

# Palliative Care for HIV/AIDS and Cancer Patients in Vietnam

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## Basic Training Curriculum

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Harvard Medical School  
Center for Palliative Care

**Eric L. Krakauer**  
*Editor-in -Chief*

Palliative Care for HIV/AIDS  
and Cancer Patients in Vietnam

**Basic Training Curriculum**



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E.L.K.

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# Sample Palliative Care Module 1 Training Schedule

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## Day 1

8am - 8:30am	<b>Introductions</b>
8:30am - 8:45am	<b>Group Photo</b>
8:45am - 9:20am	<b>Pre-conference Survey</b>
9:20am - 9:30am	<b>Goals of the Training / Agenda</b>
9:30am - 10am	<b>Life-threatening Illness in Vietnam / Current State of Palliative Care in Vietnam</b>
10am - 10:45am	<b>What is Palliative Care? Definition and Principles</b>
10:45am - 11am	Tea break
11am - 11:45am	<b>Palliative Care Assessment and Approach to the Patient</b>
11:45am - 1:30pm	Lunch
1:30pm - 2:30pm	<b>Medical Ethics, the Patient-Doctor Relationship, and Team-work in Palliative Care</b> - Ethical issues in end-of-life care - Patient-doctor relationship and communication - The palliative care team
2:30pm - 2:40pm	<b>Introduction to Role Play</b>
2:40pm - 3:50pm	<b>Small Group Role Play (Breaking Bad News)</b>
4pm - 5pm	<b>Bedside Rounds in Small Groups</b>

## Day 2

8am - 9:20am	<b>Principles of Pain Management</b>
9:20 - 10am	<b>Adverse Effects of Analgesics and Adjuvant Analgesics</b>
10am - 10:30am	Tea break
10:30am - 11:15am	<b>Barriers to Pain Relief -Opioid Policy in Vietnam</b>
11:15am - 11:45am	<b>Adult Learning Theory and Training of Trainers (TOT) Techniques</b>
11:45am -1:30pm	Lunch

CONTINUED

1:30pm - 2:45pm

**Small Group Case (Pain Management)**

2:45pm - 3pm

Tea break

3pm - 3:45pm

**Small Group Case Continued (Pain Management)**

4pm - 5pm

**Bedside Rounds in Small Groups**

### Day 3

8am - 9am

**Dyspnea**

9am - 9:45am

**Skin Problems**

9:45am - 10am

Tea break

10am - 11am

**Nausea / Vomiting**

11am - 11:45am

**Constipation / Diarrhea**

11:45am - 1:30pm

Lunch

1:30pm - 2pm

**Constitutional Symptoms**

2pm - 2:15pm

Tea break

2:15pm - 3:50pm

**Small Group Case Discussions**

4pm - 5pm

**Bedside Rounds in Small Groups**

### Day 4

8am - 9:15am

**Psychological / Psychiatric Problems**

- Depression, Anxiety and Insomnia

- Dementia and Delirium

9:15am - 9:45am

**Loss, Grief, Bereavement**

9:45am - 10am

Tea break

10am - 10:30am

**Psycho-social Support**

10:30am - 12pm

**Small Group Role Play (Psycho-social Assessment)**

12pm - 1:30pm

**Lunch**

1:30pm - 3:15pm

**Panel Discussion: Social & Spiritual Suffering and Care**

3:15pm - 4:15pm

Tea break

CONTINUED

4:15pm - 5pm

6:30pm

**Health Care Worker Self-care and Memorial Service**

**Conference dinner**

## Day 5

8am - 9:30am

**Palliative Care for IDU**

- Addiction treatment
  - Methadone substitution therapy
  - HIV prevention
- Treatment of pain in IDU

9:30am - 10am

**Integrating Palliative Care with HIV/AIDS Care and Treatment**

10am - 10:30am

Tea break

10:30am - 11am

**Integrating Palliative Care into Cancer Care and Treatment**

11am - 11:30am

**Plans for Development of Palliative Care in Vietnam**

11:30am - 1:30pm

Lunch

1:30pm - 2:30pm

**Large Group Discussion**

- Examples of efforts to develop palliative care services in hospitals and in the community
- Participants ideas for developing palliative care in their home provinces or institutions

2:30pm - 2:45pm

Tea break

2:45pm - 3:30pm

**Post-conference Survey**

3:30pm - 4:15pm

**Concluding Ceremony and Certificates**



# Day 1



## Viet Nam Palliative Care Basic Training Course: Goals and Agenda

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## Overall Goals of Training

- To prepare physicians and physician-educators in HIV/AIDS and cancer care to:
  - practice optimum palliative care
  - train other physicians as well as nurses, and other clinicians in palliative care (ToT)
  - promote integration of palliative care into HIV/AIDS and cancer care



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## Agenda of the Training

- Major Topics
  - The definition of palliative care
  - The need for palliative care in Viet Nam
  - Ethical issues in palliative care
  - Palliative care assessment
  - Pain relief
  - Relief of other symptoms in patients with life-threatening illnesses
  - Relief of psychological, social and spiritual suffering
  - Integration of palliative care into HIV/AIDS and cancer care in Viet Nam
  - Adult learning theory



3



## Agenda of the Training

- Teaching methods:
  - Lecture
  - Small group case discussions
  - Large group discussions with patients
  - Role play
  - Bedside teaching rounds



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## Thanks

- Hosts and partners
  - Department of Therapy, Ministry of Health
    - Director: Dr. Ly Ngoc Kinh
    - Vice Director Dr. Luong Ngoc Khue
    - Mme. Nguyen Thi Phuong Cham
  - National Cancer Hospital
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## HIV/AIDS and Cancer in Vietnam: Epidemiology, Treatment and Care

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 Vice- Director, Department of Therapy  
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1

## HIV/AIDS Infection in Vietnam

Up to April 30, 2007

- HIV documented cases nationwide: 124,223
- AIDS documented cases: 23,611
- Accumulative deaths due to AIDS: 13,469

Infections have been detected at:

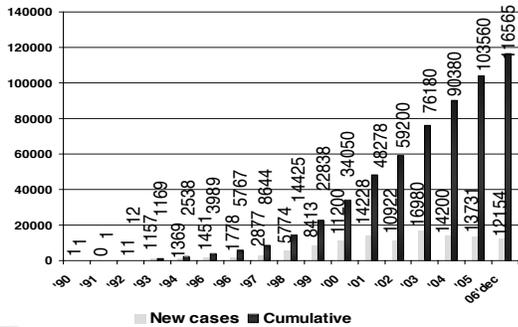
- 93% of districts; 49% of communes
- 100% of communes, wards in many provinces/cities have PLWHA

Estimation of HIV infection: 263,000 (2005), 10,000 new cases annually



2

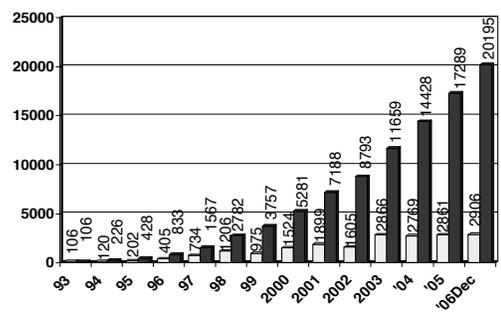
## Reported HIV Cases in Vietnam



Ministry of Health, Vietnam, 2007

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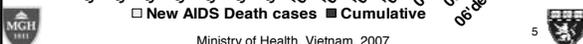
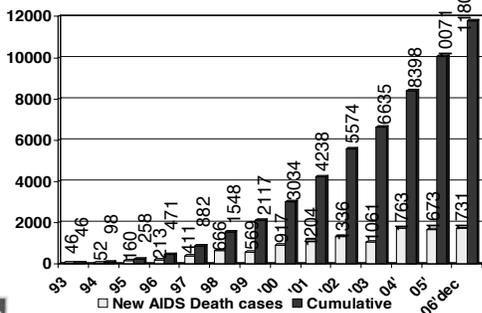
## Reported AIDS Cases in Vietnam



Ministry of Health, Vietnam, 2007

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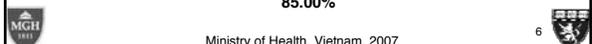
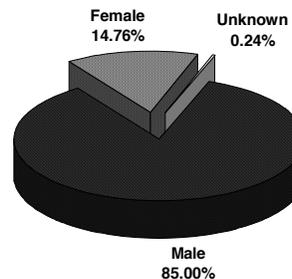
## Reported AIDS related deaths in Vietnam



Ministry of Health, Vietnam, 2007

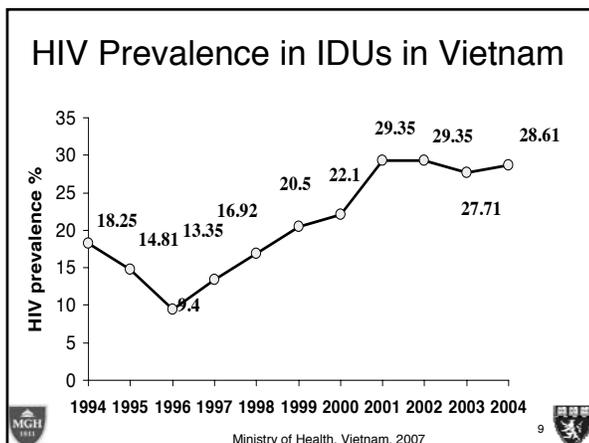
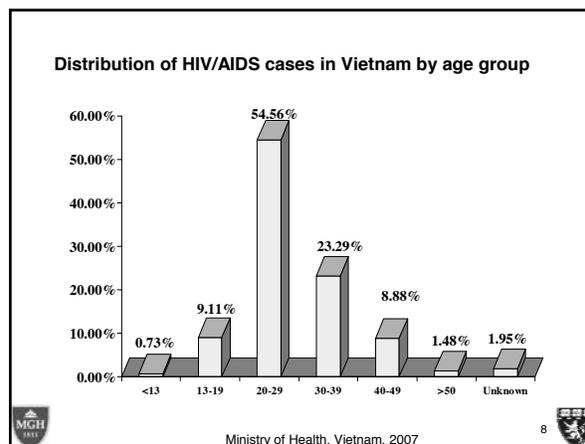
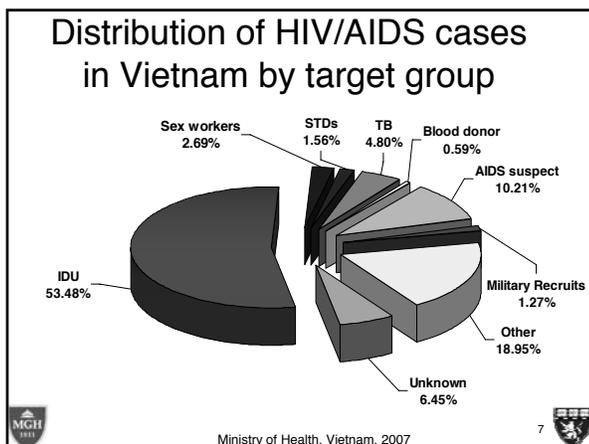
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## Distribution of HIV/AIDS cases in Vietnam by gender



Ministry of Health, Vietnam, 2007

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### Estimated Number of PLWHA needing to access Antiretroviral Therapy during 2005 – 2010

2005	14,775
2006	18,975
2007	23,040
2008	27,690
2009	33,075
2010	37,275

Ministry of Health, Vietnam, 2007

### Access to Antiretroviral Therapy in Vietnam

**Since 1995:**  
 1995 – 2003: 50 patients each year  
 2004: 500 patients  
 2005: 3,140 patients  
 11/ 2006: 6,740 patients  
 843 PMTCT

**Funding:** Vietnamese government, Global Fund, ESTHER, Clinton Foundation, PEPFAR

**Strategy for AIDS treatment & care to 2010:**  
 Increase access to care, support & treatment services for PLHA and affected by HIV/AIDS in order to prevent HIV transmission and prolong the life of PLWHA

Ministry of Health, Vietnam, 2007

### Cancer in Vietnam

**General information**

- Number of detected cancer cases increases gradually.
- It is estimated that there are 150,000 new cases and 70,000 deaths each year.
- Cancer registration system is still not completed. A few models have been applied in some provinces.
- Lack of facilities for diagnosis & treatment.
- The network of cancer prevention and control is developing

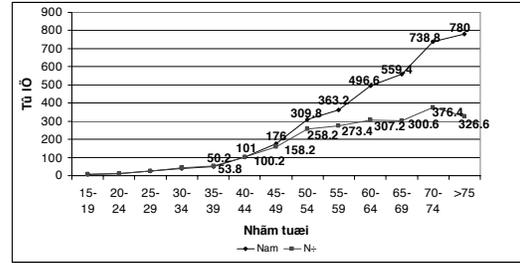
Ministry of Health, Vietnam, 2007

### Cancer in Vietnam

- A cancer registry was created from Jan. 1, 2001 through Dec. 31, 2004
  - Hanoi, Thai Nguyen, Hai Phong, TT-Hue, and Can Tho
- 32,944 new cancer cases were found
  - 32,944 (54.01% male, 45.99% female)
- Cancer incidence increases steadily by age with sharp increases after 40 in both sexes



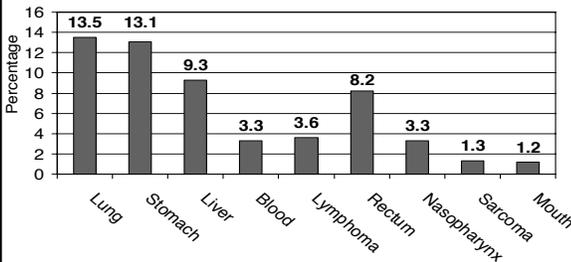
### Cancer Incidence in Vietnam



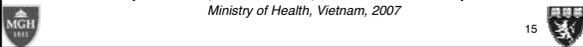
Cancer incidence by age 2001-2004 in 5 provinces (per 100,000 pop)



### Most Prevalent Cancers in Vietnam



Cancer prevalence, in both sexes, from 2001-2004 in 5 provinces  
Ministry of Health, Vietnam, 2007

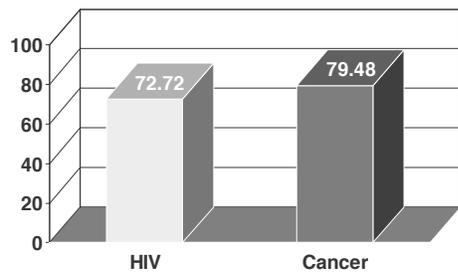


### Palliative Care: Needs and Gaps

- A Palliative Care Rapid Situational Analysis was done in 2005
- Study sites: Quang Ninh, Hai Phong, Hanoi, HCMC, An Giang
- Study subjects:
  - Healthcare policy opinion leaders (33)
  - Patients with HIV/AIDS and cancer (105)
  - Caregivers for PLWHA and cancer (62)
  - Bereaved caregivers (37)
  - Palliative care program managers (31)
  - Healthcare workers (76)
  - PLWHA focus groups (9 groups, 106 people)



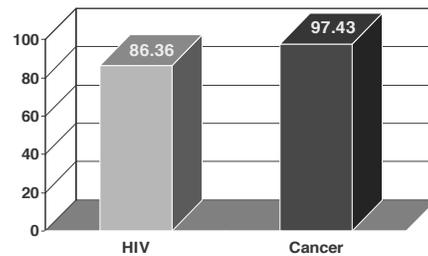
### Result 1: Pain Experiences



Percentage of people living with HIV/AIDS and cancer who report ever being in pain



### Result 2: Symptoms Experienced



Percentage experiencing physical discomfort of any kind



### Result 3: Emotional Suffering

- 48% people living with HIV and cancer reported that they felt completely or mostly dissatisfied with their life
- 79% of people with HIV and 87% of those with cancer said that they were either unhappy or very unhappy.
- 64% caregivers reported that they were spending more than 10 hrs a day providing care to the patient
- 30% caregivers reported that they were under stress because they did not know how to take care of patient



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### Result 4: Pain Relief Medication Access (Opioids)

- 39% health staff said that there were not any protocol or guidelines related to pain treatment
- 30% health staff reported that the injection form of morphine was not available in their settings
- Among 70% people who reported that the injection form of morphine was ever available, 42% reported that there were not regular supplies



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### Result 4: Pain Relief Medication Access (Opioids)

- 95% reported that their facilities had no oral morphine
- 18% health staff said that they experienced difficulty in managing pain because of the limited availability of opioids.



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### Result 5: Pain management

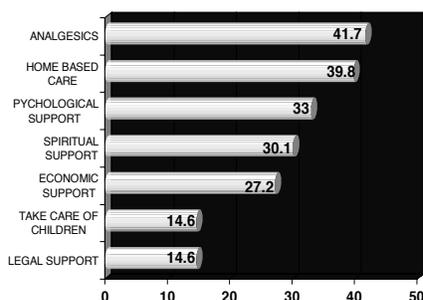
- 57% health staff providing care for PLWHA and cancer reported that they have been trained in pain management.
- 23% health staff reported that they could define level of pain and prescribe pain medication.
- 77% cancer patient and 84% PLWA remained in pain despite treatment



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### Result 6: PLWHA and Cancer Patients' Needs



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### Key Conclusions

1. Pain among PLWHA and cancer is not well controlled.
2. Social, emotional and spiritual needs of patients should be better supported.
3. Palliative care services in Vietnam are inadequate.
4. Improvement of palliative care skills and services, and development of opioids policy are important and necessary issues.
5. *Training and certification in accordance with National Guidelines is urgent!*



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**Thank you**



## Palliative Care in Viet Nam

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1



## Background

- 1980: Palliative care first received attention in Vietnam
- 1998: Vietnam signed International Convention on Drug Policy
- 2004: National Strategy on HIV/AIDS Prevention to 2010
- 2005: Palliative Care Rapid Situation Analysis conducted
- 2006: National Guidelines on Palliative Care for Cancer and AIDS Patient promulgated by the Ministry of Health.



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## Background

- Jan. 2007: Law on HIV/AIDS prevention and control were promulgated by the national assembly and became effective.
- The needs for palliative care are huge:
  - Population increasing at rate 1.5% / year
  - About 10,000 new HIV diagnosed / year
  - About 150,000 new cancer cases / year
- Opinions of the health policy makers:
  - Current palliative care services are extremely inadequate to the need
  - 70% worry about improper or illegal use of opioids
  - 100% agree that oral opioids should be made available
  - 52% agree that palliative care services should be available in the home



3



## Palliative Care Programs

- Level of program coverage: very limited
- No close collaboration between HIV/AIDS and cancer institutions.
- Concepts of palliative care only disseminated in the HIV/AIDS and cancer fields.
- Palliative care is still separated into HIV and Cancer fields without a single palliative care speciality or organization



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## Training

- Previous training was mainly on pain management and usually was short.
- No national program yet
- WHO "Pain Management" material translated into Vietnamese in 1999
- Several materials available:
  - HIV Clinical care - MoH and VCHAP
  - Palliative care material - K hospital
  - Home base care - FHI
  - End of life care - Hue central Hospital



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## Counseling and Psychological Support

- Little attention paid:
  - 79% patients feel sad,
  - 23% HIV patients do not receive psychological support
- Stigma and discrimination to HIV/AIDS patients:
  - 45% of infected patients report
- Needs for spiritual support:
  - more than 30% patients report



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## Socio - economic

- Viet Nam:
  - 74% rural;
  - 26% urban
- Health expenditures mainly paid by patients,
- Only 16% of the population have health insurance
- 56% care-givers worried about not having enough money for taking care of patients



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## Drug availability

- Non opioids widely available (84%)
  - Many different forms
- Weak opioids:
  - Codeine available only in combination formulations.
  - Combination forms available at only 50% of surveyed sites
- Strong Opioids
  - Only short acting morphine available (single dose, oral and injection)
  - Only 5% of sites surveyed (one site) had oral morphine
  - Only 40% of sites had injectable morphine
  - Long acting opioid: only fentanyl and not always available
- Adjuvant medications are available but their use for palliative care purposes is very limited



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## Other Drug Availability

- Drugs for non-pain symptoms:
  - widely available,
  - use for palliative care purposes is very limited



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## Drug availability

- In-country drug production:
  - very limited,
  - Long-acting forms not produced,
  - Small number of drugs and dosages produced.
- Opioids are listed as Poisons Schedule A which limits their use in palliative care
- Prescription regulations not convenient



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## Human resources

- Limited in number and capacity
- Cancer field: only 4 sites have pain management units
  - K hospital,
  - Hanoi oncology hospital,
  - Huế Central hospital, and
  - Chợ Rẫy hospital
- HIV/AIDS field:
  - NIITD
  - several rehabilitation centers,
  - PEPFAR-funded outpatient clinics
- Low numbers of health care workers in the palliative care field



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## Recommendations

- Active in-country production and distribution of low cost palliative care drugs including different forms of codeine and morphine
- Finalize policies on opioid prescription and pain management
- National palliative care training of health care workers
- Develop detailed guidelines on palliative care for health care workers at different levels.



