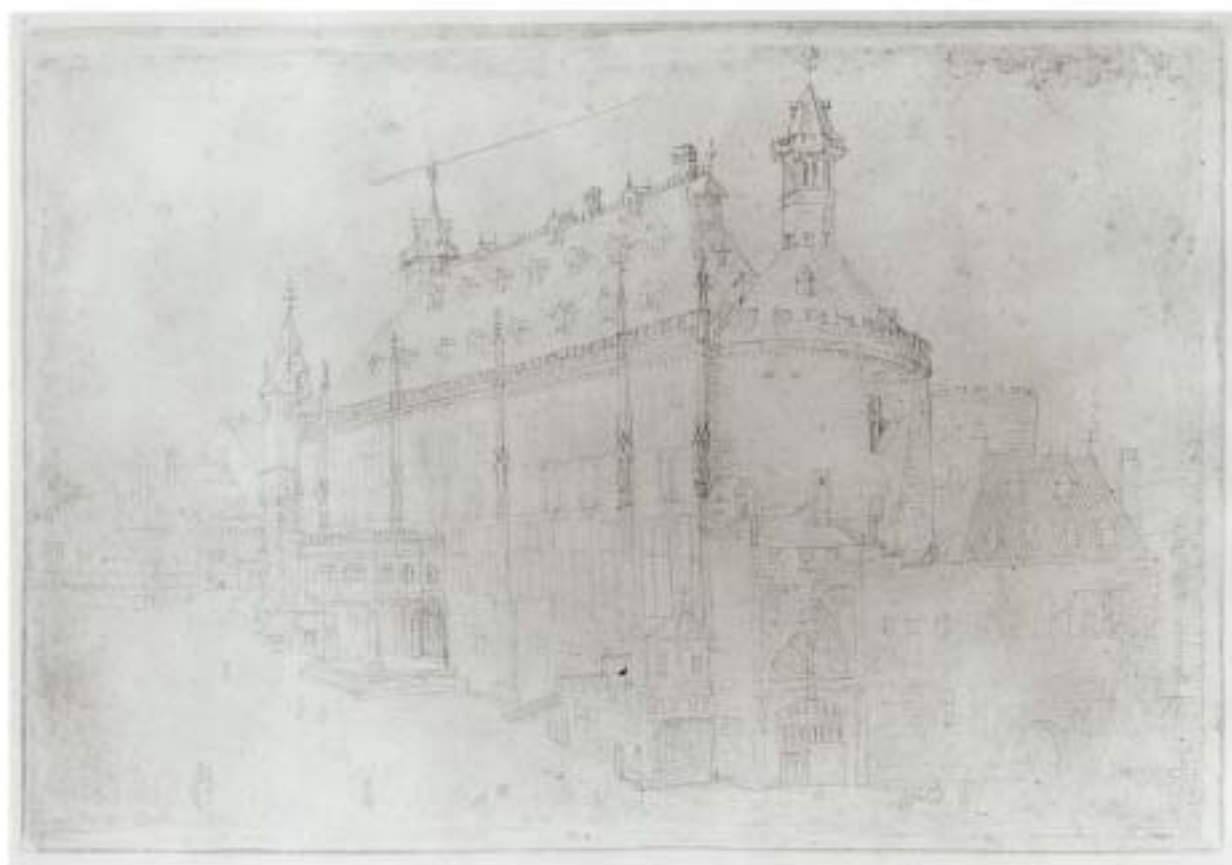

European Journal of Palliative Care



THE JOURNAL OF THE EUROPEAN ASSOCIATION FOR PALLIATIVE CARE



Plenary lectures

9th Congress of the European Association for Palliative Care (EAPC)

Aachen, Germany, 8–10 April 2005

Plenary lectures

The Scientific Committee for this Congress of the European Association for Palliative Care (EAPC) has decided to include nine plenary sessions in the programme, covering key aspects of palliative care and its development. We have invited speakers of outstanding reputation, including healthcare professionals with extensive experience in palliative care and distinguished academics and researchers.

The plenary sessions include a lecture in memory of Virgilio Floriani. This is in recognition of the Floriani Foundation and its contribution to palliative care over the years, including its support for the foundation of the EAPC.

The lectures are published in full here.

Death without suffering? <i>Robert Twycross, UK</i>	5
Anorexia-cachexia syndrome <i>Neil MacDonald, Canada</i>	8
Extending palliative care to chronic conditions <i>Julia Addington-Hall, UK</i>	15
A challenge for palliative medicine: bereavement care <i>David W Kissane, USA</i>	19
The volunteer in palliative care – a clearly defined role <i>Monika Müller, Germany</i>	24
Biology and pharmacology of the elderly: start low – go slow <i>Ola Dale and Stein Kaasa, Norway</i>	28
Palliative care communication in a cultural context <i>Daniela Mosoiu, Romania</i>	32
Palliative care in Europe: a view across the borders <i>Michael Wright, UK</i>	34
Refractory symptoms: complex problems need careful solutions <i>Sebastiano Mercadante, Italy</i>	38

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Death without suffering?

Robert Twycross, Emeritus Clinical Reader in Palliative Medicine, Oxford University, UK

Suffering is a state of severe distress caused by events that threaten the integrity of a person.¹ Benjamin Franklin is reputed to have said, 'In this world, nothing can be said to be certain except taxes and death.' However, he was wrong; change and suffering are also inevitable and inescapable parts of life – and of death. Even with sudden unexpected death, such as a cardiac arrest or a major accident, there is change and suffering for those who are left behind. Therefore, there is no such thing as death without suffering. Typically, people in pain feel threatened by the pain when:

- They feel out of control
- The pain is overwhelmingly severe
- The source of the pain is unknown
- The meaning of the pain is dire
- The pain is chronic.¹

Healthcare professionals must never forget that suffering and physical pain are not synonymous, and must always remember that pain is 'somato-psychic'. In other words, although pain is typically associated with a physical hurt, the perception of the discomfort is always modified by the person's cognitive and emotional reaction.² Thus, what an observer thinks must be a major cause of suffering for a person may in fact not be so. It is important not to make unwarranted assumptions. It is therefore helpful to ask a patient, 'What causes you the most suffering?'³

Relief of pain and other distressing symptoms is rightly seen by healthcare professionals as the primary goal of palliative care. Indeed, where palliative care is available, competent symptom management means that patients can generally expect to be free of severe pain. A high measure of relief is also expected with various other symptoms. However, no longer distracted and exhausted by unrelieved pain, patients may become distressed emotionally and spiritually as they contemplate their approaching death. Few do this with equilibrium. Most defend themselves psychologically in various ways, but some are overwhelmed with anguish, rage, or fear about what is happening to them. In consequence, it has been suggested that palliative care should be thought of as the provision of a safe place to suffer, a place where people can come to terms with their own death as fully and constructively as they can.⁴

Unfortunately, even when palliative care is available, pain sometimes remains uncontrolled and overwhelming, and the patient dies in great suffering, or heavily sedated.⁵ This tends to be associated with major unresolved psycho-spiritual distress. On the other hand, in palliative care, we meet many people who work through great psycho-spiritual distress and eventually achieve a remarkable measure of acceptance and peace.⁶

'Truth may hurt but deceit hurts more'

These words are the title of a paper published a few years ago.⁷ In it, examples are given of deliberate attempts to withhold the truth from patients, together with cases of

unintentional deception created by the use of ambiguous language. The evidence all points to the conclusion that, although truth may hurt, deceit hurts more. This has been long recognised by perceptive physicians. Over 2,000 years ago, Hippocrates wrote, 'I think the best physician is the one who has the providence to tell to the patients according to his knowledge the present situation, what has happened before, and what is going to happen in the future.'⁷

In my view, the biggest ethical challenge facing doctors globally in relation to palliative care is the question of truthfulness with patients. It is often said that telling patients that they are terminally ill destroys hope and leads to irreversible despair and depression. However, in reality, the opposite is more often the case – lies and evasion isolate patients behind a wall of words or silence that prevents them from sharing their fears and anxieties. Indeed, it is not possible to offer hopeful palliative care without a prior commitment to openness and honesty.⁸ An American surgeon wrote, 'A promise we can keep and a hope we can give is the certainty that no man or woman will be left to die alone. Of the many ways to die alone, the most comfortless and solitary must surely take place when the knowledge of death's certainty is withheld ... Unless we are aware that we are dying, we cannot share any sort of final consummation with those who love us. Without this consummation, no matter their presence at the hour of passing, we will remain unattended and isolated. For it is the promise of spiritual companionship near the end that gives us hope, much more than does the mere offsetting of the fear of being physically without anyone.'⁹

Good communication skills are essential to palliative care. As Michael Simpson said:

'Truth is one of the most powerful therapeutic agents available to us, but we still need to develop a proper understanding of its clinical pharmacology, and to recognise optimum timing and dosage in its use.'

It is important to remember that the ultimate tragedy is not death, but depersonalisation. This is commonly caused by:

- Dying in an alien environment
- Isolation from the spiritual support of other human beings
- A sense of desolation and helplessness.

Globally, isolating a person behind either a 'conspiracy of silence' or a 'conspiracy of words' is a major cause of depersonalisation – and of suffering.

Palliative care and healing

You can't die cured but you can die healed.¹⁰ The essence of palliative care is healing. A journalist wrote shortly after his wife's death, 'Of course terminal cancer is unspeakably awful. That aspect needs no emphasis. More difficult to imagine is the blessedness which is the corollary of the awfulness ... I think my wife learnt more of our love during those dreadful months than she did at any other time, and

Box 1. Where was God?

Where was God when Brian shat from his mouth?
Where was God when Elsie's belly eroded?
And liquid faeces rolled over her loins, soiled her sacred pubis
And soaked the sheets of her bed?
Where was God when spinster Jill couldn't fart or crap,
Blew up like the expectant mum we believe she never was
And cursed us all, supposedly behind our backs,
Hurling insults and expletives through the side-room door
On our departures, destroyed our All
And filling other patients with fear?
I simply don't know where God was.
All I know is that God was there.

Written by a trainee palliative care specialist.

we of hers ... The suffering of a long and terminal illness is not all waste. Nothing that creates such tenderness can be all waste. As a destroyer, cancer is second to none. But it is also a healer, or an agent of healing.'

Healing is about restoring right relationships with self, others, the environment and God. It is important to remember that the aim of healing is not to be cured or to survive, but to become whole. And to die healed includes expressing five important things: I love you; forgive me; I forgive you; thank you; goodbye.¹¹

The effect on the carers

In palliative care, one is forced to face the facts of life as they are, not as we might like them to be. All around us, everyday, there are endless examples of incredible suffering. One poignant example was that of a 68-year-old man dying of lung cancer. He had four children, three girls and one boy. All the girls suffered from an inherited disease that led to liver failure. One died as a teenager; the second survived to marry but died in her mid-20s; the third had a liver transplant and is still alive. The son was not affected. Then, two to three months after the father was diagnosed with terminal cancer, the son was killed in an accident at work.

As palliative care professionals, we have to cope with the fact that it is not always possible to achieve 'a good death' for our patients. Consider the patient with an eroded malodorous face or perineum, or the patient with end-stage dementia. Particularly in such situations, we cry inwardly in anguish as we witness the sufferings of our patients and their families (Box 1).

Looking to the future

For the people, by the people, with the people'

Earlier this year, I spent three weeks in India visiting several important palliative care centres there. In Kerala, a state in the south-west with 60 million inhabitants, I learned about the Neighbourhood Network in Palliative Care. This resulted from the realisation by one doctor in particular that enthusing and training doctors to set up doctor-led palliative care clinics in their localities would never provide community-wide coverage of holistic palliative care. As a consequence, it was decided to set up 'neighbourhood network' groups organised by trained non-professional volunteers. The volunteers were asked to identify people in their locality who would benefit from holistic palliative care. As a result, many patients have been included in

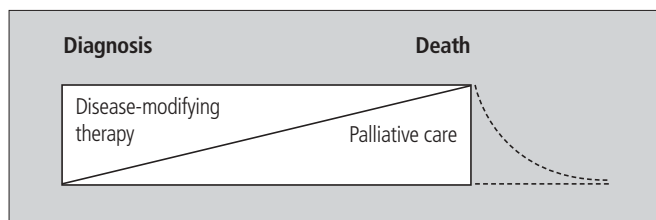


Figure 1. Traditional diagram to illustrate the relationship of palliative care to disease-modifying/curative treatment

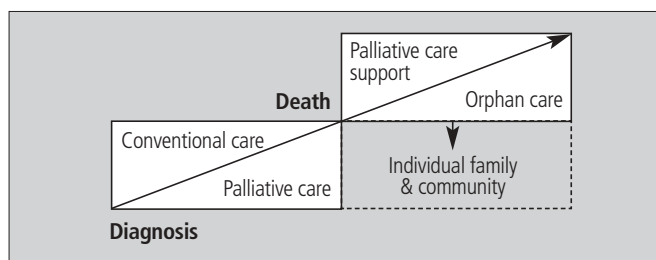


Figure 2. Modified diagram to illustrate the extension of palliative programmes in sub-Saharan Africa (Kath Defilippi, South Coast Hospice, KWazulu Natal, South Africa)

addition to those with end-stage disease. Thus, in many places, patients in the following categories are being supported socially (including financially), psychologically (extending to spiritually) and physically by the local palliative care network:

- Stable chronic disorder, such as post-traumatic paraplegia
- Fluctuating chronic disorder, such as lymphoedema, sickle-cell disease
- Slowly progressive disease, such as peripheral vascular disease, HIV/AIDS
- End-stage progressive disease, such as cancer.

The tendency for hospital-based clinics (run in several major hospitals mainly by anaesthesiologists) to be called pain and palliative care clinics is wholly appropriate. However, away from the hospitals, it is palliative care as defined by the community, namely: the active total care of patients with a chronic disorder or an advanced disease, and their families. Remarkably, one group has already extended its services to chronic psychiatric patients.

The essential task of this community-based palliative care is to help patients (and their families) to make the transition from being passive victims to empowered persons; and, in advanced disease, from fighting death to seeking peace. Already, after just three to four years, there are 70 functioning groups, with plans to expand from northern and central Kerala to the south of the state.

In parallel ways, the same reliance on community volunteers is being witnessed in parts of sub-Saharan Africa, although the emphasis is still on end-stage disease. Here, HIV/AIDS has overtaken cancer in terms of numbers and social impact. In some African countries, between 30% and 40% of the adult population is HIV positive. Often it is the main breadwinner who is struck down. Thousands of children have become 'AIDS orphans'. It has become necessary to redraw the familiar palliative care diagram (Figures 1 and 2).

These local developments in India and Africa – and no doubt elsewhere – have broadened and deepened the scope of palliative care. It is a far cry from how it was for me

before I retired as a clinician in 2001. Throughout 30 years in palliative care, more than 95% of my patients had end-stage cancer. In the UK, there were (and are) all sorts of parallel services for patients with other disorders and diseases. In many ways, I was sheltered from the harsher realities of life that appertain in most parts of the world. It is exciting that, globally, palliative care is increasingly breaking out of its original cocoon, and is imaginatively and compassionately responding to neglected and unsupported suffering of many kinds in the wider community. It calls for inspired leadership – and a true partnership between the community and the healthcare professionals. The bulk of the ‘active total care’ will be provided by trained non-professional volunteers in the patients’ homes, with the professionals providing only what they alone can do in terms of rehabilitation and symptom relief.

At the end of the day

Palliative care developed as a reaction to the attitude – spoken or unspoken – that, ‘There’s nothing more that we can do for you’, with the inevitable consequence for the patient and family of a sense of abandonment, hopelessness and despair. It was stressed that this was never true – there is always something that can be done. Even so, there are times when doctors, nurses and other healthcare professional feel that they have nothing to offer:

‘Slowly, I learn about the importance of powerlessness. I experience it in my own life and I live with it in my work.

The secret is not to be afraid of it – not to run away.
The dying know we are not God.
All they ask is that we do not desert them.’¹²

When we have nothing to offer except ourselves, a belief that life has meaning and purpose helps to sustain us in our work.¹³ However, to speak glibly of this to a patient who is in despair is cruel. At such times, actions speak louder than words, and the essential message to be conveyed is, ‘You matter because you are you; you matter to the last moment of your life. And we will do all we can to improve and sustain the quality of your life, and ultimately provide support and comfort in dying.’ (after Cicely Saunders).

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Anorexia-cachexia syndrome

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Primary cachexia is a wasting syndrome characterised by loss of muscle and fat directly caused by an aberrant host response to a wide variety of chronic illnesses. The wasting of cancer patients may also involve the actions of specific tumour factors.¹ Anorexia commonly accompanies cachexia and is usually caused by the same mediators acting upon hypothalamic centres. As a rule, the patient with primary anorexia-cachexia is fatigued and loses muscle with an associated decrease in function. Loss of appetite may be compounded by changes in taste, sensitivity to odours, a constant sense of satiety and occasionally nausea.

It is critical to identify both primary and secondary components of anorexia-cachexia. The latter category includes a group of often reversible problems – notably anxiety, pain, difficulty in swallowing, obstructions, constipation, infection and related problems that impact on appetite and energy intake.

In contrast to starvation, the patient with primary anorexia-cachexia fails to preserve muscle protein and feeding the patient by enteral or parenteral means is not beneficial. Therefore, while decreased nutritional intake associated with anorexia compounds the problem, primary anorexia-cachexia is fundamentally different from wasting associated with famine and other causes of starvation, where lean body mass is preserved and feeding reverses wasting.

Significance

Anorexia-cachexia profoundly influences family life. The patient does not always regard loss of appetite as a serious problem but families suffer greatly as they watch a loved one waste away. Providing sustenance and participating in shared family meals is of fundamental importance in all cultures.

Healthcare costs – both to the family and to society – are dramatically increased as patients progressively become incapacitated. In many countries, cachexia and the often associated problem, fatigue, are the major causes of prolonged institutional dependency towards the end of life.

Aside from functional loss, psychosocial distress and financial costs, anorexia-cachexia seriously limits patient therapeutic opportunities. Cancer wasting strongly correlates with adverse treatment effects and poor tumour response, probably arising from interference with drug metabolism and, possibly, with chemotherapy efficacy, secondary to inflammatory cytokines or the acute phase proteins induced by these cytokines.^{2,3} Aside from indirect effects on survival, primary anorexia-cachexia syndrome can directly kill patients.

