing and administering cytotoxic drugs, simulation of the use of closed systems.

In her lecture 'How to establish and run a cytotoxic preparation unit', Ms Eva Hartvig-Honoré, working in a large hospital pharmacy in the capital region in Denmark, set out the principles of planning rooms for cytotoxic drug preparation. She reinforced the need to monitor the production of cytotoxic drugs. As many hospitals in Slovenia are currently building or about to build premises for the centralised preparation of cytotoxic drugs, the lecture was very welcome and provided a good basis for further discussion.

The second day was interactive, and began with a workshop on safety in preparing and administering cytotoxic drugs. The 28 participants watched a recording of the preparation and administration of cytotoxic drugs at the Institute of Oncology in Ljubljana, Slovenia, which provided the starting point for questions and discussion on specific procedures used in individual hospitals. The participants then divided into groups which simulated the preparation of cytotoxic drugs with a closed system, reviewed different administering systems, and shared their experience in preparing chemotherapy drugs.

The meeting ended with a discussion on the problem of transporting chemotherapy drugs. Currently, shipments of carcinogenic, mutagenic and reprotoxic (CMR) drugs are not labelled dangerous, and CMRs may be combined with other drugs, or placed in cardboard boxes. Everyone agreed there was much work to be done in this area. The goal is to make the transportation of cytotoxic drugs consistent with ESOP guidelines on safe transportation, which are also included in QuapoS. CMR drugs must be transported in safe and sealed impermeable containers marked with a logo that highlights the danger and carries a warning understood by non-trained personnel. We agreed that the yellow hand logo should be used; however, problems arise with regard to realisation, as there is currently no legal basis on which to compel wholesalers to indicate CMR drugs with a special label. As a first move, wholesalers will be approached to adopt the standard for transporting cytotoxic drugs.

The meeting expressed a desire to standardise procedures in hospitals. Therefore, a working group will be set up for the oncology pharmacy service to address the issue more actively.

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The development of oncology pharmacy

This article takes a look at oncology pharmacy in countries where it is just developing to those in which it is now well established.

Oncology pharmacy in Austria

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The first oncology pharmacist in Austria, Ms Petra Mache-Dornbusch, began working in the paediatric oncology ward at LKH Graz towards the end of the 1980s. However, at that time she was not even a staff member of the pharmacy. Then in 1990 the Vienna University Hospital established the first centralised cytotoxic preparation service in its pharmacy. This was immediately followed by those of the pharmacies of the LK Wr Neustadt (Lower Austria), the Center for Social Medicine East, Donau Hospital and the Hospital Rudolfstiftung, both located in Vienna.

In the early 1990s several collaborations with German colleagues, many of which are still ongoing, began. Then in the middle of the 1990s a milestone study was initiated by Austrian oncology pharmacists [1] which showed that following current quality standards may prevent hospital pharmacy personnel working in a centralised cytotoxic preparation service from being exposed to cytotoxic drugs.

During this time educational activities in oncology pharmacy also intensified. Local symposia and meetings were followed by the organisation of the European Society Clinical Pharmacy congress in 1998 in Linz, highlighting oncology and pharmacoepidemiology.

At the end of 2000 the Austrian Society of Oncology Pharmacy was founded and accepted by the authorities in 2001. The website, www.asop.at was launched in 2007. Members of the society are involved in a number of working groups such as the interprofessional oncology expert group of the Vienna Hospital Trust and the cytotoxics' working group of the Austrian Ministry of Health, which is currently updating the regulatory framework for the safe handling of chemotherapeutic agents.

There is also cooperation with the Austrian Society of Clinical Pharmacy (ÖGKP; www.clinicalpharmacy.at) regarding continuing medical education activities such as the Annual Clinical Pharmacy Week (the 5th such week will take place in September 2010).

1. Pilger A, Köhler I, Stettner H, Mader RM, Rizovski B, Terkola R, et al. Long-term monitoring of sister chromatid exchanges and micronucleus frequencies in pharmacy personnel occupationally exposed to cytostatic drugs. Int Arch Occup Environ Health. 2000;73:442-8.

Strategy in Croatia

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Knowing that it would be extremely difficult to develop oncology pharmacy in Croatia without a well-designed development strategy, we applied for help to the professional organisation of physicians and the oncology society of the Croatian medical society. Its president, Professor Damir Vrbanec, assumed responsibility for providing education in the field of oncology. There was also considerable assistance and support from the ESOP and its president, Mr Klaus Meier. Without this wholehearted help and cooperation we would not have been able to attain the results we have. For the purpose of full coordination of our work with the Ministry of Health, the profession and legal provisions, we established a working body called 'The Commission on Oncology Pharmacy' at the Croatian Pharmacists' Chamber with the following members: Mirjana Canjuga, Ms Višnja Kopecki, Maja Koroman, Tihana Govorčinović and Ms Vesna Pavlica (President). Since May 2005 we have met regularly, and once a week in video-conferences, to discuss all topical issues. Our aim is to produce a set of regulations, based on Quality Standards for Pharmaceutical Oncology Service (QuapoS), for the handling of antineoplastic drugs, which would subsequently become part of the law on protection in the workplace.

Ten years of oncology pharmacy in the Czech Republic

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Ten years ago, oncology pharmacy in the Czech Republic was a new, fast developing part of hospital pharmacy, with only a few members. However, when the 7th International Society of Oncology Pharmacy Pratitioners (ISOPP) was held in Prague in 2000 and ESOP was established as a European oncology pharmacy society, this stimulated greater interest in the area. The Czech Republic oncology pharmacy working group began on 5 May 2004, with about 15 members. Now as part of the Hospital Pharmacy Society this number has grown to 65, meeting twice a year at national conferences. In 2000 only one pharmacy had a cytostatic compounding unit, but today there are 28 pharmacies capable of

cytostatic preparation. Since 2009 there has also been a dedicated website, as part of the Hospital Pharmacy Society (www.nemlek.cz). The Czech Republic has hosted two ESOP masterclasses in oncology pharmacy. This year, after ten years, the 12th ISOPP symposium will once again be held in Prague.

First steps in oncology pharmacy in Estonia

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In the past few years the number of oncology patients has increased significantly in Estonia, which has meant the greater use of cytostatic drugs. Hospital pharmacists now have the challenge of providing for the safe handling and administration of these drugs and also their proper waste disposal.

There are two hospitals in Estonia treating oncology patients; the North-Estonian Central Hospital in Tallinn and Tartu University Hospital. Preliminary work for the preparation of cytostatic drugs in Estonia began in 2006. But first of all basic knowledge regarding their preparation was needed, which led to Estonia joining the ESOP in 2006. Today, Estonia is represented by five members.

Estonian pharmacists have relied upon QuapoS as their basic literature guide in the preparation of cytostatics. The latest edition, QuapoS 4, has now also been translated into Estonian. From March 2008 there has been a department responsible for the preparation of cytostatic drugs in the North-Estonian Central Hospital in Tallinn, with a similar department subsequently created in March 2009 at Tartu University Hospital.

A cancer patient counselling campaign in German community pharmacies

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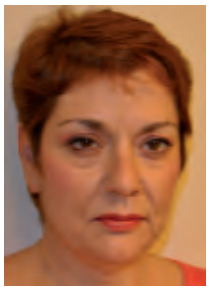
Since 1985 in some small hospitals the preparation of cytotoxics has been centralised in pharmacies in Germany. It was quickly apparent to those pharmacists involved of the necessity for the exchange of knowledge and the first national meeting (NZW) was held in 1993. In 1995 the 4th ISOPP conference was organised in Hamburg and this fostered the recognition of the need for a constant 'relationship' between pharmacists involved with oncology drug preparation. The beginning of the ISOPP society also corresponded with the establishment of the German Society for Oncology Pharmacy in 1998. German pharmacists understood that only by acting at an international level, with cooperation across Europe, would give the national movements a unique voice. Since then membership has grown, today there are around 600 members. Not only hospitals but also community pharmacies have become more and more aware that the treatment of cancer patients must not be divided between healthcare professionals.

Since many cancers become largely manageable chronic diseases with ongoing surveillance and treatment, patients need continuous counselling by healthcare professionals. Increasingly oral therapies with novel types of toxicity are prescribed, requiring close monitoring to avoid adverse events, non-compliance, incorrect use, interactions, etc. Since many patients receive their drugs, especially the supportive medication, in a community pharmacy, it is crucial for community pharmacists to be prepared for this task.

To increase their expertise the German Society of Oncological Pharmacy (DGOP) initiated a nationwide cancer patient counselling campaign for pharmacists. This advanced training consists of three steps. First of all kick-off presentations given by a total of 25 speakers took place simultaneously in every German federal state in December 2009. More than 1,000 participants attended, which gave a general introduction to pharmaceutical care for oncological patients. On the basis of a case study the management of adverse events was illustrated including specific patient recommendations.

The second step will support a consolidation of pharmaceutical knowledge regarding specific topics in supportive care, e.g. mucositis, skin changes or fatigue. Subsequently, in step three, written patient information will be developed containing descriptions of possible adverse events, explicit patient recommendations and specific information about individual prescribed drugs, to support the counselling by the pharmacists. The aim of this nationwide campaign it is to enhance the safety of anticancer therapies and optimise health outcomes for patients.

Oncology pharmacy in Greece



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The Pan-Hellenic Scientific Association Hospital Pharmacists (PEFNI) was founded in 1986 with the aim of promoting pharmaceutical science in hospital practice. Members are hospital pharmacists from public, private and military hospitals, plus pharmacists working in public assurances' hospitals. PEFNI's administrative council consists of seven elected members, and symposiums and seminars of interest to hospital pharmacists are organised by PEFNI every year.

In 2006 PEFNI signed the ESOP constitution and their delegates participate in all of ESOP's activities. Today 25 pharmacists are part of the Greek national scientific group for oncology pharmacy, which is a member of ESOP. In November 2009 a highly successful 3rd masterclass in oncology pharmacy practice was organised in Athens.