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## **Palliative Care: Definition and Principles**

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### **Objectives**

*After the lecture, the trainees will be able to:*

1. Understand:
  - The definition of palliative care;
  - The need for palliative care;
  - Who needs palliative care;
  - When palliative care should be provided;
  - Where palliative care should be provided.
2. Appreciate that palliative care is part of comprehensive care for HIV/AIDS and cancer patients.
3. Understand the steps necessary to develop a national palliative care program.

### **Contents**

#### **1. Definitions of Palliative Care**

- World Health Organization (WHO) definition: “Palliative care ... improves the quality of life of patients and their families facing the problems 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.”
- Vietnam Ministry of Health (MoH) definition: “Palliative care for cancer and AIDS patients is a combination of measures to relieve suffering and improve the quality of life of patients through the prevention, early detection, and treatment of pain and other physical and psychological problems, and to provide counseling and support to address social and spiritual problems that patients and their families are encountering.”
- Similar emphasis in both definitions on:
  - Responding to suffering by preventing and relieving it in all its forms.
  - Addressing not only physical but also psychological, social and spiritual problems.
  - Maximizing quality of life.

## 2. Principles

### 2.1. Who should be assessed for the need for palliative care?

- All patients with advanced HIV/AIDS or cancer.
- All patients with other life-threatening illnesses.
- Any patient whose death in the next 6 months would not be surprising.
- Any patient distressed by pain, any other physical symptom, or psychosocial problems that are chronic and moderate or severe in intensity.

### 2.2. When should palliative care be provided to patients with cancer or HIV/AIDS (**Figure 1**)?

- From the time of diagnosis:
  - The initial palliative care assessment and, if needed, intervention, should occur at the time of diagnosis or as soon as possible thereafter.
- Throughout the course of the illness.
  - Palliative care is applicable early in the course of HIV/AIDS or cancer along with disease-modifying treatments such as:
    - Antiretroviral (ARV) therapy.
    - Prevention and treatment of opportunistic infections (OIs).
    - Cancer chemotherapy or radiation therapy.
  - Palliative care can reduce or relieve side effects of disease-modifying therapies.
  - Palliative care can promote adherence to disease-modifying therapies.
- Increasingly important as disease-modifying therapies become less appropriate, effective, or feasible.
- After the patient's death to provide bereavement support to the family.

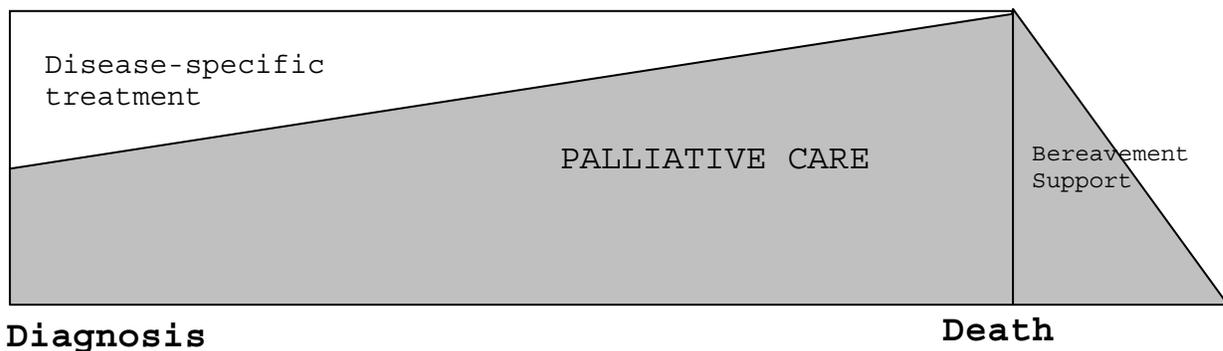


Figure 1: Diagram of palliative care throughout the course of illness and bereavement.

### 2.3. Why should palliative care be provided?

- To relieve suffering (the most basic principle and moral imperative of the medical profession).
  - Pain
  - Other physical symptoms.
  - Psychological symptoms such as depression and anxiety.

- Social distress such as isolation, homelessness and extreme poverty.
- Spiritual distress such as loss of previously cherished beliefs.
- To maximize the patient's quality of life and dignity until death.

#### 2.4. What is palliative care?

- Aggressive relief of pain and any other symptoms based on
  - Differential diagnosis of the symptom and
  - Treatment chosen for the specific symptom's cause and intensity.
- Psychological and social supports:
  - To help the patient live as actively as possible.
  - To help patients access clinical services and remain adherent to disease-modifying therapies.
  - To help dying patients prepare for death.
  - To help the patient's family cope during the patient's illness and during bereavement.
- Anticipation of potential future symptoms and psychosocial problems and planning to address them.
- Protection of the patients from unwanted or inappropriate medical interventions such as treatments that unduly sustain life.
  - Life-sustaining treatments such as mechanical ventilators, non-invasive ventilatory support, and hemodialysis are becoming more available in Vietnam.
    - These treatments can save lives but also can cause pain and suffering.
    - As these treatments become more available, decisions will be required more frequently about the relative benefits and burdens of specific life-sustaining treatments for individual patients.
  - Palliative care considers life and death a natural progression.
    - It never intends to hasten death, but it also does not try to unduly prolong the dying process.
- Ideally, palliative care is provided by an **interdisciplinary team** with the patient at the center that includes:
  - Healthcare workers:
    - Physician (or Assistant Physician in some settings)
    - Nurse
    - Community health workers
  - Family members
    - Will require training and psychosocial support
  - Peer supporters and/or volunteers
    - May require training.

#### 2.5. Where should palliative care be provided?

- Home:
  - Palliative care often can be provided in the home by the family with training and support from nurses, community health workers, peer support groups and volunteers.
- HIV Outpatient Clinic (OPC) or communal health station:
  - Prescription of analgesics and other necessary medications.
  - Occasional visits if patient ambulatory.

- Training and psychosocial support for the family.
- Hospital:
  - For palliative treatment of severe or refractory pain or other symptoms.
  - Homeless patients.
    - 09 Centers
    - AIDS Hospices

### 3. Special Principles of Palliative Care for Patients with HIV/AIDS

3.1. Comprehensive care for people living with HIV/AIDS should integrate:

- HIV prevention counseling
- OI prophylaxis and treatment
- ARV therapy
- Palliative care

3.2. There is no contradiction between ARV therapy and palliative care. A balance always should be sought between disease-modifying (ARV) therapy, curative treatment of acute complications such as OIs, and palliative care.

- Every effort should be made to treat AIDS patients with ARV therapy.
- Pain and other distressing symptoms, whether caused by the disease or side effects of medications, should be treated at any stage of HIV disease.
- In the later stages of progressive HIV disease, many patients will have an increasing need for palliative care including comprehensive symptom control and psychosocial support.

3.3. People living with HIV/AIDS suffer from severe stigmatization and discrimination.

- Many people living with HIV/AIDS are multiply stigmatized from:
  - HIV infection
  - TB infection
  - Illicit drug use
  - Sex work
  - Homosexual sex.
- Stigma leads to:
  - Discrimination of many kinds:
    - Employers
    - Landlords
    - Schools
    - Insurance companies
  - Shunning by friends, family, customers, and others
  - Shame
  - Social isolation
  - Poverty
  - Homelessness
  - Reluctance to be tested for HIV
  - Psychiatric problems
    - Anxiety
    - Depression

- Suicidality

### 3.4. HIV/AIDS creates complex family problems.

- The breadwinner may be ill, creating severe financial problems.
- Both parents may be ill, creating both financial and childcare problems, or young children may be required to care for their sick parents.
- There may be anger, fear or guilt related to actual or possible transmission of HIV within the family.

### 3.5. Many people living with HIV/AIDS will have experienced multiple losses of family members or friends from AIDS.

- Like stigma, loss can cause or exacerbate psychiatric problems such as anxiety and depression.

### 3.6. Provider stress:

- Providing palliative care for people living with HIV/AIDS, or treating AIDS patients where ARV are not available for all, can be very stressful for caregivers:
  - Healthcare workers
  - Family members
- All care givers may benefit from:
  - Regular time away from their care-giving duties.
  - Opportunities to discuss the burdens and rewards of their work with colleagues
  - Regularly scheduled recreational activities.

## 4. The WHO has described the “four pillars” of a national palliative care program

### 4.1. Policy

- National palliative care clinical guidelines are needed to set standards of care.
  - Vietnam’s Ministry of Health developed and approved national palliative care guidelines in 2006.
- National healthcare policies can include palliative care as an essential part of comprehensive care. For example, palliative care can be integrated into:
  - National primary care program
  - National cancer control program
  - National HIV/AIDS control program

### 4.2. Medication availability

- A national essential medications list can improve medication availability and should include at least one strong opioid analgesic such as oral morphine.
- Laws and regulations are needed to control import, manufacture, storage, distribution, and prescription of opioid analgesics. Such regulations can help to achieve “balance” between:
  - Assuring the availability of opioid analgesics for treatment of pain and other medical purposes;
  - Minimizing the risk of illegal diversion of opioids.

### 4.3. Education

- Training curricula and programs in palliative care are needed for:

- Physicians
- Assistant physicians
- Nurses
- Community healthcare workers
- Family caregivers

#### 4.4. Implementation

- Model palliative care programs can be developed both “from the top down” and “from the bottom up”. Palliative care programs are needed both:
  - In major national and regional HIV/AIDS and cancer centers and provincial hospitals
    - Inpatient palliative care wards for patients with severe symptoms and for homeless patients
    - Outpatient clinics at the district and commune level.
  - In the community:
    - Palliative care can be integrated into community-based HIV/AIDS care, cancer care, and primary care.

#### **Daily evaluation questions**

1. Palliative care should be offered only when the patient is dying. Yes    No
2. Goals of palliative care include:
  - a. Sustaining life at all costs.
  - b. Improving adherence to ARV therapy or cancer therapy.
  - c. Improving the quality of the patient’s life.
  - d. All of the above.
  - e. b and c
3. Palliative care can be provided
  - a. In the home
  - b. In outpatient clinics
  - c. In hospitals
  - d. a and b
  - e. All of the above.
4. The WHO recommends achieving \_\_\_\_\_ in national opioid regulations.

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## Palliative Care: Definitions and Principles



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## Learning Objectives

- Understand:
  - The definition of palliative care
  - The great need for palliative care
  - Who needs palliative care
  - When palliative care should be provided
  - Where palliative should be provided
- Appreciate that palliative care is part of comprehensive care for cancer and HIV/AIDS patients beginning at the time of diagnosis.
- Understand the steps necessary to develop a national palliative care program.



## Definitions of Palliative Care

- WHO (2002): “Palliative care ... improves the quality of life of patients and their families facing the problems 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.”



## Definitions of Palliative Care

- Viet Nam MoH (2006): “Palliative care for cancer and AIDS patients is a combination of measures to **relieve suffering** and **improve the quality of life** of patients through the prevention, early detection, and treatment of pain and other physical and psychological problems, and to provide counseling and support to address social and spiritual problems that **patients and their families** are encountering.”



## Definitions of Palliative Care

- Emphasis in both definitions:
  - Responding to and relieving all kinds of suffering:
    - Physical
    - Psychological
    - Social
    - Spiritual
  - Improving of quality of life
  - Attending to both patient and family



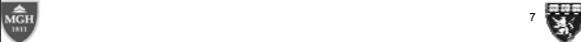
## Who should receive palliative care assessment?

- Any patient with:
  - HIV/AIDS
  - Cancer
  - Other life-threatening illness.
  - Chronic pain, another distressing symptom, or psychosocial problems, regardless of the stage of disease.
  - Potential to die in the next 6 months.

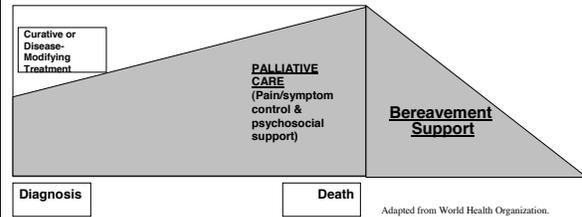


### When should palliative care be provided?

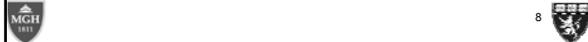
- **From the time of diagnosis**
  - Initial assessment at that time, especially if disease already advanced
- **Throughout the course of illness**
  - Complementary to disease-modifying treatments such as ARV therapy, OI prevention & treatment, cancer chemotherapy or radiation therapy
    - Can reduce side effects
    - Can promote adherence
    - Can improve morbidity and mortality
- **Especially when disease-modifying therapies are no longer effective, feasible, or appropriate**
- **After patient's death: bereavement support**



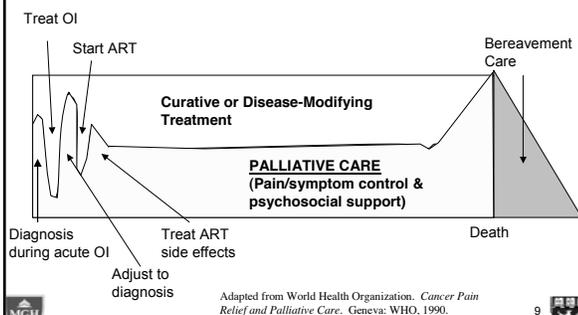
### When should palliative care be provided?



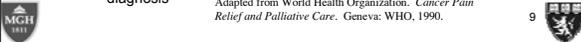
Adapted from World Health Organization. *Cancer Pain Relief and Palliative Care*. Geneva: WHO, 1990.



### Palliative Care for HIV/AIDS



Adapted from World Health Organization. *Cancer Pain Relief and Palliative Care*. Geneva: WHO, 1990.



### Why should palliative care be provided?

- High prevalence of suffering of all kinds among patients with life-threatening illnesses such as HIV/AIDS and cancer
- All human beings suffer and die
- Medicine's most fundamental task is not to cure or treat disease but to comfort suffering human beings
- Palliative care is a corrective for medicine overly focused on specific diseases, organs, or molecules
- Bac Ho: Lương y phải như từ mẫu



### Of what does palliative care consist?

- Relief of pain and other distressing symptoms
  - Careful assessment including differential diagnosis
  - Aggressive treatment
- Psychological and social support for patient and family
  - Help patient live as actively as possible
  - Help patient access and remain adherent to disease-modifying therapies
  - Help dying patients prepare for death
  - Help patient's family cope with patient's illness and death
- Anticipation of future problems



### Of what does palliative care consist?

- Protection from unwanted or inappropriate medical interventions
  - Life-sustaining treatments
- Multi-disciplinary team
  - Healthcare workers
    - Physicians (many specialties)
    - Nurses
    - Community health workers
  - Family
  - Peer supporters / volunteers
- Clinician self-care
  - Essential to avoid "compassion fatigue"



## Where should palliative care be provided?

- **Patient's home**
  - Family (with training)
  - Visiting nurses, community healthcare workers, peer supporters, volunteers
- **Communal health station / HIV OPC**
  - Evaluation & prescriptions
  - Training and psychosocial support for family
  - For patients receiving morphine, confirmation that the patient is still alive
- **Hospital**
  - Severe symptoms
  - Homeless
- **09 Centers / AIDS Hospices**



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## Palliative Care for PLHA

- Part of comprehensive HIV/AIDS care:
  - HIV prevention / harm reduction
  - OI prophylaxis & treatment
  - ARV therapy
  - Palliative care
- **NO CONTRADICTION BETWEEN ARV THERAPY AND PALLIATIVE CARE**
  - Palliative care:
    - Should promote access to ARVs when they are not available to all in need
    - Can alleviate side effects of ARVs & promote adherence to ARVs
    - Can reduce morbidity & mortality
  - ARVs and OI treatment often can relieve pain and other symptoms
- **Special foci:**
  - Fighting stigma & discrimination
  - Psychological and social supports



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## Palliative Care for PLHA

- **PLHA often stigmatized in many ways**
  - HIV infection
  - TB
  - IDU
  - Sex work
  - MSM
- **Stigma leads to:**
  - Discrimination by employers, landlords, schools, insurance
  - Shunning by friends, neighbors, customers, family
  - Social isolation
  - Poverty
  - Homelessness
  - Reluctance to be tested for HIV
  - Shame & guilt
  - **Psychiatric problems**
    - Anxiety
    - Depression
    - Suicidality



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## Palliative Care for PLHA

- HIV/AIDS creates severe financial problems and psychological tensions within families
- Many PLHA experience multiple losses
- For all of these reasons, PLHA are at particular risk for **psychological and social suffering**
- Thus, palliative care must both:
  - Work to fight stigma and discrimination at a societal level
  - Work to relieve psychological and social suffering of patients and their families



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## WHO Public Health Strategy for Palliative Care

- The “four pillars”
  - 1) Policy
    - National guidelines to set standards of care
    - Policies to integrate palliative care into national cancer, HIV/AIDS, or primary care programs
  - 2) Medication availability
    - Review and revision of laws and regulations controlling availability of opioids and other essential palliative medications
    - Goal is achievement of “balance” in national opioid policy
      - Maximize availability of opioids for medical use
      - Minimize risk of diversion for illicit use



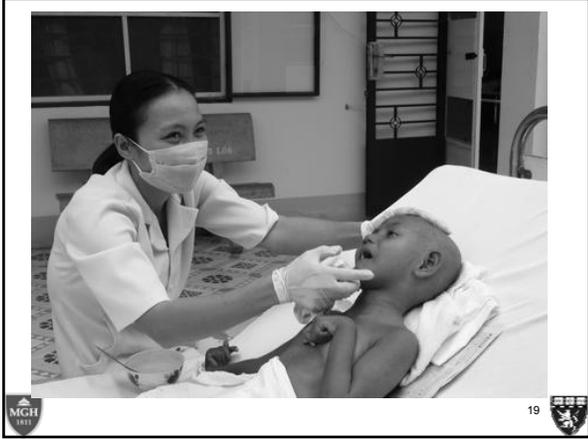
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## WHO Public Health Strategy for Palliative Care

- 3) Education
  - For clinicians: physicians, assistant doctors, pharmacists, nurses, community health workers
  - For healthcare officials
  - For family caregivers
- 4) Implementation
  - Sustainable training programs
  - Sustainable clinical programs integrated into the national healthcare system at all levels from national and provincial hospital to the community



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## **Palliative Care Assessment: Approach to the Patient in Palliative Care**

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### **Objectives**

*After the lecture, the trainees will be able to:*

1. Understand and apply the main steps of the palliative care assessment.
2. Understand the principles of assessing physical, psycho-social, and spiritual distress.
3. Do a detailed psycho-social assessment.