In stark contrast to the common presence of anorexia-cachexia and its overall impact on people and society, is the low research priority assigned to it. Perhaps we are unduly fatalistic and perhaps we do not appreciate the common features of anorexia-cachexia across multiple disease states. Consequently, we are not applying the lessons learned from the experiences of colleagues in sister disciplines.

Pathophysiology

While the complex interaction between contributing factors remains to be clearly elucidated, unbridled chronic inflammation appears to be at the centre of the problem.⁴ Enhanced activity of certain cytokines (including interleukin [IL]-1, tumour necrosis factor- alpha [TNF- α], IL-6 and related factors) and activation of eicosanoid proinflammatory pathways are of particular importance. Arising from the inflammatory state, one notes decreased muscle synthesis, lipolysis, increased muscle proteolysis, and a rise in acute phase proteins.⁵ Certain cytokines (notably TNF- α and IL-1) may suppress ribonucleic acid-dependent myosin heavy chain muscle expression or promote ubiquitin-proteasome mediated myosin proteolysis (IL-6).⁶ Abnormalities in autonomic function are common with an imbalance favouring enhanced sympathetic activity and sometimes increases in resting energy expenditure, particularly in cancer patients.⁷

The above constellation of events is also encountered in patients with an acute infection or injury. The 'switch' that activates our response to an immediate threat, causes great harm when left on over time. The resultant gene activation and downstream events lead to a cascade of metabolic and neuroimmune derangements that, in no way, appear to protect the patient against the progress of cancer or other chronic disorders. Indeed, many of the products of inflammation may 'feed the flame' in a fashion eloquently expressed by Balkwill and Mantovani in a seminal article in *The Lancet* in 1991.^{4,8}

Cancer cachexia may have specific features arising from the production of tumour factors in some patients. Tisdale and his colleagues have identified chemicals inducing proteolysis and lipolysis in the mouse and in man;^{9,10} in addition, some tumour cells are able to produce cytokines that enhance new growth.

Diagnosis and assessment

'Upon this gifted age in its dark hour
Rains from the sky a meteoric shower
Of facts ... they lie unquestioned, uncombined.
Wisdom enough to leech us of our ill
Is daily spun, but there exists no loom
To weave it into fabric'

Huntsman, What Quarry? Edna St Vincent Millay

The wide array of abnormalities outlined in the pathophysiology section may well fit into a series of specific patterns. At the present time, however, an aetiology-based anorexia-cachexia classification system does not exist. Nevertheless, certain biochemical markers reflecting the background presence of a chronic inflammatory state are associated with a poor prognosis.^{11,12} Wasting patients usually have low serum albumin, an increase in hepatic acute phase proteins (C-reactive protein [CRP] – a rough measure of chronic inflammation is an example) and are commonly anaemic with lymphocytopenia. Underlying

changes in autonomic function are manifest through the presence of tachycardia and symptoms of early satiety.¹³ An important point for the clinician – if your patient is losing weight but has a normal albumin and CRP, be particularly alert for alternate correctable causes of weight loss.

Patients with chronic illnesses associated with anorexia-cachexia should be screened at first diagnosis for the presence of nutritional problems and monitored throughout the course of their illness. A simple assessment system consists of:

- A regular recording of weight (an easy task – not always carried out)
- Reporting of variations in taste, perceptions of odours, swallowing and a sense of early satiety
- Use of an ‘aide-memoire’ to ensure that the physician has identified secondary sources of anorexia-cachexia (see Table 1)
- Performance status – questions related to home function
- CRP and testosterone levels.

In our clinic, we use the above measures complemented by a symptom scale (the Edmonton Symptom Assessment System) and tests of upper and lower limb strength (Jamar hand dynamometry, and either a quantifiable chair rise test or a two-minute walk).

While all of these procedures may be difficult to carry out in a busy general clinic, clinicians should use a quantifiable symptom scale that will focus their initial and subsequent patient interviews in a helpful fashion – it will not burden either them or their patients – and assess for the presence of chronic inflammation (CRP), and review potential causes of secondary cachexia.

Low testosterone levels are common in patients with a wide range of chronic illnesses.¹⁴ It seems reasonable to identify hypogonadal states and to offer replacement therapy, as it is difficult to maintain or rebuild muscle if one is hypoanabolic. At the time of writing, the replacement of testosterone in hypogonadal patients cannot be said to be common practice.

General principles for management

Secondary anorexia-cachexia

It is critically important to identify and treat reversible causes such as anxiety/depression, dry mouth, oral thrush, early satiety, constipation and poorly controlled pain and other symptoms, as each of these problems will reduce nutritional intake and functional status (see Table 1).

If, after a general symptom review and assessment of relevant laboratory findings, the clinician concludes that primary anorexia-cachexia is present, measures to combat this syndrome should be employed.

Historically, the emphasis in anorexia-cachexia trials has been placed on reversal of weight loss and improvement in appetite. Consequently, the evidence base is heavily tilted towards agents that might improve appetite, albeit having a neutral or even negative effect on lean body mass and patient function. Recently, there has been a shift towards prioritising maintenance and enhancement of muscle mass and function as the key attributes of successful therapy. As this reversal of priorities is relatively new, the evidence base for muscle-enhancing treatments remains modest. Nevertheless, in the author’s opinion, sufficient wisdom is present to construct a ‘platform’ for treating primary anorexia-cachexia and for

Table 1. An approach to identify potentially correctable causes of cancer cachexia

This assessment is made easier by the routine use of simple patient-completed questionnaires. These allow for ongoing quantitative data that helps physicians to ‘zero in’ on specific problem areas. Examples of such scales include the Edmonton Symptom Assessment Scale, the EORTC quality of life questionnaire (QLQ C-30) and its associated disease specific modules, and the Edmonton Functional Assessment Tool.

Potentially correctable problems	Possible approaches
Psychological factors	
Anxiety	Anxiolytics – counselling
Depression	Antidepressants – counselling
Family distress	Social assistance
Spiritual distress	Counselling
Eating problems	
Appetite	Referral to a nutrition clinic or a dietitian
Disturbed taste or smell	Zinc supplementation Multivitamins
Oral	
Dentures, mouth sores	Antifungal medication
Thrush	Oral moisteners
Dry mouth	Change medication(s)
Swallowing difficulties	
	Antifungal medication
	Oesophageal dilation
	Regurgitation therapy
Stomach	
Early satiety	Gastric stimulants
Nausea and vomiting	Cause related
Bowel	
Obstruction	Cause related
Constipation, Diarrhoea	Laxatives, especially if on opioids
Malabsorption	
Pancreas	Pancreatic enzymes
Fistulas	Cause related
Fatigue	
	Anxiolytics
Sleep disturbances	Sleep protocol
Physical limitation	Exercise protocol
Motivation	Exercise protocol
‘Cognitive fatigue’	Methylphenidate
Function	
	Exercise protocol
Home setting	Cause related
Pain	
	Appropriate analgesics
	Nerve blocks: surgical, percutaneous
	Counselling
Metabolic	
Diabetes	As indicated
Adrenal insufficiency	
Hypogonadism	
Thyroid insufficiency	

Parts of this article appear in, or are adapted from, the chapter on cachexia-anorexia published as a part of the core curriculum for Education on Palliative and End-of-life Care, Feinberg School of Medicine, Northwestern University.

The author is a contributor to this curriculum; the text reprinted or adapted in this article is solely selected from the author’s contribution. The author acknowledges the generosity of the EPEC Project in allowing access to their curricular material.

establishing a take-off point for further clinical studies. Specific agents of interest include:

Appetite-enhancing drugs

Multiple randomised clinical studies support the efficacy of corticosteroids and progestational compounds in stimulating appetite.^{15,16} Most of these studies have been carried out in cancer patients, but progestational agents have similar effects in AIDS populations and in the frail elderly.^{17,18} Probably little difference exists among the various corticosteroids, although dexamethasone is usually the drug of choice for oncologists because of reduced problems with electrolyte fluid balance and a history of common usage.

Alas – although they will clearly increase appetite over time – corticosteroids have catabolic effects that reduce muscle mass and function. Dexamethasone is a fluorinated corticosteroid – a class particularly prone to reduce muscle mass and function.¹⁹ Consequently, it is the author's practice to use dexamethasone for only short-term purposes; if a longer period of treatment appears wise, a switch from dexamethasone to a non-fluorinated corticosteroid such as prednisolone should be carried out.

Progestational agents, of which megestrol acetate is the best-studied drug, will increase appetite and weight in approximately 50% of patients. Megestrol acetate is available both in tablet form and in oral suspension, a formulation that may have improved bioavailability. Doses in the range of 400–800 mg per day are commonly employed.

The initial response to corticosteroids is usually dissipated within three to six weeks. Progestational agents appear to have a longer period of response. The weight gained is fat (not a bad outcome in its own right), not muscle. The geriatricians suggest that megestrol, which is known to have corticosteroid-like effects, also has catabolic effects on muscle,¹⁸ while in long-term use adrenal suppression has been observed. Consequently, cautions on the use and timing of therapy of corticosteroids also apply to progestational agents. Both classes are well tolerated by patients initially; those on a progestational drug may be at a slightly greater risk of thromboembolism, particularly if receiving concomitant chemotherapy. Both agents may induce sufficient adrenocortical suppression to dictate the need for adequate corticosteroid replacement in patients encountering serious infection, trauma or surgery.

The appetite-stimulating actions of corticosteroids and progestational agents are not fully understood. They both reduce the production of inflammatory cytokines, and their effect on hypothalamic feeding centres may be carried out simply through this mechanism. Progesterone also stimulates the activity of neuropeptide Y, a hypothalamic factor enhancing appetite.²⁰ The relative importance of these drug actions is not clear.

Cannabinoids

A long folk history supports the appetite-stimulating action of cannabinoids; the 'munchies' is a well-known attribute of marijuana use. There is mixed evidence of benefit when cannabinoids are used by anorectic cancer and AIDS patients.²¹ People who have used marijuana in the past where psychotomimetic effects may be viewed as a side benefit rather than an adverse event, may experience greater success, although prior non-users may also benefit.

Most studies have been carried out with an oral marijuana congener, dronabinol; and while some believe that smoking marijuana is particularly efficacious, proof is awaited. The mode of action is uncertain. Endogenous cannabinoid systems are present in the brain, with most receptor activity noted in so-called 'hedonistic centres' in the nucleus accumbens.²² Whether marijuana acts directly upon hypothalamic feeding centres is not known; its major appetite effects may come about through stimulation of cerebral pathways stimulating a sense of pleasure in eating rather than a fundamental drive to take in energy.

Anorexia and a sense of feeling 'full' go hand in hand

Patients may start with a good appetite that rapidly abates. While unknown vagal-hypothalamic mechanisms may play a role, early satiety correlates with autonomic dysfunction, and consequent delay in gastric emptying.²³ Commonly used but modestly studied agents stimulating gastric emptying may be helpful in relieving early satiety. Metoclopramide and domperidone are employed for this purpose. The 14-membered ring macrolide antibiotics (for example, clarithromycin, erythromycin) are strong stimulants of gastric emptying; their efficacy in anorexia-cachexia has been studied only in a few small Japanese studies, primarily emanating from one group.²⁴

Cachexia – agents of interest

As stated earlier, the main interest now lies in alleviating the cachexia side of the anorexia-cachexia equation. Muscles require nutrition, efficient processing of energy sources, and maintenance of the ratio between muscle synthesis and proteolysis. Moreover, muscles must receive an adequate blood supply providing a conduit for nutrition and removal of metabolic waste, while they must also be effectively stimulated by their nerve supply. Considering the complexity of muscle activity, it is encouraging that a series of single-agent trials that only address one or at most two elements of the above muscle requirement litany have been successful. Surely the efficacy of anabolic agents is reduced if the effect on muscle synthesis is truncated because of continuing excess proteolysis. That they are effective at all is most encouraging. To the author's knowledge, no one has studied combination therapies that address more than two of the constituent requirements of muscle. Agents of interest include the following.

Anabolic agents – androgens

We must learn from our athletes and sports medicine colleagues who have known for years that anabolic agents build muscle. Perhaps because of the taint associated with their use in athletics as well as concerns for adverse effects, clinicians have been slow to realise their potential benefit in cachectic patients. Where studied, however, results are encouraging. An older agent, fluoxymesterone, only modestly increased appetite when compared with megestrol.²⁵ The effects on lean body mass were not studied. Recently, a series of studies on oxandrolone, an androgen thought to be anabolic with reduced androgenic effects, demonstrated an increase in appetite, lean body mass and quality of life in both AIDS and cancer patients.^{26,27} The frail

elderly also appear to benefit from androgen treatment.²⁸ Not surprisingly, androgens are generally more efficacious if used in combination with exercise.

As stated earlier, hypogonadal states are frequently encountered across the spectrum of patients with chronic illness. Many – but not all – studies on androgen use utilised physiological doses of androgens, and specifically targeted patients with low testosterone levels. The author concludes from a review of such studies that it is reasonable to identify the presence of a hypogonadal state and to correct it if clearly evident; establishing hypogonadism is not always straightforward and programmes should employ specific assessment guidelines.²⁹ Should super-physiological doses of anabolic agents be more regularly employed? While recent results on oxandrolone are highly encouraging, this issue remains to be clearly resolved. Certainly, anabolic agent trials should receive high priority, particularly in a multi-modal setting where androgens are studied in combination with anti-inflammatory agents, amino acids, antiproteolytic compounds and exercise.

Creatine

Again, consideration of the benefits of creatine causes one to reflect that we must learn from our sports medicine community. Creatine is widely used by body builders and athletes, based on the thesis that adenosine triphosphate (ATP) is a critical energy source for the working muscle; creatine phosphate is a necessary component for synthesis of ATP. Multiple studies confirm that healthy individuals will notice an increase in lean body mass and certain aspects of muscle function after ingestion of creatine.^{30,31}

As with androgens, there is little information on the potential use of creatine in wasting disorders. A few trials in the elderly and in patients with muscular dystrophy suggest that creatine may be helpful.^{32,33} To date, creatine studies on cancer cachexia are not available. ATP infusion reduces weight and fat-free mass loss in non-small cell lung cancer patients.³⁴

Creatine appears to be a safe agent, widely used in the community, and in most countries not subject to regulation by governmental pharmaceutical agencies. Only mild abnormalities in renal function have been reported, although available studies are small and short term, with few providing data beyond 28 days' use. We look forward to the emergence of a creatine clinical trial, which should logically be carried out in situations where patients are assured of an adequate supply of nutrition, and where exercise is an inherent trial component.

Amino acids

Few trials on the use of amino acids have been carried out, which is strange as they are fundamental building blocks for muscle. Should we supply muscle with a non-selective portfolio of amino acids, or should we concentrate on certain amino acids deemed to be particularly important for function and growth? For example, a combination of glutamine, arginine and beta-hydroxymethylbutyrate (a metabolite of leucine) appears to increase weight and lean body mass in both AIDS and cancer patients enrolled in controlled clinical trials.^{35,36} N-acetyl cysteine has been reported to improve body cell mass, redox state and quality of life in advanced cancer patients.³⁷ Whey protein in

healthy populations, either alone or in combination with creatine, builds lean body mass.³⁸

Amino acids provide more than a nutrient source to muscle. Amino acid mixtures can have immune/stimulatory properties and also mediate essential cellular second messenger systems protecting against oxidative damage and undue muscle proteolysis.^{39,40} Specific amino acids that may be key in these roles include glutamine, the branch chain amino acids (leucine, isoleucine and valine) and cysteine–cystine. Future studies may tell us that we should employ specialised amino acid formulations to assist waiting patients. While awaiting the conduct of these trials, it is reasonable to ensure that our patients have an adequate supply of amino acids, readily available as supplementary whey protein.

Omega-3 fatty acids

Key omega-3 fatty acids include eicosapentaenoic acid (EPA), and docosahexanoic acid (DHA), natural oils present in fish with dark oily flesh (salmon, sardines, herring and mackerel). In wasting syndromes, EPA is of particular interest as Tisdale *et al* offer evidence that it may have a specific inhibitory on the action of proteolysis-inducing factor.⁴¹ Both EPA and DHA are strong anti-inflammatory compounds that divert cellular prostaglandin metabolism away from eicosanoid mediators of inflammation.^{42,43} The omega-3 fatty acids inhibit tumour growth in a variety of animal systems, while enhancing antitumour effects and reducing adverse effects of a number of common chemotherapeutic drugs.^{44,45}

Omega-3 fatty acids carry a positive pedigree supporting their use in a wide variety of human ailments, including the anorexia–cachexia syndrome. The extraordinary promise of animal studies has yet to be fully realised at the bedside. Indeed, because of their modest effects on appetite stimulation and weight gain, some have concluded that they are not useful compounds.⁴⁶ Part of this current negativity relates to the dashing of earlier expectations – a small controlled trial and a carefully carried out uncontrolled study in pancreatic cancer suggested that the omega-3 fatty acids may even have life-sustaining properties.^{47,48} Two large recent controlled trials have failed to find evidence to this effect, but one of these trials once again demonstrated that omega-3 fatty acids can sustain and increase lean body mass if adequate amounts of EPA (2 grams a day) are ingested.⁴⁹ The other 'negative trial'⁴⁶ did actually show that the omega-3 fatty acid supplement has a modest effect on increasing appetite and weight, albeit not equal to that of megestrol. This trial did not, however, measure lean body mass or function. Trials are currently under way to study the efficacy of omega-3 fatty acids in combination with chemotherapy.

In view of the weight of animal reports and data suggesting that lean body mass may be sustained, the author concludes that an increased intake of omega-3 fatty acids may be recommended for patients with wasting syndromes. Caution is needed because these are oxidant agents and they should always be accompanied by the use of antioxidant vitamins. They are safe agents – some patients may notice a sense of bloating and 'fishy returns' and occasional increased bowel movements (often a blessing). Omega-3 fatty acids require further study in combination with other muscle-enhancing agents, and with chemotherapy.