Greek hospital pharmacists collaborate closely with other healthcare workers and participate as an association in many multidisciplinary symposiums. They are also willing to collaborate, and exchange valuable oncology knowledge and experience, with their European colleagues.

Oncology pharmacy in Hungary - the beginning of the journey

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The first national guidelines for the preparation of IV admixtures in a hospital setting was issued in 1998, although this guideline provided standards for not only cytotoxic admixtures but also for TPN and other IV admixtures. The first centralised pharmacy-controlled cytotoxic preparation service in Hungary also started that year.

Substantial changes took place at the end of 2004, when the first quality standards of cytotoxic reconstitution were published. By that time the number of hospital pharmacies providing centralised cytotoxic preparation had increased to 12.

At the beginning of 2005 a working group of oncology pharmacists was formed as a section of the Hungarian Society of Hospital Pharmacy, and Hungary joined ESOP. A detailed survey on cytotoxic preparation was conducted for the first time. Since then workshops and seminars on oncology pharmacy topics have been organised during the annual congresses for hospital pharmacists.

The national guidelines underwent further significant changes in December 2007 and in many aspects were harmonised with the ESOP guidelines. That year a Hungarian translation of Cato software was made available and some hospital pharmacies began gravimetric preparation. As a further educational tool, *Oncology for oncology pharmacists*, was published in 2008.

By the end of 2009 three of our members had finished the ESOP masterclass, and there are currently seven hospital pharmacies where Cato software has been installed.

Our plans for 2010 include a 1-day educational seminar for oncology pharmacists, in cooperation with Berner International, and a survey of cytotoxic preparation.

Cooperation in oncology pharmacy in Italy

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The Italian Oncology Group was officially established in 1996 as a special interest group of the Italian Society of Health System Pharmacy (SIFO). Since then the group has been very active, particularly in education. The first event, of which, was held in Turin and involved colleagues discussing oncology issues. The course has been repeated three times. This was unique in that it was coordinated by a pharmacist and an oncologist and was the first experience of a multidisciplinary approach in this field. Since then there have been many more steps taken and now, for example, it is possible to obtain a Masters degree in Oncology Pharmacy at Milan University.

There has also been increased collaboration between oncologists, occupational health physicians, nurses and haematologists. This year SIFO and the Italian Association of Medical Oncologists (AIOM) organised a 'multicentre' meeting on 'the integrated management of oncological therapies' dealing with the issues of new oncological drugs or targeted therapies. The Italian Oncology Group has just published the results of a survey on the prevention of medication errors in oncology, which involved more than 40 oncological centres and pharmacies. The results highlighted the role of oncology pharmacy in preventing medication errors. CytoSIFO, a computer programme developed by pharmacists for pharmacists, was recognised as a very important instrument in managing prescription errors and preparation. Last, but not least, closer cooperation between the Italian Agency of Medicinal Products (AIFA), oncologists, haematologists and pharmacists has been established. Thanks to this cooperation the Italian project of the Register of Oncological Drugs has been set up. This has given important results with regards to the promotion of the appropriate use of new, expensive drugs.

Certification for oncology pharmacists in Spain

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Oncology patients in Spain are usually treated in general hospitals, belonging to the National Health Service. There are very few specific cancer centres in the country (San Sebastian, Valencia, Barcelona, La Coruña, Madrid). Many of them are private hospitals, but they usually have an agreement with the National Health Service and treat patients through the National Health Service insurance.

According to data from year 2000, 80% of hospitals prepare cytotoxic drugs in the pharmacy service. In Spain cytotoxic drugs are prepared in biological safety cabinets; the use of isolators is not widespread. In recent years, pharmacists have paid special attention to the quality of the preparation facilities and environmental matters, with many facilities being renovated. Of the pharmacy services, 71% use computerised programmes for preparation and 11% have computerised oncology prescription programmes. In recent years hospital pharmacists have, importantly, also increased their visibility and participation within the oncology team. They collaborate with oncologists and nurses in many activities with a final goal: to offer a better therapy and care to the oncology patient. This has been well accepted by both patients and other health professionals.

At a national level, oncology pharmacists have GEDEFO (Spanish Group for the Development of the Oncology Pharmacy). The group was founded as a cooperative working group in 1995 after ISOPP IV in Hamburg, Germany. In January 2003 the group was transformed into a Foundation, in order to achieve an appropriate legal framework. At the moment it works closely with the Spanish Society of Hospital Pharmacists (SEFH) and is one of its working groups. GEDEFO brings together 225 oncology hospital pharmacists in more than 130 hospitals.

According to its constitution, the main aims are:

- To promote appropriate education and training for pharmacists who work or are interested in oncology.
- To develop pharmacist's integration in the health team in order to improve oncology care of the patients.
- To foster and develop cooperative projects in oncology.
- To provide an appropriate framework for the collaboration and the exchange of experiences among its members.

In 2003 GEDEFO and SEFH began an important educational project in order to help pharmacists working in oncology to achieve the BCOP (Board Certified Oncology Pharmacist) from the American Board of Pharmaceutical Specialities (BPS). They offered 20 grants for oncology pharmacists with at least three years experience in oncology. The grants provide and facilitate all arrangements for the exam. This includes a programme of teaching activities with at least 3–4 intensive educational weekends organised in order to help with preparation for the exams.

After the US, Spain has, at the moment, the highest number of certified pharmacists. This project has been very successful in all aspects and pharmacists specially appreciate the level of knowledge and confidence in clinical aspects acquired throughout the programme. This background helps them to integrate into the multidisciplinary oncology team.

Other highlights of the activities of the group include a number of investigational projects and studies such as the use of taxanes, ondansetron versus granisetron (meta-analysis) and a study of chemotherapy treatment of breast cancer in Spain. There have also been numerous publications such as brochures for patients on chemotherapy side effects and on oral cytotoxics and supportive therapies. The group has also published breast cancer, colorectal, lung and ovarian protocol guidelines, as well as consensus documents for medication prevention errors in oncology, the use of oncology drugs for 'compassionate use' and oral chemotherapy.

Over the last ten years oncology pharmacists have gained and consolidated a strong position within the oncology team in Spanish hospitals. Our national group, GEDEFO, is very active and provides a strong platform of support for hospital pharmacists interested in oncology.

The start of oncology pharmacy in Turkey

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There were initially seven founder members of the Oncology Pharmacists Association in Turkey (*Onkoloji Eczacilari Dernegi*, OED). The association now has 15 members from university, public and private hospital's cytotoxic units. Interestingly the logo of OED was chosen by 1,238 people, the vote being held on Facebook! The association also has a website, www.onkoeczader.org with the OED Journal of Oncology Pharmacists Association also published on the Internet. A training programme has been organised called *Cytotoxic drug preparing techniques and safe room management* in collaboration with Gaziantep University of Medicinal Faculty Oncology Hospital. This involved 11 trainers from five different units, with the curriculum including the rules and regulations from the Ministry of Health together with ESOP QuapoS criteria. In 2009, with guidance and support from experts in the area, OED and ESOP, two new cytotoxic preparation units came into operation.

An introduction to mucositis

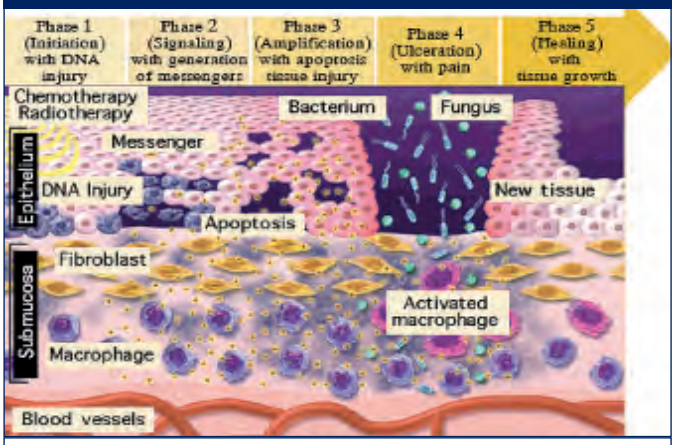
Mucositis is a burdensome adverse reaction to chemotherapy (CTX) and radiotherapy (RTX) that significantly impairs the quality of life. Damage to the mucosa leads to anorexia and cachexia, preventing the full dose of CTX from being used or delaying the scheduled RTX, jeopardising the treatment.

Definition and pathophysiology

Jürgen Barth

The high rate of proliferation and short duration of the cell cycle, which are the results of the high capacity for growth and regeneration of oral and gastrointestinal mucous membrane epithelia, are the reasons for the tremendous non-specific destructive effect of adverse reaction to chemotherapy/radiotherapy (CTX/RTX). Synergistic damage of mucous membrane function, differentiation and regeneration caused by CTX + RTX are symptoms of this direct toxicity. Functional breakdown primarily of serous and mucus glands, resulting in a reduction or complete breakdown of the physiological protective barrier, provide ideal conditions for microorganisms in an adhesive, saliva. Consequently, breakdown of the barrier to infection leads to thrush and a serious danger of sepsis as depicted in Figure 1 [1, 2]. Mucositis contributes to the morbidity and mortality of cancer patients. Few options for alleviating the symptoms of mucositis are available to date.

Figure 1: The five phases of mucositis



After breakdown of the physiological barrier systemic infection is a serious danger.

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Guidelines

Guidelines for supportive measures have been published by the Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology (MASCC/ISOO). They are available in English, German and Greek on www.mascc.org. They contain a list of substances and procedures that are **not recommended**: no sucralfate for prevention (RTX), no antimicrobial rinses (RTX), no chlorhexidine (CTX + RTX), no acyclovir (or analogues) for prevention, no pentoxifylline with autologous haematopoietic stem cell transplantation. **Positive recommendations** are good oral hygiene and basic oral care; patient, caregiver and staff education, appropriate use of oral rinses, ice chips, palifermin, appropriate use of analgesics, proton-pump inhibitors, anti-diarrhoeal agents and the avoidance of agents without proven evidence [3].