### **Contents**

#### **1. General Principles**

- 1.1. Patients with HIV/AIDS, cancer and other life-threatening illnesses suffer from many kinds of distress.
  - All forms of distress are under-diagnosed and under-treated in these patients.
- 1.2. Palliative care requires comprehensive evaluation of the patient and the family.
- 1.3. Evaluation of the patient should discover and determine the severity of any of the following:
  - Pain
  - Other physical symptoms.
  - Psychological symptoms or problems
  - Social problems
  - Spiritual problems
- 1.4. Basic components of palliative care assessment (**Figure 1**):

#### **Figure 1: Main steps of the palliative care assessment**

- History of present illness
- Past medical history
- Review of symptoms
- Thorough social history
- Drug allergies
- Current medications
- Physical examination
- Review of laboratory data and diagnostic imaging
- Assessment including differential diagnosis of symptoms
- Intervention plan

- History of the present illness
  - Patient's understanding of the illness and prognosis.
  - Date of diagnosis.
  - Previous treatments.
  - Performance status
    - Karnofsky scale (0 – 100):
      - 0: Dead
      - 50: Requires considerable assistance with activities of daily living
      - 100: Normal
    - ECOG scale (0 – 4):
      - 0: Fully active
      - 1: Ambulatory, able to do light work
      - 2: Can do self-care but no work, ambulatory >50% of waking hours.
      - 3: Limited self-care, confined to bed or chair >50% of waking hours.
      - 4: Completely disabled.
- Past medical history
  - Illnesses
  - Treatments
- Review of symptoms
  - Basic symptoms:
    - Pain
    - Dyspnea
    - Nausea/vomiting
    - Diarrhea
    - Constipation
    - Anorexia
    - Anxiety
    - Depressed mood
    - Delirium
    - Insomnia
    - Others that commonly are caused by the patient's type of illness
  - Chronology: start date, frequency
  - Location (if relevant)
  - Severity
  - Symptom characteristics or qualities (for example, is the pain dull and constant or sharp and intermittent)
  - Factors that make it worse or better
  - Impact on functioning (activities of daily life)
  - Impact on other symptoms (for example, severe pain can cause vomiting, insomnia, fatigue)
  - Patient's perception of cause
  - Prior treatments and their effectiveness
- Social history
  - Members of immediate family

- Living situation
- Impact of disease:
  - On patient
  - On family (including financial situation)
- Impact of symptoms on quality of life
- Social supports
- Education
- Work history
- Religious beliefs
- Substance abuse history
- Other stressors:
  - Other ill family members
  - Previous deaths in the family
- Goals of care
- Drug allergies
- Current medications
- Physical examination
- Review of any available laboratory of imaging studies
- Assessment Summary
  - Major medical issues
  - Likely prognosis
  - Goals of care
  - Palliative care issues
  - Differential diagnosis of each symptom or problem when the cause is not obvious.
- Intervention plan
  - Immediate interventions to relief suffering
  - Plan to prevent or relieve potential future suffering

## 2. Principles of Symptom Assessment

2.1. **Symptoms** are subjective experiences perceptible only to the patient. They cannot be seen by the clinician.

- Examples:
  - Pain
  - Nausea
  - Dyspnea
  - Anxiety

2.2. **Signs** are objective or physical manifestations of a symptom or disease that are perceptible by the clinician.

- Signs do not reveal the severity of a symptom or the degree of the patient's distress.
- Some symptoms may have no signs.
- Therefore, only the patient knows how distressing a symptom is, and clinicians should **believe the patients report of pain or distress.**
- Symptom assessment and control is more difficult in preverbal children or cognitively impaired adults who are unable to describe their symptoms and report their level of distress. In these

situations, the clinician must use on less reliable evidence of a patient's distress such as signs and reports of caregivers.

2.3 The *diagnosis* is the underlying cause of a sign or symptom but is not itself a sign or symptom. Signs and symptoms are clues to the diagnosis.

- A given symptom, abdominal pain for example, can have many causes. In other words, the *differential diagnosis* of abdominal pain is large.

2.4. Before treating any symptom, it is important to:

- Complete as thorough a history as possible of the symptom.
- Complete a focused physical examination.
  - Focus the physical examination on the body areas or organ systems most likely to be associated with the symptom.
  - Minimize discomfort to the patient during the examination.
    - For example, if sitting up would cause pain or dyspnea and auscultation of the back is not essential to good care of the patient, listen only to the front of the patient's chest.
- Develop a differential diagnosis of the symptom (if the cause is not obvious).

2.5. Optimal treatment for most symptoms will vary depending on their cause.

- For example, bone pain is treated differently than neuropathic pain, and vomiting caused by bowel obstruction is treated differently than vomiting caused by radiation therapy to the abdomen or by a brain tumor.

2.6. Treating the symptom versus treating the cause of the symptom

- In some cases, symptoms can be relieved by treating their underlying cause.
  - For example, antiretroviral therapy can improve some symptoms associated with AIDS, and cancer chemotherapy sometimes can improve cancer-related symptoms.
  - But improvements in symptoms from disease-modifying therapies often take time.
- Palliative or symptom-specific interventions usually can relieve symptoms quickly and effectively.
- Often, disease-modifying and palliative treatments should be used together.

2.7. Acuteness of symptom:

- When a patient is in severe distress, evaluation should be as brief as possible and treatment should be initiated as rapidly and aggressively as is possible and clinically indicated.
- The full assessment can be completed later when the patient is more comfortable.

### 3. Principles of Symptom Control

3.1. Always choose treatments based on a rational assessment of the most likely cause of the symptom (based on a differential diagnosis of the symptom).

3.2. Treatment of symptoms should be based on the patient's goals.

3.3. Be aware of potential side effects and toxicities of any treatments and try to minimize them.

- Many medications used to treat pain, dyspnea, and other distressing symptoms can cause sedation. Ask the patient whether s/he would prefer to be completely comfortable even if the treatment causes sedation or whether s/he would prefer to tolerate some discomfort in order to remain fully alert and able to interact with family.

3.4. Principle of Double Effect (see Ethics syllabus)

- If desired by a terminally ill patient, medications intended purely to provide relief from severe pain or other symptoms may be used even at the risk of foreseen but unintended side effects.
- For example, high-dose opioids may be given to relieve severe pain or dyspnea even at the risk

of foreseeable but unintended sedation, hypotension, respiratory depression, and hastening of death.

#### 4. Evaluation of Pain as an Example of Symptom Evaluation

4.1. It is essential to ask about pain because:

- Pain is highly prevalent in HIV/AIDS and cancer patients.
- Most physical pain can be well controlled.

4.2. Taking a pain history:

- Because pain is inherently subjective, patient self-report is the standard for evaluation. There is no reliable way to determine what the patient is experiencing other than by asking the patient.
  - Use open-ended questions as much as possible.
- Thorough evaluation:
  - Affords the best chance of diagnosing the underlying cause of the pain.
  - Facilitates determination of the best treatment.
  - Conveys to the patient that pain control is important to the physician.
- Aspects of pain evaluation
  - Chronology
    - How long have you had this pain?*
    - Did it begin gradually or suddenly?*
    - Does it come and go, or do you have it all of the time?*
    - How has your pain changed over time?*
  - Location:
    - Where does it hurt most?*
    - Does it radiate anywhere?*
  - Quality:
    - What words might you use to describe the pain?*
  - Severity (**Figure 2**):
    - How bad is it on average? At its worst?*

#### **Figure 2: Pain Severity Scales (following page)**

Despite pain being subjective, patients can accurately and reproducibly indicate the severity of their symptom by using a scale. They enhance the ability of the patient to communicate severity to health care professionals and the ability of clinicians to communicate among themselves. Thus, they facilitate optimum pain treatment. Numeric scales (0-10), visual analog scales, and faces scales (using a sequence of faces from happy to sad) have been scientifically validated as pain assessment tools. The specific scale used is less important than using one consistently with a patient over time.

The Brief Pain Inventory (BPI), a comprehensive pain assessment tool designed primarily for research, has been validated in Vietnamese and is included as an appendix to this section.



## - Results of pain intensity assessment

Pain Intensity	Pain Intensity Scales	Wong-Baker Faces Pain Rating Scale
Mild	1 – 3	Hurts a little bit
Moderate	4 – 6	Hurts a little more Hurts even more
Severe	Above 7	Hurts a whole lot and hurt worst

- Modifying factors:
  - Does it feel better when you are in a certain position?*
  - Do you notice any change with (various activities)?*
- Impact on function:
  - To what extent does your pain interfere with normal activities?*
  - Your sleep?*
  - Your ability to walk?*
  - Your relationships with others?*
    - Perform a neurologic exam including cranial nerves, motor and sensory function, reflexes, and gait.
- Patient perspectives:
  - What do you think is causing the pain?*
  - What does the pain mean to you?*
  - Would you like me to prescribe something for the pain?*
- Effect of treatments:
  - What have you been doing for the pain?*
  - Have you taken any medications?*
  - How much relief does that provide?*

## 4.3. Physical examination of the pain patient

- Focus the physical examination on the body areas or organ systems most likely to help you determine the cause of the pain.
- Minimize discomfort to the patient during the examination.
  - For example, if sitting up would cause pain and auscultation of the back is not essential to good care of the patient, listen only to the front of the patient's chest. If palpation of the abdomen causes pain and a thorough abdominal exam is not essential to good care of the patient, perform only those parts of the exam that are essential to achieving the patient's goals.
  - When the pain interferes with normal activities, a neurological examination should be performed if possible and not too uncomfortable. The neurologic exam may include:
    - Mental status
    - Cranial nerves
    - Cerebellum
    - Motor function
    - Sensory function

- Reflexes
- Gait

## 5. Evaluation of Psychosocial and Spiritual Problems in the Palliative Care Assessment

### 5.1. Overview:

- All patients have an emotional response to serious illness.
- Serious illness may challenge the patient's:
  - Sense of self.
  - Self-esteem or sense of personal worth.
  - Religious beliefs.
  - Some people struggle with many different emotions or move through emotional stages, not always in a predictable order.
  - Emotions may come in surprising waves or may be persistent.
- Emotional, social, and spiritual distress typically is not evaluated adequately or at all because:
  - Psychosocial and spiritual evaluation typically is not taught in medical school or residency.
  - Physicians are not aware that they can help patients with these types of distress.
- It is now well established in western countries that physicians can both effectively evaluate psychosocial and spiritual suffering and effectively intervene to relieve it.
  - Ask about how the patient is responding to the fact of being ill. Consider naming some common responses, such as anger, grief, hopelessness, determination, or resignation.
  - It helps to give the patient (or parent if the patient is a child) a sense that feeling many different emotions is normal.
    - One way to do this is to inquire about his or her emotions, then actively listen to the patient's responses.
  - It frequently helps the patient if the physician acknowledges the emotion in an accepting way and thereby normalizes it.
  - The emotional responses of the parents and the siblings of a dying child require particular attention because they will directly affect the child.
    - It can be very helpful for the parents and siblings of a dying child to speak about their emotions with the physician or another clinician as this can help them understand and accept their emotions and decide how best to express them when with the patient.

### 5.2. Evaluation of emotional state:

- General: Not all questions suggested below are appropriate for every patient. They are listed just to help you think about the best way to assess each individual patient.
- Meaning of illness:
  - What is your understanding of your illness?*
  - Why do you think this is happening to you?*
- Emotional state:
  - How are your spirits?*
  - Are you depressed?*
  - Are there times when you feel anxious? sad?*
- Unresolved issues:
  - As you think about the future, what matters most to you?*

*Let me ask a hypothetical question (or a “what if?” question): if someone were able to tell you with certainty that you have only six more months to live, what would you want to do in those six months?*

- Grief:
  - Many patients already will have suffered losses of many kinds:
    - HIV/AIDS patients often will have lost their spouse, friends and children; their work; even their family and home.
    - Patients with any serious chronic illness may be impaired physically or mentally and therefore have partially or entirely lost the ability to perform their daily activities independently (dressing, washing, walking, eating, using the toilet). They may have lost control entirely over their bladder and bowels.
    - Patients with any terminal illness may be feeling the loss of their hopes and dreams such as the hope to see their children grow up, marry, and have children.
  - Many patients will be grieving these losses and yet have no opportunity to speak about or otherwise express their grief. The physician can provide this opportunity.  
*It seems to me that you have experienced significant loss. Would you like to tell me about that?*
  - Fears:  
*What concerns you the most about your illness?*  
*Do you have particular worries or fears?*
  - Coping Style:  
*How have you coped with hard times in the past?*  
*How are you coping with what is happening to you?*  
*What strengths help you cope with your illness?*  
*Are there things that help you to take your mind away from your illness and bring you comfort?*  
*How do you like to make decisions? For example do you like to know every detail or do you prefer to know only the major issues?*

### 5.3. Evaluation of social situation

- Domestic needs of the patient:  
*Where do you sleep?*  
*How many people live with you?*  
*Is anyone else sick at home?*  
*Do other people depend on you to take care of them?*  
*Do you have electricity? Running water? Easy access to clean water?*  
*Do you have enough to eat?*
- Financial situation of the patient:  
*How much of a concern are financial issues for you?*  
*Is income from your work crucial to your family?*  
*Are you able to pay the rent?*  
*Are you able to afford the medications that have been prescribed for you?*  
*Are you able to afford the cost of transportation to see the doctor?*  
*Has it been necessary for you or your family to borrow money to pay for medical expenses?*
- Caregivers for the patient:  
*Who takes care of you at home now?*

*Who can help to take care of you at home in the future if you are not able to take care of yourself?*

*Does your caregiver work? Have children?*

- Community supports and support persons available to the patient and family:

*Who are the important people in your life now?*

*Who do you depend on and confide in?*

*What others could you ask to provide emotional, domestic, or financial support?*

*How are the important people in your life coping with your illness?*

#### 5.4. Evaluation of spiritual issues

- The spiritual is the conviction, sentiment, or hope that life has a fundamental meaning or purpose.
- These convictions, sentiments, or hopes:
  - May be religious or non-religious.
  - Give many people a sense of having a place or role in the world and a connection to others.
- The loss of this sense of place or connectedness is called a “spiritual crisis” and causes spiritual suffering.
- Such a crisis may be caused by:
  - Life-threatening illnesses such as HIV/AIDS and cancer, especially when they occur at a young age.
  - Loss of a loved one.
  - Stigmatization, discrimination and rejection (too often experienced by HIV positive people).
- Spiritual suffering often can be relieved through counseling or support from peers or community support groups.

#### 5.5. Anticipatory planning for death

- A terminally ill patient’s normal “anticipatory grief” should be distinguished from pathological depression or anxiety.
- Even very debilitated and poor patients can be helped to recognize that there often is much they can do to plan for their death and take care of their families:
  - Giving directions for dispersal of their possessions or for their funeral.
  - Complete unfinished business.
  - Reconcile with estranged family members or friends.
  - Say good-bye.
  - Tell their children how proud they are of them.
  - Leave a legacy for children or other family members such as a “memory box” containing pictures; audio or video tapes; messages for important occasions like the anniversary of death day, Tet, or a child’s wedding day; treasured or meaningful items.

### Daily evaluation questions

1. In general, symptoms are subjective and can be best assessed by listening to the patient.

**Yes**    **No**

2. The same symptom can have many causes. Therefore, after completing the history and physical examination, the clinician must make a \_\_\_\_\_ of the symptom in order to decide on the most likely cause of the symptom and to provide the treatment that is most likely to be effective.

**differential diagnosis**

3. Important aspects of pain assessment include:

- a. Location
- b. Severity
- c. Modifying factors
- d. Effect on daily activities
- e. Criminal record

**f. a, b, c, and d only**

g. All of the above

4. Important aspect of social assessment include:

- a. Living situation
- b. Financial situation
- c. Home caregivers
- d. Community supports

**e. All of the above**

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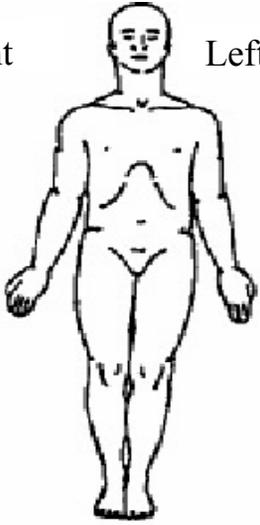
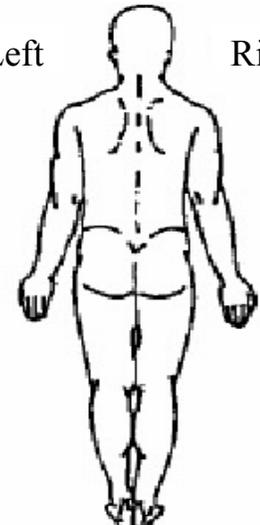
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**Appendix 1**  
**BRIEF PAIN INVENTORY**

Date: <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/>	Study Title: (used when needed) -----
(date) (month) (year)	
Patient's name:	
Study Code: (used when needed) <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Study Number: (used when needed)
<b>Brief Pain Inventory</b>	
1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today ?	
<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.	
Front	Back
<div style="display: flex; justify-content: space-between; width: 100%;"> <span>Right</span> <span>Left</span> </div> 	<div style="display: flex; justify-content: space-between; width: 100%;"> <span>Left</span> <span>Right</span> </div> 
3. Please rate your pain by ticking the one box that best describes your pain at its worst in the past 24 hours.	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10 No pain <span style="float: right;">Pain as much as you can imagine</span>	
4. Please rate your pain by ticking the one box that best describes your pain at its least in the past 24 hours.	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10 No pain <span style="float: right;">Pain as much as you can imagine</span>	
5. Please rate your pain by ticking the one box that best describes your pain on the average.	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10	

No pain	Pain as much as you can imagine
6. Please rate your pain by ticking the one box that tells how much pain you have right now.	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10	
No pain	Pain as much as you can imagine
7. What treatments or medications are you receiving for your pain ?	
-----	
8. In the past 24 hours, how much relief have pain treatments or medications provided ? Please tick the one box that shows how much relief you have received.	
0%    10%    20%    30%    40%    50%    60%    70%    80%    90%    100% <input type="checkbox"/> <input type="checkbox"/>	
No relief	Complete relief
9. Tick the one box that shows how much pain, in the last 24 hours, has interfered with your:	
A. General activity	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10	Completely interferes
Does not interfere	
B. Mood	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10	Completely interferes
Does not interfere	
C. Walking ability	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10	Completely interferes
Does not interfere	
D. Normal work (including work outside the home and housework)	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10	Completely interferes
Does not interfere	
E. Relations with other people	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10	Completely interferes
Does not interfere	
F. Sleeping	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10	Completely interferes
Does not interfere	
F. Enjoyment of life	
<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10	Completely interferes
Does not interfere	

**Appendix 2**  
**PSYCHOSOCIAL ASSESSMENT**

**1. Mental Health:** Mark  (if applicable to patient concerns) Client

Needs/Comments: \_\_\_\_\_

Any mental health-related hospitalizations?  No  Yes

Risk assessment (if above warrants - important to be direct)

Have you ever thought of harming yourself or others?  No  Yes (details if yes)

Substance and/or alcohol use: Mark  (if applicable to patient)

Do you currently routinely use any substances?  No  Yes (specify type): \_\_\_\_\_

In the past, did you ever routinely use substances?  No  Yes

What did you use? \_\_\_\_\_ When was the last time you used? \_\_\_\_\_

Have you ever overdosed?  No  Yes When? \_\_\_\_\_ What from? \_\_\_\_\_

**2. Sleep:** Mark  if applicable to patient

Sleep patterns: \_\_\_\_\_ Number of hours: \_\_\_\_\_

restful  naps  restless  fatigue  insomnia  night sweats  sleep walking

Use sleeping pills? \_\_\_\_\_ Other method to improve sleep? (specify) \_\_\_\_\_

Preferred location for sleep: \_\_\_\_\_

Client Needs/Comments: \_\_\_\_\_

**3. Complementary Therapy / Alternative Medicine** Mark  (if applicable to patient)

Complementary therapies and Alternative medicine presently used:  No  Yes

Client Needs/Comments: \_\_\_\_\_

**4. Spiritual Assessment:** Mark  (if applicable to patient)

Any religious/spiritual practices we should be aware of?  No  Yes

Any cultural customs/practices we should be aware of?  No  Yes

Client Needs/Comments: \_\_\_\_\_

Who do you turn to for spiritual guidance and support? \_\_\_\_\_

Client Needs/Comments: \_\_\_\_\_

*If the Client expresses need for spiritual support, refer to appropriate service (e.g. local pagoda, church)*

**5. Coping and Support Systems:** Mark  (if applicable to patient)

What do you do to help cope with your illness and related issues? \_\_\_\_\_

How have you managed in the past? \_\_\_\_\_

Counseling Needs?  No  Yes (specify) \_\_\_\_\_

---

Who do you count on for support? \_\_\_\_\_

Have you told family/partner or friends about your illness, treatment?  No  Yes

Comment: \_\_\_\_\_

What is your family's/partners understanding of your illness? \_\_\_\_\_

---

Do you want help in disclosing your diseases to your family/partners?  No  Yes

Comment: \_\_\_\_\_

**6. Main concerns of the patient and family/partner:**

Caregiver support needs (i.e. home-based care team, respite, etc.) \_\_\_\_\_

---

Any home-based care/volunteer support needs?  No  Yes

Comments: \_\_\_\_\_

---

Are there young children in this situation that may require support services during this illness?