Cardiovascular agents

If chronic inflammation is the core aberration governing the onset of anorexia-cachexia in chronic diseases, presumably a wide range of drugs that reduce chronic inflammation may have positive effects on wasting. Patients with cardiovascular diseases, usually for other reasons, take large amounts of anti-inflammatory drugs. Statins have anti-inflammatory activity as evidenced by their action in reducing C-reactive protein.^{50,51} Angiotensin-converting enzyme (ACE) inhibitors also reduce inflammatory cytokine production. Moreover, the ACE inhibitors may directly improve muscle synthesis and decrease proteolysis.⁵² An international trial is currently looking at the effects of a highly lipophilic ACE inhibitor, imidapril, in cachectic cancer patients. A recent study in the geriatric literature is encouraging – hypertensive women on ACE inhibitors demonstrate improvement in the extensor muscles, strength and walking speed in comparison with women with hypertension who are otherwise treated.⁵³

Dependent upon our genetic profile, some of us may be more likely to do well with ACE inhibition than others. Approximately 20% of the population has a particular gene polymorphism for ACE, which enables the fortunate fifth to respond with improved muscle performance following adherence to an exercise programme.⁵⁴

Beta-blockers are widely used in the management of patients with advanced congestive heart failure. They could possibly affect cachexia through modulation of increased sympathetic activity and the consequent useless drive on energy expenditure.⁵⁵

To date, the wisdom garnered by cardiology colleagues has not been applied to other fields where cachexia is encountered. Herein lies a case study in the need to cross traditional disciplinary lines to conduct clinical studies enlisting a blend of patients with chronic illness and wasting.

Non-steroidal anti-inflammatory drugs (NSAIDs)

The chronic inflammatory state is associated with PGE2 activity. As well, a downstream eicosanoid 15-hydroxyeicosatetraenoic acid (15 HETE) may mediate the activity of proteolysis-inducing factor (PIF).⁴¹ In animal studies, NSAIDs may reduce tumour growth and tumour-induced wasting.⁵⁶ Studies in Sweden and Britain demonstrate the benefits of indomethacin or ibuprofen in reducing cachexia in cancer patients;^{57,58} in the Swedish clinic, use of NSAIDs is part of their basic platform for management of anorexia-cachexia.⁵⁹ Despite widespread use for other conditions, at least in North America, NSAIDs are not commonly employed in the management of anorexia-cachexia. Concerns about drug toxicity in frail populations and ‘polypharmacy’ may influence this point of view. Further clinical trials on these promising agents are welcome.

Multivitamins

Malnourished patients may have unrecognised vitamin deficiencies, while geriatric studies support the routine use of multivitamins for institutionalised patients. Antioxidant vitamins have been incorporated into a few studies, together with other anti-cachexia measures. Initial results are encouraging.⁶⁰

Other agents of interest

There is no lack of candidates for clinical study in the anorexia-cachexia field. Readers may wish to follow the literature on carnitine (fatigue), thalidomide, and specific TNF- α and Il-6 inhibitors (perhaps too specific considering the multifactorial genesis of anorexia-cachexia), melatonin, macrolide antibiotics, and b-2 (beta-2) agonists. At a more fundamental level, biotechnology groups are attempting to find specific blockers of muscle synthesis inhibitor myostatin, inhibitors of certain genes that activate the ubiquitin-proteasome system, and compounds that may favourably influence the ‘yin and yang’ of appetite control, notably inhibition of the melanocortin C₄ neurotransmitter, which may stimulate a panorama of undesirable events, including undue sympathetic stimulation and increased resting energy expenditure. Stay tuned.

Exercise – rehabilitation

‘If you don’t use it, you lose it’ – muscles only thrive if they are active. Our patients readily appreciate this common wisdom, and welcome encouragement to exercise within safe limits. Common wisdom is increasingly accompanied by immunological and biological studies informing us that exercise can lower cancer incidence, improve fatigue and reduce the adverse effects of treatment.^{61–65} Studies on rehabilitation in cancer lag behind research and practice in geriatrics, which clearly supports the benefit of defined rehabilitation activities in improving patient function. Exercise, when used in conjunction with anabolic and nutrient supplements, has positive muscle mass and functional effects on people with AIDS, and on healthy body builders and athletes.

Considering the interest of the community in exercise, and the wealth of supportive studies, why have we failed to formally introduce rehabilitation programs into our disease management strategies? Resources are limited, and while we welcome physiotherapists as members of our team, we may not have the funds to hire a dedicated therapist. In addition, the mantra of ‘preservation of energy’ that we preach to patients who are fatigued and losing weight may often be erroneous. Fatigue is not relieved by inactivity, while some aspects of energy preservation may encourage a general spiraling down of muscle usefulness. In light of current evidence, efforts should be made to prioritise rehabilitation with chronic disease care, and to provide specific advice and opportunities to patients at the first evidence that they are beginning to waste.

Obviously, advice in this realm is tailored according to the patient’s capacity, and the need to consider dangerous situations that may be exacerbated by exercise, such as bone metastases (usually a regional problem) and cardiovascular capacity.

‘I must tell you how beneficial my husband’s participation in your programme was to his sense of wellbeing and control. Exercise was his therapy, which he controlled, while he had little control over the chemotherapy and radiotherapy administered by others.’ These comments from the wife of a young man who underwent numerous courses of therapy, without benefit, for a steadily advancing sarcoma, bear witness to a major benefit of exercise. So often our patients feel caught as passive recipients of care. Participation in rehabilitation and

nutritional therapy programmes, in which patients see themselves as members of a team, sustains a sense of control and dignity.

Influence of public understanding and biology on programmes

The updated World Health Organization definition of palliative care stresses the importance of including the principles of palliative care into the care of patients at the onset of a predictably fatal chronic illness.⁶⁶ This concept, plus the understanding that anorexia-cachexia should be treated as early as possible,⁶⁷ has moved a number of institutions to develop programmes encompassing these tenets. In Europe, the careful work of Dr Lundholm and his colleagues, who have steadily developed a platform of care based on a series of progressive studies, is worthy of note. As the author understands their approach, patients are treated with anti-inflammatory agents, notably indomethacin, nutrient supplementation and, more recently, measures to ensure that haemoglobin is maintained in the range of 12 grams with consequent beneficial effects on fatigue.

In Montreal we have formed a Cancer Nutrition Rehabilitation Group working with patients with advanced lung and gastrointestinal cancers as early in their course as possible. Our current 'interventional platform' consists of nutritional counselling, regular use of omega-3 fatty acids, low-dose antioxidant vitamins, whey protein supplementation, and an invitation to take part in a tailored rehabilitation programme. We are considering changes in the platform; at present we are not regularly identifying hypogonadal patients and offering physiological replacement. The author thinks we should. Dr Lundholm's work with NSAIDs influences our thinking. Should they be included in our regular programme? To date, we have simply held off because of the already evident polypharmacy to which our patients are exposed, together with safety issues in certain patients. Should we ensure maintenance of haemoglobin using erythropoietin if necessary? Again, the author supports this activity, but cost and government regulatory activities may limit universal adherence to this approach. Moreover, the overall effect of erythropoietin on the course of cancer remains to be clearly defined.⁶⁸

Conclusion

Surely we have reached the time when the false dichotomy between 'active disease treatment' and palliative care must be set aside. Model programmes that place palliative care people and/or principles in immediate contact with patients and those who traditionally manage them at the onset of chronic illness should be encouraged. A 'ticket of entry' centred on concerns of chronic inflammation management and consequent problems with anorexia-cachexia and fatigue may provide a particularly effective model for moving from rhetoric to reality.

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Extending palliative care to chronic conditions

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Since its inception in the 1960s, hospice care has been primarily focused on the care of terminally ill cancer patients. The lack of effective remedies for pain and other symptoms, poor communication with healthcare professionals, and inadequate practical and emotional support resulted in considerable distress for patients and families, and provided much of the impetus for the original development and rapid spread of what has become the hospice movement.¹ This initial focus on cancer, together with rapid advances in science and management of pain, allowed swift progress to be made in both the science and the practice of palliative care.² As the principles and practice of hospice care have been disseminated across the world, they have been adapted to fit local circumstances. In some settings there has been historically greater emphasis on, and provision for, people with conditions other than cancer, particularly in those countries where pioneers and champions of hospice care have come from backgrounds outside oncology. Nevertheless, in many settings, hospice and palliative care have been (and remain) synonymous with terminal cancer care. This situation is increasingly challenged, especially in those countries where hospice care has the longest history.³ In this paper, I will review the reasons for this and consider the obstacles to extending the borders of palliative care beyond cancer.

Background

Despite the focus on terminal cancer, some hospice and palliative care services in the UK, as in other settings, have always cared for some non-cancer patients, particularly those with motor neurone disease (MND). With a life-expectancy of two or three years at best and a course of rapidly increasing physical deterioration, the needs of patients and families are perhaps seen to 'mirror' those of terminally ill cancer patients, thus justifying to these services the decision to extend hospice care to them. Other services have offered care to MND and other neurological patients at points in the service's development, but have not continued to do so, instead concentrating on terminal cancer services as demand has grown.

It has been recognised by hospice pioneers since the beginnings of hospice care that the philosophy and practice of this care would also apply to people dying from other conditions. As the following quote shows, however, the hope and expectation was that clinicians in other specialties would apply what was being learnt within hospice care about caring for terminally ill cancer patients to their specialty, and develop their own terminal care services.

'Many of the symptoms to be treated and much of the general management will be relevant to other situations ...

Terminal care should not only be part of oncology but of geriatric medicine, neurology, general practice and throughout medicine.⁴

Thus, during the AIDS/HIV epidemic in the 1980s, there was considerable (and sometimes acrimonious) debate about whether the increasing numbers of people dying from AIDS should be able to access care from hospices, or whether new AIDS-specific services should be set up.⁵ These patients were mainly young, and experienced severe symptom distress, in addition to having complex psychological and existential concerns heightened by the stigma associated with the diagnosis. General issues about the focus and funding of hospice care combined with specific anxieties about caring for AIDS patients led to a difficult debate within the UK and elsewhere. Initially in the UK, new AIDS-specific hospice services were set up, helped in part by ring-fenced government funding. Over time, ring-fenced funding has disappeared, new treatments have radically changed the prognosis in HIV/AIDS, and the at-risk populations have changed. Many hospice and specialist palliative care services in the UK now care for AIDS patients, and the passion of the initial debates seems a distant memory. Importantly, the history of the development of services for AIDS patients has demonstrated that hospice and palliative care can adapt to accommodate new client groups.

The reforms of the UK National Health Service (NHS) in the late 1980s/early 1990s split the NHS into healthcare providers on the one hand, and healthcare purchasers (later commissioners) on the other.⁶ Purchasers held NHS budgets and were given the task of assessing the healthcare needs of their population and purchasing care accordingly. This led to them seeking information on population-based estimates of palliative care need,⁷ and to them subsequently beginning to question the focus of service provision on the care of terminally ill cancer patients. By 1996, there was definite recognition from the government that palliative care was relevant not only to these patients, but also to patients with other life-threatening conditions, including AIDS, neurological conditions, and cardiac and respiratory failure.⁸ The rhetoric of palliative care in the UK has shifted from one almost entirely concerned with terminally ill cancer patients to one that argues for the provision of palliative care to all patients who need it.

Despite this, in 2003 cancer patients still made up 95% of patients cared for by hospice and specialist palliative care services, with the remainder made up mainly of patients with neurological conditions or AIDS/HIV. The change in rhetoric in the UK does not seem to have been followed by much change in practice.

This may suggest, as some have argued, that patients with conditions other than cancer are currently being discriminated against in palliative care, a situation that would be difficult to justify morally or ethically given the increasing emphasis within the UK healthcare system on equality of provision.⁹ There is, however, another possible explanation. Terminal cancer patients may simply have more palliative care needs than patients with chronic conditions. If this is so, then the current situation may indeed be justifiable.

Palliative care needs beyond cancer

The World Health Organization currently defines palliative care as, 'An approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual'.¹⁰ The growing research evidence on the palliative care needs of people with life-threatening chronic diseases demonstrates that terminally ill cancer patients are not the only people to experience uncontrolled symptoms, psychological and spiritual distress.³ Many also experience inadequate communication with healthcare professionals in the last year of life, akin in some cases to the experiences of cancer patients before the widespread movement, at least in northern Europe, towards open communication. Surveys of bereaved relatives were an important initial source of this evidence,^{11,12} and subsequent work from prospective studies has supported these findings in demonstrating palliative care needs at the end of life in, for example, heart failure,^{13,14} chronic respiratory diseases¹⁵ and stroke.¹⁶

An example of a chronic condition associated with palliative care needs is chronic heart failure (CHF). This is becoming an increasingly common diagnosis as the acute care of myocardial infarction improves and, because of its association with older age, as populations age. It is a progressive condition with symptomatic deterioration over an unpredictable period of time, and has worse age-adjusted long-term survival rates than bowel cancer and breast cancer.¹⁷ People with the most severe CHF are breathless at rest, severely fatigued and may be cachexic. Although pain is less prevalent and usually less severe than in cancer, a significant minority are in pain that they find to be distressing, and for which they receive inadequate analgesia. Nausea and constipation can also be problems. Not surprisingly given the often extremely disabling nature of their illness, many people with CHF are depressed. Bereaved relatives report that almost half knew or suspected that they were dying, and that most had worked this out for themselves, with little open communication with healthcare professionals.¹⁸ Differences in prognostic certainty and lay perceptions of the two conditions mean that issues around communication are different in CHF than in cancer;¹⁹ nevertheless, there is growing evidence that more open communication about the future is wanted by at least some patients. Informal carers of patients with CHF experiences have received little attention, although it is clear that in the UK at least they receive much less support than carers of cancer patients from health and social

services even when caring for bed-bound relatives. Although more work is needed to fully understand the palliative care needs of people with severe CHF and of their families, it is clear that these needs are substantial, albeit different in some respects from those of terminally ill cancer patients.

It is clear that palliative care needs are not restricted to terminally ill cancer patients. What is less clear is how the palliative care community should respond to this, especially given the very limited evidence, outside MND and AIDS, for the benefits of palliative care in chronic conditions. Extending the boundaries of palliative care to chronic conditions presents a number of challenges.

Challenges to extending palliative care

Many healthcare professionals in palliative care, and the organisations they work in, have important concerns about moving beyond cancer.

A lack of relevant expertise

Generally, but by no means exclusively, many palliative care practitioners in the UK have professional backgrounds in oncology. They are concerned that their expertise and knowledge will not be relevant to non-cancer patients, and they are right to be so; there are important differences between cancer and non-cancer patients (and between patients with different chronic conditions). For example, a comparison of people with severe CHF with those dying from lung cancer identified that the latter had a clearer terminal phase, facilitating planning for death, and a good understanding of diagnosis and prognosis.²⁰ In comparison, people with CHF experienced a gradual decline with episodes of acute deterioration, often dying suddenly with no distinct terminal phase, and little understanding of diagnosis and prognosis. Differences such as these mean the manner in which palliative care practitioners organise and provide psychological, social and spiritual support may need some re-thinking.

Continuing with active treatment is also likely to play a more important role than is the case traditionally in cancer, particularly in chronic conditions such as CHF where in any case the focus of treatment is on controlling symptoms. This raises understandable concerns among practitioners with little general medical, cardiology or care of the elderly experience (although it will be less of a concern for palliative care practitioners from these backgrounds). In addition, the physical causes of symptoms may differ significantly from those in cancer, again limiting the generalisability of palliative care practitioners' knowledge. A further difference is that although cancer patients are often older and do have co-morbidities, many people with chronic conditions are older still and have a number of co-morbidities contributing to the complexities of their condition. Given these differences there is a real risk, as some recognise, that the involvement of palliative care practitioners could impair rather than improve patient care.

These risks are real, but while healthcare professionals need to recognise and understand differences between cancer and other conditions, they probably underestimate the extent to which skills in assessment, in counselling and in the basics of pain and symptom control are generally applicable.²¹

Overwhelming need for palliative care beyond cancer

In her influential epidemiological-based assessment of palliative care need, Higginson estimated that the percentage of patients with 'progressive non-malignant diseases' who require palliative care may be 50% to 100% of the number of cancer patients requiring care.⁷ Similarly, Addington-Hall *et al* estimated on the basis of data from the Regional Study of Care for the Dying that making specialist palliative care fully available to non-cancer patients in the UK would result in an increased caseload of at least 79%.²² Not surprisingly, palliative care practitioners became (and in many cases remain) concerned that their services would be inundated with non-cancer referrals, resulting in a reduction in care for cancer patients. There are also worries that pressure on existing healthcare services may make referrals to palliative care attractive for services seeking to empty their beds or reduce their workload.

Although evidence for palliative care need beyond cancer continues to grow, anecdotal evidence from the UK suggests that even when services have developed an 'open door' policy for non-cancer patients and have encouraged referrals, few – if any – have been overwhelmed and many have been distinctly underwhelmed, with referrals. This is encouraging for services wanting to slowly extend their boundaries beyond cancer but it cannot be presumed this will be the case everywhere: in the USA the growth in both the number and proportion of patients cared for by hospice who have conditions other than cancer has been much more rapid. It is important to begin to understand the reasons for low referral rates as they can provide important insights into the acceptability of palliative care to patients who do not necessarily see themselves as 'dying', and into the appropriateness of current models of care.

Lack of funding for palliative care

Although increasing amounts of NHS funds are going into palliative care in the UK, independent hospices depend on local fundraising and contributions for upwards of 30% of their income, and some are concerned about the impact of caring for non-cancer patients on their local support and fund-raising activities. In addition, cancer care charities, particularly Macmillan Cancer Relief, play an important role in 'pump-priming' services and in direct service provision. Charities set up for cancer patients are prevented legally from using their charitable funds on other patient groups. Therefore, they are unable to play a direct role beyond cancer, and it is unclear who will do so in their place. The example of the USA, where the availability of MEDICARE funding is likely to have contributed to the rapid expansion of care to non-cancer patients,²³ illustrates the important influence funding has on the ability of palliative care to extend its borders beyond cancer.

Lack of evidence for the effectiveness of palliative care beyond cancer

There is an almost complete dearth of evidence for the effectiveness and acceptability of hospice and palliative care services beyond cancer. Evidence is urgently needed to enable services to make informed decisions, to support negotiations for healthcare funding, and to ensure moving beyond cancer benefits service users and their families. While there is an increasingly substantial body of evidence

for the effectiveness of palliative care services in general, it cannot be presumed that these conclusions would hold true if these services were extended to non-cancer patients. It is important that those services across the whole international palliative care community that provide care to non-cancer patients audit their care and share their experiences and, where appropriate, initiate and participate in research.