Therapeutic options

Traditional approaches

Since virtually no evidence-based studies are available for the prophylaxis of mucositis, no recommendations besides general oral hygiene are possible. Treatment strategies lack evidence-based studies as well.

Mucositis mouthwashes are often (multi-component) mixtures of pharmaceuticals based on historical clinical tradition lacking proof of efficacy, or even worse, compatibility. The wide variety of formulations should be considered doubtful even if they possess euphonic names such as 'magic mouthwash'. Allopurinol mouthwash did not have any of the desired effect in humans that was seen in animal models [4, 5].

Uridine 10% adhesive paste seems to be a real antidote to palmar-plantar erythrodysesthesia (PPE) and 5FU-related mucositis. It was developed by the Pharmaceutical Department of the University of Essen, Germany; see EJOP 2009; 3(2):22-3. Calcium folinate 4% adhesive paste against mucositis after high-dose methotrexate has also been developed in Essen and seems to work as a local antidote. Clinical trial data do not exist, but positive clinical experience allows this paste to be recommended. The formula is:

R

Calcium folinate	0.6 g	
Paraffin	10.1 g	
Carbopol 974 P	4.3 g	or alternatively:

Calcium folinate	0.6 g
Paraffin q.s.	
Hypromellose adhesive paste 40% (*Neues Rezeptur Formularium 7.8*)	ad 15.0 g

Flavouring can be added as required.

Many popular global, non-specific prophylaxis and therapeutic remedies show few or only subjective effects. Sage tea and chamomile extract both reduce inflammation with subjective benefit. According to Fidler et al, chamomile did not show any benefit for 5FU-induced mucositis and dysphagia [6]. Dexpanthenol remedy, myrrh tincture, suspensions of sucralfate or diluted Betaisodona (Betadine), chlorhexidine, locally used

antibiotics and anaesthetics such as Lidocaine and Tetracain or H_2O_2 1-3% are examples of lots of suspensions used without measurable usefulness.

Contradictory opinions have been reported for glutamine suspension 50%. In animals, a glutamine-enriched diet has been shown to reduce chemotherapy-induced enterotoxicity [7]; however, no significant positive effects in mucositis have been reported for supplementation of oral and parenteral glutamine in humans [8-10].

New developments

Recombinant keratinocyte growth factor (rHuKGF) stimulates epithelial cells that physiologically play an important role after damage. Palifermin (Kepivance) claims to induce cell proliferation and increase epithelial thickness, upregulate cytoprotective mechanisms, reduce DNA damage, upregulate levels of detoxifying enzymes and therefore protect against oxidative stress. So it claims to reduce proinflammatory cytokines, reduce apoptosis (in oral mucous membranes) and accelerate re-epithelisation of tissue leading in short to fewer ulcerated areas and less pain. Kepivance was approved in 2005 for patients with haematological tumours, myeloablative CTX (which bears a high risk of oral mucositis) and patients who are targeted for autologous stem cell transplantation only. Application of 60 µg/kg/d as IV bolus must take place three days prior to and three days after myeloablative CTX (not during CTX). In total, six doses have to be given, the last injection 24–48 hours before further CTX. Subcutaneous application will not be tolerated. In a clinical trial, administration of palifermin within 24 hours of chemotherapy resulted in increased severity and duration of oral mucositis. The safety and efficacy of palifermin have not been established in patients with non-haematological malignancies. KGF receptors are present on epithelial cells in many tissues including the tongue, buccal mucosa, oesophagus, stomach, intestine, salivary gland, lung, liver, pancreas, kidney, bladder, mammary gland and skin. One case of aggravation of PPE after BEAM (carmustine 300 mg/m^2 day 1, etoposide bd 100 mg/m^2 days 2-5, cytarabine bd 100 mg/m^2 days 2-5, melphalan 140 mg/m^2 day 6) has been reported, raising the question whether palfermin might have contributed to the severity of this side effect on the skin, usually seen after cytosine arabinoside [11].

Traumeel S, a mixture of homeopathic extracts from plants and minerals, is used in Germany for the treatment of traumatic, inflammatory and degenerative processes. The manufacturer is developing a new formulation for use as protection against mucositis [12].

Benzydamine is one option supported by an evidence base that inhibits the development of mucositis and might be given prophylactically [13]. Dr Dirk Keiner, from the Pharmacy Department of the Head and Neck Clinic in Suhl, Germany, has developed a benzydamine-containing but alcohol-free, palatable mouth gel adhesive to mucosa. Fast effectiveness against bacteria lowers the risks of ulceration and infection, local anaesthesia and high affinity to membranes explain the advantages for the patients. The gel contains benzydamine HCl, sodium hydrogen carbonate, saccharine sodium, polysorbate, polyvidone, glycerol and hydroxyethyl cellulose and is able to cover lesions and protect against painful stimulation [14]. Several mucoadhesive products (Gelclair, MuGard), or the hypersaturated $CaPO_4$ solution in Caphosol are coming onto the market. These medical products form a barrier in order to reduce pain. Whether or not these film-forming solutions will reduce the duration and severity of mucositis in clinical practice remains to be seen.

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New horizons in cytotoxic therapeutic drug monitoring

In many cancers, cytotoxic drugs have only a marginal long-term effect and resistance develops quickly. Optimal dosing is needed and drawbacks exist with traditional dosing calculations. Therapeutic drug monitoring (TDM) using population-based methods may hold promise to optimise therapy.

Dosing of cytotoxic drugs

Cytotoxic drugs are characterised by a narrow therapeutic margin with high toxicity, causing many and severe side effects. This points to the obvious need for therapeutic optimisation.

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Most doses of cytotoxic drugs are empirical, coming from previous experience and mainly tailored to avoid the most serious toxicity. There is an obvious large variation in the disposition of these drugs not just between patients but even within the same patient on different occasions. The variation in tumour response can partly be imposed by the variability in disposition. The pharmacokinetics and pharmacodynamics (PK-PD) is influenced by age, comorbidities and other patient-specific factors. Cytotoxic drugs may act as pro-drugs and may have active metabolites. This has to be taken into account when dealing with the pharmacokinetics of cytotoxic drugs. The tumour usually exhibits genetic polymorphism conferring a certain degree of drug resistance. Furthermore, blood supply for many tumours is highly irregular due to malfunctioning of blood vessels in the microenvironment surrounding the tumour. On both the disposition side and effect side there are interactions with endogenous and exogenous substrates in and around the tumour. The cytotoxic effect is difficult to measure and usually it takes a long time before it becomes obvious. The effect measures are difficult to quantify, although techniques using biomarkers or imaging with positron emission tomography might be useful.

Dosing of cytotoxic drugs is usually based on body surface area (BSA) and in the last 50 years most chemotherapy doses have been individualised according to this measure. There are several problems related to dose adjustment by BSA. Indeed, most studies have shown that BSA-based dosing does not reduce pharmacokinetic variability. Furthermore, BSA does not account for different body compositions, organ function, activity of metabolising enzymes, drug resistance, sex, age, concomitant diseases or co-administration of other drugs. There is also no relation between BSA and tumour size and type, or for accessibility of the drugs to the tumour. These difficulties with current practice warrant a change in dose adjustment routines. Other methods such as dosing per body weight or even flat dosing have, as expected, not improved the tailoring of dose.

Therapeutic drug monitoring of cytotoxic drugs

TDM means that therapy is followed by plasma concentration measurements and dose is adjusted accordingly. It is used for drugs with a narrow therapeutic margin, and for drugs with large inter- and intra-individual variations in dose – concentration relationships because of formulation, drug interactions, lifestyle, comorbidities, and also genetic variation in metabolism. The requirement to use TDM is when there are:

- no direct clinical measures that provide clear evidence of efficacy or toxicity
- therapeutic or toxic effects that are clearly related to plasma concentration of the drug
- drugs with a narrow therapeutic window
- drugs that are used for prophylaxis, e.g. epilepsy, mania, diabetes
- drugs that do not form active metabolites.

TDM is used to adjust the dose from the plasma concentration in order to achieve maximum effect and minimise drug-related toxicity, to monitor ongoing therapy and also to indicate patient compliance. TDM is routinely performed in the clinic for epilepsy drugs (phenytoin, carbamazepine), lithium, digitalis, cyclosporin and most antibiotics.

Can TDM significantly affect cytotoxic drug therapy? Yes, since it predicts toxicity better in some cases and increases efficacy in other cases. TDM gives an increased understanding of the large patient variability encountered regarding responses to drugs. Yet TDM is not used routinely for cytotoxic drugs. In fact, it is only commonly used for methotrexate. However, there is also long-term follow-up on 6-mercaptopurine in children with acute lymphoblastic leukaemia, as steady-state concentrations that are not high enough are associated with an increase in relapses. There is also some interest in monitoring 5FU as well as the new drugs for chronic myelogenous leukaemia and metastatic renal carcinoma. There are several reasons for this including:

- a lack of established therapeutic ranges
- a poor understanding of dose-concentration-response relationships
- a time lag between drug measurement and clinical effect.

TDM has not found its way into clinical oncology. Cytotoxic dosing is much more complicated than dosing for non-onco-

logical treatments. Good efficacy and low toxicity depend on an array of factors related to the individual patient, the cancer type itself and its genetic properties, and the tumour burden. Indeed, statistical methods exist to account for all these factors in the analysis of the optimal dose for any given patient. Population-based PK-PD, one such statistical approach, is increasingly being investigated in the field of oncology.

Population-based methods to optimise therapy

Population-based PK-PD models seek to determine how patient factors affect not just exposure to a drug but their response as well. The models, through the use of sophisticated software, simulate different dose regimens and treatment options. Indeed, such services are of importance to the pharmaceutical industry, with the aim of providing useful information from clinical studies in terms of how patients react to drugs. For example, by better identifying appropriate dose regimens fewer clinical trials may be needed, thus saving money.