No  Yes

Comments: \_\_\_\_\_

---

**7. Intimacy**

Mark  (if applicable to patient)

Intimacy is still needed throughout life especially when you are ill.

Has your illness affected your sense of intimacy with others?  No  Yes

Client Needs/Comments: \_\_\_\_\_

---

Are you concerned about your relationships?  No  Yes

Client Needs/Comments: \_\_\_\_\_

---

Other Needs/Comments: \_\_\_\_\_

## Palliative Care Assessment

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1



## The palliative care evaluation should be thorough

- **History of present illness**
- Past medical history
- Review of **symptoms**
- **Thorough psychosocial history**
- Drug allergies
- Current medications
- Physical examination
- Review of laboratory data and imaging
- **Assessment including differential diagnosis**
- **Plan**



2



## The history of present illness

should focus on:

- 1) patient's understanding of the illness
- 2) past & present treatments
- 3) the patient's distress

### Treatments:

- HIV: CD4 count, OIs, ARVs
- Cancer: chemotherapy, radiation therapy surgery, past pain medications



3



## Distress: There are two parts to the evaluation

- **Symptoms:** subjective, perceptible to the patient
  - Pain
  - Dyspnea
- **Signs:** objective, can be seen by the doctor
  - Swelling
  - Rapid breathing



4



## It is difficult to know what the patient is experiencing

- Believe the patient's report of pain or distress
- Use scales to help measure improvement or worsening of a symptom

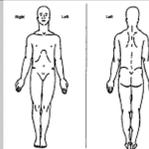


5



## Scales can help you know if a symptom is getting better or worse

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its **worst** in the last 24 hours.

0 1 2 3 4 5 6 7 8 9 10  
 No Pain Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain at its **best** in the last 24 hours.

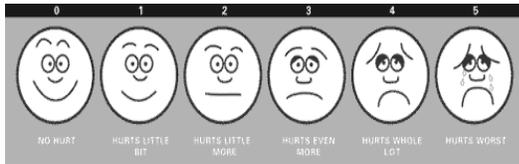
0 1 2 3 4 5 6 7 8 9 10  
 No Pain Pain as bad as you can imagine



6



Have a pediatric patient point to the face that describes the pain



7



A symptom evaluation should be very detailed

- **Chronology**
  - How long have you had the pain?
  - Did it begin suddenly or slowly?
- **Location**
  - Where does it hurt the most?
  - Does it radiate anywhere?
- **Quality**
  - What words would you use to describe the pain?
- **Severity**
  - How bad is it on average? At it's worse?



8



A symptom evaluation should be very detailed

- **Modifying factors**
  - What makes it better or worse?
- **Impact on function**
  - Does it effect your ability to sleep? Walk?
- **Patient perspectives**
  - What do you think is causing the pain?
- **Effects of treatments**
  - What have you been doing for the pain?
  - Have you taken any medications?



9



The palliative care evaluation should be thorough

- History of present illness
- Past medical history
- Review of symptoms
- **Complete psychosocial evaluation**
- Drug allergies
- Current medications
- Physical examination
- Review of laboratory data and imaging
- Assessment including differential diagnosis
- Plan



10



A complete psychosocial evaluation is typically not done adequately because:

- Psychosocial evaluation is not taught in medical school
- Doctors are not aware that they can help patients with psychosocial problems



11



All patients have an emotional response to serious illness

- It is well established in western countries that doctors can evaluate and treat psychosocial suffering
- Simply acknowledging emotional distress helps patients



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## The psychosocial evaluation has four components

- 1. Evaluation of the emotional state**
  - Feelings about the illness
  - Hopes for the future
  - Fears
- 2. Evaluation of the social situation**
  - Domestic needs
  - Financial situation
  - Supports, caregivers, community



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## The psychosocial evaluation has four components

- 3. Evaluation of spiritual issues**
  - Maybe religious or non-religious
  - Loss of sense of meaning, place or connectedness: "spiritual crisis"
- 4. Anticipatory planning for death**
  - Plan for funeral
  - Reconcile with estranged family members
  - Say good-bye



14



## The palliative care evaluation should be thorough

- History of present illness
- Past medical history
- Review of symptoms
- Thorough psychosocial history
- Drug allergies
- Current medications
- Physical examination
- Review of laboratory data and imaging
- **Assessment including differential diagnosis**
- Plan



15



## Even for a dying patient, a proper assessment should be completed

- Complete a full physical exam
- Review any available laboratory data and diagnostic imaging
- Construct a differential diagnosis of any symptom or type of distress when the cause is not obvious
- Consider which interventions are likely to be most helpful



16



## For example, a differential diagnosis of a patient with HIV and abdominal pain might include:

- Possible infections
  - TB (sputum BK often negative even in active TB due to partial treatment or extrapulmonary disease)
  - Other OIs: MAI, CMV
  - Other infections: Abscess, typhoid, appendicitis, cholecystitis, peritonitis, etc.
- Medications side effects
  - ARVs (pancreatitis, hepatitis)
  - NSAIDS (gastritis or PUD)
  - Opioid (constipation)
- Mechanical problems
  - Renal or gall stones
  - Constipation
- Other causes
  - Malignancy
  - Ischemia
  - Etc.



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## The palliative care evaluation should be thorough

- History of present illness
- Past medical history
- Review of symptoms
- Thorough psychosocial history
- Drug allergies
- Current medications
- Physical examination
- Review of laboratory data and imaging
- Assessment including differential diagnosis
- **Plan**



18



## The plan may have many parts:

- Treat infections if appropriate based on patient's goals
- Start ARVs or palliative radiation therapy if appropriate
- Treat pain or other symptoms
  - Patients in severe pain may need morphine immediately
  - Most pain can be controlled quickly
- Anticipate future problems such as worsening pain or dyspnea
- Help the patient and family to cope with:
  - Grief over the illness and the possibility of the patient's death
  - Social and financial consequences of the illness
  - Caregiving responsibilities



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## Summary of today's lecture: Palliative Care Evaluation

- **History of present illness**
- Past medical history
- Review of **symptoms**
- **Thorough psychosocial history**
- Drug allergies
- Current medications
- Physical examination
- Review of laboratory data and imaging
- **Assessment including differential diagnosis**
- **Plan**



20



## **Ethics and Communication with the Patient and Family in Vietnamese Palliative Care**

Eric L. Krakauer, MD, PhD & Craig D. Blinderman MD, MA

Harvard Medical School & Massachusetts General Hospital

### **Objectives**

*After the lecture, the trainees will be able to:*

1. Understand the major ethical principles of palliative medicine.
2. Apply the ethical principles of palliative medicine in the context of Vietnamese culture.
3. Understand and apply guidelines for good communication and trusting relationships with patients and their families.

### **Contents**

1. The moral imperative to prevent and relieve suffering that accompanies medical training is guided by several ethical principles.

1.1. These principles increase in importance proportionally with the vulnerability of the patient.

- Palliative medicine deals with patients who are physically and often also psychologically and financially severely weakened by advanced life-threatening illnesses such as AIDS and cancer.
  - These are the most vulnerable of patients.
- Thus, ethical principles and guidelines are a particularly important part of palliative medicine.

2. Ethical Principles of Palliative Medicine

2.1. Social justice

- According to UNAIDS and others, palliative care is a human right for people with AIDS or cancer, and providing it to all who need it is a medical and moral imperative.
- Understood in its fundamental sense as a response to suffering, palliative care has a special responsibility to those who suffer the greatest morbidity and mortality: the poor.
- Because of inadequate availability of effective disease-modifying interventions for HIV/AIDS and cancer in developing countries like Vietnam, it is imperative that efforts to pilot and scale-up palliative care for the poor be accompanied by or integrated with efforts to pilot and scale-up comprehensive HIV/AIDS and cancer care including HIV and cancer prevention and ARV therapy.
  - To try to scale-up only palliative care for diseases that can be prevented, controlled, or cured would be unjust.

- Palliative care must improve access to preventive and disease-modifying interventions where they can prevent unnecessary suffering and death and yet are not available.
  - In this way, palliative care will uphold medicine's fundamental responsibility, codified in the Hippocratic Oath, to keep the sick from harm and injustice.

## 2.2. Autonomy and Shared Decision-Making

- In western industrialized nations, great moral value is placed on "autonomy".
  - Autonomy may be defined as self-rule by an individual person, free from:
    - Controlling influences by others.
    - Personal limitations such as delirium, dementia, or mental illness.
  - The western principle of autonomy requires that each individual patient be given the respect, opportunity, and information needed to make decisions for himself or herself.
- In Vietnam, where decisions about medical treatment often are made by the family or by specific family decision-makers on behalf of family members, the principle of autonomy may still apply in **shared decision-making** between patients or families and physicians (see section on "Shared Decision-Making" below).
- **Respect for cultural differences** is essential. Local culture often:
  - Determines the most appropriate mode of decision-making and the most appropriate decision-maker: the patient, the family, someone else.
  - Strongly informs the patient's values and preferences.

## 2.3. Beneficence / Non-maleficence

- The principle of beneficence requires the physician to do good for the patient, to help the patient, without regard to personal gain or the interests of other people.
- The principle of non-maleficence requires the physician to protect the patient from harm.
- In Vietnam, perhaps these principles were expressed by Bac Ho with the words: "Luong y phải như từ mẫu."
- Practical application:
  - The potential benefits and burdens of all treatments should be weighed prior to initiation and continuously during therapy.
  - Treatments that may sometimes be more burdensome than beneficial include:
    - Chemotherapy or radiation therapy for cancers.
    - Other medications with potentially severe side-effects.
    - Life-sustaining treatments such as mechanical ventilation or hemodialysis.
  - The benefits and burdens of a treatment must be assessed in light of each individual patient's goals, values and beliefs.
  - It is ethical to limit even a life-sustaining treatment if it is deemed more burdensome than beneficial according to the patient's goals, values and beliefs.
- **Withholding / Withdrawing Life-sustaining Treatments**
- In western industrialized nations, there is no moral or legal distinction made between **withholding** (not starting) a life-sustaining treatment and **withdrawing** a life-sustaining treatment.
  - Therefore, it is ethically acceptable, and often imperative, to withdraw a life-sustaining treatment if it is no longer desired by the patient or is more burdensome than beneficial according to the patient's values.

*Quote from Truyện Kiều 2611-2614 - (The Tale of Kieu, lines 2611-2614):*

Thân sao thân đến thể này,  
Còn ngày nào cũng dư ngày ấy thôi.  
Đã không biết sống là vui,  
tấm thân nào biết thiệt-thời là thương

*English Translation:*

How could a body sink to reach this state?  
Each day on earth was just a wasted day.  
If while alive the body knows no joy,  
Why mourn a loss it will not know as loss?

#### 2.4. Principle of Double Effect

- An ancient doctrine for deciding what to do when any action risks bad effects.
- It is frequently applied in end-of-life care.
- If desired by a terminally ill patient, medications intended purely to provide relief from severe pain or other symptoms may be used even at the risk of foreseen but unintended side effects.
  - For example, high-dose morphine may be given to relieve severe pain or dyspnea even at the risk of foreseeable but unintended sedation, hypotension, respiratory depression, and hastening of death.
  - There are four conditions for applying the principle.
    - The act itself must not be immoral.
    - Only the good effect (relief of suffering of a dying patient), not the potential bad side effect (death), may be intended.
    - The bad effect (death) may not be the means to the good effect (comfort).
    - The potential benefit of the good effect must outweigh the potential burden of the bad effect (rule of proportionality).

#### 2.5. It is considered unethical to intentionally cause the death of a patient.

- Definitions:
  - Physician Assisted Suicide: The patient commits suicide using medications, information, or other means provided by a physician with the intention of facilitating the suicide.
  - Euthanasia: The physician performs an action with the intention of directly causing the patient's death.
- In western industrialized nations, there is a generally accepted moral and legal distinction between:
  - Intentionally causing the death of a patient, and
  - Withholding (not starting) or withdrawing a life-sustaining treatment if it is no longer desired by the patient or if it is more burdensome than beneficial according to the patient's values.
    - In these situations, the patient dies of the disease, not by the hand of the doctor.
- Intentionally causing the death of a patient is:

- Illegal in most countries
- Widely considered to be unethical under virtually any circumstances.

## 2.6. Non-Abandonment

- Withholding or withdrawing life-sustaining treatment or disease-modifying treatment (such as ARV therapy or cancer chemotherapy) should not result in the patient or family being ignored or abandoned.
- Palliative care, including psychosocial support, can be provided as an alternative.

## 2.7. Duty to Treat

- According to Vietnam's "Law on HIV/AIDS Prevention and Control" (No. 64/2006/QH11) Article 8, item 9 (June 29, 2006): "It is prohibited to refuse to provide medical examination or treatment to a patient because of the knowledge or suspicion that such person is infected with HIV."

## 3. Guidelines for Ethical Practice and Good Patient-Physician Communication

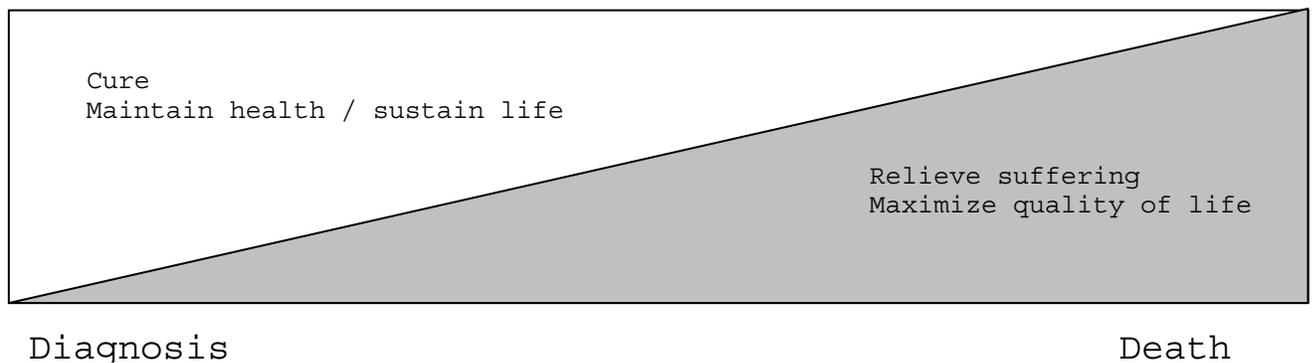
### 3.1. Developing a therapeutic alliance

- Patients do better, and patients and their families feel better, when they trust the doctor, feel respected by the doctor, and believe the doctor is an ally in the struggle to achieve their medical goals. They are more likely to:
  - Follow doctors' orders.
  - Take medicines as prescribed.
  - Return for follow-up appointments.
- A good therapeutic alliance has several components:
  - Empathy: The empathetic presence of a physician can itself comfort a suffering patient and family.
  - Respect: Treat each patient and family as you would want your own family members treated if they were sick.
  - Trust: Honesty and genuine empathy as well as technical competence evoke the patient's trust.
  - Confidentiality:
    - Patients must reveal extremely intimate and potentially embarrassing secrets about themselves to their doctors if the proper diagnosis is to be made and the best treatment to be found.
    - It is the doctor's responsibility to keep these secrets in the strictest confidence and to reveal them only for the good of the patients (for example, to a clinical colleagues who can help care for the patient and who is bound by the same requirement for confidentiality).

### 3.2. Determining the goals of care

- As more disease-modifying treatments for HIV/AIDS, cancer, and other life-threatening illnesses become available, more patients will suffer from side effects of these treatments and more patients will live longer with severe disabilities such as chronic pain, incontinence, blindness, or paralysis.

- Therefore, patients increasingly will have to decide about the goals of care.
- Typical goals of care:
  - **Cure** (not possible with HIV/AIDS, many cancers, and chronic major organ failure).
  - **Maintain the current or best possible state of health** using disease-modifying treatments such as ARV or palliative cancer chemotherapy.
  - **Sustain life** with technologies such as mechanical ventilators, cardio-pulmonary resuscitation, and hemodialysis when cardiac arrest or end-stage major organ failure occurs.
  - **Comfort** and best possible **quality of life**.
  - Some patients will have multiple goals
    - One goal may take priority over another.
    - Goals may change over the course of an illness (**Figure 1**).



**Figure 1:** Typical goals of care over the course of a chronic, life-threatening illness such as HIV/AIDS or cancer.

- Shared decision-making:
  - Whenever the goal or goals of care are not obvious, it is important to determine them in discussion with the person or persons of the patient's choice as culturally appropriate:
    - The patient.
    - The family or specific family member(s).
    - Sometimes, the patient or family may ask the physician to decide.
  - Guidelines for discussing goals of care:
    - Find out what the patient or decision-maker understands about the illness and prognosis.
    - Find out what the patient or decision-maker is hoping for.
    - Gently educate the patient or decision-maker about the illness and prognosis and correct misconceptions.
      - Since prognosis often is uncertain, provide a range and average.

- Avoid creating false hope (example: a cure for AIDS or for advanced metastatic lung cancer).
- Help the patient or decision-maker to set realistic goals.
- Review the goals periodically or when the patient's condition changes.
- Patients without decision-making capacity
  - Determining decision-making capacity:
    - Does the patient have the ability to understand the information needed to make a decision?
    - Does the patient have the ability to communicate the decision?
  - When a patient lacks the capacity to make or communicate medical decisions for himself or herself a family member or close friend can make decisions for the patient.
    - In western countries, this is called “substituted judgment” by a “surrogate decision-maker.”
    - In wealthy western countries, patients often prepare “advance directives” to facilitate decisions about their care when they are no longer able to decide for themselves. They do this by:
      - Designating a surrogate decision-maker.
      - Preparing a “living will” describing their goals and values and the kind of care they would like under various circumstances.