Shared concerns with non-palliative carers

Palliative care providers and practitioners are, of course, unlikely to be alone in having concerns about palliative care extending its borders. Those healthcare professionals and services currently providing care for people with life-threatening chronic conditions are likely to share palliative care's concerns about its lack of expertise beyond cancer; they may have concerns about palliative care seeking to build its empire at their or their patients' expense (perhaps particularly likely to be of concern in healthcare systems where market share can have a significant impact on a service or individual's resources or income); and differences in philosophy of care between palliative care and acute medicine may lead to concerns that patients will be 'given up on' inappropriately, or receive sub-standard care. These concerns highlight the challenges involved in extending palliative care's borders in ways that truly benefit users and their families, which enable collaborative working with other providers and practitioners, and which are commensurate with local and national healthcare systems and resources.

What role for palliative care beyond cancer?

There will be more than one role for palliative care beyond cancer, just as there is more than one model of palliative care provision for cancer patients. This is not least because of the broad spectrum of diagnoses subsumed under the heading of 'non-cancer'. The appropriate response of palliative care will differ; for example, between patients who have a short, predictable prognosis with increasing symptoms (such as in end-stage renal failure post-dialysis), those with more unpredictable conditions where symptoms and quality of life vary over time and individual prognosis is difficult to judge (such as CHF and chronic respiratory diseases), and those with conditions characterised by cognitive decline (such as Alzheimer's disease and Creutzfeldt-Jakob disease). It will also differ according to the characteristics of the existing services caring for these patients, their funding and their philosophies of care. The origin, composition, funding and workload of the palliative care service will also impact on the role they are able to adopt, and for whom.

A starting point is to focus on what palliative care has to offer. Although increasingly palliative care is developing a role in providing support for cancer patients throughout the disease trajectory, for most services their key skills remain in end-of-life care, where this is broadly defined to include issues and problems arising out of the fact that death is certain and not too far off, rather than that it is imminent within the next hours and days. Palliative care has undoubtedly – and unique – expertise in dealing with the physical, psychological, social, spiritual and ethical issues that emerge at the end of life; it can offer assistance to healthcare teams in end-of-life decision-making; supply

expert symptom control when required; and offer support in adjusting to multiple losses caused by disease progression, as well as family support during illness and in bereavement. End-of-life care is what palliative care has to offer beyond cancer. The fact that individual prognosis is currently difficult to judge in many people with conditions other than cancer (and many will be recognised to be 'actively dying' shortly before death, if at all) presents challenges,²⁴ but does not detract from the fact that what palliative care has to offer beyond all else is its familiarity with, and expertise in, end-of-life care.

A major role for palliative care will be in working with patients' existing care providers to increase palliative care knowledge and skills, to support them in moving outside their 'comfort zones' to talk to patients and their families about prognosis and treatment options, and to address the psychological and existential concerns of patients and families,²⁵ and to support them in making end-of-life decisions. As in cancer, collaborative working through shared ward rounds, team meetings, outpatient consultations and home visits will be important. A key difference may be the fact that the education and support will need to be truly two-way, with the palliative care practitioner learning about, for example, CHF at the same time as sharing their knowledge and skills in palliative care.

In the UK setting, there remain important questions about whether and how palliative care services should directly provide care to non-cancer patients. The history of palliative care involvement in neurological conditions and in AIDS/HIV indicates that education and support for colleagues outside palliative care will not always be sufficient to meet the palliative care needs of patients and families. It can be hypothesised that hospice day care might, for example, have a role in helping people with severe CHF to find meaning and social support, that access to the growing numbers of hospice-at-home services might enable some end-stage heart failure patients to die at home, and that some CHF patients have such complex physical, psychological and spiritual needs that an inpatient hospice admission is warranted. It is becoming clear that hospital palliative care teams can have an important role beyond cancer, not surprisingly given that many patients will be identified as dying close to death following an acute exacerbation; care pathways such as the Liverpool Care Pathway for the Dying are an important innovation here.²⁶ Community palliative care teams can also provide useful support to patients and their families. In the UK, as elsewhere, imagination, commitment and (crucially) collaborative working are needed to develop and test appropriate roles for palliative care beyond cancer.

Conclusion

There is now good evidence that terminally ill cancer patients are not alone in having physical, psychological, social and spiritual needs in the last months and weeks of life. Despite the rhetoric of palliative care emphasising that it should be provided on the basis of need not diagnosis, it remains focused on terminal cancer care with, in many European countries, very few people with life-threatening chronic conditions receiving palliative care. Challenges to

be addressed when seeking to meet the needs of these patients and their families include:

- The need for palliative care professionals and services to recognise the differences between cancer and non-cancer patients, and thus the limits of their own knowledge, and the importance of working collaboratively with those currently caring for these patients
- The need to see beyond 'non-cancer' as a group and to seek to understand the needs of different diagnostic groups
- The potential impact of increasing the workload of palliative care
- The need to identify appropriate long-term funding sources
- The difficulties and dangers of operating without evidence for the effectiveness and acceptability of palliative care beyond cancer.

Imagination, flexibility, commitment and collaborative working are needed to develop and test appropriate roles for palliative care. The extension of the borders of palliative care to chronic life-threatening conditions needs to be underpinned by a clear sense of what palliative care has to offer. Beyond all else, this is familiarity with, and expertise in, end-of-life care.

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A challenge for palliative medicine: bereavement care

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Bereavement care is well recognised as the final phase of the palliative care continuum.¹ Prevention of the morbidity and increased mortality associated with bereavement is a desirable goal of family-centred care. Despite the nobility of such objectives, the evidence for palliative medicine's success in accomplishing these outcomes is the poorest of all its endeavours. This represents a substantial challenge for contemporary research and practice: to develop effective models of prevention and care provision for the bereaved relatives of our palliative care patients.

What impact do palliative care services have on the bereaved?

In a recent meta-analysis of 26 studies of palliative and hospice care teams, Higginson and colleagues contrasted a slightly positive effect size on patient outcomes (26 studies, weighted mean 0.33, standard error (SE) 0.12 [95% CI 0.10, 0.56]) with no proven benefit on carer and family outcomes (13 studies, weighted mean 0.17, SE 0.16 [95% CI -0.14, 0.48]).² The large US National Hospice study failed to demonstrate an effect on carers.³ A recent Norwegian study randomised patients to receive comprehensive palliative care versus conventional oncological care and discerned no difference in bereavement outcome despite efforts from the palliative care teams to achieve this.⁴ Funnel plots (whose precision increases with sample size) suggested significant publication bias and statistical heterogeneity in many of these studies reporting carer outcomes, but the broad conclusions remain bleak.

Another systematic review of interventions to help carers identified 22 studies, of which nine focused on a single index carer.⁵ This review helps us to appreciate the current state of the art. Some straightforward facts emerge.

- The provision of information and psychological support for carers are substantial priority needs.
- As in the US National Hospice study,^{3,6} complicated bereavement is associated with increased physician utilisation. Clear evidence, substantiated by a wide body of other research, documents the medical (including psychosocial) morbidity suffered by the bereaved.
- Intervention to promote problem-solving skills in carers is only found to be effective for the distressed subsample.⁷
- Pilot studies of carer groups show little promise of inducing significant outcome in the psychosocial wellbeing for carers.⁸⁻¹⁶ The latter finding is noteworthy, given the Level I evidence within psychooncology studies for the effectiveness of group therapy.¹⁷ The failure of such programmes to use trained and experienced group therapists might be one explanation.

While lamenting the methodological difficulties with many studies of carers, Harding and Higginson conclude that evidence is lacking to support benefit for carers being derived from broadly offered individual, group and family interventions.⁵ As carers value self-reliance and independence, these researchers called for an approach that respects the resilience of those destined to cope well and targets those at risk of significant psychosocial and psychosomatic morbidity. Screening for predictors of morbid outcome, with appropriate triage to a comprehensive range of therapies, seems mandatory for clinical services to begin to redress this striking area of apparent neglect.

When is grief pathological?

The intensity and time course of the phenomena of grief, together with the presence of maladaptive behaviours, are generally used to differentiate normal from complicated grief. The latter can then become expressed as one of the following common psychiatric disorders: depression, anxiety, alcohol and other substance abuse/dependence, psychotic disorders and post-traumatic stress disorder. When psychiatric disorders complicate bereavement, their recognition and management is straightforward; subthreshold states present the greater clinical challenge, as studies of the bereaved indicate groups in which clusters of intense grief symptoms are distinct from uncomplicated grief.¹⁸⁻²⁰ In practice, the location of these patients in high-risk groups and the application of preventive models of bereavement care might eliminate some of the academic debate about their characteristics.

Inhibited or delayed grief

While the use of avoidance may serve some as a temporary coping mechanism, its persistence is usually associated with relationship difficulties or the emergence of a hypomanic state in individuals with bipolar disorder. Grief may be understandably absent, however, when there has been no bond of attachment to the deceased. Cultural variation obviously influences grief expression. Empirical studies have generally identified inhibited grief in up to 5% of the bereaved – it may not always present clinically, but can reappear in later years as an unresolved issue.

Chronic grief

This common form of complicated grief is particularly associated with overly dependent relationships, in which a sense of abandonment is avoided by the perpetuation of the relationship through memorialisation of the deceased and maintenance of continuing bonds. A situation emerges in which tearfulness is induced by any reminder of the deceased, without any cognitive transition being achieved

in the world view of the bereaved. Social withdrawal and depression are common.

Traumatic grief

When death has been unexpected or in some way 'shocking' – be it traumatic, violent, stigmatised or perceived as undignified – its integration and acceptance may be interfered with by the increased distress that memories can trigger. Intensive recollections, including flashbacks, nightmares and recurrent intrusive memories, cause hyperarousal, disbelief, insomnia, irritability and disturbed concentration, which distort normal grieving.²¹ The shock of the death can precipitate mistrust, anger, detachment and an unwillingness to accept its reality. These reactions at a subthreshold level merge with the full features of post-traumatic stress disorder, but the subthreshold state has been observed to persist for years and contribute substantial morbidity.

Depressive disorders

Rates of major depression in the bereaved vary in studies between 16 and 50%, peaking over the first two months,^{22,23} and gradually decreasing to 15% across the next two years.^{24,25} The features of any major depressive episode post-death resemble major depression at other points of the life cycle.²⁶ There is a tendency to chronicity, considerable social morbidity and risk of inadequate treatment.

Anxiety disorders

These take the form of adjustment disorders, generalised anxiety disorder and phobic states and occur in up to 30% of the bereaved.²⁷ Patients commonly present to GPs with a range of somatic concerns. Separation anxiety of a heightened nature can be distinguished from anxiety symptoms of a general kind.

Alcohol and substance abuse/dependence

Individuals predisposed to alcohol abuse or dependence on other substances, such as benzodiazepines, relapse during bereavement.²⁶ This is typically an exacerbation of pre-existing problems and other family members often raise the alarm.

Post-traumatic stress disorder

While primarily related to unnatural deaths (such as homicide and suicide), those that involve profound breakdown of bodily surfaces, gross disfigurement due to head and neck cancers or loss of dignity through illness may generate traumatic memories in the bereaved.

Psychotic disorders

Bereavement is a common precipitant of relapse in psychotic illnesses such as bipolar disorder or schizophrenia among individuals so predisposed; occasionally mania presents for the first time in such a setting.

Identifying those at risk of morbid bereavement outcome?

Palliative care teams are ideally placed to recognise those at increased risk of complicated grief and plan preventive interventions in an endeavour to circumvent morbidity. To accomplish this, bereavement care planning should not begin after death, but at the point of entry by the patient

Table 1. Risk factors for complicated grief*

Category	Range of circumstances
A. Nature of the death	1. Untimely within the life cycle (eg death of child) 2. Sudden and unexpected (eg death from septic neutropenia during chemotherapy) 3. Traumatic (eg shocking cachexia, bedsores, disfigurement or debility) 4. Stigmatised (eg AIDS or suicide)
B. Strengths and vulnerabilities of the carer/bereaved	5. Past history of psychiatric disorder (eg depression) 6. Personality and coping style (eg intense worrier, low self-esteem) 7. Cumulative experience of losses (eg multiple deaths, financial problems)
C. Nature of the relationship with the deceased	8. Overly dependent (eg clinging, symbiotic) 9. Ambivalent (eg angry and insecure with alcohol abuse, infidelity, gambling)
D. Family and support network	10. Dysfunctional family (eg poor cohesiveness and communication, high conflict) 11. Isolated (eg new migrant, new residential move) 12. Alienated (eg perception of poor support, disenfranchised)

*Reproduced with permission from Kissane DW. Bereavement. In: *The Oxford Textbook of Palliative Medicine*, 3rd edition.

and their family into the palliative care service. The continuity of supportive care that flows from this builds a strong therapeutic alliance, which will be more likely to survive any ambivalence about the death than if a bereavement counsellor first attempts contact only after death.

When preventive interventions are targeted to those at risk, benefits ensue,²⁸ whereas when they are broadly offered to a bereaved population regardless of risk, no such benefit is discernible.²⁹ In the latter type of study, those who are functioning well hide any evidence of benefit to those at risk. In contrast with broadly supportive, generic follow-up programmes (for example, those that utilise condolence cards and invitations to memorial services), formal bereavement interventions should be directed towards those at increased risk.

Risk factors to aid recognition of those at greater risk of complicated grief are summarised in Table 1. These should be documented at service entry and updated over time, including revision shortly after the death. Completion of the family genogram presents an ideal time for assessment of relationships, prior losses and coping to be considered. Some palliative care services have developed checklists based on such risk factors to generate a numerical measure of risk. There has been insufficient validation of such scales at this stage, but the presence of any single bereavement risk factor signifies greater risk and therefore the potential benefit of a preventive intervention. Continued observation of the pattern of grief evolution over time is appropriate whenever such concern exists.

A family model of risk recognition

Systemic theory recognises the salience of family processes to mourning and bereavement outcome.³⁰ Indeed,

exploration of the association between family functioning and bereavement morbidity highlighted the manner in which family dysfunction predicts increased rates of psychosocial morbidity in the bereaved.³¹ Family-centred care that focuses on the wellbeing of the family during palliative care is uniquely placed to reduce rates of morbidity in those subsequently bereaved.

A typology of family functioning during both palliative care and bereavement was created using cluster analysis in the Melbourne-based family grief studies.^{32,33} Dimensions of cohesiveness, expressiveness and conflict from the Family Environment Scale determined five classes of families illustrated in Table 2.³⁴ While approximately half the families that met in a palliative care setting demonstrated resilience through their family functioning, and did not need particular psychological assistance to achieve an adaptive outcome post-death, the remainder had identifiable characteristics predictive of a higher risk of morbid bereavement outcome and were targeted through a preventive model of family care.³⁵

During early bereavement, families at risk have been shown to decompensate through deterioration in their functioning with loss of cohesiveness, communication breakdown and increased conflict. A proportion of families with intermediate characteristics of functioning changes to become sullen or hostile in type. Importantly, these dysfunctional families carry the bulk of the psychosocial morbidity observed to occur during bereavement, thus highlighting the potential benefits of a family approach to intervention. Screening of families on their admission to palliative care through the use of a well-validated measure such as the Family Relationships Index (FRI) provides an ideal means to recognise those families at greater risk of morbid outcome during bereavement.³⁵ Rules to interpret family functioning and thus recognise those at risk when screening (on admission to the palliative care service) are summarised in Table 3.³⁵ The FRI has satisfactory sensitivity and specificity as a screening tool.^{36,37} Let us turn now to consider approaches to intervention.

Models of bereavement care

Once the patient has died, the palliative care team should routinely review the death and any bereavement-related risk factors in the next available multidisciplinary team (MDT) meeting. Was the death perceived to impact significantly on family members? What level of bereavement follow-up should be adopted?

Two broad models of follow-up are possible. The first is generic and involves the expression of condolences via the telephone, sympathy card, visit by the nurse or GP, staff attendance at the funeral and subsequent family invitation to a periodic commemorative service arranged by the palliative care team. This approach provides both encouragement and support, while normalising the grief that relatives express and respecting their mourning process without undue intrusion. Where greater concern does emerge, an opportunity presents to intervene appropriately. Generally, staff that have developed closer relationships with the family are wisely selected by the team to take up this observing role as it also provides them with a means of gradual farewell. Their formal identification and documentation in MDT meeting records

Table 2. Typology of palliative care and bereaved families³⁴

Category	Family type	Rate of occurrence	Features
Well-functioning types	Supportive	32%	Strongly cohesive families who grieve adaptively
	Conflict resolving	20%	Cohesion and effective communication empowers tolerance of difference of opinions; adaptive grief
Dysfunctional types	Hostile	6–12%	Poorly cohesive with high conflict, ineffective communication and relationships; families tend to resist help and develop complicated grief
	Sullen	9–18%	Muted anger generates highest levels of depression; families seek help; complicated grief
	Intermediate	20–33%	Mid-range levels of communication, cohesion and conflict place these families at risk of deterioration when stressed by life events; complicated grief

Table 3. Screening rules to recognise families at greater risk of dysfunction and complicated grief through use of the Family Relationships Index* (FRI)³⁵

- a. Well-functioning families (low risk)**
Cohesiveness score of 4 (out of maximum 4) plus FRI > 9 (out of maximum 12)
- b. Families considered at some risk**
Cohesiveness score <4 or FRI ≤9

FES* subscales	Typical range of scores for family types		
	Intermediate	Sullen	Hostile
Cohesiveness	3–4	2–3	0–1
Expressiveness	1–3	1–2	0–1
Conflict	0–1	1–2	2–4
FRI	8–9	5–7	0–4

* FRI is derived from the Family Environment Scale.³⁴ FRI is the sum of the cohesiveness, expressiveness and reversed (out of 4) conflict score; its maximum sum is 12.

[Plenary address given at the 2005 Congress of the European Association of Palliative Care, Aachen, Germany]

is nonetheless important to ensure completion of the process over time. Final contact is often shortly after the first anniversary of death.

The second model of follow-up is for those individuals or families judged to be at greater risk and thought likely to benefit from being offered a preventive intervention. Such prevention effectively reduces morbidity when delivered to those 20% likely to otherwise develop complicated grief.²⁷ Teams vary in their pursuit of this depending on staff availability; in other instances, GPs provide active individual support. Individual, group or family approaches are valid and selected on the basis of personal needs. Where continuity of involvement of the counsellor from palliative care into bereavement is possible, direct knowledge of the deceased is advantageous, as is the continuing relationship with the bereaved. Attempts to establish bereavement

counselling only after the death can meet high rates of defensive avoidance blocking this support form.