More knowledge about cytotoxic PK-PD and the introduction of Bayesian modelling to aid in the prediction of optimal dosage of cytotoxic drugs may improve therapy outcome. Bayesian estimations have allowed for fine-tuning of doses as well as administration schedules to be accurately adjusted for cytotoxic drug therapies. It goes without saying that predictive methods and more individualised therapy are of value in optimising treatment outcomes. The ability to model PK-PD relations in the individual patient may optimise dosing of cytotoxic drugs with respect to both dose and dose intensity.

The advantages of population-based methods are that data from all patients given cytotoxic drugs can be modelled simultaneously in a population non-linear mixed effects analysis. The data include all information of cytotoxic drug kinetics in the patient, patient characteristics, disease properties, as well as effects on the tumour or encountered side effects. This method treats the population, rather than the individual, as the unit of analysis. By doing so, sparse data from many individuals can be analysed, and a more representative sample of the target population is obtained. It is possible not only to describe the mean tendencies in the population, i.e. the typical values, but also to describe the random effects, including variability between subjects, between occasions, and within a subject (residual variability). The model-building process is performed in a stepwise fashion. Covariates are entered in the model by forward inclusion and backward deletion. The procedure is to include all covariates one by one into the basic model and retain the model with the covariate-parameter relation causing the largest significant improvement in the objective function value. Several criteria are used to validate the resulting model, e.g. objective function values and best goodness of fit. This model serves as the new basic model and the stepwise inclusion procedure is repeated until no significant improvement is seen and this model then constitutes the full model. In the backward deletion the covariates in the full model is eliminated one by one until no more covariates can be eliminated from the full model without causing a significantly detrimental effect to the model fit. The computer software NONMEM (nonlinear mixed effect modelling) is usually used.

Conclusion

A better knowledge of the relationships between pharmacokinetic parameters or drug exposure variables, tumour growth, and treatment outcomes may improve treatment efficacy and patient outcomes by using *a priori* determination of the first dose and *a posteriori* Bayesian adjustment of the subsequent doses using population-based methods. Such models have the potential to eliminate many of the difficulties associated with BSA-based dose adjustments. Patient characteristics are used in the model to provide suggestions for optimal dosing of cytotoxic drugs. The method has shown success in several studies and is also used routinely to improve therapy. This is the way to reach the difficult goal of individualised and tailored dosages for optimal therapeutic results in the individual patient. The benefit of the population-based method promises to be optimisation of cytotoxic drug dosages, leading to better efficacy, fewer side effects, and more cost-effective treatment.

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Contamination from handling cytotoxic agents

Contamination of personnel who handle cytotoxics has been proven via traces in urine. Despite safety standards for handling cytotoxics, operators can still be exposed to them, mainly through skin contact. Identification of sources of contamination is recommended to improve working procedures.

Previous studies

Studies of contamination on vials, plungers of syringes, gloves, infusion bags, and work surfaces have been published.

Jean François Latour PhD

Vials

Some authors have measured the amount of cytotoxic drug present on the outer wall of vials containing these agents, on receipt from the pharmaceutical supplier. A significant number of vials had a quantifiable level of external contamination (up to 2.5 ng of 5FU per vial) [1-3].

Plungers of syringes

The contamination of the plungers of syringes used for handling cytotoxic drugs was measured [4]. The results showed that all the plungers were contaminated, amounts varying from 3.7 ng to 445.7 ng of cyclophosphamide.

Gloves

Gloves offer the first line of protection when handling cytotoxic drugs and are frequently in contact with these agents. A few studies showed that gloves used for biological safety cabinets (BSCs) were frequently (42–100%) contaminated during preparation of the drugs and cleaning of the hood [4, 5]. Favier et al. showed a contamination rate of 100% after only one dose was prepared. The amounts of cytotoxic agent detected were significant: Sessink et al. demonstrated up to 87 μg, and Favier et al. 180 μg [5, 6]. Because of the number of potential sources of contamination (drug preparation, vials, syringes, infusion bags, various surfaces), it is almost impossible to prevent contamination on the outside of gloves during normal work. Therefore changing gloves is recommended at least every 30 minutes. In addition, the quality of gloves must be carefully checked as shown by Wallemacq et al. [7].

Infusion bags

Infusion bags are an important source of contamination of gloves and environment. Studies carried out on the external surface of bags prepared in a pharmacy have shown that they became contaminated with cytotoxic agents, independent of the equipment used for their preparation (isolators or BSCs) [8, 9]. Favier et al. [8] found measurable amounts of 5FU on infusion bags varying from 70% to 100% for isolators, and 10% for BSCs.

Work surfaces

In several publications, surface contamination with different cytotoxic drugs (mainly cyclophosphamide, ifosfamide, 5FU and methotrexate) was estimated using a wipe sampling method [5, 8-10]. These studies were carried out on different surfaces, inside and outside the isolators and BSCs. The samples selected were potentially contaminated areas such as the work surface inside the isolator or the BSC, the floor in the preparation room, computers and furniture. Substantial levels of several antineoplastic agents were detected at various sites in drug preparation areas, whatever the equipment used. For example, Connor et al. indicated that 76% of the pharmacy samples were contaminated with measurable amounts of cytotoxic drugs.

Rhône Alpes studies

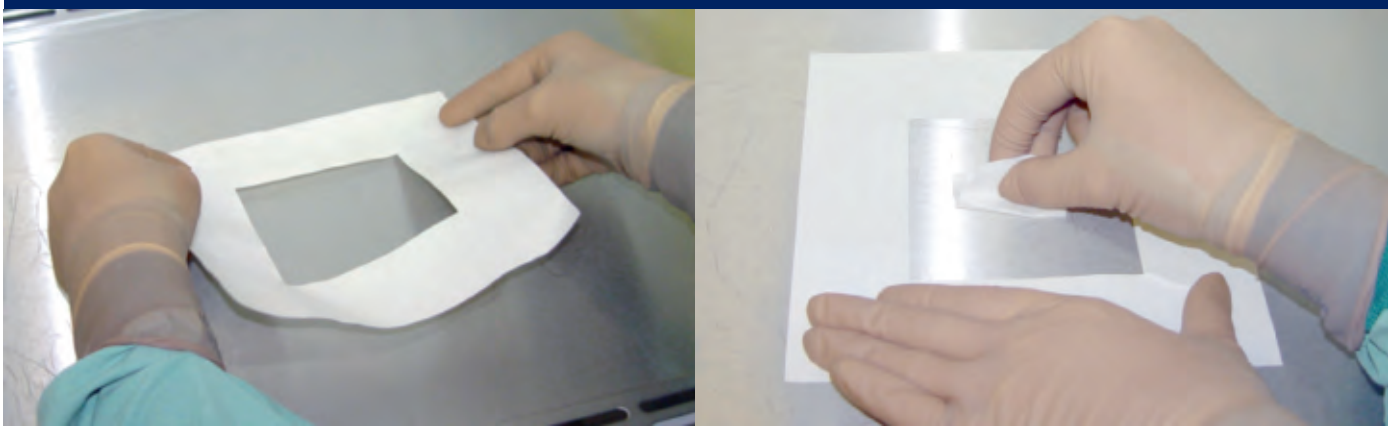
In 1999 we carried out a similar study in six French hospitals that perform between 3,500 and 26,500 preparations per year with the objective of determining the level of contamination with 5FU of different cytotoxic drug preparation units, three using BSCs and three using isolators [8]. The main results were:

- A higher rate of contamination inside and outside isolators compared with BSCs, with measurable amounts of 5FU detected in 79.2% (19/24) of the surface samples within isolators and 8.3% within BSCs (1/12). In the preparation rooms, 29.6% (8/27) of the surface samples outside isolators were found contaminated and no positive samples outside BSCs (0/29).
- 86.2% (25/29) of the samples collected on the outside of infusion bags prepared within isolators were contaminated but only 3.3% within BSCs (1/30).

In 2007, we carried out a larger study in 30 hospitals of the French Rhône Alpes region that are monitored by the ONCORA cytotoxics laboratory. The aims of this study were to measure the contamination with 5FU at various hospital sites (including the drug preparation and administration areas), to observe practices during the preparation of cytotoxic drugs and to make a comparison with the 1999 study.

The sampling locations were selected as potential areas of contamination on the basis of the results of previous studies. In each cytotoxic drug preparation unit, at least two samples were collected on the work surface within BSCs or isolators (one before cleaning and one after in order to evaluate the effectiveness of the decontamination procedures). Four more samples were also taken: two samples on the outer operator's gloves

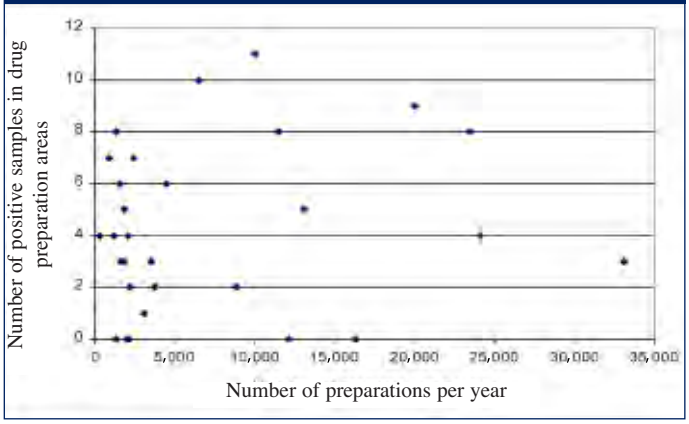
Figure 1: How we obtained standard samples from flat surfaces



and two on the outside of infusion bags. In addition, it was possible to get samples in some outpatient clinics. Samples from objects and surfaces were performed with moistened filters wiping calibrated surfaces when possible (for gloves and infusion bags, immersion in distilled water was used), see Figure 1. The preparation of cytotoxic drugs was centralised under the control of a pharmacist in 24 hospitals, 16 using BSCs and eight using isolators. It was under the responsibility of nurses in the last six hospitals, all equipped with BSCs. The number of doses prepared ranged from 325 to more than 33,000 per year. The preliminary results on the 555 collected samples were:

- Measurable amounts of 5FU were detected in 28% of the samples collected in preparation areas and 23% in the administration areas.
- A high rate of contamination of the outer preparation gloves (more than 60%) and a 20% rate of contamination of infusion bags were found. Some gloves were heavily contaminated.
- The level of contamination in the immediate preparation areas did not correlate significantly with the number of doses of chemotherapy prepared per year (see Figure 2). This confirms the importance of establishing strict working procedures under the control of a pharmacist.
- If we compare the results of the first two groups of hospitals performing preparation under the control of a pharmacist with BSCs or with isolators to those of the preliminary study, we still find a difference in terms of contamination between the two techniques, but with a smaller gap, suggesting that operating procedures have been improved.
- In the areas where the drugs are administered, many samples taken on nurses' gloves after they had connected or disconnected infusion bags were found to be contaminated. 5FU was detected in nearly half of the samples, but the number of samples collected was a little bit too low (only 18 samples collected): these preliminary results need to be confirmed by a larger study of contamination at the time of administration.