### 3.3. Communicating Bad News

- Why is it important to communicate bad news carefully and well?
  - The patient can be emotionally injured if it is not done well and in accordance with his or her cultural values.
  - When done well, it strengthens the patient-physician relationship.
  - It allows patients and families to plan realistically and grieve.
- Practical Guidelines for Communicating Bad News
  - Initial planning:
    - Determine whether the patient would like to receive information herself/himself or whether s/he prefers to designate others such as one or more family members or friends to receive the information
    - Think in advance about what to say.
    - Allow adequate time.
    - Find a place where you will not be interrupted. Turn off mobile phone.
    - Ask the patient (or family) if they would like to have others present (for example, other family members, friends, or clinicians) and if they would prefer that someone not be present.
    - Find out what the patient or family understands about the illness and prognosis.
    - Assess the patient's (or family's) ability to comprehend information.
    - Inquire how much the patient (or family) wants to know.
  - Sharing the information:
    - Sit down if possible.
    - Avoid talking too much. Pause frequently to allow the patient or family to react and ask questions and to assess whether your words are being understood.

- Avoid using medical jargon that patients or families may not understand.
- Be prepared for a broad range of reactions including anger, sadness, tears. Listen patiently. Express empathy.
- Plan next steps:
  - Any changes in goals or preferred location of care.
  - Additional tests or treatments (disease-modifying or palliative).
  - Discuss potential sources of support.

### 3.4. Obtaining informed consent for treatments that have risk of bad side effects

- Informed consent is based on the principle of autonomy.
  - The patient or surrogate decision-maker requires information about the risks and potential benefits of a specific intervention to make a rational decision whether to accept or decline the treatment.
  - The riskier an intervention, the more important it is to obtain informed consent.
- The amount of information desired by a patient will depend on the patient's culture, beliefs, and values.
  - Some patients may not wish to receive any information or to make any medical decisions and direct that all information be given to someone else such as a family member.
  - Some patients may wish to know everything themselves (common in western countries, may be becoming more common in Vietnam?).
- Elements of informed consent:
  - Nature of the intervention
  - Risks (common or severe)
  - Potential benefits
  - Alternatives
  - Time for the patient or surrogate decision-maker to deliberate (in non-emergent situations)
  - Consent (or refusal) should be based on understanding each of these.
  - Consent must be free of coercion.
  - Documentation in the medical record.

### 3.5. Responding to requests for physician-assisted suicide or euthanasia:

- Clarify the request with the patient (What exactly is the patient requesting?)
  - Avoid conveying personal biases.
  - Use open-ended questions (to allow the patient to explain what he or she means).
  - Show empathy with words and actions (sit down, speak softly, take extra time).
- Assess the reason for the request:
  - Suffering? (physical, psychological, social, spiritual)
  - Fear? (of future suffering, loss of function, control or dignity, abandonment, being a burden to others)
  - Clinical depression? (usually treatable)
- Affirm your commitment to care for the patient (non-abandonment)
- Address the reason for the request as well as possible:
  - Offer to provide or make referrals for palliative care to relieve all types of suffering and many fears.
    - Offer only those services that you know are available (honesty is crucial).

- Treat clinical depression
- Educate the patient and discuss alternatives
  - Explore with the patient the potential consequences of suicide:
    - To the family.
    - Related to any religious beliefs.
  - Discuss alternatives to physician-assisted suicide or euthanasia:
    - Refusing further disease-modifying or life-sustaining treatments.
    - Reducing or stopping eating.
    - In rare cases of extreme distress refractory to standard palliative interventions, palliative sedation (sedating the patient until death).
  - Explain honestly but compassionately what actions you are and are not willing to take.
  - Consider consulting with colleagues for advice and support while maintaining patient confidentiality.

### Daily evaluation questions

1. The more physically, psychologically, or financially vulnerable a patient is, the more important ethical principles become.   **Yes**   **No**

2. Major ethical principles in palliative medicine include

- a. Social justice
- b. Autonomy
- c. Beneficence
- d. Non-maleficence
- e. Euthanasia
- f. All of the above

**g. a to d only**

3. In order to provide the most appropriate treatment, it often is necessary to understand the patient's \_\_\_\_\_ of care.                   **goals**

4. It is important to communicate bad news well because:

- a. It takes less time when done well.
- b. The patient can be injured emotionally if it is not done well.
- c. The patient-physician relationship is strengthened when it is done well.
- d. All of the above.
- e. None of the above.

**f. b and c only**

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## Ethical Issues and Patient-Physician Communication in Palliative Care: Principles and Practice

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## Objectives

- Understand the major ethical principles of palliative medicine.
- To apply ethical principles of palliative medicine in the context of Vietnamese culture.
- To understand and apply guidelines for good communication and trusting relationships with patients and families.



2



## Introduction

- The moral imperative to prevent and relieve suffering is guided by several ethical principles.
- These principles increase in importance proportionally with the vulnerability of the patient.
  - Large power differential between patient & doctor
- Palliative medicine deals with the weakest and most vulnerable of patients.
- Thus, ethical principles and guidelines are a particularly important part of palliative medicine.



3



## Ethical Principles of Palliative Medicine



4



## Social Justice

- UNAIDS: palliative care is a human right
  - Providing palliative care (pc) is a moral imperative
- Because pc is a response to suffering, it has special responsibility to those who suffer most: the poor.
- In resource-limited settings, it would be unjust to scale-up only palliative care for diseases like HIV/AIDS and cancer that can be prevented, controlled, or cured.
- In these settings, efforts to scale-up pc must be accompanied by efforts to improve access to comprehensive HIV/AIDS & cancer care including prevention and treatment.
  - These interventions can prevent unnecessary suffering.



5



## Autonomy and Shared Decision-Making

- In western industrialized nations, great moral value is placed on autonomy
  - Autonomy may be defined as self-rule by an individual person, free from:
    - The controlling influencing of others
    - Personal limitations, e.g., delirium, dementia, or mental illness
- Requires that each individual patient be given the respect, opportunity, and information needed to make decisions for him/herself.



6



## Respect for local cultures

- Local culture often:
  - Determines the most appropriate mode of decision-making and the most appropriate decision-maker: the patient, family, or someone else
  - Strongly informs the patient's values and preferences



7



## Shared-decision making

- In Vietnam, where decisions traditionally are made by the family or by specific family decision-makers on behalf of particular family members, the principle of autonomy may still apply in **shared decision-making** between patients or families and physicians



8



## Beneficence/Non-maleficence

- Beneficence requires the physician to “do good” for the patient, to help the patient, without regard to personal gain or the interests of others.
- Non-maleficence requires the physician to protect the patient from harm.



9



## Application of Beneficence/ Non-Maleficence

- The benefits and burdens of all treatments should be considered
- Treatments that may be more burdensome than beneficial include:
  - Chemotherapy / radiotherapy
  - Mechanical ventilation
  - Hemodialysis
  - Rarely ARVs
- Benefits and burdens should be assessed in light of the patient's goals/values



10



## Withholding/Withdrawing Life-sustaining treatments

- In western industrialized nations, there is a generally accepted moral and legal distinction between:
  - Intentionally causing the death of a patient (unacceptable)
  - Withholding (not starting) or withdrawing a life-sustaining treatment that is no longer desired by the patient or that is more burdensome than beneficial by the patient's criteria (part of good care)



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## Withholding/Withdrawing Life-sustaining treatments

- In western industrialized nations, there is no moral or legal distinction made between
  - **Withholding** (not starting) a life-sustaining treatment and
  - **Withdrawing** a life-sustaining treatment
  - Both are fine as long as the treatment is no longer desired by the patient or is more burdensome than beneficial according to the patient's values.



12



## Quote

Truyện Kiều 2611-2614 - (The Tale of Kieu, lines 2611-2614)

How could a body sink to reach this state?  
Each day on earth was just a wasted day.  
If while alive the body knows no joy,  
Why mourn a loss it will not know as loss?

Thân sao thân đến thế này,  
Còn ngày nào cũng dư ngày ấy thôi.  
Đã không biết sống là vui,  
tám thân nào biết thiệt-thòi là thương



13



## Principle of Double Effect

- Ancient principle for deciding what to do when any action risks bad effects
- It is frequently applied in end-of-life care when treating pain and other severe symptoms with medications that may have important side effects.



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## Principle of Double Effect

- If desired by a terminally ill patient, medications intended purely to provide relief from severe pain or other symptoms may be used even at the risk of foreseen but unintended side effects.
  - For example, high-dose morphine may be given to relieve severe pain or dyspnea even at the risk of foreseeable but unintended sedation, hypotension, or respiratory depression and a hastening of death.



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## Principle of Double Effect

1. The act itself must be morally neutral
2. Only the good effect (relief of suffering of a dying patient), not the potential bad side effect (hastened death), may be intended
3. The bad effect (hastened death) may not be the means to the good effect (comfort).
4. The potential benefit of the good effect must outweigh the potential burden of the bad effect (rule of proportionality).



16



## Prohibition Against Intentionally Causing the Death of a Patient: Physician Assisted Suicide and Euthanasia

- **Physician Assisted Suicide:**
  - The patient commits suicide using medications, information, or other means provided by a physician with the intention of facilitating the suicide.
- **Euthanasia:**
  - The physician performs an action with the intention of directly causing the patient's death

**Intentionally causing the death of a patient is:**

- *Illegal in most countries*
- *Widely considered to be unethical under virtually any circumstances.*



17



## Non-Abandonment

- Withholding or withdrawing life-sustaining treatment or disease-modifying treatment (ARV therapy or chemotherapy) should not result in the patient or family being ignored or abandoned
- Palliative care, including psychosocial support, can be provided as an alternative



18



## Duty to Treat

- “It is prohibited to refuse to provide medical examination or treatment to a patient because of the knowledge or suspicion that such person is infected with HIV.”
  - Vietnam’s “Law on HIV/AIDS Prevention and Control” (No. 64/2006/QH11) Article 8, item 9 (June 29, 2006)



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## Guidelines for Ethical Practice and Good Patient-Physician Communication



20



## Therapeutic Alliance

- Patients feel better, are more adherent, and have better outcomes when they trust and feel respected by their doctor.
- Components of a good therapeutic alliance:
  - **Empathy**
    - The empathetic presence of a physician can itself comfort a suffering patient and family.
  - **Respect**
    - Treat each patient as you would want your own family member treated if he or she were sick.
  - **Trust**
    - Honesty and genuine empathy as well as technical competence evoke the patient’s trust.
  - **Confidentiality**
    - It is the doctor’s responsibility to respect the patient’s intimate and potentially embarrassing secrets.



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## Goals of Care

- As more disease-modifying & life-sustaining treatments become available in Vietnam, more patients will:
  - Suffer severe side effects
  - Live longer with severe disabilities such as chronic pain, paralysis, or blindness
- For some patients, these conditions may make their quality of life unacceptable to them.
- In order to decide whether to use treatments that either entail a high risk for serious side effects or may prolong an unacceptably poor quality of life, it is useful to determine the patient’s goal(s) of care.



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## Goals of Care

- Typical goals of care:
  - **Cure**
    - Not possible with HIV/AIDS, many cancers, and chronic major organ failure.
  - **Maintain the current or best possible state of health**
    - Using disease-modifying treatments such as ARV or non-curative cancer therapies.
  - **Sustain life at all costs**
    - Using life-sustaining treatments such as mechanical ventilators, cardio-pulmonary resuscitation, and hemodialysis.
  - **Comfort and best possible quality of life**



23



## Goals may change over the course of an illness

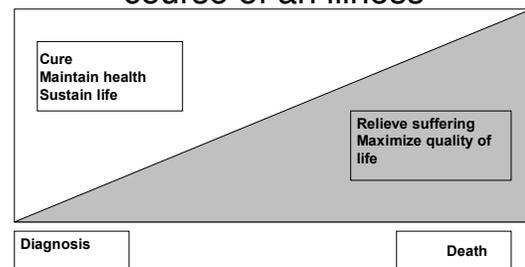


Figure 1: Typical goals of care over the course of a chronic, life-threatening illness such as HIV/AIDS or cancer.



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## Goals of Care: Shared Decision-Making

- Whenever the goal(s) of care are not obvious, it is important to determine them in discussion with the person(s) of the patient's choice, as culturally appropriate.
  - Patient
  - Family or specific family members
  - Sometimes the patient may ask the physician to decide.



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## Guidelines for discussing goals of care

1. Find out what the patient or decision-maker understands about the illness and prognosis.
2. Find out what the patient or decision-maker is hoping for.
3. Gently educate the patient or decision-maker about the illness and prognosis and correct misconceptions



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## Guidelines for discussing goals of care

4. Avoid creating false hope (example: a cure for AIDS or for advanced metastatic lung cancer).
5. Help the patient or decision-maker to set realistic goals.



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## Decision-making capacity

- When a patient lacks the capacity to make or communicate medical decisions for him/herself, a family member or close friend can make decisions for the patient using:
  - Substituted judgment
  - Best interests standard
- In western countries, this person is called a **“surrogate decision-maker.”**



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## Decision-making capacity

- In wealthy western countries, patients often prepare **“advance directives”** to facilitate decisions about their care when they are no longer able to decide for themselves
  - Living Will
  - Health Care Proxy



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## Communicating Bad News

- It is important to communicate bad news well because:
  - The patient can be emotionally injured if done badly.
  - Patient-physician relationship is strengthened when done well.
  - Allows patients and families to plan realistically and grieve.



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## Communicating Bad News: Initial Planning

1. Determine whom the pt would like to receive information.
2. Think in advance about what to say.
3. Allow adequate time.
4. Find a place where you will not be interrupted. Turn off mobile phone.
5. Ask the patient (or family) if they would like to have others present and if they would prefer that someone not be present.
6. Find out what the patient or family understands about the illness and prognosis.
7. Assess the patient's (or family's) ability to comprehend information.
8. Inquire how much the patient (or family) wants to know.



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## Communicating Bad News: Sharing Information

1. Sit down if possible.
2. Avoid talking too much. Pause frequently to allow the patient or family to react and ask questions and to assess whether your words are being understood.
3. Avoid using medical jargon that patients or families may not understand.
4. Be prepared for a broad range of reactions including anger, sadness, tears. Listen patiently.
5. Express empathy.



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## Communicating Bad News: Discuss Next Steps in the Patient's Care

1. **Any changes in goals or preferred location of care**
2. **Additional tests or treatments (disease-modifying or palliative).**
3. **Discuss potential sources of psycho-social support.**



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## Informed Consent

- Informed consent is based on the principle of autonomy.
- The riskier an intervention, the more important is informed consent.
- The amount of information desired by a patient will depend on the patient's culture, beliefs, and values.



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## Elements of Informed Consent

- Nature of the intervention
- Risks (common or severe)
- Potential benefits
- Alternatives
- Time for the patient or surrogate decision-maker to deliberate (in non-emergent situations)
- Consent must be free of coercion
- Documentation in the medical record



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## Responding to requests for physician- assisted suicide or euthanasia

- Respectfully explore exactly what the patient is requesting.
- Assess the reason for the request:
  - Suffering? (physical, psychological, social, spiritual)
  - Fear? (of future suffering, loss of function, control or dignity, abandonment, being a burden to others)
  - Clinical depression? (usually treatable)
- Affirm your commitment to care for the patient (non-abandonment)
- Address the reason for the request as well as possible. Refer to specialists if needed and possible.



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### Responding to requests for physician-assisted suicide or euthanasia

- Educate the patient and discuss alternatives
  - Refusing further disease-modifying or life-sustaining treatments
  - Reducing or stopping eating/drinking
  - In rare cases of extreme distress refractory to standard palliative interventions—palliative sedation
- Explain honestly but compassionately what actions you are and are not willing to take
- Consider consulting with colleagues for advice and support while maintaining patient confidentiality.



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### Summary

- Review of the basic ethical principles of palliative care
- Review of guidelines for ethical practice and good patient-physician communication
- Discussion of the role of culture in caring for patients in the end of life

QUESTIONS OR COMMENTS?



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## Giving Bad News Role Plays

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### **Case #1: Mr. Tho, a patient with HIV**

(Note this case uses the same patient as the Psychosocial Assessment case.)

#### **Patient Mr. Tho**

You are a 41 year old male construction worker who has been having weight loss and difficulty swallowing for 2 months. For some time you thought it was the flu, but you have lost 5 kg and your wife insisted that you see a doctor. The first doctor you see told you to go to another clinic. There, the doctor said she wanted to order an HIV test and you were shocked. The doctor asked you about sexual partners and intravenous drug use. While you have been with sex workers a few times and used IV drugs sometimes, you did not want to discuss either of these things with the doctor and simply said that you would go ahead with the blood test.

Since giving the blood, you have been very worried about what the doctor will tell you today. You only know that, if you have AIDS, you would bring shame on your family and probably would die soon and in pain. You also worry that you might have infected your wife. You have no idea what you would tell your wife (you came to clinic by yourself today) or your children (ages 1, 2, and 5).

#### **Dr. Hung**

You are a physician in a busy outpatient clinic and are seeing Mr. Tho for the first time. You know from his chart that he was seen in clinic a week ago with weight loss, low grade fevers, and thrush, had an HIV test performed, and that he is coming to hear the results today. His laboratory tests reveal that he is HIV positive and that his CD4 is 50. You think he should start ARV therapy as soon as possible.

\*\*\*\*\*

### **Case #2: Mr. Thieu, a patient with lung cancer**

(Note this case uses the same patient as the Psychosocial Assessment case.)

#### **Patient Mr. Thieu**

You are a 56 year old veteran of the American War and a married father of two teenagers. You came to the hospital because of a recent fever and a cough that has lasted for about 3 months. You have smoked cigarettes for many years and have had bronchitis in the past; so you think this is likely to be the same kind of problem and are not particularly worried. The physician in the emergency department ordered a chest x-ray and then told you that you have pneumonia and must be admitted to the hospital for treatment. You are now

waiting for the doctor to see you the next morning and want to know when you can go home.

You own a successful restaurant and do not want to be away from your work for too long. Your wife and children are visiting your wife's parents in Nghe An Province. You know that you have lost weight over the last few months, but you attribute this to a busy schedule. You also notice that you are having a few more aches than usual, especially in your back.

**Dr. Oanh**

You are a doctor in the district hospital. Your patient, Mr. Thieu, is a 55 year old man who was admitted yesterday with fever and a cough. His chest x-ray shows a large right lung mass with a post-obstructive pneumonia and obvious bone metastases.

Your diagnosis is that Mr. Thieu has metastatic lung cancer, and you need to talk to him about the chest x-ray results because you want to transfer him to the cancer hospital for further evaluation and treatment. You would prefer to tell his family rather than Mr. Thieu himself, but no family is present. When you ask Mr. Thieu when his wife will come, he says that he wants to know what treatment is needed and when he can go home and get back to work at his restaurant.

# Day 2



## Principles of Pain Assessment and Relief

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### Objectives

*After the lecture, the trainees will be able to:*

1. Understand the definition of pain and the basic principles of pain medicine.
2. Understand the basic causes and classification of pain.
3. Evaluate a patient with pain and provide a differential diagnosis of the pain.

### Contents

#### 1. Pain in cancer and AIDS

- 1.1. Studies have shown that over 75% of advanced cancer patients and up to 75% of advanced AIDS patients have moderate or severe pain.
- 1.2. A Rapid Situation Analysis of palliative care needs in Viet Nam revealed similar results:
  - 73% of HIV/AIDS patients reported pain since diagnosis.
  - 79% of cancer patients reported pain since diagnosis.
- 1.3. Numerous studies show that cancer pain is often under-treated, for several reasons:
  - Physicians underestimate the pain that patients feel.
  - Physicians doubt the patients' reports of pain.
  - Patients sometimes underreport their pain because they feel that there is little to be done or are afraid to take medications for pain.