Where social isolation is noteworthy, the additional support derived from a group approach maximises relational connectedness.^{38,39} Others will seek the personal support of individual therapy. For many, a family approach is cost-effective in reaching several at risk simultaneously, when the nature of the family's functioning has been shown by screening to be dysfunctional. Family-focused grief therapy (FFGT) offers continuity from palliative care through to bereavement and, in promoting family functioning, it fosters the role of the family as a prime source of support.³⁵ Asian cultures, including the Chinese and Japanese, are especially suited to family models of care.⁴⁰

The diverse range of clinicians in palliative care teams, including nurses, social workers, GPs, psychologists or psychiatrists, chaplains or pastoral care workers, volunteers and generic bereavement counsellors, ensure that there is no shortage of staff to support the bereaved. Nevertheless, staff caught up with the business of acute patient care will neglect the bereaved despite their best of intentions. Team leadership needs to monitor actively programmes of bereavement follow-up to ensure its adherence to an intended protocol and to initiate appropriate cross-referral of those at greater risk.

Family-focused grief therapy

Family-focused grief therapy is a brief, focused and time-limited intervention that targets at-risk families identified by screening and typically comprises four to eight family sessions of 90 minutes' duration, arranged flexibly across nine to 18 months.³⁵ The patient starts off as an active member of the family meetings during palliative care, therapy then continuing with the relatives after the patient's death. The intervention aims to prevent the complications of bereavement by enhancing the functioning of the family, through exploration of its cohesion, communication (of thoughts and feelings) and handling of conflict. The story of illness and related grief is shared in the process. FFGT has three phases: assessment (one to two weekly sessions) that concentrates on identifying issues and concerns relevant to the specific family and on devising a plan to deal with them; intervention (typically two to four sessions), which focuses on the agreed concerns; and termination (one to two sessions), in which gains are consolidated and the end of therapy is confronted. The frequency and number of sessions in each phase are modified to meet the needs of the family. The techniques, themes met in FFGT and a range of approaches to the challenges of complex families have been described in a recently published book.³⁵

Therapy can be conducted in the clinic or hospital setting, but most commonly in the family home in an effort to accommodate ill patients. Although the problems and challenges associated with therapy in the home are well documented, the patient's home emerges as a much appreciated place to meet.

In a controlled trial of FFGT,⁴¹ 81 families were randomised in a 2:1 ratio to conditions of FFGT (53 families, 233 individuals) or usual care (28 families, 130 individuals). Assessments occurred at baseline and at six and 13 months after the patient's death. Primary outcome measures were

the Brief Symptom Inventory (BSI), Beck Depression Inventory (BDI) and Social Adjustment Scale (SAS). Analyses allowed for correlated family data by employing generalised estimating equations (GEE) that controlled for site and were based on an intention-to-treat. The overall impact of FFGT was a reduction in distress (BSI) at 13 months ($p=0.02$). Importantly, significant improvement in both distress and depression were demonstrated for individuals with high BSI and BDI baseline scores. Sullen families improved most overall, whereas depression remained unchanged in some hostile families. FFGT has the potential to prevent complicated grief, particularly for intermediate and sullen families, but care is needed to avoid increasing conflict in hostile families.

As part of an analysis of the fidelity of FFGT in this RCT,³⁶ insight was gained into what techniques work best for therapists conducting such family sessions. Competence was evidenced by a strong therapeutic alliance (94%), affirmation of family strengths (90%) and focus on agreed themes (76%). Therapists averaged ten grief-related questions per session, seven on communication-related issues during assessment, seven on conflict late in therapy and four on cohesiveness across the course of therapy.

Overall, 86% of therapists adhered faithfully to core elements of the model in the trial. Nevertheless, some aspects of FFGT proved more difficult to apply. Thus, therapists did not elicit family values, strengths and beliefs in 58% of assessments. Some therapists neglected to emphasise the positive, while some families had given little thought to their traditions or motto. Moreover, although therapists provided some direction to therapy in 75% of sessions, progress summaries were only found in half the sessions, this process necessitating greater confidence in understanding what has emerged.

These insights are instructive in guiding supervisors seeking to build skills in novice therapists and therapists aiming to optimise their interventions. A fundamental goal in any appraisal of family functioning is for the therapist to make sense of the family's strengths alongside their concerns, and to be able to summarise such appreciation. This direct feedback to the family builds rapport and empowers a focus for continued work. To achieve such global understanding of the family, therapists need to think regularly during a session about what they have learnt regarding the family's functioning.

The model of family-centred care offered by FFGT ensures continuity of care and is an effective model for most at-risk families who would benefit from a preventive approach. Nevertheless, a comprehensive bereavement support programme should offer a diverse range of therapies that complement a family approach with individual and group options as well.

Directions for the future

While individual care plans for continued support of those at risk can be readily developed, services able to offer a greater breadth through group and family models of care will be better equipped to respond to all their patients' needs. A group model is appreciated by spouses who are socially isolated, and can offer benefit to bereaved siblings and parents, where the homogeneity of the group adds to its benefit. For such programmes, selection of those at risk was

a key message coming from Harding and Higginson's systematic review. Our own work with FFGT offers considerable promise that such a targeted approach can be useful and cost-effective. Replication studies that more precisely ascertain the dose-response curve for level of family morbidity are now needed. Thus far, FFGT has been applied to adult and adolescent families; appropriate modification to suit paediatric oncology is desirable.

Until the empirical evidence for clear benefit is demonstrated, justification for the employment of dedicated 'bereavement counsellors' as an add-on to a palliative care programme is lacking. In contrast, approaches that promote continuity of care with the psychosocial staff encountered during palliative care seem worthwhile, with a particular emphasis on recognising those relatives at greater risk of a morbid outcome. Further research is needed urgently to garner the evidence to justify the establishment of effective bereavement programmes.

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The volunteer in palliative care – a clearly defined role

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First, I want to state that I am giving this lecture on volunteers as a qualified professional person, employed full-time, working within a clearly structured and financially rewarding field. The fact that someone outside the field under discussion has been invited to give this talk is already part of the problem. In the literature and at congresses, the role of volunteers is mainly discussed by members of staff. It is not the volunteers themselves who define their own role. This is done by others who are not members of the same club, so to speak.

Second, I would like to suggest that the story of the good Samaritan from the Bible could have been a story about a non-professional carer. You may remember how a man walks the road from Jerusalem to Jericho and falls among thieves. Passers-by like a priest and a Levite – professional carers, if you like – do not stop and come to the man's assistance. Then a socially less-privileged person enters the scene, he shows empathy and helps the badly injured man lying on the ground. Strangely enough, those who should have felt it their professional obligation to stop and help continued on their path regardless, but the person at the bottom of the social ladder took on the job in their stead. Is charity and empathy (only) the role of the volunteer?

Contribution of volunteers to palliative care

Theoretically, the involvement of volunteers is an indispensable part of the palliative care concept. In the catalogue of values of both hospice work and palliative medicine, voluntary aid and support are regarded as a constituent part of paramount importance. This is not to be understood as a cost-cutting measure to meet the challenges of caring for the dying in terms of healthcare and the changing social and political situation. Volunteers are also not intended as substitutes for professionals, where the latter can no longer be afforded. The contribution of volunteers in hospice work is seen as an independent but nonetheless complementary contribution which 'ensures, that in the public opinion aid for the dying cannot be delegated entirely to the professionals'.

There is hardly a leaflet in the field of palliative care in which volunteers are not mentioned. Textbooks and congresses discuss volunteers as one of their subjects, and sometimes it is even possible to find articles written by volunteers – in which they will not define their role, unfortunately, but describe the problems and challenges of their work from a more emotional point of view. Hospice and palliative care services rely on the contribution of volunteers and could not achieve their social and political aims without them.

Problems of voluntary work

The German hospice movement proudly announces that it relies on the contribution of about 50,000 volunteers! Due to recent legislative initiatives in Germany, resources for the promotion, recognition and social coverage of voluntary workers have been made available. Why then do we need to talk about the problems of voluntary work?

Perhaps we need to talk about it, because the practice of voluntary work in palliative care shows a less than ideal picture.

- Institutional and outpatient services increasingly decline to co-operate with volunteers (they may mention the existence of voluntary services in the daily team meetings but the contribution of voluntary workers is hardly ever seen as one of the cornerstones of their delivery of palliative care).
- Volunteers may become surrogate family members.
- Often enough, volunteers have a negative attitude towards administrative measures, such as documentation, and regard qualifications as incompatible with their general status as informal and empathic carers.
- One of the German translations of 'voluntary work' is 'ehrenamt', meaning 'honorary post'. But in our country it is now not uncommon that such a post carries expectations of some kind of employment security.
- We know that a significant number of people refuse to work as volunteers because their efforts have been frustrated in the past.
- Volunteers may suffer from helper's disease.
- Volunteers are being misused as substitutes for professional staff.
- Some voluntary organisations decline to work alongside professionals, because they believe that only those who have experienced the same kind of suffering, such as bereaved parents in the organisation 'Compassionate Friends', are able to show real understanding.

What are the reasons for the difference between lip service, vision and reality? What are the duties, roles, obligations and rights of voluntary workers? Is a concept of care that relies on volunteers 'old hat'?

Personalities in the volunteer field

And, furthermore, exactly who is this mysterious stereotypical volunteer whom the professionals in the palliative care field seem to know so well? I think, we probably take too simplistic a view of voluntary workers. As there is no such thing as 'a stereotypical dying person', why should there be 'a stereotypical volunteer'? Let us take a closer look.

- Take, for example, a 48-year-old woman. Her children have left home and she is looking for another meaningful occupation. Having been a housewife, she would like to take up 'some kind of social work' and care for others in a different way. Furthermore, she longs for social contact and interaction.
- Take the 62-year-old widow. Two years ago, her husband died from cancer after a long period of suffering. During the course of his illness, she had a very hard time. She experienced doctors who were always in a hurry and not very empathic, overstretched and exhausted nurses, endless therapies, and in the end her husband's death became an isolating and segregating experience in a multi-purpose room. At the time she resolved to help work towards a better dying culture.
- Take the man in his mid-fifties, a renowned and extremely respected member of his community with real organisational talent and many connections. He wants to fulfil his communal and social responsibilities, and he also likes being asked for advice and to exert his authority a little. Perfect material for a committee chairperson!
- Take the young mother-of-two, who temporarily neglected her career for the sake of her children, but she left it too long and lost touch with her profession. She hopes that working as a volunteer will give her some additional qualifications, good references and therefore increase her chances to return to her employment as a social worker. She is also interested in personal challenge and development.
- And finally, take the newly qualified physician in his first job. He is disappointed by the reality of work in a hospital and would like to find a place where he can put his ideals into practice, ideals that made him want to become a doctor in the first place.

These five types, chosen at random, may nevertheless be typical examples of personalities working in the voluntary sector.

Common denominators

What is it that these five personalities with five different sets of motivation and five different reasons to take up voluntary palliative care have in common? Is there even the tiniest common denominator? And, furthermore, is the make-up of volunteers completely different from that of professionals? Maybe looking at some of the terms in this field will give us a clue.

Could the status of layperson be the binding factor between these five persons? Not really, because the doctor mentioned above is not a layperson, and the four others bring along life experience and emotional maturity and compassion. This indicates a core competence that is not compatible with the term layperson.

'Honorary post' is a historical term with many promising connotations. But where is the honour? And is there really a post? Outsiders, acquaintances and friends may still have this rather colourful historic meaning in mind when they make comments like, 'This is what you do in your spare time? I couldn't do this kind of job!' A post or a job should have clear descriptions of what it encompasses – this is not true for voluntary work. Whatever needs to be done depends on the varying wishes of those who require support in whichever field is applicable at the time, and, of course, it

depends on the co-ordinator, who sets up varying task schedules for volunteers.

The term voluntary work is also ambiguous. You may take up voluntary work, but at the same time you have to make commitments and work according to the schedule you are given – not unlike a professional, who also goes to work every morning according to his/her own will, almost.

Unpaid work – this is what seems to be left at last as the binding factor. But does the term unpaid work, and this means unpaid work done by tens of thousands in each country, somehow belittle the huge commitment of those who do it?

Other terms I found in the literature were charity – a personal obligation to do social good; solidary action; informal care; non-commercial (not-for-profit) work; and acts of social and civil responsibility. They all seem to be rather vague and contrived terms and not very helpful.

If there is no stereotype of a volunteer, then there is also no predefined role that a volunteer should take on. Their roles seem to be as individual as the volunteers themselves. Nevertheless, a volunteer's role is not to be defined by the volunteer him/herself at his/her individual will. We could stop here and answer the title question of this lecture in the negative. 'No, the term volunteer does not imply a clearly defined role.' But this is not a satisfying answer.

The benchmark for contributions of volunteers, their duration and intensity of commitment, can be none other than what a dying person and his/her family need, in addition to pain and other symptom control, palliative nursing care and the social support of professionals.

Therefore, from the viewpoint of a dying person and his/her family, a volunteer is expected to act as a kind of chameleon within the environment of their wishes. What volunteers should not have are aims, ideas or needs of their own. Because the services to be delivered by a volunteer should fit exactly the expectations of those who are in need of support, volunteers can by no means act according to their will/'voluntas', not even according to their wishes. In practice, their commitment is not inclination-oriented, but rather ability-oriented.

This leaves the question as to who would make a good volunteer and who is going to decide this? And furthermore, who places the volunteers according to their abilities and with which families? The co-ordinator has a very important and responsible part in this field. First, she organises information events. Those who are interested in taking up voluntary work will then take part in a qualification course. This early encounter is of paramount importance for further developments; it lays the foundation stone for further commitment and is the key to future success or disappointment. If this early chance to build mutual trust, a feeling of solidarity, co-operation and an openness to honest self-appraisal on both sides is not handled well, the first step to a regressive development is already taken. Therefore, the aims and content of these qualifications need to be well considered. The same applies to the teaching content and the role model aspect presented by the co-ordinator.

Content of training courses for volunteers

How to communicate with oneself?

A professional carer must employ a twofold attitude towards the suffering nature of the human existence. On the one

hand, the carer needs to detect the reasons for suffering and other people's pain in order to eliminate them. The carer is expected to give a practical, positive answer to problematic matters of existential and physical suffering. On the other hand, the carer is expected to accept his/her own existential suffering as an indispensable part of the human nature and to live life in harmony with the knowledge of one's own inevitable mortality. In working with a patient facing death, a carer must be able to reflect on his/her own life and attitude towards his/her own mortality. Otherwise, real and true support cannot be given.

Therefore, work on one's own biography is seen as the central element for the delivery of good care. Experiences of loss, death and dying must be considered in terms of one's own concepts of dealing with these experiences. We know that further training programmes that address matters of death and dying are not fruitful unless the participants have previously been given enough room to reflect on their own experiences in this field and make a comparison with the experiences and attitudes of others.

If – for example – a person who still bears a grudge against institutions like hospitals or nursing homes, has not been able to deal with his/her own feelings of guilt or cannot express his/her true hopes and fears, these feelings and unreflected attitudes may surface involuntarily and unexpectedly within inappropriate care contexts and get in the way of delivering good quality care.

Another important aspect of training courses, which include units on autobiographical work and self-assessment, is that participants will learn what impact their previous experience of death and dying has on their expectations of their own death. Every experience has left its mark on one's own concept of what other people's and one's own death should or should not be like. There is a danger of promulgating one's own concept of death, which does not allow others their own individual experience of death.

'As a student, I worked at the university clinics of Bonn during my vacation. One day, all of a sudden I found myself involved in the care for an old patient who, even from his hospital bed, continued to reign over his family members like a despot, so that none of them came to see him. Fearing his death would be a lonesome experience, I undertook measures to make up for his behaviour. The old chap sensed what I was up to and was luckily not too weak to stop me by saying, "Don't even think of dragging my family to my bedside when I'm going to die. This is a moment I will celebrate on my own." I learned a lot from that man.'

Reasons and motivation for caring

The reasons behind the social involvement of voluntary workers, especially in the field of care, must be thoroughly questioned and reflected on. This is quite the opposite of mistrust: it is the first and most important step towards truly autonomous and responsible action. What is it that I am doing? To whose benefit are my actions? What are my intentions?

Some people do what they do because it was the only possible role they were given within their own family, and maybe they were loved and adored only when caring for others. Some people do what they do because they want to rid themselves of the fear of their own mortality, and they may think that dealing with other people's death would

Box 1. What volunteers need and contribute

Volunteers contribute:

- Personality
- Openness to self-reflection
- Dependability
- Identification with the care concept and its practical implications
- Willingness to serve and cater for someone else's needs
- Personal strength and life experience that are not limited to the process of helping
- Acceptance of the necessity of training and documentation.

Volunteers need:

- Trust and respect
- Competent, sensitive and (tutelary/protective) co-ordinators
- Continuing training, work assistance and supervision.

Then they can find their roles:

- Voluntarily
- Reliably
- Not oriented to material gains
- In the public arena
- Co-operatively
- Supportively
- Responsibly and autonomously
- Within a framework of limited time and resources.

cure them of their own fears. Other people do what they do because they feel unimportant, maybe even 'invisible' in their ordinary life, and they may like this new position of someone who is in charge. None of these reasons are bad in themselves, but it is very important that volunteers and co-ordinators are aware of them. Otherwise, these reasons may become secretly counterproductive, and they may result in volunteers burdening, rather than supporting, patients; or lead to burnout on the part of the volunteers.

People who work in the care of the dying are often described by others as brave, strong, selfless, empathic, compassionate, kind, warm-hearted, ready to help, altruistic and so on. Before accepting descriptions such as these as self-evident, volunteers should ask themselves whether or not these adjectives describe the true attitudes behind their contribution. They should also ask themselves whether or not some selfish reasons may in fact determine their action, something that would be neither unusual nor 'forbidden'. To be able to do so, volunteers need support from the early stages of their involvement onwards. As already mentioned in my own example of caring for a dying old man, two 'real selves' meet in the process of support. They should see each others as partners, who are responsible for their own actions, and not as 'a help automaton' or 'a mere passive recipient of help'. This means that the helper is truly grounded in his/her own self and able to be open to other people.