Figure 2: Contamination does not correlate with number of doses prepared



Conclusion

Contamination studies show that occupational exposure of workers handling cytotoxic agents can be controlled only if all the possible sources of contamination are identified and if suitable systems of protection are used. The validation of work procedures should include surface analysis of critical points such as gloves and various surfaces in pharmacies and wards. In addition, initial and continuing education of technicians, pharmacists and nurses is highly recommended to obtain as low a level as possible of cytotoxic contamination.

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Medical devices for safe handling of cytotoxic drugs

The main objectives of these devices are to protect patients against bacterial contamination and healthcare workers against chronic exposure to chemical contamination. Many manufacturers have developed medical devices for the safe reconstitution of cytotoxics.

For many years, the use of chemotherapy has been growing considerably. Because of the increase in this activity and the risk incurred by healthcare workers when handling cytotoxic drugs, safety devices have been developed to improve quality in the preparation of these drugs. Pharmacy technicians also require training.

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PharmD, PhD

Selection criteria for medical devices

Limitation of contamination

The imperative to limit both microbial and chemical contamination has led to the adoption of closed systems. According to the American Society of Health-System Pharmacists (ASHP), closed-system drug-transfer devices mechanically prevent the transfer of environmental contaminants into the system and the escape of drug or vapour out of the system [1]. This echoes the definition adopted by the National Institute for Occupational Safety and Health (NIOSH) [2]. This definition, taking into account drug vapour, clearly indicates that air-venting devices, even those with a 0.20 μm filter membrane, are not strictly closed-system devices. The recommendations of the GERPAC-Europharmat workgroup (the French isolators users' group - *Les Journées Nationales d'Etudes sur les Dispositifs* Médicaux) based their definition on that of the ASHP, but specified that closed systems should protect the operator against the escape of vapour, liquids and solids [3].

Compliance with these recommendations cannot be considered a substitute for ventilated cabinets or isolators.

Avoidance of needle risks

Avoiding the use of needles achieves several goals. Needles increase the risk of operator exposure to cytotoxic drugs by contact or injection. Moreover, the absence of a needle is a good way to decrease contact with liquid aerosols. These are caused by drug droplets squirting out, when the needle is withdrawn from the vial, if overpressure has been caused during manipulation. For these reasons, ASHP, GERPAC and Europharmat recommend needleless systems if possible. Unfortunately, the use of air-venting systems is not always possible, e.g. if the vial opening is too small, or for soap solutions. Needles are necessary in such cases. A needle safety transfer device may protect operators against the risk of puncture, but does not decrease the risk of aerosol formation.

Container–contents interactions

It is important to take into account the possible physico-chemical interactions between anticancer drugs and the device. In particular, devices containing plasticisers such as PVC should be avoided as much as possible [4-6]. It is then preferable to use devices made of polyolefins (polyethylene, polypropylene) or polyurethane. In addition, chemical contaminants from the surroundings cross the wall of a device (permeation). It can occur during sterilisation with peracetic acid [7] or hydrogen peroxide. Permeation through medical devices is a potential toxic risk to the patient and the loss of stability of the drug may be revealed by a pH change.

Figure 1: BD Blunt safety transfer device

Figure 2: PCHIMX-1

Figure 3: Tevadaptor

Figure 4: Closed-system device Phaseal

Classification of devices

The latest International Society of Oncology Pharmacy Practitioners (ISOPP) standards [8] classify special devices for the reconstitution and administration of cytotoxic drugs as follows:

(1) Devices to protect the handler of the vial/ampoule
(2) Devices to protect the operator during preparation
(3) Devices to protect the administrator during administration of the cytotoxic drug to the patient.

Devices/systems used to transfer the drug solution from a vial to an infusion bag fall in class 2. ISOPP standards specify that manufacturers have to indicate if the device can be used for the entire or only a part of the preparation process, if the device can be used if more than one vial is necessary for a preparation, and if studies demonstrate the ability of the device to reduce or eliminate environmental contamination.

Class 2 devices may be divided into two groups, based on their function: devices to access the primary vial (access and reconstitution devices) and devices to access the infusion bag (dilution devices). For the reconstitution devices, four points have to be strictly controlled: limitation of aerosol formation, asepsis, safe use and the residual volume. For dilution devices, we have to be vigilant on the universality of use, maintenance of asepsis, safe use and minimal chemical contamination.

Access and reconstitution devices [9]

If a needle is required, a safety transfer needle can be used to decrease the risk of needlestick. The Blunt Fill needle (see Figure 1) has a special bevel (45° angle). This bevel is sufficient to penetrate the cap, but ten times the force is needed to puncture the skin or the operator's gloves. Nevertheless, the risk of an aerosol is not reduced.

Spikes are widely used to access the vial. The syringe connection to the spike must be the Luer-lock type for safety. Important criteria include the type of connection (bidirectional valve or not), a single or double channel, the residual volume, or pore size of the air filter (0.45 μm or 0.20 μm). The double channel spikes (Baxter's Chemo-Aide Pin, Codan's Spike, Hospira's CS-51 Spike, B.Braun's Chemo-Spike) incorporate an air vent protected with a 0.22 μm hydrophobic filter. B.Braun's Mini-spike has a 0.45 μm hydrophobic air filter. Hospira's CS-53 spike only has one channel.

Dilution devices

Dilution devices allow access to the bag contents. The selection criteria for these devices are the polymer used for manufacture, a bidirectional valve to allow needle-free operation, a Luer-lock connection, and the residual volume.

Chemo-set and Connect-Z are two extension sets. They are used with special infusion devices to which they are connected by a bidirectional valve, allowing needle-free manipulation. The Luer lock between the extension set and the infusion set ensures safe transfer of the anticancer drug solution. PCHIMX-1 (see Figure 2) is a recent special extension set. It is a device with two independent entrances made to be connected to two infusion bags. Like the other devices, it allows safe handling because it has a bidirectional valve on the tube that is connected to the cytotoxic drug infusion bag.

Devices called in practice 'closed systems'

The Tevadaptor (see Figure 3) is a 3-part device including a vial adapter, a syringe adapter and an infusion bag adapter. The vial adapter fixes firmly to the vial. It has a dual channel perforator with a hydrophobic 0.22 μm air-filter. The infusion bag adapter contains a perforator with two channels: one for the injection of the cytotoxic drug solution and another for the administration. The syringe adapter allows the transfer of the solution from the vial to the infusion bag using a Luer connection to reinforce safety. Nevertheless, the Tevadaptor cannot be considered, or recommended, as a closed-system device.

PhaSeal from Carmel is the only closed-system device suitable for handling cytotoxic drugs (see Figure 4). It allows the drug to be transferred from the vial to the syringe and then to the infusion bag without any contact between the drug and the environment at any time. This multi-component system uses a double membrane to enclose a specially cut injection cannula as it moves into a drug vial, Luer-lock, or infusion-set connector. Several studies comparing PhaSeal to traditional techniques show a significant reduction in environmental contamination if this device is used [10, 11].

Conclusion

Cytotoxics can be safely reconstituted if aseptic handling is strictly respected and chemical contamination is minimised. Devices decrease the risk of chemical contamination and maintain a good level of asepsis. However, these devices must be used in a clean environment and operators must wear protective clothing and must be regularly trained and evaluated.

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Asian activities in oncology pharmacy

The Asia for Safe Handling of Cytotoxic Drugs Interest Group aims to further develop guidelines and training for oncology pharmacists in the region.

Oncology pharmacy in Asian countries including Thailand really began to develop around 1996. The main focus was to enhance safety in the handling of cytotoxic drugs, which was mainly carried out by nursing staff. Initially some pharmacists in the region received training in Australia and the US in order to learn how to safely handle cytotoxic drugs. Since then the handling of cytotoxic drugs has become part of the growing responsibilities of pharmacy departments in Thailand. This has brought about new opportunities not just for professional career advancement, but also for collaboration among hospital pharmacists in Asian countries. This will undoubtedly help oncology pharmacy practice advance in the region.

Kamonsak Reungjarearnrung RPh

The Asia for Safe Handling of Cytotoxic Drugs Interest Group was formed in 2004 in response to Asian pharmacists' concerns over the safe handling of cytotoxic drugs in their workplaces. Whilst in some places there may already be protocols, procedures or guidelines for safe handling, there was not a common platform in Asia to share experiences and 'best practices'. The intention of the Asia for Safe Handling Interest Group is to provide practical guidance for pharmacies, clinics and community settings. Therefore, guidelines have been developed by a panel of experts utilising data from published evidence or from accepted 'best practice'.