#### 2. Principals of Pain Medicine

- 2.1. All patients with pain must be treated to relieve their suffering and improve their quality of life at any stage in the course of their illness.
- 2.2. Pain medicine includes:
  - Eliminating pain or, if this is not possible, at least reducing the severity of pain to a tolerable level.
  - Preventing pain from recurring.
  - Making it possible for the patient to carry out their normal activities of daily life.
- 2.3. Treatment of pain can be conducted in medical facilities, at home and in the community.
- 2.4. Believe patients' descriptions of their pain and of the efficacy of pain treatment, including patients with a history of illicit drug use or opioid addiction.
- 2.5. Both pharmacologic and non-pharmacologic interventions can be effective to relieve pain.
- 2.6. Psycho-social problems may cause or exacerbate pain or reduce the effectiveness of treatment. Therefore, comprehensive pain management requires attention to psycho-social problems.
- 2.7. Individualize pain interventions and doses.

2.8. Children feel pain even though they may not always outwardly express that they are in pain. Younger children may be unable to report pain. Assessment needs to include observation and caregiver report.

### 3. Pain Definition

3.1. *Pain* is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of tissue damage.

### 4. Causes of Pain:

4.1. Actual tissue damage from infection, inflammation, neoplasm, ischemia, trauma, invasive medical procedures, drug toxicity, etc.

4.2. Potential tissue damage from recognized disease entities where no tissue damage can be demonstrated such as fibromyalgia.

4.3. Psychological factors

- Major depression and anxiety disorders can cause or exacerbate physical pain, and chronic physical pain also can be a cause of major depression and anxiety disorders.
- Other psychological syndromes that predispose patients to chronic pain include somatization disorder, conversion disorder, post-traumatic stress disorder, hypochondriasis, and psychogenic pain disorder.
- Psychological syndromes that predispose to or exacerbate pain have specific definitions but often are difficult to diagnose both because most physicians are not familiar them and because patients fear the stigma of being diagnosed with a psychiatric illness.
- In some cases pain cannot be relieved unless underlying depression, anxiety, or other psychological problems are properly diagnosed and treated.

4.4. Severe emotional stress can also exacerbate pain. Family, friends, clinicians, and peer supporters as well as employment and faith can help the patient handle the stress, promote medication adherence, and moderate the experience of pain.

### 5. Classification of Pain

5.1. There are 2 major categories of pain:

- *Nociceptive pain*: is caused by the stimulation of intact nociceptors or sensory nerves that mediate pain. Nociceptive pain is further subdivided into somatic and visceral pain:
  - *Somatic pain*: nociceptors in the skin, soft tissues, muscle, or bone are stimulated, and the resulting pain usually is localized. Pain in the skin is often sharp, strong, burning, or throbbing. Pain in the muscle is often gnawing or dull. Pain in the bone is gnawing and dull, but can become sharp with movement.
  - *Visceral pain*: nociceptors in internal organs and hollow viscera organs are stimulated due to metastasis, or to blockage, swelling, stretching, or inflammation of the organs from any cause. This pain is often non-localized and causes feelings of being compressed.
- *Neuropathic pain*: is caused by damage to nerve tissue. Neuropathic pain is burning or like an electric shock. There also can be numbness, tingling, or allodynia (pain resulting from a stimulus that normally is not painful such as light touch) in the area innervated by the injured nerves.

5.2. Pain can be acute or chronic.

- *Acute pain* is usually related to an easily identified event or condition. Resolution is anticipated within a period of days or weeks.

- *Chronic pain* may or may not be related to an easily identified pathophysiologic phenomenon and may be present for an indeterminate period of time.

## 6. Evaluation of Pain (see chapter on Palliative Care Assessment)

### 6.1. Taking a pain history:

- Chronology:
  - When did the pain start?*
  - How long does it last?*
  - Is it constant, or does it come and go?*
- Location:
  - Where is the pain?*
  - Does the pain radiate? To where?*
- Quality:
  - Ask the patient to describe the pain. Try to differentiate neuropathic pain from nociceptive pain.
    - Can you describe the pain to me?*
    - Is the pain burning or like an electric shock? Do you feel any numbness or tingling?* (characteristic of neuropathic pain)
    - Is the pain throbbing, dull, or aching?* (characteristic of nociceptive pain)
- Severity:
  - Assess the baseline level of pain using simple, validated methods such as a visual analog scale, numerical scale (for example, from 1 to 10), or pictorial scale (for example, faces). (**Table 1**)
  - Use the same scale to follow the patient's pain over time.
  - Each patient will use pain scales differently. For example, two patients may have the same severity of pain, but one will report the pain as 10/10 and another will report the same pain as 5/10. Therefore:
    - Pain levels can be compared between different assessments of the same patient but not between patients.
    - Pain treatment should not be based on a pain scale alone.

\*\*\*\*\*

### **Table 1: Pain Severity Scales**

Despite the fact that pain is subjective, patients can accurately and reproducibly indicate the severity of their symptom by using a scale. Scales enhance the ability of the patient to communicate the severity of their pain to health care professionals and the ability of clinicians to communicate among themselves. Thus, they facilitate optimum pain treatment. Numeric scales (0-10), visual analog scales, and faces scales (using a sequence of faces from happy to sad) have been scientifically validated as pain



Pain Intensity	Pain Intensity Scales	Wong-Baker Faces Pain Rating Scale
Mild	1 – 3	Hurts a little bit
Moderate	4 – 6	Hurts a little more Hurts even more
Severe	Above 7	Hurts a whole lot and hurts worst

\*\*\*\*\*

- Modifying factors  
*What makes the pain better? (Positions? Touching or rubbing painful area? Time of day?)*  
*What makes it worse?*
- Effect of previous treatments  
*What medications or other interventions have been tried?*  
*What were the doses?*  
*What was the duration of therapy?*  
*How effective was the treatment?*
- Impact on functioning (activities of daily living):  
*To what extent does the pain interfere with your normal activities?*  
*(Sleep? Work? Walking? Washing and toileting? Relationships with others?)*
- Patients perspectives:  
*What do you think is causing the pain?*  
*What does the pain mean to you?*

#### 6.2. Past Medical History

- Pain may be related to:
  - Previously diagnosed disease
  - Past traumatic injury
  - Past surgical intervention
  - Psychiatric illness.

#### 6.3. Social History

- Pain may be related to social problems. Examples:
  - Grief
  - Loss of employment or income
  - Homelessness or inadequate housing
  - Poor nutrition
  - Excessive use of alcohol
  - Illicit drug use

#### 6.4. Physical Examination

- Focus the physical examination on the body areas or organ systems most likely to help you determine the cause of the pain.
- Minimize discomfort to the patient during the examination.
  - For example, if sitting up would cause pain and auscultation of the back is not essential to good care of the patient, listen only to the front of the patient's chest. If palpation of the abdomen causes pain and a thorough abdominal exam is not essential to good care of the patient, perform only those parts of the exam that are essential to achieving the patient's goals.
  - When the pain interferes with normal activities, a neurological examination should be performed if possible and not too uncomfortable.

#### 6.5. Laboratory and Imaging Studies

- Many studies may help to diagnose the cause of pain or to develop a differential diagnosis.
  - Radiographs and Computed Tomography (CT) scans may reveal tumors, fractures, nerve compression, or other causes of pain.
  - Biopsies and cytologies may reveal a malignancy or inflammation.
  - Hematology and microbiology studies may reveal infection.
  - Serologic studies may reveal rheumatologic or auto-immune disease.

#### 6.6. Allergies and Medications

#### 6.7. Assessment of pain (differential diagnosis):

- Type(s) of pain:
  - Neuropathic
  - Nociceptive
    - Somatic: skin, soft tissues, muscle, bone
    - Visceral: internal organs
- Most likely causes of the pain

\*\*\*\*\*

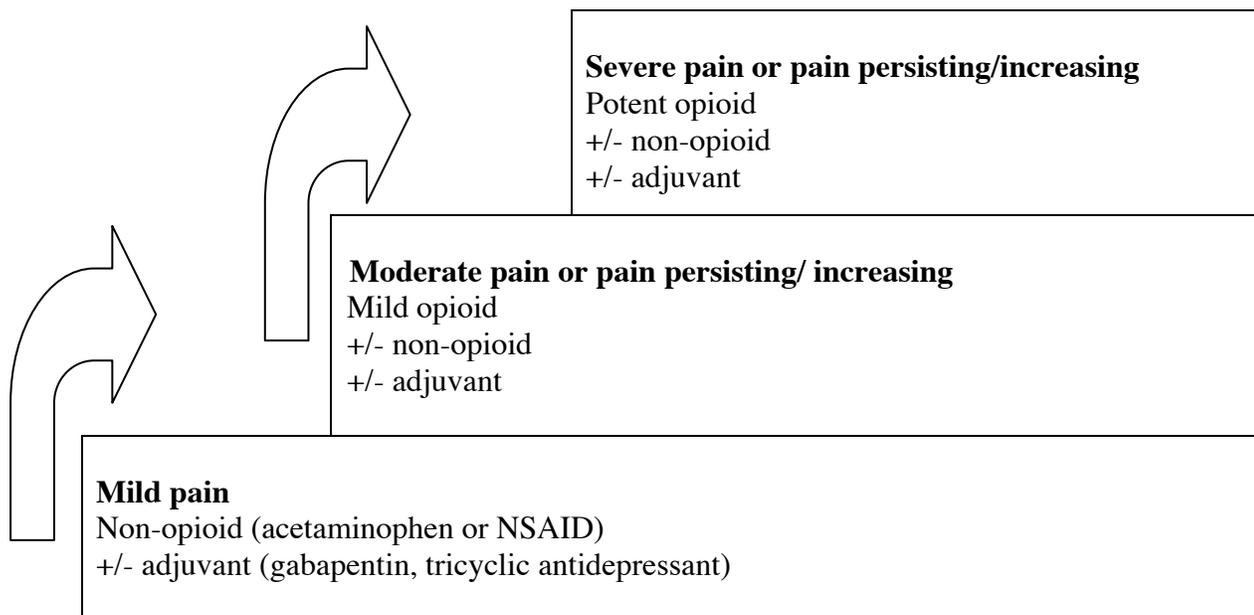
## 7. Principles of Pharmacotherapy of Pain

### 7.1. General principles

- Therapeutic Route: Oral therapy is preferred unless the patient is unable to take oral medication or unless the pain is so severe that more rapid and aggressive parenteral therapy is necessary.
- Individualize the treatment: The correct dose is the one that is sufficient to relieve an individual patient's pain.
- Monitor the response closely to maximize benefit and minimize side effects.

### 7.2. Use the WHO three-step Pain Ladder (Figure 1):

**Figure 1. The WHO 3-Step Ladder: A Step-by-Step Approach to Pain Relief**



- *Mild Pain* (WHO ladder step 1): Use a non-opioid. Consider using an adjuvant pain medications if the pain is neuropathic.
  - Non-opioids:
    - Acetaminophen (Paracetamol)
    - NSAIDS (Ibuprofen, Diclofenac, many others)
  - Adjuvants (tricyclic antidepressants, anticonvulsants, corticosteroids, muscle relaxants)
    - *Definition:* Adjuvant medications can relieve pain independently or enhance effects of and help to reduce dosage of NSAIDs and opioids.
    - *Main indications:* Useful for neuropathic pain. Some adjuvants also are useful in treating bone pain and muscle spasm. When one of these types of pain is suspected and pain is not sufficiently relieved with an NSAID or acetaminophen, add an adjuvant medication.
- *Moderate or severe pain* (WHO ladder steps 2 and 3)

- Opioids

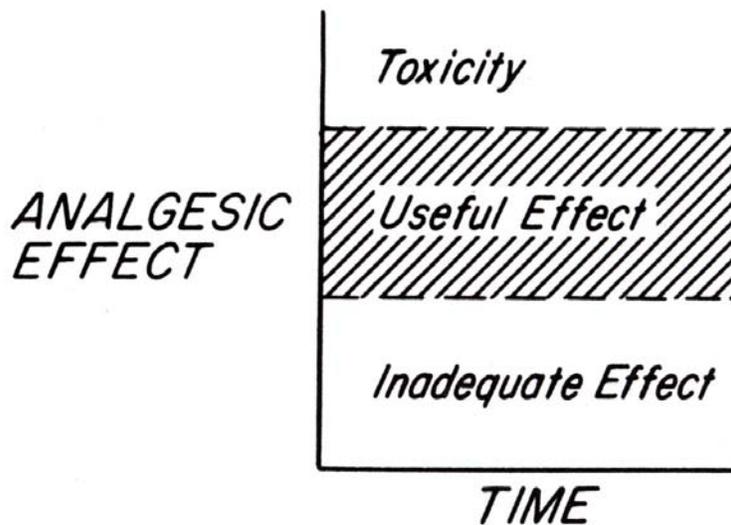
- For moderate pain or pain that persists despite an NSAID or acetaminophen, use a weak opioid (or a low dose of a strong opioid) with or without a non-opioid, and consider adjuvant pain medications if the pain is neuropathic.
- For severe pain, use a strong opioid with or without a non-opioid, and consider adjuvant pain medications if the pain is neuropathic.
- Short-acting opioids for chronic pain should be dosed frequently so that they can maintain their analgesic effect.
  - If the patient has trouble sleeping at night because the effect of the pain medication wears off, try doubling the bed-time dose.

### 7.3. Definitions

- *Around-the-clock dosing*: For moderate or severe chronic pain, pain medications should be given regularly at fixed time intervals or “around-the-clock.” This allows the following dose to be taken before the effect of the previous dose wears off.
- *Pharmacokinetics*: The study of the metabolism and action of drugs; in particular, the time required for absorption, duration of action, distribution in the body, and method of excretion.

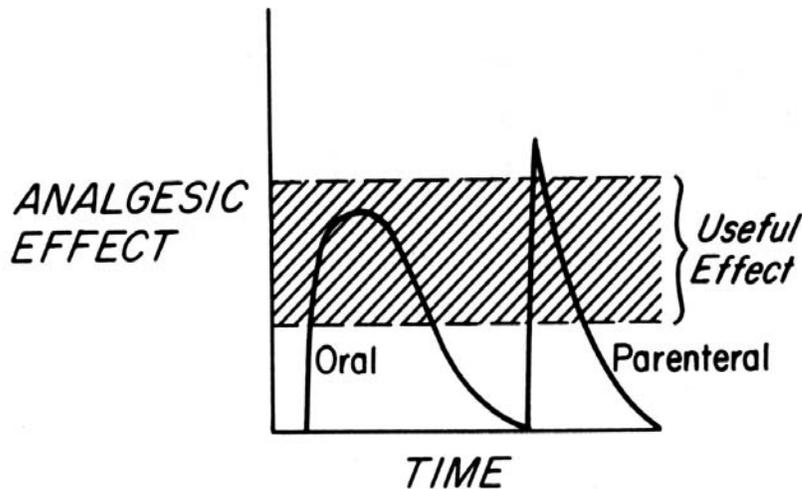
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**Figures 2-4. Basic Opioid Pharmacokinetics**

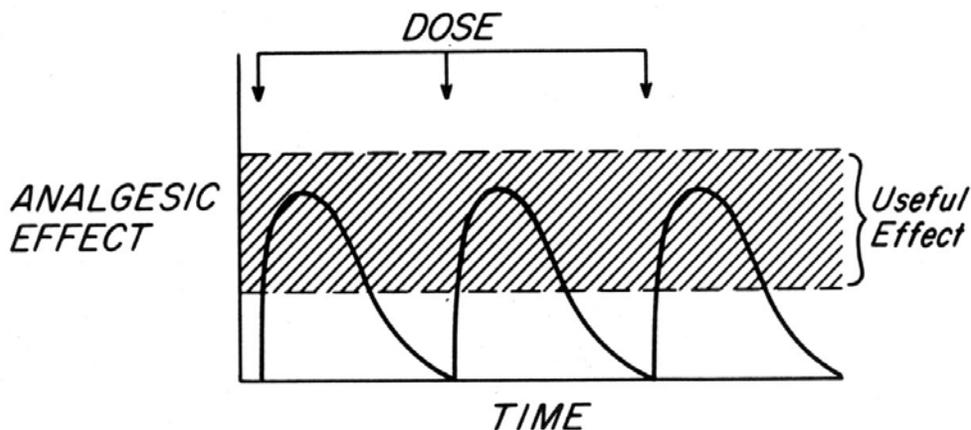


**Figure 2. Simple graph of pharmacokinetics.** This graph plots time against analgesic effect (or blood level of the medication). The goal of medical therapy for chronic pain is to maintain the “useful effect”

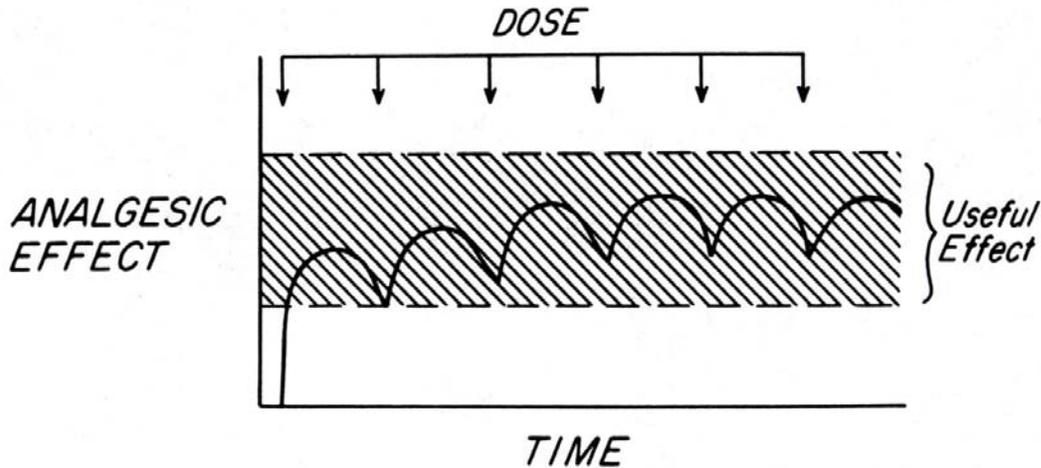
(a therapeutic blood level and thus adequate pain relief) without overdosing (causing toxicity) or underdosing (causing an inadequate effect and thus the return of pain).



**Figure 3. Difference in pharmacokinetics between oral and intravenous dosing.** An intravenous opioid takes effect more quickly but may have a slightly shorter duration of action than an oral opioid. An intravenous opioid takes effect within 10 minutes, and the analgesic effect usually lasts about 3-4 hours. The oral opioid usually takes effect in 30 minutes if the gastro-intestinal system is working properly, and the analgesic effect usually last about 4 hours.



**Figure 3. Excessively long dosing interval of an opioid.** When the dosing interval of an opioid is too long, the useful (therapeutic) effect is lost before the next dose. As a result, pain recurs before each dose and the patient suffers. For example, the useful (therapeutic) effect of short-acting oral opioids usually is about 4 hours. Short-acting oral opioids given at longer intervals will lose their useful effect.

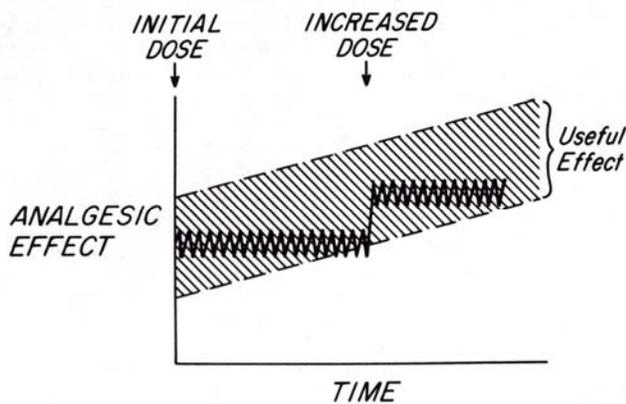


**Figure 4. Proper dosing interval of an opioid.** When the opioid is dosed appropriately, pain usually will not recur before the next dose because an adequate blood level of the drug is maintained. For example, short-acting opioids dosed every 4 hours usually maintain their useful effect.