Attitude rather than technique

A qualification concept, in which the wishes and needs of dying people and their families are the highest aim, must strive to build up and strengthen certain attitudes rather than techniques. If the aim were to learn a number of techniques, this would imply that those who are cared for, are treated as objects, not subjects. The dying person is not in need of care methods but rather of human care and solidarity. Humanity and solidarity are attitudes, not methods or techniques.

One of the greatest challenges facing the co-ordinator is to act as a role model for volunteers and potential volunteers in terms of understanding the paramount importance of attitudes in human contacts. She should be able to show clearly the importance of a dialogical approach to others as well as the indispensability of respect for the dignity and integrity of others. She should also be a living example of a well-balanced person in terms of talking about feelings, meaning that she can keep the necessary distance while at the same time still being empathic.

Nevertheless, the wishes and needs of dying patients and their families must be known to the volunteer or – if they are not clear – carefully evaluated. By the same token, patients and families may be under such agonising physical or mental stress that it is difficult for them to define clearly what they want.

Even so, volunteers cannot assume that the wishes and needs of the dying and their families conform to a certain pattern, for each person deals individually with anticipated and real losses. Therefore, the volunteer should be taught to listen carefully to what is being said and to understand non-verbal information.

‘During a supervision session a volunteer once reported about an aphasic patient, to whom she recited a prayer at the end of each of her visits. After the patient’s death she learned from his daughter, when they were preparing the funeral ceremony, that the patient had not been a member of a church for many years. The volunteer felt very insecure about her action in retrospect. When asked why she had believed that the patient would have liked to say a prayer, she answered that she had assumed this were the case. In a role play, where she then took on the role of the patient and reflected on all the observed gestures, it became obvious that the patient must have given enough signs of refusal and ‘inner emigration’ and that the volunteer had been too sure of her assumption to detect those signs.’

This example clarifies how important it is that qualification measures include unprejudiced attention to the patient. Volunteers must understand that perception of a patient should not be based on interpretation and assumptions but on the most attentive listening and observation, without any preconceived conclusions. Therefore, a training unit on ‘how to perceive’ is of the utmost importance.

The neutral point of view that should be taken by the volunteer is not to be misunderstood as being that of a distant observer of the process of dying and the network of family relationships. Neutrality is not indifference, but an independent look at things and processes, unbiased by ideology, prejudices and assumptions.

Let me assume the role of a mature volunteer who might say the following, ‘It is not only us who are in need of training. Those who co-ordinate our services and the institutions and services we are supporting need to be enabled to work along with volunteers. It is not our

responsibility to find out what the targets of voluntary support of these services should encompass. Therefore, these services must clearly define their roles first before they go and develop training aims for us and ask themselves on the basis of these definitions the following questions:

- What is it that the volunteers should do?
- Where should they do it?
- In co-operation with, and complementary to whom, should they do it?

It is the institutions and services and not the volunteers that are responsible for connecting professionals with voluntary workers. The field of care is still largely influenced by the attitudes of professionals. Whenever voluntary informal carers are to be integrated in care, it is also the professionals who have to make certain adjustments. These are necessary, for example, in the field of manifest structures of co-operation and routines. The co-operation with volunteers must be oriented to changing needs and contexts.

Integration

An artificial division of professional and voluntary contributions in the delivery of ‘proper’ treatment and supplementary care, and a reduction of the volunteer to a mere ‘holding of the patient’s hand’, is discriminating and does not comply with the patient’s needs for a holistic approach. In order to deliver a trustful atmosphere of all-encompassing care, volunteers need to be integrated in the early stages of care. They are not some kind of last resort when the professionals are becoming less involved. Rather, they represent an additional and assisting social service of everyday care with certain qualifications of its own. Professionals and volunteers must find the appropriate way to link one with the other most effectively.

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Biology and pharmacology of the elderly: start low – go slow

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Aging is a continuous process beginning early in life. However, age is a relative term, as a person may be considered old at a nominal age of 65. Social and medical advances have changed the age composition of advanced industrialised countries. These demographic changes are dramatic. For example, in 1950 the number of persons above 65 years of age constituted about 8% of the total US population. This figure increased to about 13% in 2000 and is expected to reach about 20% in 2030.¹ It is estimated that the cancer incidence in Norway will increase by 26% over the next two decades.² Approximately 50% of the increase in cancer incidence is caused by an aging population; as around 60% of cancer occurs in those above 65, the incidence of cancer in this group being more than ten times that of younger people.¹ Pain accompanies cancer; in addition, the older person may have a high prevalence of pain, regardless of cancer.^{3,4} The older generation are more exposed to disease in all organs, and therefore are more complex with more co-morbidities. Many patients now live longer with active disease and intensive oncology treatment for a longer period of time. This may influence palliative care with regard to symptom complexity and need for care over a longer time period. Furthermore, an older population means potentially having older family members at home, and will probably influence and limit the possibility for many patients to stay at home since it is well documented that most patients will need a close relative to be able to stay home. As a consequence, the number of patients in need of palliation will increase substantially over the next decades. This dramatic change in the composition of the patient population is a major challenge for the healthcare system, both at an organisational level and at staff level.⁵ Unfortunately, the paucity of clinically controlled studies in older people limits the possibilities to make evidence-based recommendations for this group of patients.

The older palliative care patient

In general, palliative care patients are bothered by a series of distressing symptoms such as fatigue, pain and reduced appetite, often concurrently. Many older patients, especially those in nursing homes, are cognitively impaired together with impaired mobility, sleeping problems, anxiety/depression and cachexia. Pain is one of the most feared symptoms. Despite efforts to control pain, a substantial number of older patients still suffer from pain, either due to lack of a proper diagnosis or appropriate treatment.⁵⁻⁷

In palliative care, most of the treatment is symptomatic and most symptoms are of subjective nature. Consequently, symptom assessment should be undertaken as a patient self-report. Cognitive impairments such as dementia and delirium are major threats to symptom assessment. It follows that the aging of society will be very challenging for society, and not least for palliative care.

Aging

A person above 65 is considered old, those above 80 the oldest old, and those above 90 as the very old. Aging is a continuous process of functional decline; apparent changes of aging come after puberty, or at the time when mortality rates are at the lowest. Functional decline with age reduces the capacity to adjust to a variety of everyday stress. A major problem is that aging is not readily distinguished from disease and disability. Aged is a state or condition that may or may not correlate with chronological age, and more often than not reflects the loss of a person's capacity to maintain an independent life. Aging is described as continuous set of time-dependent processes that generally mirrors chronological age, but is variable and highly individual. Unfortunately, there are no validated indices of biological age,⁸ however, the Comprehensive Geriatric Assessment (CGA) is used by geriatricians to classify patients by their biological (or physiological) age rather than the chronological.^{1,3} Regardless, a prominent feature of aging is reduction in the capacity of functions, vital and non-vital functions. These may reduce the ability to perform the daily activities of living (ADLs) as well instrumental activities (IADLs), such as driving.³

Organ functions

Cross-sectional studies of functional capacity in humans clearly demonstrate numerous functional declines starting at 30 years of age. However, optimal accommodation of the eye and high frequency hearing are observed much earlier, while personality on the other hand remains unchanged throughout life. Gender differences in aging are also shown, for instance female hearing is much more robust to aging than male hearing. Aging of the sensory perceptual systems contributes significantly to the problems of older people. The aging of these senses correlate more closely to chronological age than other systems. Important consequences of such reduced functions are interference with appetite (smell, taste) or communication and social functioning (vision, hearing).⁸

Longitudinal studies of aging may display different results to cross-sectional ones. Cardiovascular function was apparently stable when measured with cardiac output in the seventh and eighth decades of life, when individuals with occult disease were excluded from the sample, in contrast to the 25% reduction reported in the cross-sectional studies. This shows how difficult it is to separate aging from disease.⁸

Homeostasis

In addition to reduction in single organ functions, impairment in homeostatic mechanisms in the older population also develops; for example, impairment in:

- Fluid balance, which may increase the risk of both overhydration and dehydration
- Blood pressure control, causing orthostatic hypotension
- Temperature control (risk for hypothermia and infection without fever)
- Balance, which may lead to fall injuries
- Cognition, especially psychomotor speed (affecting driving skills and instrumental command, which may lead to isolation)

Pain

When discussing age in a palliative context, pain is an important subject. Pain in the geriatric population may be named presbyalgos (presby = old, algos = pain) similar to presbycusis of presbyopia (age-related reduction in hearing and vision, respectively). Thus, presbyalgos is the age changes in pain sensitivity, perception, effect and behaviour.⁹ Little is known about presbyalgos as the interest from the scientific community has been low.

Pain sensitivity

Many people seem to believe that the sensitivity for painful stimuli is reduced with age similar to sensory systems such as hearing and vision. However, pain threshold studies in the laboratory have given contradictory results, and the present view is that aging itself has minimal effect on superficial, acute pain.⁴ Also, little is known about aging and procedural pain, as well as post-surgical pain.⁹

On the other hand, there is clinical experience and some evidence that age may change pain as a symptom resulting in atypical pain presentation. The elderly have more silent myocardial infarctions than the young, indicating an age difference with respect to referred pain. In line with this, the elderly more often than the young have an atypical or vague pain presentation towards reduced pain under such conditions.⁹

Chronic pain

Older people have more arthritis, bone and joint disorders, back problems and other chronic conditions.^{4,9} Moreover, the elderly report significantly higher pain intensity than the young. Also, it is observed that pain gives more limitations of activities of daily living than for the young. Authors claim that there is no difference in Stage 1 pain effect (the immediate unpleasantness of pain) between younger and older persons. When it comes to Stage 2 pain effect, more or less the suffering that is related to pain, the elderly present lower scores on all domains such as depression, anxiety, fear, frustration and anger than the young.⁹

Special considerations in geriatric pain

Pain is one of the most prevalent and challenging symptoms in this group of patients, both to treat and to diagnose. The old person with age-related reduction in functions as described above must be assessed with respect to these in order to appreciate the functional consequences of pain. The concept, both in patients and healthcare providers, that pain is a normal consequence of aging may be harmful, as this may lead to unnecessary pain-related suffering in the elderly.^{3,4,9}

Pain is a subjective symptom; therefore the application of self-assessment methodology is recommended. A series of instruments have been developed, but there is no consensus internationally as to which methodology to apply. The EAPC has recommended the use of a Numerical Rating Scale (NRS) to assess pain intensity and the Brief Pain Inventory (BPI), if more comprehensive instruments are applied. However, recently there has been raised doubt about the ability of BPI to distinguish the impact of pain on functions from other causes.¹⁰ For the moderately cognitively impaired patient, an NRS scale is easy to use. For patients with major cognitive impairment, proxy ratings (by healthcare providers and/or family members) are recommended. If such an approach is used, systematic assessment is recommended. However, there is no consensus on which method to use for proxies.¹⁰ In most of the assessment methods, behavioural indicators are often used, such as verbal, facial expressions, movement, action and mental functioning.

Pain interventions in the elderly

Few studies have addressed the outcome of pain center interventions in the geriatric population. Cutler *et al* concluded that geriatric patients were distinctly different from younger pain patients,¹¹ the geriatric patients showed significant and meaningful improvement with pain center treatment, and their improvement was by and large as great as for the younger groups. Thus, pain in the elderly benefits from treatment; although the old person requires special attention as given in guidelines of the American Geriatrics Society.^{4,9}

Consequently, in daily clinical practice one must take age into consideration during assessment and treatment of symptoms. There is a great need to perform clinical studies, including high enough numbers of older patients, and patients with cognitive impairment. There is an urgent need to develop and agree upon common assessment methodology for subjective symptoms in palliative care in general and specifically for the older and cognitively impaired patients. At the European and national level, it is necessary that palliative care is regarded as a subspecialty for key health care providers, specifically in medicine, and that plans on how to organise palliative care for the elderly preferably as an integrated part of the public health care symptoms is developed. It will be helpful with European guidelines, including curricula for specialist training as well as guidelines on how to organise palliative care.

Pharmacology

The pharmacotherapeutics of the older patient differs considerably from the young one. In general,

pharmacological responses vary more among old individuals, thus the effect of standard doses are less predictable. Age-related factors may change the disposition of drugs (altered pharmacokinetics) or pharmacodynamics (sensitivity). Increased sensitivity may result from the decrease in homeostatic functions in the elderly. Such age-related functional changes may not be distinguishable from disease-related changes as the older person becomes more ill. The older person uses more drugs, which may increase the likelihood for drug interactions,¹² and the older person may also have problems with compliance – that is, taking the drugs as prescribed. Adverse effects in the elderly often comprise confusion, ataxia, falls, orthostatic hypotension, urinary retention and constipation.¹³

Pharmacokinetics

Pharmacokinetics describes drug uptake, distribution and excretion; or more simply, what the body does to the drug. The major contributing factors are age-related changes in body composition and reduction in the excretory organs such as the liver and kidney. By and large, age-related changes will tend to increase serum drug concentrations resulting in more pronounced drug actions, or increase the duration of action by means of a longer terminal half-life.

Fat content is increased, and water content is reduced in the older person. This may decrease the volume of distribution for water-soluble compounds, which combined with decreased renal excretion, may lead to higher concentration of ethanol, for example. Fat-soluble drugs may or may not have increased volume of distribution; for example, is the longer terminal half-life of diazepam in older people caused by a larger volume of distribution and not by reduced clearance by the liver?¹³

Hepatic mass and blood flow are reduced in the elderly. However, this change is small compared with the normal variation between individuals regardless of age. Thus, the clinical significance of age-related changes in the liver metabolism of drugs is uncertain.^{13,14} Age seems to have little significance on the hepatic pharmacokinetics of the opioids,^{15,16} although methadone should be used with care in older patients due to its long and variable half-life.⁴

The picture is much clearer when it comes to renal excretion. Age causes a fairly consistent reduction of renal function. Serum creatinine is not a good indicator of renal function in an older person due to reduced muscle mass; instead creatinine clearance should be calculated.^{17,18} It is important to stress that the older person is more prone to dehydration than their younger counterpart, which further reduces renal clearance. Reduced renal clearance may be harmful when an active drug or active metabolite depends on renal excretion to terminate their actions. Examples of such drugs are aminoglycosides, lithium, digoxin and chlorpropamide.¹³ Non-steroidal anti-inflammatory drugs (NSAIDs) excreted by the kidneys should be used with great care in old people due to increased risk for accumulation.¹⁸ Also, one should be aware that the morphine-6-glucuronide is pharmacologically active, and its elimination depends on renal excretion. Thus, morphine should be used with care in the older patient with a renal function at risk.¹⁹ These considerations are major arguments for active hydration in patients exposed to a variety of drugs.

Fentanyl is administered as a patch or by the oral transmucosal route. Barriers such as skin undergo age-related changes. For the fentanyl patch, this may lead to increased absorption in the elderly,²⁰ while no difference has been found for the oral transmucosal fentanyl.¹⁶

Pharmacodynamics

Pharmacodynamics is the action that a drug exerts; that is, what a drug does to the body. Drug action is usually considered to be the result of the binding of the drug to receptors, an interaction that elicits a biological response. If more drug is needed to produce a response, sensitivity is decreased. Little is known about age-related alterations in man, but it is conceivable that sensitivity can both increase and decrease. Studies in humans indicate that beta-receptor sensitivity may be decreased with age. Increased sensitivity is reported for psychotherapeutic drugs; for example, psychomotor function impairment by diazepam.¹³ For the opioid agonist fentanyl, on the other hand, the data indicate that the sensitivity for this drug is increased in older people,^{15,16,20} which is probably true for the other opioids as well.¹³ However, these data are largely experimental and their relevance for palliative care remains unsettled.

Homeostasis

Decreased renal function does not only reduce excretion of water-soluble drugs and metabolites, but the older patient also has less capacity to excrete both free water and salt, that is to maintain salt-water homeostasis. Due to the lower capacity to maintain homeostasis, drugs such as diuretics may increase the likelihood of hyponatremia or dehydration (volume depletion) resulting in oedema or hypotension. Also NSAIDs are likely to cause salt retention in older people.¹³

Drugs and cognitive function

Cognitive impairment is associated with aging. Elderly people are also more at risk of developing cognitive impairment as a result of medication, ranging from major confusional syndromes and dementia to subtle cognitive abnormalities. Early diagnosis and drug withdrawal is essential.²¹

Age-drug relationships in general

It is not easy to determine when pharmacological age-related changes may have clinical significance. Cusack *et al* have drawn up a table of drug classes,¹³ and described the mechanism of action for a significant age-related change, whether dose adjustments were necessary, and the common adverse event related to the actual drug-age circumstance.

Prescribing and compliance

Several 'non-pharmacological' circumstances amplify problems related to geriatric pharmacotherapy. First, the elderly person may have several prescribers/specialists due to co-morbidities.²² These specialists do not necessarily communicate well, and at least for the US population, they may fill out prescriptions at multiple pharmacies. The result is polypharmacy with the consequences described below. Second, compliance is the other circumstance that causes significant problems in geriatric pharmacotherapy. It is easy

to understand that compliance may be considerably reduced in the older person. First, the older patient may have to keep track of more drugs than a younger person. Second, the older patient may have more or less reduced cognitive functions. Non-compliance with medication may represent 10% of all hospitalisations in older patients.¹³

As indicated above, polypharmacy is common in the elderly patient, and the risk for drug interactions increased. In a survey conducted in Europe on drug-drug interactions (DDI) in the elderly patient it was found that the elderly on average used seven drugs per person, and the 46% had at least one drug combination that could lead to a DDI.²³ Almost one potential DDI was found per person. Ten per cent should have been avoided. The risk for subtherapeutic effects was as common as the risk for adverse reactions. Lists of drug combinations that should be avoided in the geriatric populations are available.²³ Data can also be found on drugs that are inappropriate for use in the elderly.²⁴ In the perspective of palliative care, opioids such as pethidine, pentazocine and propoxyphene are listed. In this publication some NSAIDs are also listed.²⁴ NSAIDs are listed in tables of drug-disease combinations that should be avoided in the elderly. NSAIDs are shown to increase the risk for serious adverse effects in the elderly.²⁵ This risk is not trivial, as serious gastric complications increase tenfold in the very old population. Furthermore, NSAIDs may, especially in the elderly population, precipitate renal and cardiac failure with significant morbidity and also mortality. Thus, NSAIDs should only be used in elderly with good reason, and when they are used the patient should be monitored closely for adverse effects.¹⁸

Consequently, the following principles should be used for safe prescription in the elderly:¹³

- Is drug therapy required?
- If drug therapy is required, which drug is appropriate?
- Is the patient being asked to take more drugs than are tolerable or manageable?
- Which type of preparations should be used?
- Should the standard dose or dosage schedule be modified?
- Which adverse effects are likely to occur, and which drugs should be avoided if possible?
- Should the drugs be specially packaged and labelled?
- Can the patient living at home manage self-medication?
- Is there a need for continued medication?