The highlights of the work and collaborations of the group are:

- An annual aseptic dispensary training programme held in Malaysia, Singapore and Thailand, which is designed also for pharmacy students.
- An exchange training programme for oncology pharmacists through grants provided by the Asia for Safe Handling Group of Cytotoxic Drugs Interest Group and others.
- The 1st Asia Pacific Oncology Pharmacy Congress, 3–5 August 2006 in Bangkok, Thailand, served as a platform for those in areas of oncology pharmacy sciences to get together to share recent developments and network with international colleagues, with the aim of improving cancer care through scientific research and evidence-based practice.
- The 2nd Asia Pacific Oncology Pharmacy Congress, 11–13 September 2008 was entitled 'Translating Evidence-based Medicine into Oncology Pharmacy Practice'. The congress focused on the practical application of evidence-based medicine and intended to highlight advancements in oncology to improve the quality of pharmaceutical care. These events also acknowledged members who have made outstanding contributions to oncology pharmacy practice in this region.

Most Asian nations now have mandated that the handling of cytotoxic drugs is part of good practice in drug management systems and that the pharmacy department in the hospital is responsible. Therefore, practical guidance on the safe handling of cytotoxic medicines is a necessity. We have been working on the establishment of a residency training programme, as well as Board certification, research grants and scholarships, and also exchange training programmes, including those designed for pharmacy students.

The Asia for Safe Handling of Cytotoxic Drugs Interest Group is also working to support those countries, such as Cambodia, Laos, Myanmar, and the Philippines which need help in developing practice standards. We plan to review guidelines at regular intervals to ensure they reflect current knowledge and changes in health and safety legislation.

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EJOP – Call for papers

The main objectives of the *European Journal of Oncology Pharmacy* (EJOP) are providing information on current developments in oncology treatment, sharing practice related experiences as well as offering an educational platform via conference/seminar reports to practising oncology pharmacists and pharmacy technicians. The editorial content covers scientific, clinical, therapeutic, economic and social aspects. Prospective authors are welcome and invited to share their original knowledge and professional insight by submitting papers concerning drug developments, safety practices in handling cytotoxics and breakthroughs in oncology treatment along with practice guidelines and educational topics which fall within the scope of oncology pharmacy practice. Manuscripts must be submitted in English, the journal offers English support to the manuscript content. The EJOP 'Guidance for Authors' can be found on the website (www.ejop.eu), where the journal is freely available in PDF format. You are encouraged to discuss your ideas for manuscripts with us at editorial@ejop.eu.

Highlights of the Joint ECCO 15–34th ESMO Multidisciplinary Congress

This new partnership has launched a strong congress. The first joint ECCO 15–34th ESMO Multidisciplinary Congress took place in Berlin, Germany, 20–24 September 2009 and attracted 15,000 delegates from near and far. EJOP highlights a selection of topical reports, the latest advances in oncology.

Professor Branko Zakotnik, MD, PhD

Professor Dirk Schrijvers, MD, PhD

With a strong commitment to unite oncology in Europe, the European CanCer Organisation (ECCO) and the European Society for Medical Oncology (ESMO) have joined forces to combine the two leading educational opportunities in European oncology — the ECCO and ESMO congresses — every other year. Offering a unique platform to embrace all oncology specialities, the joint congress reflects the mission of both societies to promote a multidisciplinary focus on oncology and uphold the right of all patients to the best treatment and care available.

Thanks to the tremendous efforts of Professor Alexander Eggermont, ECCO President and 2009 Congress President, Professor José Baselga, ESMO President, Professor Chris Twelves, Co-Scientific Chair (ECCO), Dr Fortunato Ciardiello, Co-Scientific Chair (ESMO) and other leading figures, the Scientific Committee assembled an in-depth and comprehensive programme. This report discusses the highlights of the congress scientific programme.

Several important abstracts confirmed the importance of *KRAS* as a predictive biomarker of anti-epidermal growth factor receptor monoclonal antibodies in first-line metastatic colorectal cancer (mCRC) in combination with chemotherapy.

The randomised phase III study of panitumumab with FOLFIRI versus FOLFIRI alone as second-line treatment in patients with mCRC was presented by Peeters. A total of 1,186 patients were randomised. For patients with wild-type (WT) *KRAS*, median progression-free survival was 5.9 months with and 3.9 months without and panitumumab ($p = 0.004$); median overall survival 14.5 months with and 12.5 months without and the monoclonal antibody; and response rate (by blinded central review) was 35% and 10%. There was no difference in progression-free and overall survival or response rate among patients with mutated *KRAS*.

Intermittent versus continuous oxaliplatin-based combination chemotherapy was tested in a randomised non-inferiority trial (MRC COIN) in 1,630 patients with advanced colorectal cancer[1]. Median overall survival on continuous treatment was 15.6 months versus 14.3 months on intermittent treatment. The primary analysis of the ± cetuximab comparison was in the cohort of WT *KRAS* patients. Tumour samples from 1,305 (80%) patients were available for *KRAS* analysis. WT *KRAS* patients numbered 724 (56%), while 561 (43%) had a *KRAS* mutation. Patients in the second arm experienced significantly greater grade 3/4 diarrhoea, skin rash, lethargy, hand–foot syndrome, and hypomagnesaemia, but significantly less grade 3/4 peripheral neuropathy. The researchers observed no evidence of any differences in treatment-related or 60-day all cause mortality between the two arms. Presenting results, Maughan said that the estimated difference in favour of continuous treatment needs to be balanced against the reduced toxicity observed with intermittent treatment.

A randomised phase III study comparing epirubicin, docetaxel, and capecitabine (EDC) to epirubicin and docetaxel (ED) as neoadjuvant treatment for early breast cancer was reported by Steger[2]. The primary aim of the study was an improvement of the pathological complete response rate. Five hundred and twelve patients were eligible for the toxicity and efficacy study. In the intention-to-treat analysis there was no significant difference in the incidence of serious adverse events. In the EDC arm significantly more patients had documented a pathological complete response (23.8% vs. 15.2%; $p = 0.036$) despite the fact that significantly fewer patients completed the scheduled six cycles (EDC: 75% vs. ED: 97%; $p < 0.0001$) mainly due to capecitabine-induced side effects.

Results of a randomised phase III study comparing denosumab versus bisphosphonate zoledronic acid for the treatment of breast cancer patients with bone metastases was presented by Stopeck[3]. Denosumab significantly delayed the time to first on-study skeletal-related event (SRE) compared with zoledronic acid ($p = 0.01$) in this 34-month study. The median time to first on-study SRE was not reached for denosumab, and was 806 days for zoledronic acid. Denosumab also significantly delayed the time to first and subsequent on-study SRE (multiple event analysis) compared with zoledronic acid ($p = 0.001$).

Three presentations focused on patients with advanced non-small cell lung cancer (NSCLC) harbouring epidermal growth factor receptor EGFR mutations underlying the growing body of evidence of genotyping tissue for taking clinical decisions. Tsurutani presented on behalf of the West Japan Oncology Group results of a comparison of gefitinib versus cisplatin plus

docetaxel for patients with advanced or recurrent NSCLC harbouring activating mutation of the EGFR gene[4]. Two hundred patients were randomised showing that gefitinib significantly prolonged response rate (56.3% vs. 25.3%) and progression-free survival (9.2 months vs. 3.6 months; $p < 0.001$) compared to chemotherapy. Haematological toxicity was more pronounced in the chemotherapy arm while skin rash and liver function test disturbances were more seen in the gefitinib arm.

Similar results were found also by Kris who presented pooled results of the four main studies comparing gefitinib (ISEL, V-15-32-INTEREST-IPASS) versus placebo or chemotherapy in 1,006 patients with EGFR mutations[5]. In every study, overall response rate (ORR) was numerically better for gefitinib than comparator in EGFR-mutation positive patients, and similar or poorer than comparator in EGFR-mutation negative patients: in patients with EGFR mutations, ORR with gefitinib was 71% when used initially and ranged from 38–67% in studies where gefitinib was given after chemotherapy. A trend similar to ORR was observed for progression-free survival or time to treatment failure, with longest median values in gefitinib-treated EGFR-mutation positive patients (range 7–11 months).

Taken together, these analyses indicate that efficacy of gefitinib in EGFR-mutated patients is consistent across all lines and ethnicities (Asians versus non-Asians) and stresses the importance of the knowledge of EGFR mutation status when selecting a treatment with tyrosine kinase inhibitors regardless of line of therapy.

The treatment of locally advanced head and neck cancer recently underwent important changes with the introduction of new radiotherapy techniques and the addition of chemotherapy or targeted agents to radiotherapy. These techniques can produce better treatment outcomes in terms of local control and survival but add higher acute and late toxicity. However, long-term results of newer treatment modalities in relation to outcome are still scarce.

Rivera looked at the recurrence patterns in 50 patients with squamous cell carcinoma of the head and neck (SCCHN) treated with intensity-modulated radiotherapy (IMRT) with or without chemotherapy[6]. At a median follow-up of 22 months, 14 loco-regional failures (persistent disease or relapse) were observed. Five were in-field, five were marginal, and four occurred out-field. Two of those marginal failures had received more than 95% of the prescribed dose on more than 95% of the failure gross tumour volume. The 2-year overall survival, local disease-free survival and loco-regional disease-free survival rates were 73%, 78% and 72%, respectively. The authors concluded that despite a high rate of loco-regional and overall disease-free survival, target volume delineation and definition of margins should be analysed with accuracy because local failure remains a major issue.