\*\*\*\*\*

- *Breakthrough pain:* a transitory flare of pain of moderate to severe intensity that occurs on a background of otherwise controlled pain.
- *Rescue dose:* An extra dose of pain medication that is given to treat breakthrough pain.
- *Opioid tolerance:* when a fixed dose of drug produces a decreasing effect so that a dose increase is required to maintain stable analgesic effect. Opioid tolerance occurs in all chronic opioid therapy and is not pathological. (Figure 5)

\*\*\*\*\*



**Figure 5. Opioid tolerance.** Over time, a fixed dose of drug produces a decreasing effect. Thus, an higher dose is needed to maintain the same level of pain relief even if the disease (the underlying cause of the pain) does not change.

- 
- *Equianalgesic dose*: The dose of one opioid that is calculated to be equal in potency to another opioid and therefore to provide the same pain relief as the other opioid.
  - *Incomplete cross-tolerance*: Due to the differing molecular structure of each opioid, patients who switch from one opioid to another have less tolerance of the new opioid than they did of the first one. Therefore, the dose of the second drug should be 25-33% lower than the calculated equianalgesic dose.
  - *Opioid physical dependence*: a state in which withdrawal symptoms will occur if a patient suddenly stops using an opioid or when the effects of an opioid are reversed with an opioid antagonist. Opioid physical dependence occurs in all chronic opioid therapy and is not pathological.
  - *Opioid psychological dependence or addiction*: a disorder characterized by compulsive use of a drug resulting in physical, psychological, and/or social dysfunction to the user and by continued use despite this dysfunction.
  - *Pseudo-addiction*: drug-seeking behavior resulting from inadequate treatment of pain by physicians that resolves when pain is adequately treated. Must be distinguished from true addiction in which drug-seeking behavior continues despite adequate analgesia.

### Daily evaluation questions

1. Since pain can be measured objectively and accurately, it is not necessary to believe the patient's report of pain.      Yes    **No**
2. There are two major categories of pain: \_\_\_\_\_ pain is caused by stimulation of intact sensory nerves, and \_\_\_\_\_ pain is caused by injury to nerves.    **nociceptive    neuropathic**
3. According to the WHO 3-Step Pain Treatment Ladder, severe pain should be treated with some combination of the following:
  - a. Strong opioid
  - b. Non-opioid
  - c. Adjuvant
  - d. All of the above**
  - e. b and c only
  - f. a and c only
4. A transitory flare of pain that usually is well controlled is called \_\_\_\_\_ and requires a \_\_\_\_\_ of pain medication.      **breakthrough pain    rescue dose**

**References (Suggested reading)**

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## Pain Assessment and Treatment

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1



## Cancer and AIDS Cause Pain

- Over 75% of advanced cancer and AIDS patients have pain

### In Vietnam:

- 73% HIV/AIDS patients report pain since diagnosis
- 79% cancer patients report pain since diagnosis



2



## Reasons why cancer pain is often under-treated:

- Doctors underestimate the patient's pain
- Doctors are afraid to prescribe opioids
- Doctors doubt the patient's report of pain
- Patients underreport their pain because:
  - they feel there is little to be done
  - they fear taking pain medications



3

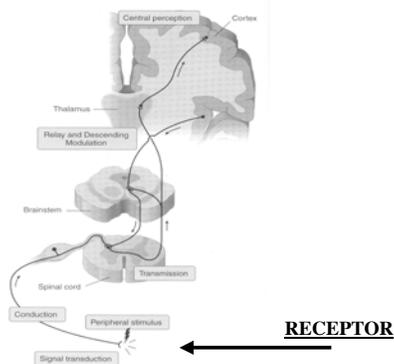


## There are many causes of pain

- Tissue damage
  - infection, tumor, ischemia, trauma, drug toxicities, inflammation, invasive medical procedures
- Psychological factors
  - Depression, anxiety, or stress can exacerbate pain



4



5



## There are two major categories of pain

- Nociceptive pain
  - Caused by stimulation of intact nociceptors (sensory nerves that mediate pain)
- Neuropathic pain
  - Caused by damage to nerves



6



## Nociceptive pain is due to damaged tissue

- Tissue injury is usually apparent
- Direct stimulation of intact nociceptors
- Transmission along normal nerves
- Sharp, aching, throbbing
- Two types of nociceptive pain:
  - Somatic: skin, soft tissue, muscle, or bone
    - easy to describe and localize
  - Visceral: internal organs and hollow viscera
    - difficult to describe and localize



7



## Neuropathic pain is due to damaged nerves

- Many different types of nerve damage:
  - Compression, transection, toxicity, infiltration, ischemia, metabolic injury
- Pain may exceed observable injury
- Described as burning, tingling, shooting, stabbing, electrical



8



## Pain should also be classified as acute or chronic

- Acute pain
  - identified event, resolves in days or weeks
- Chronic pain
  - cause often not easily identified or multifactorial
  - prolonged duration



9



## Pain treatment

- Don't delay for diagnostic tests or disease treatment
- Neuro-plasticity: Uncontrolled pain often causes pathological chemical and anatomic changes in the nervous system that may:
  - Become permanent
  - Amplify pain and make it very difficult to treat
- Seek the underlying cause and treat it if possible. For example:
  - For a painful bone metastasis: radiation therapy
  - For Candida esophagitis: fluconazole



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## Placebos

- Placebos are not considered ethically acceptable means to assess or treat pain



11



## General principles of pain relief

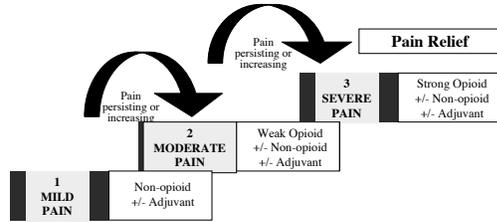
- Assessment:
  - Chronology
  - Location
  - Severity
  - Character
  - Mediating factors (What makes it better or worse?)
  - Previous treatments
- Differential diagnosis
- Management
  - pharmacologic
  - nonpharmacologic



12



Figure 1. The WHO three-step analgesic ladder



Adapted from World Health Organization. *Cancer Pain Relief*. Geneva: WHO, 1990.



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## WHO Step 1: Non-opioid analgesics

- Acetaminophen
  - Starting dose 500-1000 mg every 6 hours
  - Site, mechanism of action unknown
  - Minimal anti-inflammatory effect
  - Hepatic toxicity if > 4 g / 24 hours
    - Increased risk in hepatic disease, heavy alcohol use



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## WHO Step 1: Non-opioid analgesics

- NSAIDs (for example, ibuprofen, diclofenac)
  - Inhibit cyclo-oxygenase (COX)
  - Effective for bone pain, inflammatory pain
  - Individual variation, overall no NSAID works better than any other
  - Side effects:
    - renal failure, gastro-intestinal ulceration, hemorrhage
  - Caution in:
    - Renal/liver impairment, coagulopathy, impaired platelet function, peptic ulcer disease



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## Adjuvant Pain Medications

- Definition
  - Adjuvants are non-opioid medications that help to relieve pain
  - Help to reduce the amount of NSAIDs or opioid medications needed
- Most useful for:
  - Neuropathic pain, bone pain, and muscle spasm



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## WHO Step 2: Weak opioids Routine oral dosing

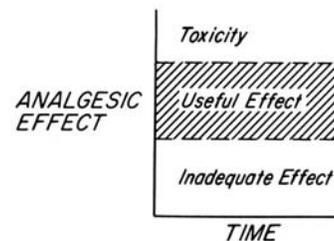
- Codeine:
  - Starting dose 30-60 mg orally every 3-4 hours
  - Maximum dose of 360 mg per day
- Dextropropoxyphene (not recommended)
- Tramadol
- Recommended for mild pain
  - Many patients do not receive adequate analgesia with codeine
  - For these patients, use to morphine



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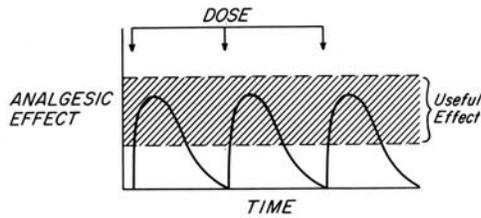
## Opioid Pharmacology



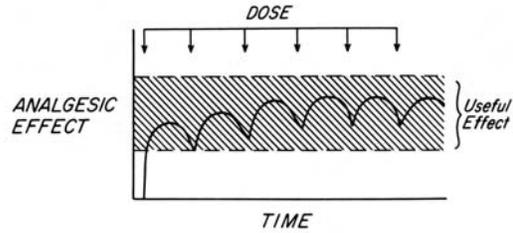
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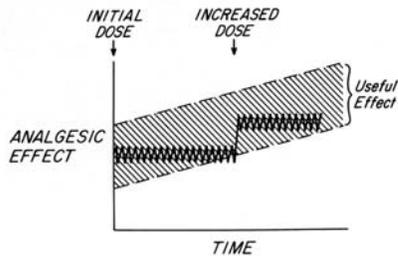
Short-acting opioids dosed infrequently will lose their effect



Dose short-acting opioids frequently (around-the-clock dosing)



Opioid tolerance: over time, a fixed dose produces a decreased effect



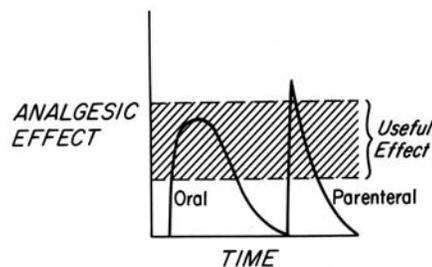
WHO Step 3: Strong opioids  
Routine oral dosing

- Morphine
  - Oral route is preferred except:
    - When patient unable to swallow or absorb oral medications
    - When pain has very severe pain
  - Start with 5 mg orally (for opioid-naïve patient)
    - Reassess after 30 – 60 minutes
  - For chronic pain, dose every 4 hours (if renal function normal)
  - If pain remains unrelieved after 30 minutes, repeat same dose or increase by 50%–100%
  - If pain disturbs sleep, consider doubling the evening dose.

Parenteral

- Morphine SC, IV
  - Starting dose 2-5 mg IV or SC in opioid-naïve patient with normal renal function
  - For chronic pain, dose every 3–4 hours
  - Peak effect reached in 15 minutes
  - If pain remains unrelieved after 15 minutes, repeat same dose or increase by 50%–100%
  - Continuous infusion
    - Easier to administer
    - More even pain control

Peak effect of oral vs. IV morphine



## Routine oral dosing extended-release preparations

- Improve compliance, adherence
- Dose every 8, 12, or 24 hours
- Don't crush or chew tablets
- Steady plasma level reached in 2 – 4 days



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## Transdermal patch

- Fentanyl
  - Peak effect after application  $\approx$  24 hours
  - Patch lasts 48–72 hours
  - Bad for titrating
  - Very expensive-should not be used routinely
  - Analgesia not better than morphine



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## Useful definitions:

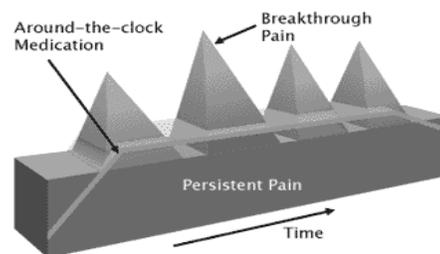
- *Around-the-clock dosing*: pain medication given regularly at fixed dosing intervals
- *Breakthrough pain*: transitory flare of pain
- *Rescue dose*: an extra dose of pain medication to treat breakthrough pain



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## Breakthrough pain



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## Breakthrough pain should be treated with a rescue dose

- How to calculate the rescue dose:
  - 5%–10% of 24-hour dose
    - Give the rescue dose and reassess in 15 minutes if IV/SC or 30 minutes if oral
  - If pain unchanged: double the dose
  - Pain decreased by  $<50\%$  : repeat same dose



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## To change opioids:

- For example: codeine is not adequately effective for your patient and you want to use morphine
- 1) Calculate the dose of codeine the patient is taking
  - 2) Use the equianalgesic table to convert this dose to morphine



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### Equianalgesic Table Used to convert from one opioid to another

Drug	Approximate equianalgesic dose	
	Oral	Parenteral
Morphine	<b>30 mg every 3-4 hours</b>	10mg every 3-4 hours
Codeine *	<b>200mg every 3-4 hours</b>	120mg every 3-4 hours

\*Available only in fixed dose tablet combination with acetaminophen or aspirin.



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### Reduce the new dose by 33%

- Cross-tolerance
  - The molecular structure of each opioid is different
  - When changing from one opioid to another, the patient is not 100% tolerant to the new opioid
  - start with 67% of standard equianalgesic dose



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### Morphine pharmacokinetics

- Metabolized by the liver to active and inactive metabolites
- Excreted mostly by kidneys
- Liver disease:
  - Mild (no change on prothrombin time): no change in dose
  - Severe (increase in prothrombin time): lengthen dosing interval to every 6 or 8 hours
- Renal failure:
  - Increase dosing interval or decrease dose size
  - If anuria renal failure develops, stop routine dosing of morphine and use only as needed
  - Treat symptomatic myoclonus with benzodiazepine or by changing to another opioid, if possible



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### Important concepts

- Opioid physical dependence
- Opioid psychological dependence (addiction)
- Pseudoaddiction



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### Physical dependence

- A normal process of neuro-adaptation
- Abruptly reducing or stopping opioid therapy may cause withdrawal syndrome
- If dose reduction required, reduce by no more than 50% every 2–3 days



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### Psychological Dependence (Addiction)

- Compulsive use even when continued use creates problems in patients work or personal life
- Loss of control over drug use
- Loss of interest in pleasurable activities
- A rare outcome of pain management
  - particularly, if no history of substance abuse

*continued...*



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- Differential diagnosis of addictive behavior...
  - substance use (true addiction)
  - pseudoaddiction (undertreatment of pain)
  - behavioral / family / psychological disorder
  - drug diversion



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## Pseudoaddiction

- Drug-seeking behavior that results from inadequate treatment of pain
- Resolves when pain is adequately treated
- Must be distinguished from true addiction



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## Substance users

- Can have pain too
- Treat with compassion
- Protocols, contracting



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## Ongoing assessment of patients with pain

- Increase analgesics until pain relieved or adverse effects unacceptable
- Be prepared for sudden changes in pain
- Driving is safe if
  - pain controlled, opioid dose stable, no adverse effects



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Thank you



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## Pharmacotherapy for Pain

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### Objectives

*After the lecture, the trainees will be able to:*

1. Use the WHO Analgesic Ladder to treat pain effectively.
2. Prescribe non-opioids effectively and safely.
3. Understand indications for and proper use of adjuvant pain medications.
4. Understand safe and effective use of opioids.

### Contents

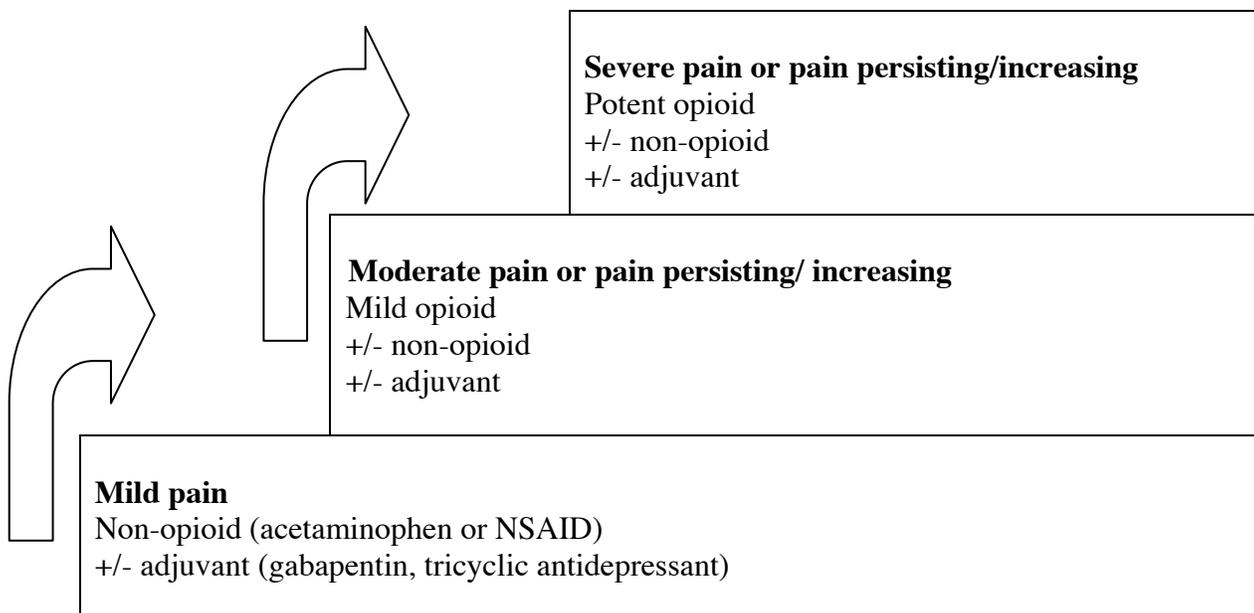
#### 1. General principles:

- 1.1. Therapeutic Route: Oral therapy is preferred unless the patient is unable to take oral medication or unless the pain is so severe that more rapid and aggressive parenteral therapy is necessary.
- 1.2. Individualize the treatment: The correct dose is the one that is sufficient to relieve an individual patient's pain.
- 1.3. Monitor the response closely to maximize benefit and minimize side effects.

#### 2. Use the WHO three-step Pain Ladder (Figure 1):

\*\*\*\*\*

**Figure 1.** The WHO 3-Step Ladder: A Step-by-Step Approach to Cancer Pain Relief



2.1. Mild Pain (WHO ladder step 1): use a non-opioid and consider adjuvant pain medications if the pain is neuropathic. (**Tables 2 and 3**)

- Paracetamol
  - Dosing
    - Starting dose: 500-1000mg every 6 hours
    - Daily maximum dose: 4000 mg
    - Reduce dose (2000mg/day) or avoid completely in patients with liver disease.
  - Side effects: hepatotoxicity
    - May be hepatotoxic if recommended dose is exceeded
    - Do not use in patients who may be heavy alcohol users.
- NSAIDs (Ibuprofen, Diclofenac)
  - Dosing
    - Ibuprofen: start 400-800 mg every 6-8 hours; maximum dose 2400 mg/day.
    - Diclofenac: start 25-75 mg every 12 hours; maximum dose 200 mg/day
    - No NSAID works better than any other
  - Side effects: renal failure, gastrointestinal ulceration and hemorrhage
    - Use with caution in patients with renal impairment, liver impairment, coagulopathy, or impaired platelet function.
    - Prolonged prescription requires gastrointestinal prophylaxis with an H<sub>2</sub>-receptor blocker or proton pump inhibitor (omeprazole)
- Adjuvants (tricyclic antidepressants, anticonvulsants, corticosteroids, muscle relaxants)
  - *Definition:* Adjuvant medications can relieve pain independently or enhance effects of and help to reduce dosage of NSAIDs and opioids.
  - *Main indications:* Useful for neuropathic pain. Some adjuvants also are useful in treating bone pain and muscle spasm. When one of these types of pain is suspected and pain is not sufficiently relieved with an NSAID or acetaminophen, add an adjuvant medication.
  - *For neuropathic pain:*
    - Amitriptyline
      - Start with 10-25 mg once per day at night.
      - Maximum dose 200 mg/day
      - Side effects: drowsiness, initial postural hypotension, anticholinergic effects.
      - Overdose: life-threatening cardiac toxicity.
    - Gabapentin
      - Start with 300 mg at night
      - Then increase every 1 – 3 days to 300mg twice per day, then 300mg three times per day. Titrate to effect.
      - Maximum dose 3600 mg/day
      - Side effects: Drowsiness with each dose increase, dizziness, tremor.
      - Reduce dose in renal failure.
    - Corticosteroids (prednisolone, dexamethasone)
      - Dosing: see ( **Table 3** )
      - Side effects: psychosis, agitation, myopathy, gastrointestinal bleeding,

hyperglycemia.