Conclusion

Aging results in the reduction of most functions. This functional reduction threatens the all-over wellbeing related to good health and an active social life. The elderly are more susceptible to both disease and the actions of drugs. Their

ability to comply with the inevitable increase of prescriptions is also reduced. These changes are apparent in many palliative care patients, and they make it more difficult to diagnose and treat symptoms.

Most of the age-related changes in pharmacology cause stronger effects from drugs in the elderly. A critical and conservative approach to drug therapy is therefore of the utmost importance, and when a drug is indicated, the slogans 'start low, go slow' seems justified and highly recommended. Moreover, repeated evaluation of the treatment with respect to desired effects or troublesome adverse effects is required. Stopping of treatment is often required to evaluate whether the patient benefits from pharmacotherapy or not.

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Palliative care communication in a cultural context

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Palliative care as a model of care was developed in the West. With Christian roots, it stems from the needs of a population suffering and dying from degenerative diseases occurring late in life.¹ On a global level, 85% of the 56 million deaths per year in the developing world² occur at a younger age and are often due to infectious diseases. So can this standard model be imported into the developing world and can it answer all the questions or is it doomed to fail? If it is transported there, what are the challenges? How can it be adapted to the cultural context, to the existing healthcare system and to the economic challenges? The purpose of this paper is to highlight some of the ethical aspects about communication in various cultures.

Culture, ethics and communication

Culture is the aggregate of people's way of life; in particular, a group of people's knowledge, beliefs and attitudes, but also those practices and ideas that may be non-verbal and go unstated.³ Culture is a body of beliefs and customs that defines a group of people as being connected and that determines their identity.

Attitudes towards end of life are relative to particular cultures, societies and times. Culture influences the way we see and understand the world, shapes interpretation and gives meaning to suffering and death. Culture establishes acceptable behaviours regarding communication and emphasises the role of different patients, families, communities and life events relating to illness.⁴

Autonomy, a popular concept in North America, seems to have become in some countries the pre-eminent ethical value, ahead of beneficence, non-maleficence and justice, the other three ethical principals identified by Beauchamp and Childress.⁵ But autonomy has to be compatible with other values like liberty, loyalty, friendship and faith. Part of being an autonomous person lies in discovering how to strike a balance between the desire to choose and the desire to belong; to follow or to be led; how to forgo the opportunity to choose in order to protect one's welfare or to demonstrate membership to a larger whole. These are important components of the individual identity.⁶

Through this perspective, we might understand why in many non-Western cultures the family or community members are perceived as the ones entitled to receive and disclose information necessary to decision-making and to the organisation of patient care. This is different from Western medicine, which assumes that the person experiencing the illness is the best person to make healthcare decisions. In non-Western contexts, other factors seem to be important like respect for the traditional authority of the medical profession, coupled with strong religious observance and greater reliance on intrafamilial support during

disruptive life events.¹ In places such as China, Spain, Portugal and in societies where the sense of family remains stronger and where the family acts as an interface between the patient and the healthcare system, autonomy is no longer the backbone of biomedical ethics and can never describe the whole picture of morality satisfactorily.^{7,8}

Communication in palliative care

Effective doctor-patient communication is the means by which the confidence and co-operation of the patient are secured, and an appropriate diagnosis is made. It is a part of the treatment that may be as important as drug prescription. Communication should be viewed as a core clinical skill as doctors and nurses usually talk and listen to patients and families more often than they perform any other single medical or nursing procedure.⁹

Communication extends beyond conveying information, to conveying emotional and social support. Indeed, supportive communication with family members appears to be an important means of reducing psychological distress.¹⁰

Care

Communication is an essential part of the patient's care. It is a two-way process that, besides sharing information, also involves listening skills, especially to patient's questions and concerns. It is the means by which we have a glimpse into a patient's understanding of the nature of illness and of his expectations regarding the evolution of the disease.

It is interesting to note that Greek¹¹ and Arabic patients identify two types of cancer: good cancer described as a 'male form of cancer' and bad cancer described as a 'female form of cancer'. I encounter the same beliefs in Romanian patients living mainly in the rural areas.

Consent

Consent should be given voluntarily, competently and in an informed manner, so it should be based on sufficient knowledge and understanding by the patient of the procedure for which consent is sought. In my experience of Romania, most patients leave the decision-making to the doctor, because the doctor has the knowledge and they trust he/she will act in their best interest.

Disclosure

Disclosure about diagnosis and prognosis is the main focus of research in the field of communication. Diagnosis disclosure to cancer patients is still a controversial issue and attitudes vary in different countries with diverse cultures.¹² Disclosure contains five dimensions: who tells, when to tell, whom to tell, how to tell and how much to tell.¹³ At the moment there is only consensus on who should tell, in a context where the physician is seen as the person who has

the right and the responsibility to tell. Consensus about the other aspects is lacking.

Whereas in America and Northern Europe, the debate has moved on from whether to disclose to how to disclose, much of the rest of the world has not readily accepted the idea of fully informing the individual with cancer.

When it comes to the information needs of patients regarding the diagnosis and prognosis, Fallowfield *et al* argue that, 'The evidence for substantial cultural differences ... is rather thin or inconclusive'.¹⁴ but there are other well conducted studies on Asian patients introducing the idea that cancer patients and their families want less information than their Western counterparts.¹⁵

Unfortunately, there have been very few studies examining current experiences of communication preferences or interventions from the perspectives of non-English speaking patients and doctors. A review of surveys of patients and families around the world shows there is a nondisclosure dominant culture in countries like Italy, Spain, Russia, Japan and South Eastern Europe.¹⁶ For professionals newly involved in palliative care who come from the emerging services of the developing world, the chief source of information available regarding communication originates from the West. Applying the rules of the West non-selectively, without paying attention to local traditions and values might result in practices that are inappropriate for that culture.

Conclusion

There is no evidence that full disclosure carries the same benefit to patients from in all cultures. Autonomy is not

necessarily the sovereign ethical principle in non-Western cultures. Recognition of culturally based attitudes and beliefs is a key issue, but caution should be taken to avoid cultural stereotyping; it is important that doctors tailor the information to the needs and preferences of each individual patient and their family members.

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Palliative care in Europe: a view across the borders

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Reviewing European palliative care development presents methodological challenges due to different interpretations of 'palliative care' and disputed evidence on the ground. These problems are compounded by varying definitions of 'Europe' and the resultant inclusion/exclusion of countries or regions. A dictionary definition suggests that Europe extends west from the Dardanelles, the Black Sea and the Ural Mountains – in effect, a peninsula of the Eurasian land mass; these borders, however, rule out the British Isles, Ireland, Iceland, Cyprus and Malta. By contrast, the World Health Organization (WHO) European region reaches east as far as Kyrgyzstan, incorporating countries more usually associated with 'central Asia'. The Council of Europe's member states end at the Urals, and while the aforementioned isles are included, Monaco and Belarus are excluded. The European Association for Palliative Care (EAPC) counts Israel among its collective members.

Service development

In view of these flexible boundaries, the breadth of this paper is not constrained by one definition. Rather, it attempts to acknowledge the imaginative ways in which hospice and palliative care services have become established in a wide range of settings, and in the context of different world views, cultures and faiths. Consequently, an inclusive view is adopted that embraces the totality of these definitions, ranging north as far as Iceland, west to encompass Portugal, east to include Kyrgyzstan, and south as far as Israel.

Across this region, local pioneers have woven a rich tapestry of provision. Founding services give a glimpse of the perceptions of these early pioneers regarding the essence and landscape of palliative care. Looking towards what is sometimes called the British model, freestanding hospices were established in Cyprus (Arodaphnousa Hospice, Nicosia), the Netherlands (Johannes Hospice, Vleuten), Romania (St Laurence's Hospice, Cernavoda) and Russia (Lakhta Hospice, St Petersburg). A community focus underpinned the home care services of Armenia (Yerevan), Austria (Vienna), Bulgaria (Sofia), Iceland (Reykjavik) and Slovenia (Ljubljana); whereas a public health perspective encapsulated the hospital inpatient services in Czech Republic (Babice), Germany (Cologne), Luxembourg (Esch-sur-Alzette), Slovakia (Bratislava) and Spain (Santander). In some cases, services overlapped as attempts were made to strengthen the links between hospital and home care, as seen in Sweden (Motala)¹ and Switzerland (Ticino).²

Inspiration for these newly founded services came from many sources. Religious institutions played a part. In

Norway, Franciscan Aid established the first European service outside Britain (Oslo, 1974);³ the congregation of Lord's Ark Church, Nowa Huta (1976), foreshadowed the hospice movement in Poland⁴ and the Lithuanian Caritas Federation forged innovative links with the Public Health Department of Kaunas Municipality.⁵ Cancer organisations also featured prominently, as seen in Cyprus,⁶ Greece,⁷ and Iceland.⁸ No single group had a monopoly on innovation. Palliativists in Holland refer to the influence of the nursing home network⁹ and in Spain to the impact of a country-wide group of physicians that had a special interest in care for the dying.¹⁰

Some organisations arose from local need – the 'bottom-up' model that frequently draws on the goodwill of volunteers – and these may be clearly seen in Hungary¹¹ and Slovakia.¹² Others, as in St Petersburg,¹³ became established with the assistance of national or local government. And there were those prompted by international organisations; such as the WHO – as in the Catalonia initiative,¹⁴ the American International Health Alliance – as seen in Kyrgyzstan,¹⁵ and the British/Romanian partnership Hospice of Hope Romania.¹⁶

Cross-boundary collaborations such as the 'twinning' of services have proved beneficial. These are typified by the relationship forged between the Hungarian Hospice Foundation, Budapest, and the Tbilisi-based (Georgia) Cancer Prevention Centre; and also by the three-way relationship that has developed between the Malta Hospice Association, the UK-based Hayward House Hospice, and the Mary Potter Centre for Palliative Care in Albania.

With the exception of Poland, founding services in Western Europe were mostly established before 1990 whereas in central and eastern Europe (CEE) developments have occurred since the decline of communism. Founding services in only two countries focused exclusively on children: Belarus Children's Hospice, established in Minsk from 1993¹⁷ and St Laurence's Hospice, Cernavoda (Romania, 1992).

International reviews

Throughout Europe, there is growing interest in the nature and scope of palliative care developments and recognition of the need for comparative data. This requirement has come into sharper focus with the Council of Europe recommendation (Rec 2003/24), recently accepted by ministers: that all 45 member states adopt policies, legislative and other measures necessary for a coherent and comprehensive national framework policy for palliative care.

Among current activities is a review of services in 16 European countries led by Reimer Gronemeyer of the

University of Giessen (Germany). Also in Germany, Thomas Schindler and Birgit Jaspers have received a Bundestag commission to review hospice/palliative care provision in Germany compared with nine other European countries. In their detailed report, Schindler and Jaspers made numerous recommendations, including: the right for each individual to receive palliative care according to need; the establishment of paediatric palliative care services; paid leave for relatives caring for family members dying at home; and for palliative medicine to be an obligatory component of medical training. Also, a Spain-based EAPC task force led by Carlos Centeno Cortés has been designed to produce a 'European atlas of palliative care' by April 2005 and with its focus on the elderly, a European Federation of Older Persons (EURAG) initiative, led by Johann Baumgartner and Markus Narath (Graz, Austria), has sought to make palliative care a priority on the European Health Agenda.¹⁸

A study by Clark *et al* focused on seven countries in western Europe, paying attention to factors like early origins, patterns of provision, and structural and policy integration.¹⁹ Among the findings was a disparity of provision relating to the ratio of hospice beds to population: one bed to around 18,000 people in the UK; one bed to 1.9 million in Italy. The study concluded that despite different processes of development, the emergent discipline of palliative care now finds its most congenial home within the structures of the formal healthcare system.

More recently, a review was undertaken of palliative care developments in 28 countries of central/eastern Europe and central Asia;²⁰ an area that reaches from the Czech Republic to the Bering Sea with a population of over 400 million. This study focused on service development and current levels of provision, on policy implications, education and training, opioid availability and local, national and international partnerships.

The findings suggest that the distribution of services is patchy. Only Poland and Russia had more than 50 services (identified by type); 13 countries had between one and five; and five countries had none. Most commonly found were home care services (221 in 17 countries), and inpatient services (172 in 13 countries). Rarely found were hospital mobile teams (five in four countries), and nursing home teams (five in one country). Paediatric care was sparse, a finding confirmed by Dangel in his broader survey of provision in 24 European countries.²¹

Among ten recommendations was a proposed International Observatory on End of Life Care (IOELC) and this new initiative has been established at Lancaster University, UK. It is designed to work in partnership with organisations and individuals internationally to provide accessible, research-based information on the global analysis of palliative care, disseminated via the world wide web (www.eolc-observatory.net). Much work centres on the production of country reports with data collected against an agreed template. Around 40 country reports are available to view and download and the number continues to rise.

International and national associations

Alongside the development of palliative care services has been the growth of organisations designed to provide support and representation. In Britain, the first associations were for those who performed specialist roles: social workers

Table 1. Decades during which services were established in European countries since the founding of St Christopher's Hospice, 1967

Decade	Country
1970–1979	Norway, Sweden, Scotland, Cyprus
1980–1989	Italy, Israel, Poland, Jersey, Northern Ireland, Germany, Belgium, Spain, Wales, Ireland, France, Iceland, Malta, Finland, Austria
1990–1999	Denmark, Guernsey, Switzerland, Russia, Hungary, Netherlands, Bulgaria, Romania, Slovenia, Albania, Lithuania, Portugal, Czech Republic, Slovakia, Estonia, Latvia, Luxembourg, Ukraine, Azerbaijan, Bosnia, Macedonia, Moldova, Armenia, Bosnia–Herzegovina, Kyrgyzstan
2000	Croatia, Serbia and Montenegro, Georgia

(1982), hospice managers (1984) and physicians (1986). As these professional associations proliferated, Help the Hospices was founded (1984) to champion the cause of independent hospices, followed in 1991 by the more inclusive National Council for Hospice and Specialist Palliative Care Services now called The National Council for Palliative Care.²² This model is not generally replicated in other parts of Europe where national umbrella organisations feature more prominently. In France, for example, over 110 associations fall under the auspices of one organisation, the Société Française d'Accompagnement et de Soins Palliatif.²³

Since the early 1980s, the WHO has advocated globally for pain relief and opioid availability. A public health approach is promoted in which palliative care programmes are integrated into existing health systems, and tailored to the cultural and social context of the target populations. These programmes are supported by a variety of means that include the establishment of demonstration projects, collaborating centres, and focal points.²⁴

The EAPC was founded in 1988. At present there are collective members from 30 national associations, and the organisation represents over 50,000 members in 40 countries of the world. Among the aims of EAPC is the promotion of palliative care for all who need it, together with the training of professionals and the development of research. Task forces consider issues around euthanasia, standards, service development and paediatric palliative care.^{25,26} Since 1990, EAPC Congresses have been held biennially and from 2000, a Research Forum has met in the intervening years.

The Eastern and Central Europe Palliative Taskforce (ECEPT) is an international association administered from Poznan (Poland) that brings together palliative care professionals from across the region. Participants at the 9th annual conference at Puszczkowo issued a statement that became known as the Poznan Declaration. This proclamation called for the development of national policies, a programme of palliative care education, increased drug availability and a growth in palliative care services. ECEPT was formed in 1999 to pursue these goals.²⁷

The Open Society Institute's (OSI) Network Public Health Programme is based in New York and includes many projects, of which palliative care is one. Regardless of location, the goals of the OSI programme are the same: public education; professional training; changes in laws and policy governing healthcare delivery; drug availability; and advocacy.²⁸ In addition to international initiatives and

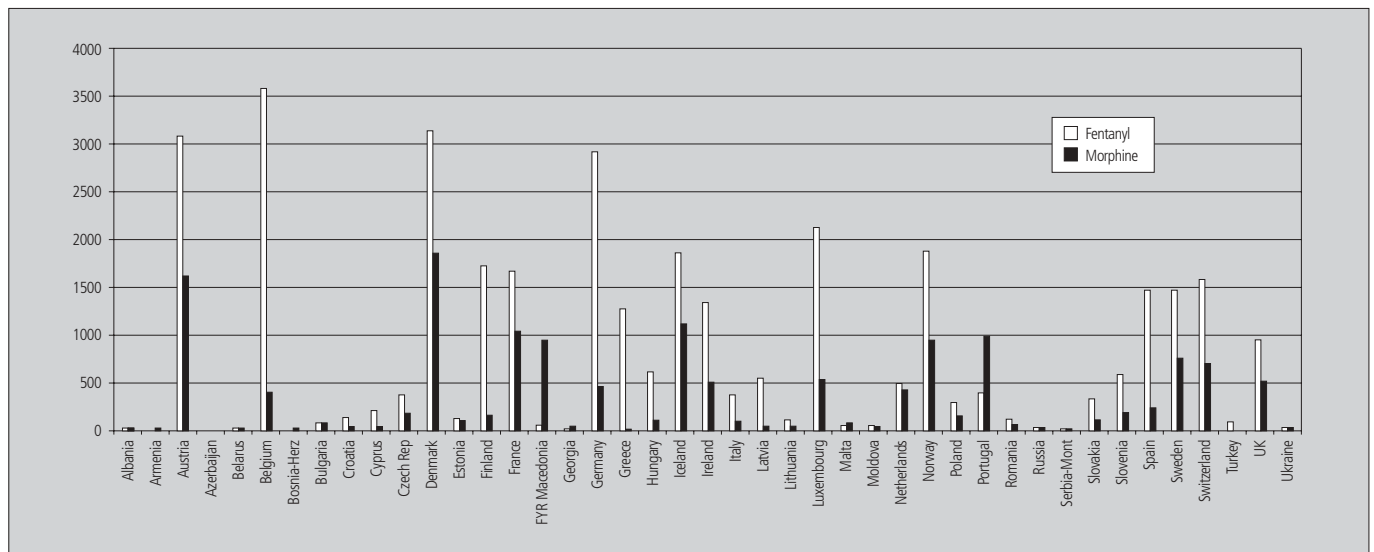


Figure 1. Average daily consumption of defined daily doses of fentanyl and morphine per million inhabitants in the countries of Europe, 2000–2002

leadership conferences,²⁹ OSI have funded the EAPC Co-ordination Centre established at Stockholm’s Sjukhem Foundation (2001), designed to support palliative care developments in eastern Europe.³⁰

Prior to the EAPC conference at The Hague (2003), the UK Forum for Hospice and Palliative Care Worldwide (established 2002) brought together more than 50 individuals from over 30 palliative care organisations around the world. The purpose of the meeting was to share experiences and discuss how closer working arrangements might promote palliative care globally.³¹ Working groups have been established and the next meeting is to be held before the Asia-Pacific conference in Seoul, Korea, 2005.