The PARSPORT trial showed that sparing the salivary glands through the use of IMRT significantly reduced the incidence of xerostomia in patients with pharyngeal tumours (Nutting)[7]. In this trial two radiotherapy delivery methods were compared in the treatment of 94 patients with pharyngeal tumours. After a median follow-up of 31.9 months; 12-month LENT-SOMA ≥G2 xerostomia scores (an international scoring system for Late Effects on Normal Tissues) were observed in 74% of radiotherapy and 40% of IMRT patients ($p = 0.005$). Corresponding values at 18 months were 71% and 29% ($p = 0.004$). On the Radiation Therapy Oncology Group (RTOG) scale, 12-month ≥G2 xerostomia was reported in 64% radiotherapy versus 41% IMRT patients ($p = 0.06$). The 18-month incidence was 81% for radiotherapy versus 20% for IMRT ($p < 0.001$). Acute radiotherapy related ≥G2 fatigue was more prevalent in the IMRT group (76% vs. 41%; $p = 0.001$). No differences in acute mucositis or pain scores were seen. At 12 months, no statistically significant differences were seen in other late toxicities. No differences were observed between overall survival and loco-regional control rates.

This year, the *35th ESMO Congress, 8–12 October 2010 in Milan, Italy*, will build upon the success of last year's ECCO-ESMO Congress. Likewise in 2011, the *ECCO 16 – 36th ESMO Multidisciplinary Congress, 23–27 September 2011 in Stockholm, Sweden*, will capitalise on the 2010 Congress, resulting in continual and dynamic advances in research and technology as well as a wealth of oncology resources and best practices to be shared by oncology professionals across Europe.

Congress webcasts
www.ecco-org.eu/Conferences-and-Events/ECCO-15-ESMO-34/Webcaptured-Sessions/page.aspx/1835

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[1] Maughan Abstract 15LBA
[2] Steger Abstract 4BA
[3] Stopeck Abstract 2LBA
[4] Tsurutani Abstract O-9002
[5] Kris Abstract O-9003
[6] Rivera Abstract P8515
[7] Nutting Abstract G4

Clinically relevant news from the ASH 2009 meeting

Highlights of the 51st American Society of Hematology Annual Meeting in New Orleans, USA, December 2009, included increasing knowledge about thrombophilia and integration of aspects of complementary medicine in oncologic care.

The American Society of Hematology is the world's largest professional society concerned with the causes and treatment of blood disorders. ASH organises an annual scientific and educational meeting, the complete programme and abstracts for which can be found at www.hematology.org/2009abstracts. ASH also provides an online resource addressing bleeding and clotting disorders, anaemia and cancer, called Blood: The Vital Connection (www.bloodthevitalconnection.org).

Professor Günther J Wiedemann, MD, PhD — Professor Wolfgang Wagner, MD, PhD

Cancer and venous thromboembolism

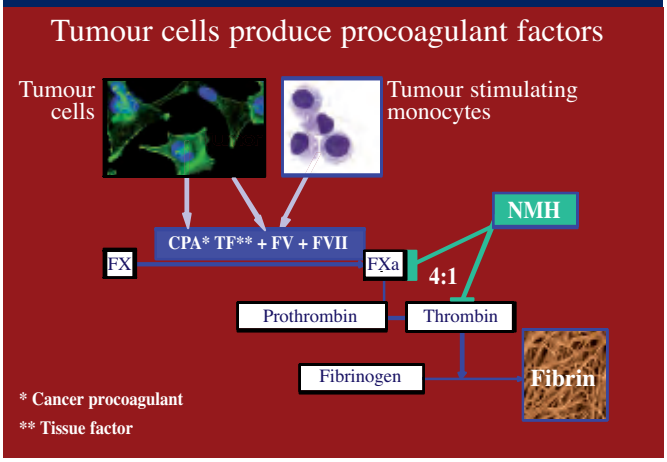
Thromboembolism is a well known complication of malignant disease. The standard treatment for acute venous thromboembolism consists of initial therapy with low-molecular-weight heparin (LMWH) followed by long-term therapy with an oral anticoagulant. This approach is highly effective in most patients, but patients with cancer have a substantial risk of recurrent thromboembolism and haemorrhagic complications. The pathogenetic mechanisms of thrombosis involve a complex interaction between tumour cells, the haemostatic system, the genetic risk factors of the patient, long-term immobilisation, surgery and chemotherapy, with or without adjuvant hormone therapy. The activation of blood coagulation in cancer patients is complex and multifactorial (see Figure 1). Briefly, prothrombotic mechanisms are related to the host response to the malignant disease and include the acute-phase reaction, paraprotein production, inflammation, necrosis, and haemodynamic disorders.

Chemotherapy and radiotherapy support these procoagulant effects. Tumour cells produce procoagulant factors, i.e. tissue factor (TF) and cancer procoagulant (CPA). TF, which is the primary activator of blood coagulation, forms a complex with factor (F) VII to activate FX and FIX by proteolysis. In malignant cells, TF is constitutively expressed. In addition, tumour cells induce platelet activation and aggregation by direct cell-cell contact or by releasing soluble factors, such as ADP, thrombin, and other proteases.

Genetic risk factors of thrombosis

Venous thrombosis is more common in the elderly (the majority of cancer patients are older than 65 years). Interactions between various risk factors determine the development of the disease, and the proportion of variance attributable to genetic factors may be as high as 50–60%. There are six strong genetic risk factors. The first three are heterozygous deficiencies of the natural anticoagulant protein C, protein S, and antithrombin. These deficiency states are quite rare in the general population. The risk for the development of venous thrombosis may be increased 10–20 fold in these deficiency states. There are also three genetic factors associated with an increase in the procoagulant potential of the coagulation system: blood-group non-0, factor V Leiden (APC resistance) and prothrombin G20201A. The increase in thrombotic risk is about threefold or sevenfold for prothrombin G20201A and factor V Leiden, respectively. However, blood group non-0 is the most common of the prothrombotic genetic risk factors, and approximately doubles the risk of venous thrombosis.

Figure 1: LMWH for the prevention of recurrent venous thromboembolism in cancer patients



In a study by AYY Lee et al, published in N Engl J Med. 2003;349:146-53, dalteparin (200 IU/kg body weight, once daily) or warfarin was given to cancer patients over a six-month study period. Dalteparin was more effective than the oral anticoagulant in reducing the risk of recurrent thromboembolism without increasing the risk of bleeding. These are exciting results since it is known that the oral anticoagulants warfarin and phenprocoumon have several severe problems: narrow therapeutic margin, delayed onset of action, difficulty with reversal, many interactions with other drugs, dietary effects, wide variation in sensitivity and the need for frequent laboratory monitoring. Poor anticoagulant control can result, leading to recurrent thrombosis with undertreatment or to bleeding with excessive effect. The risk of major bleeding on warfarin is between 1–5% per year, and bleeding complica-

tions due to anticoagulants are among the most frequent adverse drug effects. New developments in oral anticoagulation are necessary to improve patient care.

Rivaroxaban

Rivaroxaban is a significant new substance in oral anticoagulation inhibiting factor Xa. In a large, double-blind, phase III study, 1,197 patients with a high risk of thromboembolism received either once-daily oral rivaroxaban 20 mg (Xarelto) or placebo to measure the efficacy (reduction of symptomatic venous thromboembolism) and undesired effects (bleeding) of rivaroxaban. Treatment with rivaroxaban was found to be both safe and effective. Only 8 out of 602 patients (1.3%) on rivaroxaban showed signs of recurrent venous thromboembolism, compared with 42 out of 594 patients (7.1%) in the placebo arm. In the rivaroxaban arm, 4 patients (0.7%) experienced major bleeding, though none of these were fatal or at a critical site (see Abstract #LBA-2).

Integrating complementary medicine

Integrative therapies have been 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'. Although this field is still in its infancy, there is much that is now evidence-based in integrative therapies that can assist the medical oncologist or pharmacist in improving the quality of life of the patient. In addition, the majority of patients with malignant diseases are utilising one or more integrative therapies during their conventional treatment with or without the knowledge of their physicians or pharmacists.

There are now evidence-based studies using complementary therapies, such as acupuncture and mind-body medicine, that illustrate reduction of disease or treatment-related side effects and overall improvement in well being and quality of life. There are still, however, areas of complementary and alternative medicine that are troubling and raise ethical concerns.

At the recent ASH meeting various cellular, immunological and related mechanisms for specific compounds found in traditional herbal medicines, used as supplements for standard chemotherapeutic treatments, were also reviewed. This included beta-glucan in medicinal mushrooms, arsenic trioxide, and propolis. Studies are focusing on the different classes of herbal-derived compounds which may enhance distinct immune cell populations and even target cancer stem cells. Some might potentially contribute to the holistic anticancer treatment regimen in the future.

Some European studies examining the effects of complementary and integrative medicine in supportive care, integrative psycho-oncology, and quality of life, especially in cancer survivors, were summarised. The results from interventions with Tai Qi, Qi Gong, Reiki, Nordic walking, aroma-massage, phytotherapy, music-therapy and gymnastics are impressive especially in treating fatigue, cognitive impairment and psychologic/social problems.

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12th Annual Symposium of the British Oncology Pharmacy Association

The need for clear, accurate pharmacy data was a key topic at the 2009 annual symposium for UK oncology pharmacists.

For the first time the British Oncology Pharmacy Association (BOPA) and the UK Oncology Nursing Society joined forces in a combined annual conference. Around 700 delegates and speakers converged in Brighton, UK, where they enjoyed a programme of more than 60 presentations and themed work-streams that ran from 15–18 October 2009.

Janis Smy
BSc

Development of clinical pharmacy standards in oncology

Ms Joanne Robinson, Senior Oncology Pharmacist at NHS Forth Valley, Scotland, and a member of the Scottish Oncology Pharmacy Practice Group (SOPPG), outlined how the aseptic capacity plan for Scotland has been updated, to take account of the increasing complexity of chemotherapy preparation, the use of dose-banded products, the management of both inpatients and outpatients, and the varying requirements of oncology and haematology.

To inform the care model, pharmacists across Scotland were asked to 'test their assumptions' by measuring the actual time taken to provide various aspects of care for outpatients and in-patients. The subsequent updated model has been endorsed by the Scottish Directors of Pharmacy Group, and will undergo validation. It will be shared nationwide, and SOPPG will work with BOPA to develop UK quality standards for cancer pharmacists.