A common feature of many associations is a drive towards the development of standards, exemplified in Romania by collaboration between the Romanian Palliative Care Organisation and the US-based National Hospice and Palliative Care Organisation.³² Lunder *et al* have identified 18 sets of standards worldwide,³³ 13 of which are found in European countries. Such standards reflect the view of national organisations regarding the expertise of staff and the level of care that can be expected by patients. Once recognised these standards also have a relevance to legislation, policy development and funding issues.

Issues

At the policy level, far-reaching influences have impacted on palliative care development. Central and eastern Europe has been affected by monumental political and social upheavals. A region in transition, it has become inscribed by a movement towards democracy and the development of a market economy. In this scenario, hyperinflation has coincided with the decentralisation of health services, which in many countries have already been chronically underfunded.

Across the region, reimbursement from government ranges from total to none. In Sweden, palliative care is seen as an integral part of the formal healthcare system and is reimbursed as such. This contrasts sharply with Azerbaijan, where the home care service provided by the Jewish Women’s Organisation of Azerbaijan received no

government funding and came to an end when charitable donations ceased. Between these extremes are services that have a symbiotic relationship with national health systems, relying on government- or insurance-based funding supplemented by income from fundraising; such services are found in Czech Republic, Hungary and the UK (independent hospices).

Despite the global consumption of morphine having doubled since 1994 – from around 14,000 to 29,000 kg per year – the availability and accessibility of opioid drugs remain a cause for concern. Europe is no exception and there have been many reports of an imbalance between the need for regulatory control and medical availability. Prohibitive prescribing and dispensing procedures, coupled with long-standing fears about patient addiction, militate further against their use. This is strikingly apparent in Italy, where changes to legislation and free dispensation of opioids have failed to secure an increase in overall consumption,³⁴ prompting reforms to the national policy for cancer pain relief and opioids.³⁵

Figures from the International Narcotics Control Board³⁶ show the average total consumption of defined daily doses of opioids for statistical purposes (S-DDDs)[†] worldwide. In Europe, most daily doses were consumed in Denmark (22,524) and Switzerland (11,272), whereas the least were consumed in Azerbaijan (6) and Armenia (21).

Regarding fentanyl; the most S-DDDs were consumed in Belgium (3,580) and Austria (3080); the least in Azerbaijan (2) and Bosnia (3). Turning to morphine, most doses were consumed in Denmark (1,857) and Austria (1,612); the least in Azerbaijan (4) and Bosnia (10) (Figure 1).

While these consumption figures bear a close relationship to the drug’s availability, they are also influenced by customs and beliefs. The dying experience does not occur in a vacuum, but in a cultural milieu that raises fundamental questions about what it means to be human.^{37,38} These factors are powerfully articulated by Núñez Olarte and Gracia Guillen in the case of Spain.³⁹ Challenging the universal applicability of the term ‘hospice’, rejected in Spain due to its negative undertones, the authors point to different patterns of truth-telling and outline the cultural

importance of agony. This turning away in the last few hours of life signals the nearness of death and traditionally excludes family members in favour of highly valued others: close friends and/or a priest.

Influences on ethical viewpoints are many and varied. In some contexts, religious perspectives predominate; humanist approaches prevail in others. Among a range of ethical dilemmas, euthanasia and physician-assisted suicide have assumed a high profile.⁴⁰ Many 'palliateurs' are implacably opposed to euthanasia whereas others seek an element of accommodation – giving rise to fears about an emerging slippery slope.⁴¹ Addressing these issues, a recent publication from the EAPC Ethics Task Force acknowledged the complexity of requests for euthanasia, but argued that such provision should not be part of palliative care.⁴² The topic is subject to widespread debate, however, as indicated by responses from Africa⁴³ and the Asia-Pacific⁴⁴ regions.

Conclusions

As aspirations for palliative care development increase, the challenges ahead are clearly apparent. Activists readily identify difficulties posed by insufficient funding; low social and professional awareness of palliative care; poor pain control; lack of trained staff; and the absence of legislation – a critical issue in many countries. Without doubt, these challenges must be addressed if palliative care is to become fully integrated into European healthcare systems and accessible to all who need it.

There is much to build on, however, and an air of timeliness is evident that transcends many current difficulties. Supportive networks – across a variety of borders – seek to nurture the developing services, which in many cases are firmly grounded in local communities and 'owned' by deeply committed activists. Education and training programmes flourish, pain relief is gradually improving, and reimbursement issues are being addressed more fully. But significantly, at the level of government there is growing ministerial awareness that has recently been stimulated by recommendations from the Council of Europe. In this scenario, the contribution of imaginative activity across borders and barriers can only be beneficial.

† 'The term defined daily doses for statistical purposes (S-DDD) replaces the term defined daily doses previously used by the Board. The S-DDDs are technical units of measurement for the purposes of statistical analysis and are not recommended prescription doses. Certain narcotic drugs may be used in certain countries for different treatments or in accordance with different medical practices, and therefore a different daily dose could be more appropriate.' International Narcotics Control Board. Narcotic Drugs: estimated world requirements for 2004. Statistics for 2002.

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Refractory symptoms: complex problems need careful solutions

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Refractory symptoms are challenging for palliative care physicians. Despite available guidelines and protocols, a minority of patients do not respond favourably. Even such guidelines are not supported by scientific evidence. There remain large areas of clinical practice in palliative care that are based on clinical experience rather than high-quality evidence, and this applies even to core activities such as the control of pain and distressing symptoms. Unfortunately, research in palliative care remains in the doldrums despite of the continued development of new clinical services across the world and the apparent wide recognition of its importance among palliative care practitioners. This is probably due to the poor attention paid to distressing clinical problems and the tendency to apply 'low tech-high touch' techniques. Indeed, physicians involved in palliative care need a robust knowledge of physiopathology and pharmacology, as well as the capacity to understand from experimental data what is happening in difficult clinical situations. The development of a scientific basis for symptom treatment is an imperative for the field of palliative care. While there is an urgent need to explore this field scientifically and to establish a more substantial evidence base to spread information to practitioners, many problems remain difficult to resolve. Some rigid protocols and approaches are hard to apply in difficult conditions, because of the uniqueness of subjects, which, in turn, are hard to reproduce in a scientific framework. Experience, knowledge of basic mechanisms, appropriate application of experimental data, in-depth reasoning to recognise and diagnose clinical facts may all be helpful in some circumstances to provide the best treatment in that specific situation.

Undoubtedly, pain remains the most spectacular symptom for its emotional impact on patients and their relatives. A range of new treatments has been made possible by advances in neurosciences and therapeutic technology, which increase the chances of success – even in those very complex clinical presentations that were previously considered untreatable.

Similarly, interesting data from experimental work have given the impetus to improve knowledge about the physiopathology of bowel obstruction (BO) and to provide new therapeutical lines that seem to be effective in relieving gastrointestinal symptoms due to inoperable BO. There are also opportunities to reverse the pathological condition, when it is due to an initial functional mechanism that tends to become mechanically irreversible, if an early and aggressive treatment with a combination of drugs is initiated.

Escalating opioid doses in unresponsive patients

Opioid dose escalation in patients with poor analgesic response is a critical phase. Paradoxically, with the more liberal use of opioids, the incidence of neuroexcitatory adverse effects (including hyperalgesia, allodynia, myoclonus and seizures) in patients administered with large doses of systemic morphine or its structural analogues to relieve uncontrolled cancer pain has been increasing.¹ In recent years, opioid switching has gained popularity as a pharmacological practice that alleviates the analgesia adverse effect balance in patients presenting a poor response to a previous opioid. The chances of success seem to be relatively high, ranging between 60 and 80%, although no controlled study has ever confirmed this level of efficacy in comparison with other alternative treatments. The rationale of opioid switching is based on the different levels of tolerance induced by opioids and individual variability.² It is commonly used in patients in the presence of adverse effects that limit further dose escalation. However, a poor analgesic opioid response could be treated with higher opioid doses and may still improve analgesia if no adverse effects develop, according to the concept of opioid responsiveness.³ Patients requiring rapid opioid dose increases or receiving opioids for prolonged periods of time may develop tolerance, which in itself can be unexpectedly associated with hyperalgesia, sharing common molecular mechanisms. Opioid-induced hyperalgesia is an iatrogenic syndrome and may add a further element of confusion in choosing the initial conversion ratio, because the opioid dose should be chosen before developing hyperalgesia, rather than the dose achieved in a condition where increasing doses resulted in a worsening of the clinical condition. Unfortunately, diagnosis of hyperalgesia is difficult and often made 'a posteriori', if it is not suspected that increasing doses of opioids may stimulate rather than inhibit the central nervous system, by different mechanisms. Declining analgesia (assumed as tolerance), requiring further opioid escalation to maintain the previous level of analgesia, and then a worsening of pain intensity (assumed as hyperalgesia), more or less associated with adverse effects, is one clinical picture, although variants may exist.

In such circumstances, opioid switching should be anticipated and hyperalgesia, manifested as increasing pain, should be considered an adverse effect, with an hyperexcitatory profile different from the most frequent opioid-induced adverse effects. Opioid conversion ratios have been the subject of controversy in the literature. In particular, these calculations have never taken into account

the modality of the previous opioid escalation from a dynamic point of view – that is the short time used to increase the dose, or other causes – as a driving force for opioid escalation, such as the development of opioid-induced hyperalgesia. Recently, more attention has been paid to these specific clinical conditions, and complex therapies have been able to regain analgesia in patients who had previously been considered unresponsive or required symptomatic sedation for overwhelming pain.

Intensive observation while providing ‘personalised’ opioid switching or the judicious use of alternative routes, including the spinal route that allows administration of relevant adjuvant drugs, such as local anaesthetics and clonidine, and the use of ketamine as an infusion or as a periodical burst, may help in limiting the occurrence of tolerance-hyperalgesia syndrome. Paradoxically, the therapeutic difficulties remain in accepting the widespread concept of opioids as a pure agonist, with a linear dose–response curve expressed as the more pain, the more drug. This may correspond to a therapeutic paradox where the consequence (increasing pain), is treated favouring its cause (opioid escalation).⁴

The conversion ratio to be used when switching to methadone has also been the subject of controversy, the approach used having its own rationale. In the case reported (Figure 1), the concern about facing a situation of fentanyl-induced hyperalgesia was confirmed by the absence of opioid requests in the subsequent days, when minimal doses of methadone were added to achieve a final stabilisation dose of 21 mg in a couple of days; that is, about 1/10th of the initial dose calculated, with a conversion ratio of about 1:20. Even by using a more prudent methadone–morphine conversion ratio; for example 1:15, the calculated doses of methadone would be 80 mg per day, which is still four times higher than the final dose of methadone. Possibly, patient-controlled analgesia, spontaneously realised in this clinical circumstance after an initial raw calculation, according to the patient’s response and careful clinical monitoring, would be an effective and safe alternative, as dosing is clinically mediated in some way, regardless of possible calculations, which are unreliable in such a clinical situation.⁵

There are some reports in the literature that can be interpreted in the light of more recent knowledge regarding opioid-induced hyperalgesia.^{6,7} At those levels of opioid tolerance (and hyperalgesia), it is impossible to quantify any approximate dose conversion rate, as in the case reported. Such megadoses of opioids have been subject to debate, as they could be prevented with other available methods or route of administrations. It is likely that patients receiving grams of parenteral morphine, or any other opioid, may have a prevalent hyperalgesic component, so that the elimination of the first opioid implicates a consequent reduction of the state of hyperexcitation. Although the possible anti-N-methyl-D-aspartate (NMDA) activity of methadone may play a role, it is difficult to take this into consideration for calculation.

The problems of hyperalgesia, tolerance and nociception remain only partially understood and are quite difficult to interpret in the clinical setting of the cancer patient, where multiple factors are able to confound the picture. However, an integration of basic

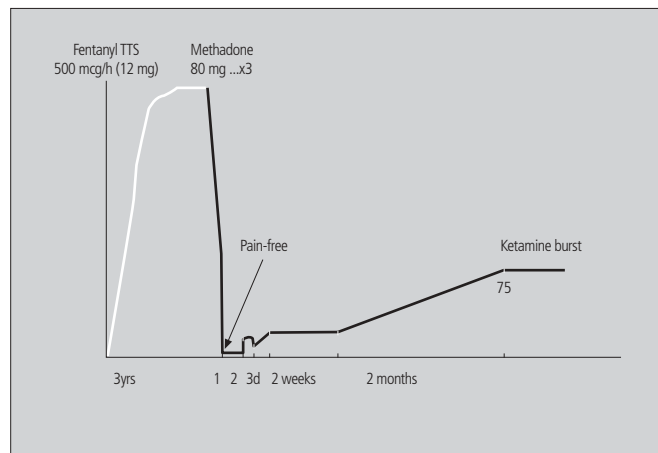


Figure 1. Case report

knowledge and clinical aspects may help to assist clinicians in applying specific alternative approaches in daily activity when such difficult conditions occur.⁸ A slowly declining analgesia may also be afforded by a sort of pharmacological desensibilisation. In cancer pain treated with opioids, there is discharge of afferent C-fibers, set off by the cancer injury, directly or indirectly, causing a state of central sensitisation. This is whereby wide-dynamic-range and nociceptive-specific dorsal horn neurones become sensitised to input in low threshold mechanical sensitive A-fibers. In the experimental setting, it has been demonstrated that the development of tolerance and hyperalgesic states involves the activation of excitatory glutamate receptors at the NMDA type in the central nervous system. Animals made tolerant to morphine analgesia can ultimately become hyperalgesic in this way, indicating that interactions occur between the mechanisms leading to hyperalgesia and tolerance. If NMDA receptors play an important role in the generation of central sensitisation, any manipulation targeted to prevent NMDA receptor activation, its intracellular consequences or calcium influx would inhibit the induction of tolerance. The development of hyperalgesia and the rightward shift of opioid antinociceptive in the dose–response curve can be prevented by the administration of NMDA receptor antagonists. NMDA antagonists do not affect the initial fast synaptic transmission in dorsal horn neurones but selectively inhibit the increase in neural responses to successive stimuli. Thus, ketamine per se produces only a weak analgesic effect, but significantly influences central hyperexcitability and inhibits wind-up in dorsal horn neurones.⁹

In the clinical setting, the development of tolerance requires increased doses of opioids, which may produce hyperalgesia. Ketamine may act predominantly by reversing morphine tolerance and or opioid-induced hyperalgesia, rather than as an analgesic. It has been suggested that intermittently administered ketamine would bring about a more long-term reversal of the central changes. With these experimental observations in mind, a clinical approach with pulse ketamine could be effective in reversing opioid tolerance in patients taking high doses of opioids, who are potentially at risk of future adverse effects.¹⁰

Translational research could make important contributions to basic pain research and its application,

according a two-way approach, one being from bedside to bench and the other from bench to bedside,⁸ integrating information and co-ordinating research efforts between these two fields.

Gastrointestinal symptoms associated with malignant bowel obstruction

Bowel obstruction (BO) is a serious complication in advanced cancer patients, commonly affecting abdominal and pelvic tumors. Conservative management with a combination of antisecretive drugs, analgesics, and antiemetics proves to be effective in reducing gastrointestinal symptoms of inoperable patients. However, most of the cases described in the literature were probably too advanced and feasibly presented in an irreversible condition, where it is only possible to reduce the number of vomiting episodes. Previous reports have shown that such treatments may allow a recovery of bowel transit and may improve the local condition before surgery preventing the pathological alterations of BO.^{11,12} Thus, an early and intensive treatment may not only reduce gastrointestinal symptoms, but also reverse BO, improving both quality of life and survival. On the basis of previous experience reporting an impressive outcome, a series of 15 consecutive advanced cancer patients presenting signs and symptoms of inoperable BO were prospectively surveyed using a drug combination composed of metoclopramide 60 mg, octreotide 0.3 mg, desamethazone 12 mg, daily, which was given intravenously and then maintained in the therapeutic regimen as an intravenous infusion, and an initial bolus of 50 ml of amidotrizoate orally. Almost all the patients surveyed showed a recovery of the intestinal transit within 1–5 days, more commonly within two days, and vomiting mainly disappeared within 24 hours. In three patients, different episodes of malignant bowel obstruction (MBO) were treated, whenever the treatment was discontinued for different reasons, mainly due to drug unavailability after hospital discharge. On each occasion, a prompt response was obtained with resolution of vomiting and recovery of the intestinal transit. One of these patients, who had refused

surgery previously, was readmitted for a further surgical evaluation and then gave authorisation to reoperate for a new gastroenteroanastomosis. Only one patient was considered unresponsive to the treatment and after two days a nasogastric tube was inserted to drain gastric secretions. This patient presented an outlet gastric syndrome. Mean hospital stay was 6.4 days. Mean survival was 44.9 days (excluding the patient operated). Symptom control was prolonged, as no patient died with gastrointestinal symptoms of BO.¹³

This case series establishes that the combination of propulsive and antisecretive agents acts synergistically to allow a fast recovery of bowel transit without inducing unpleasant colics. This underlines the point that the most important mechanism of MBO in these circumstances is functional and can be reversible even in advanced cancer patients, if an aggressive treatment is initiated early before faecal impaction and oedema render MBO irreversible.

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