Can pharmacy collect better data?

Following a report by the UK National Chemotherapy Advisory Group, calling on pharmacy departments to improve the collection of data on chemotherapy use, Dr Calum Polwart, Network Pharmacist at the North of England Cancer Network, considered how the acquisition of data can be improved in practice.

Dr Polwart warned that clear reference cost data were essential to the formulation of the forthcoming national chemotherapy tariff. Not all trusts are using the regimen codes stipulated by the Office of Population, Censuses and Surveys, and it is possible that the list of codes might not be adequate for all the treatments used. Citing FEC (fluorouracil, epidoxorubicin and cyclophosphamide) as an example, he asked the delegates to consider just some of the potential sources of confusion. Does FEC mean FEC-50, FEC-60, FEC-75 or FEC-100? Is FEC the same thing as ECF?

He urged pharmacists to make sure they include all the costs, including those associated with for example, consumables, staff, outsourcing, maintenance and cleaning. But he also delivered a reminder that clinical data must also be collected.

Radiotherapy side effects

Around 60% of patients with cancer receive radiotherapy, yet few cancer nurses have sufficient knowledge of its side effects. Professor Sara Faithfull, Cancer Nursing Practice at the University of Surrey, Guildford, UK, pointed out that many of the side effects appear several months or even years after the treatment has ended, at a time when patients may be undergoing chemotherapy and/or biological therapy. She called for improved treatment pathways and patient surveillance, to ensure prompt, effective management of late side effects.

On the topic of the early side effects of radiotherapy, Ms Mary Wells, Senior Lecturer in Cancer Nursing at the University of Dundee, Scotland, considered the management of acute skin reactions. Over 90% of radiotherapy recipients develop erythema, and 10–46% experience moist desquamation. The problem is complicated by the skin toxicities of other treatments. Good communication between services is vital because skin toxicities tend to be at their worst at the end of treatment, when the patient is under the care of the GP rather than the specialist centre.

Dr Isabel White, Macmillan/Remedi Clinical Research Fellow in health and social care at King's College, London, UK, explored the long-term effects that radiotherapy can have on sexual health. For example, up to 80% of men who receive external beam radiotherapy go on to experience erectile dysfunction, with an onset as late as three years after the completion of treatment. Thirty per cent of women who undergo radiotherapy of the cervix and endometrium report sexual dysfunction, and 50% report dyspareunia.

Dr White said that all radiotherapy treatments can diminish sexual expression, and that the effects are compounded by other treatment modalities. The time had come, she said, to make sexual rehabilitation in oncology a mainstream issue for funding, service development and delivery.

The 2010 BOPA Annual Symposium will be in Brighton, UK, 15–17 October.

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Polish-German conference on oncology pharmacy

Polish-German conferences in oncology pharmacy have become an established tradition. The 6th conference took place in Dresden, Germany, on 12–13 June 2009, with the theme 'Training close to practice with certainty'.

The programme of the conference included plenary lectures, workshops and a satellite symposium organised by GlaxoSmithKline on oral therapy in oncology. The lectures covered different aspects of advances in the treatment of malignant tumours and practical problems of quality and safety of oncology pharmacy services.

In a key lecture 'Targeted treatment of haematologic malignancies shows a new way in oncology', Professor Holowiecki, Oncology Institute in Gliwice, Poland, said that thanks to recent advances in our understanding of the molecular pathology of leukaemia, targeted therapies directed toward specific genetic lesions within malignant cells have been developed. These have contributed to advanced cure rates with low toxicity. Such progress is best exemplified by the use of all-trans retinoic acid (ATRA) as part of therapy for acute promyelocytic leukaemia, which nowadays is curable for 84% of patients. For example, the introduction of the tyrosine kinase inhibitor, imanitib, has also revolutionised the treatment of chronic myelogenic leukaemia and significantly improved the prognosis. Imanitib inhibits the BCR-ABL fusion protein, a constructively activated form of the ABL tyrosine kinase, which plays a crucial role in the pathogenesis. However, due to the development of imanitib resistance, new drugs have recently been registered: dastinib and nilotinib. In acute myeloid leukaemia (AML) studies have focused on FLT-3, *c-kit* and farnesyl transferase inhibitors. It has been found that for optimal results FLT-3 inhibitors in combination with other agents will probably be required. Tipifarnib, a farnesyl transferase inhibitor, for instance, was found to enhance the etoposide activity in resistant AML, while as a single agent it has limited efficacy. Many small molecule drugs are currently in trials for the therapy of solid tumours such as breast cancer (lapatinib), renal cancer (sorafenib and sunitynib) and non-small cell lung cancer (erlotinib). Over the last two decades, detailed studies have led to the selection of targets for humanised monoclonal antibodies and immunoconjugates. Their success is best demonstrated as part of the treatment of non-Hodgkin lymphomas and B cell-derived leukaemias. Monoclonal antibodies are also useful for the treatment of T cell malignancies and myeloblastic leukaemia as well as some solid tumours (breast and renal carcinoma). Professor Holowiecki concluded his lecture by saying that recent advances in targeted treatment should lead to a significant improvement in cancer therapy.

Dr Gil from Poznań, Poland, continued the topic by discussing tyrosine kinase inhibitors in the treatment of chronic myelogenic leukaemia, while Professor Palka from Bialystok, Poland, focused on new strategies of inhibition receptors of epidermal growth factor and vascular growth factor. The topic of patient information was also discussed by Y Remane from Leipzig, Germany, and information leaflets for patients about the correct use of dasatinib were also presented by E Korczowska and H Jankowiak-Gracz from Poznań, Poland.

Participants of the workshop

Three German (aseptic work, case reports and psycho-oncology) and two Polish (case reports and psycho-oncology) workshops were also excellently prepared and led, with all the participants engaged in lively discussions.

I am sure that all the conference delegates went back home enriched with new knowledge and ideas, as well as with a feeling of a stronger friendship between oncology pharmacists in both countries.

We are already looking forward to the 7th Polish-German Conference, which will be held in June 2010 in Wroclaw, Poland.

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10th Annual Meeting of Polish oncology pharmacists

This meeting highlighted both the necessity and opportunities for oncology pharmacy in Poland as in other European countries.

This meeting, held in Warsaw, 19-22 October 2009, was also the 10th anniversary of the oncology pharmacy movement in Poland, and invitations were extended to important guests such as Ms Carole Chambers, the President of ISOPP, Mr Klaus Meier, President of ESOP, and Dr John Wiernikowski, Paediatric Oncology Pharmacist, Canada.

During the opening ceremony Ms Carole Chambers explained to participants (nearly 150) the activities of the International Society of Oncology Pharmacy Practitioners and highlighted the benefits of being a member. This was followed by the opening lecture entitled 'To be patient. To be ill, to cure, to die and to live', given by Professor Tadeusz Kobierzycki, Professor of Philosophy, Music University, Warsaw. This was an anthropological perspective and overview of how the problems of life, disease, and death were treated in ancient and modern philosophy. He defined also disease and health from a philosophical point of view and characterised patients in relation to their behaviour in disease.

Recent advances in oncology were highlighted by Professor Dr Jedrzejczak who spoke about new drugs and targets in haematological malignancies. He focused on target therapy, underlining the role of imanitib in the development of new therapeutic agents and discussed some of the most recent clinical trials involving dasatinib, nilotinib and bosutinib. Professor Dr Szczylik examined the molecular basis of carcinogenesis, and the ways in which to affect different molecular pathways, using, as an example, targeted therapy of renal cell carcinoma with sunitinib, sorafenib, temisirolismus and bevacizumab.

Delegates were also treated to lectures on the optimisation of pharmacotherapy in the elderly; antitumour treatment in pregnancy and practical considerations in paediatric oncology pharmacy. This was presented by Dr J Wiernikowski from McMaster Children's Hospital in Hamilton, Canada. He discussed known risk factors and facts about childhood cancers. Dr Wiernikowski also spoke about specific drug and treatment issues and also gave an overview on clinical aspects including assessing toxicity, neutropenia, infections, neuropathies, thrombosis and nausea and vomiting which differ from those in adults. The subsequent effects of paediatric cancer treatment are very often unperceivable and unappreciated. These include a lower health quality of life for survivors than in the general population; cardiac complications (especially with anthracyclines); neurocognitive deficiency; obesity; endocrine complications (GH deficiency, primary hypothyroidism and hyperthyroidism); metabolic complications; decreased bone mineral density; and secondary cancers. People who were cured of cancer in their childhood have also very often poorer social outcomes. Dr Wiernikowski described some possible interventions.

During the last plenary session of lectures Dr Filipczyk-Cisarz looked at the cardiotoxicity of cytostatics. She described the mechanisms of cardiotoxicity of anthracyclines and vinca alkaloids. Cardiotoxicity can also be a side effect of target therapy drugs such as lapatinib and imatinib as well as hormonal agents, especially aromatase inhibitors. Dr Filipczyk-Cisarz gave practical advice on how to cope with the problem, and also emphasised that while qualifying patients for treatment the risk of cardiac complications should be taken into consideration.

In his presentation, the ESOP President, Mr Klaus Meier, emphasised the need for good patient support as the basis for improved collaboration between all health professionals. The oncology pharmacist can make an important contribution to this collaboration. He also emphasised the continued necessity and opportunities for oncology pharmacy in Poland as in other European countries.

During the conference there was also the opportunity for delegates to meet with the Chief Pharmaceutical Inspector. This, importantly, was the first time Polish oncology pharmacists had the chance to discuss their problems directly with the most important pharmacy officer in Poland. The discussion was often heated and lasted long after the scheduled time, but was indeed thorough. Attendees were reassured that the Chief Pharmaceutical Inspector is very interested in the problems of the oncology pharmacist and will try to solve some of them! It was agreed that this was a successful meeting which should be continued in the future.

Author

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