- *For bone pain:*
  - NSAID
  - Corticosteroid (do not use together with NSAID)
  - Bisphosphonate, if available, for painful bone metastases.
- *For muscle spasm*
  - Anticholinergics (for digestive smooth muscle spasm)
    - Dosing of scopolamine butylbromide: 10-20 mg every 6-8 hours
    - Side effects: anticholinergic effects including constipation, dry mouth, tachycardia, delirium, sedation.
  - Skeletal muscle relaxants
    - Dosing of diazepam: 2-10 mg orally every 8-12 hours
    - Side effects: drowsiness, delirium, ataxia.

2.2. Moderate or severe pain (WHO ladder steps 2 and 3): use a weak opioid (or a low dose of a strong opioid) with or without a non-opioid, and consider adjuvant pain medications if the pain is neuropathic.

- Short acting opioids
  - For moderate pain or pain that persists despite an NSAID or acetaminophen, use a short-acting opioid with or without an NSAID or acetaminophen.
  - Codeine may be effective in some patients. However, side effects such as nausea and vomiting are fairly common with codeine therapy, and codeine is a weak opioid analgesic from codeine. If pain is not adequately relieved by codeine, use a strong opioid.
  - Use oral medication if possible.
  - If the patient has trouble sleeping at night because the effect of the pain medication wears off, try doubling the bed-time dose.
  - When treating chronic pain, short acting opioids should be dosed regularly and frequently to maintain their analgesic effect.
- Weak Opioids (**Table 4**)
  - Codeine:
    - *Dosing:* start 30-60 mg every 3-4 hours, maximum dose of 360 mg per day.
    - Recommended for mild pain, but many patients do not receive adequate analgesia with codeine. These patients should receive a strong opioid such as morphine.
  - Dextropropoxyphene: not recommended
- Strong opioids (**Table 5**)
  - Morphine sulfate
    - *Oral dose:* start with 5 mg, re-assess after 60 minutes. If pain remains severe, double the dose every hour. After an effective dose is identified, give every four hours around-the-clock. May increase dose by 50% to 100% after each day if pain is refractory.
    - *IV or SC dose:* start with 2-5 mg IV or SC. For severe pain, double the dose every 20 minutes if the first dose is not effective. Once an effective dose is reached, give every 3-4 hours around the clock.
  - Transdermal fentanyl patch

- *Description:* Adhesive patch that is changed every 48-72 hours.
- *Indications:* Useful for patients who have trouble taking oral medication due to nausea, to difficulty swallowing, or to gastrointestinal tract dysfunction.
- *Mechanism of action:* Fentanyl, a lipophile, diffuses into the fat of the skin and then into the bloodstream. The patch should be placed over an area of the body with subcutaneous fat such as the abdomen, upper arm, or buttocks.
- *How to use:* The patch is not an effective initial treatment for severe pain because it takes at least 12 hours to take full effect. Frequent rescue dosing is needed for the first 12-24 hrs until the blood level of fentanyl stabilizes.
- *Contraindications:* The fentanyl patch should not be used:
  - In cachectic patients who do not have adequate subcutaneous fat.
  - In febrile patients because of increased absorption and possible toxicity.
  - In sweaty patients because the patch will not stick.
  - In poor patients who cannot afford to pay for it (use long-acting morphine if available, short-acting morphine, or a continuous morphine infusion)

### 3. Opioid side effects

3.1. The risk of serious side effects of opioids is minimal when standard prescribing rules are followed.

3.2. Elderly patients and patients with hepatic or renal insufficiency will be more sensitive to the medication and experience side effects such as sedation or delirium at lower doses. Start with a low dose and increase slowly.

3.3. *Dosing:* prescribe the lowest dose of opioid that relieves the pain completely or to the degree acceptable to the patient.

3.4. Common side effects:

- *Nausea and vomiting:* usually mild, and usually resolves within one week.
- *Sedation:*
  - Usually resolve within one week. However, patients should not operate heavy machines or perform dangerous tasks for two weeks after beginning an opioid or for one to two weeks after a change in their regimen. This waiting period gives patients time to become tolerant to the sedative effect of the opioid.
  - Somnolence that occurs when an opioid is started or increased is not always due directly to the opioid. Many patients with persistent or frequent pain are sleep-deprived and will go to sleep when their pain is adequately relieved. Normal sleep can be distinguished from opioid-induced sedation by testing the patient's arousability. A normally sleeping patient will be arousable.
- *Delirium:* Most common in elderly patients and those taking other psycho-active medications such as benzodiazepines. Delirium can improve with a slight reduction in the opioid dose.
- *Constipation:* unlike other side effects, constipation does not resolve with long-term use. Therefore give all patients on opioids a bowel regimen such as a stimulant laxative (example: senna 2 tablets orally twice per day).
- *Respiratory depression:*
  - Respiratory depression is rare in a patient on a stable opioid dose. If it does occur, evaluate for a change in the patient's underlying medical condition such as renal failure, liver failure, or sepsis.

- Sedation virtually always precedes respiratory depression. Therefore, it is safe to treat pain aggressively with opioids at least until sedation occurs. When respiratory depression is due to an overdose of opioids, it is always preceded by somnolence.
- *Treatment for opioid-induced respiratory depression:*
  - In the sedated but otherwise stable patient, reduce the opioid dose, provide supplemental oxygen, and attempt to arouse the patient.
  - For significant respiratory depression, dilute 0.4 mg naloxone into 9 cc of normal saline and administer 1 – 2 cc every one to two minutes until the respiratory rate is satisfactory.
  - When using naloxone, the clinical goal is to reverse the respiratory depression without reversing the analgesic effect of the opioid. Beware that too rapid infusion of naloxone may precipitate a pain crisis in a patient on chronic opioid therapy for pain.
- Allergic reactions:
  - Rash, urticaria, pruritis
    - May be due to mast cell activation and histamine release.
    - Treat with a systemic antihistamine such as diphenhydramine.
  - Anaphylaxis is very rare.

#### 4. Starting a long-acting opioid

4.1. For a patient with intermittent pain, short-acting opioids may suffice. However, for a patient with continuous pain or with a combination of continuous pain and intermittent worsening, use long-acting opioids when available.

4.2. Long-acting opioids are preferable because they maintain a more constant blood-level of the drug and thus a more constant state of analgesia than short-acting opioids.

4.3. To choose the long-acting opioid dose, start the patient on a short-acting medication and titrate the dose to control the pain. Once the patient is on a stable dose of a short-acting formulation, switch to the same dose in its long-acting formulation. Long-acting opioids include a 12-hour oral formulation of morphine and the 72-hour fentanyl transdermal patch (expensive).

4.4. Long-acting opioid should be used only “around-the-clock” (at regularly scheduled intervals), never as treatment for “breakthrough” pain (a transitory flare of pain that occurs in the context of otherwise well-controlled pain). A short-acting opioid – ideally the short-acting form of the long-acting opioid – should be used for breakthrough pain.

#### 5. Treating breakthrough pain

5.1. Each patient should be instructed to take a rescue dose of opioid if their pain is severe.

5.2. The rescue dose for outpatients is 10% of the total daily dose taken by the patient. (**Figure 6**)

##### **Figure 6. Calculating a rescue dose**

*Example: a patient receiving oral morphine takes 10mg every 4 hours:*

- Total daily dose:  $10 \text{ mg} \times 6 = 60 \text{ mg}$

- Breakthrough dose:  $10\% \times 60\text{mg} = 6 \text{ mg every } 2 - 4 \text{ hours as needed}$

5.3. If frequent rescue doses are required, the total amount of rescue medication needed in 24 hours

should be added to the total daily dose of medication given around-the-clock. (**Figure 7**)

5.4. If the patient requires rescue pain medication for incident pain such as pain caused when the patient is washed or walks, a rescue dose should be given 20 – 30 minutes prior to the inciting cause.

\*\*\*\*\*

### Figure 7. Recalculating the regular dose in a patient who requires many rescue doses

*Example: a patient receives morphine 10mg every 4 hours also requires a rescue dose of 6mg five times during the day;*

*- Total around-the-clock dose: 10 mg taken every 4 hours = 60 mg/day*

*- Total rescue or breakthrough dose: 6mg x 5 times = 30mg/day;*

*- Total amount of morphine taken daily= 60 mg + 30 mg = 90 mg*

*- New around-the-clock dose: 90 mg/6 = 15 mg every 4 hours*

*- Thus the regular around-the-clock dose can be increased from 10 mg every 4 hours to 15mg every 4 hours*

\*\*\*\*\*

## 6. Equianalgesic Dosing

6.1. Definition: Finding the equivalent dose when switching from one opioid to another.

6.2. Different opioids have different potency and a table must be used to convert from one opioid to another. (**Table 6** and **Figure 8**)

6.3. *Incomplete-cross tolerance* among opioids: Due to the differing molecular structure of each opioid, patients who switch from one opioid to another have less tolerance of the new opioid than they did of the first one. Therefore, the dose of the new drug should be 25-50% lower than the calculated equianalgesic dose.

**Table 6: Opioid equianalgesic doses**

Drug	Oral or Per Rectum (mg)	IV or Subcutaneous (mg)
Morphine	30	10
Codeine	200	120
Hydro- morphine	7.5	1.5
Pethidine	300	75
Fentanyl		0.1 (100 mcg)
Oxycodone / Hydrocodone	20	

**Table 7: Switching from  
injected morphine to Fentanyl  
Transdermal Patch**

Injected morphine (mg/24 hours)	Fentanyl patch (mcg/hr)
18-35	25
36-59	50
60-83	75
84-107	100
108-131	125
132-156	150

**Figure 8. Switching from codeine to morphine**

*For example, to change a patient from codeine to morphine:*

1.) Calculate the 24-hour codeine dose:  
 $60 \text{ mg codeine orally every 24 hours} = 360 \text{ mg codeine/24 hrs}$

2.) Look up the equianalgesic conversion from oral codeine to oral morphine:  
 $\text{Codeine dose} \times 0.15 = \text{morphine dose}$

**3.) Morphine dose =  $360 \text{ mg codeine} \times 0.15 = 54 \text{ mg morphine/day}$  or **9mg every 4 hours****

\*\*\*\*\*

**7. Discontinuing Opioid Therapy**

7.1. Opioid therapy can be discontinued when the patient's pain has resolved and sometimes when an alternative type of analgesic therapy is effective.

7.2. When opioid therapy of two weeks or longer is discontinued, care must be taken to avoid causing opioid withdrawal syndrome.

- Signs and symptoms of opioid withdrawal syndrome may include fever, chills, sweating, nausea, vomiting, painful abdominal cramping, diarrhea, muscle aches, insomnia, runny nose, and hypertension.
- To avoid this syndrome, the opioid dose should be tapered slowly over 2 – 3 weeks.
- When symptoms occur, they can be treated by giving opioid at a dose slightly higher than the previous dose.

**8. Difficult-to-Control Pain**

8.1. Even when the principles of pain relief are followed, the pain of some patients will be difficult to control.

8.2. Patients with severe pain may need rapid upward titration of opioid medications.

8.3. When pain is difficult to control, consider the following reasons:

- Under-medication (the most frequent reason), including tolerance
  - Consider increasing the opioid dose or changing the opioid.
- Neuropathic pain
  - Treat with adjuvant medications.
- Incident pain
  - Before dressing changes or planned activity, provide an extra dose of short-acting opioid.
- Psychological dependence (addiction)
  - Rare in cancer patients treated with opioids, but patients who have a history of substance abuse have a higher risk.
- Somatization
  - Consult a psychiatrist, if possible.

## 9. Case Example

Mr. Cuong, a 45-year-old man with advanced AIDS, complains of abdominal pain. The pain has not responded to treatments for TB or MAI. Treatment for CMV is not available. The patient has end-stage AIDS, and his HIV is resistant to the only available anti-retroviral medications. For pain, the patient is currently taking 10 mg of oral morphine every 6 hours around-the-clock. He complains that his pain medication wears off, and he is frequently in pain.

**What are the problems with this pain management?**

**How should the morphine be dosed?**

**How would do you convert him to a long-acting opioid (if available)?**

The first problem is that he is not taking an adjuvant that would minimize the toxicity of the opioid. Start an adjuvant medication such as acetaminophen (it is best to avoid using an NSAID in a patient with abdominal pain of uncertain cause). If this helps, it may be possible to reduce his opioid dose.

The second problem is that his current dosing interval of six hours is too long: the effect of the short-acting opioid lasts only four hours. He should take the morphine more frequently, every four hours, and take a double dose before sleep so that the medication can last longer and not interrupt his sleep. Alternatively, he could take a long-acting opioid every 12 hours, if available.

**What dose should you give for breakthrough pain?**

**What does breakthrough pain indicate?**

Whenever you treat a patient with an opioid analgesic around the clock, provide the patient with medication for breakthrough pain. The usual dose for breakthrough pain is 10% of the total 24-hour dose. An opioid prescribed for breakthrough pain may be safely dosed as often as every 1-2 hours. Short-acting opioids that are orally dosed reach peak analgesic effect at one hour and last no more than 4 hours. In this example, prescribe for Mr. Cuong an additional 5-10 mg of morphine every 1-2 hours as needed.

Our goal is to control Mr. Cuong's pain so well with an around-the-clock opioid regimen that he does not need more than one or two breakthrough doses per day. When a patient needs frequent breakthrough pain medication, the patient's "around-the-clock" opioid dose is too low (or the dosage interval is too long). To calculate the necessary increase in the around-the-clock dose, calculate the total amount (including around-the-clock and breakthrough medication) that the patient requires in 24 hours. Then divide this number by 6 to get the new dose to be given every 4 hours. In this example, if Mr. Cuong consistently takes 10 mg of morphine every four hours, the total around-the-clock dose is 60 mg per day. If he requires another 10 mg four times a day for breakthrough pain, the 24-hour total would be 60mg + 40mg = 100 mg. The new around-the-clock dose should be 100mg in 6 divided doses or approximately 15 mg every four hours.

**Daily evaluation questions**

(TYPES OF QUESTIONS: Yes/ No; Select the single best answer multiple choice questions A, B, C, and D ... ; Fill in the blanks with suitable words or sentence.)

1. What type of pain is often difficult to control, even with morphine?
  - a) somatic pain
  - b) visceral pain
  - c) neuropathic pain**
  - d) bone pain
  
2. According to the WHO analgesic ladder, what should be the first treatment for cancer pain?
  - a) A mild opioid such as codeine
  - b) Non-opioid analgesics such as paracetamol or ibuprofen**
  - c) Morphine
  - d) Reassurance
  
3. What is a typical indication for starting morphine?
  - a) Pain with swallowing in a patient with AIDS.
  - b) Persistent pain despite treatment with codeine and paracetamol in a patient with cancer**
  - c) Mild chronic lower back pain in a patient who does not have cancer
  - d) A patient with cancer and bony metastases but without pain
  
4. Which of the following is not a common side-effect of morphine?
  - a) nausea
  - b) sedation
  - c) constipation
  - d) anaphylaxis**
  
5. What is an appropriate morphine dose for breakthrough pain?
  - a) 5 mg of morphine
  - b) 10 mg of morphine
  - c) 10% of the daily dose**
  - d) 25% of the daily dose
  
6. Paracetamol in doses greater than 4000mg per day can cause injury to the \_\_\_\_\_. **liver**
  
7. NSAIDS such as ibuprofen and diclofenac are safe to use in patients with renal failure. Yes **No**

**References (Suggested reading)**

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**References for writing the lecture**

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## APPENDIX

**Table 2: Use of Non-opioid Analgesics**

<b>Analgesic / Routes</b>	<b>Starting Dose</b>	<b>Duration</b>	<b>Daily maximum dosage</b>	<b>Comments</b>
<b>Recommended Analgesics:</b>				
<b>Acetaminophen</b> (Paracetamol Tablets, and syrup for children with strength depends on producers)  Oral route	Adults: 500 – 1000 mg	Every 4-6 hours	4000mg	- Reduce dose or do not use in patients with liver disease. - May be hepatotoxic if exceeds recommended dose.
	Children: 10-15mg/kg		Children: no excess of recommended dose	
<b>Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)</b>				
<b>Ibuprofen</b> (Tablets of 200, 300, 400, 600, 800mg; Syrup for children with strength depends on producers)  Oral route	Adults: 400-800mg	Every 6- 8 hours	Adults: 2400mg	- Prolonged prescription requires gastrointestinal prophylaxis. - Lower dosage for patients with severe liver disease. - Use with caution in patients with kidney disease.
	Children: 5-10mg/kg		Children: no excess of recommended dose	
<b>Alternatives</b>				
<b>NSAIDs</b>				
<b>Choline magnesium trisalicylate</b>	Adults: 500-1000mg	Every 8-12	Adults: 3000mg	- No inhibition of platelet function

Oral route	Children: 25mg/kg	hours	Children: no excess of recommen ded dose	- Less gastrointestinal toxicity. - Reduce dose in patients with renal failure.
<b>Diclofenac</b> (immediate release)  Oral route	Adults: 25- 75mg	Every 12 hours	200mg	- Prolonged prescription requires gastrointestinal prophylaxis. - Reduce dose in patients with renal failure
<b>Diflunisal</b>  Oral route	Adults: 500mg	Every 12 hours	1000mg	
<b>Etodolac</b> (immediate release)  Oral route	Adults: 200-400mg	Every 8 hours	1200mg	
<b>Fenoprofen</b>  Oral route	Adults: 200mg	Every 6 hours	3200mg	
<b>Ketoprofen</b> (immediate release)  Oral route	Adults: 25-75mg	Every 6-8 hours	225mg	- No longer than 5 days. - Prolonged prescription requires gastrointestinal prophylaxis. - Reduce dose in patients with renal failure.
<b>Ketorolac</b> IM/IV  Oral route	Adults: - High dose for the first time 30- 60mg, followed by 15-30mg; or  - Oral: 10mg	Every 6 hours	-Injection: 120mg  - Oral: 40mg	- Danger of gastrointestinal hemorrhage. - Short course (5 days at most). - Gastrointestinal prophylaxis recommended. - Reduce dose in patients with renal failure.
<b>Meloxicam</b>  Oral route	Adults: 7,5- 15mg	Every 24 hours	30mg	- Prolonged prescription requires gastrointestinal prophylaxis. - Reduce dose in patients with renal failure.

<b>Piroxicam</b> Oral route	Adults: 20mg	Every 24 hours	20mg	- High risk of gastrointestinal hemorrhage. - Gastrointestinal prophylaxis recommended. - Reduce dose in patients with renal failure. - Do not use in patients with liver disease.
<b>Opioid-alike Analgesics</b>				
<b>Tramadol</b> Oral route	Adults: 50- 100mg	Every 4 – 6 hours		An analgesic that has similar effects to weak opioid.

**Table 3: Use of Adjuvant medications for Pain Management**

Adjuvant and rout	Dose and administration	Side effects
<b>Corticosteroids</b>		
<b>Prednisolone</b>	Adults: 20-80 mg in the morning, orally	Hyperglycaemia, agitation, psychosis, myopathy, gastrointestinal bleeding
	Children: 1mg/kg x 1-2 times/day, orally	
<b>Dexamethasone</b>	Adults: 8-20 mg in the morning, orally or IV	
	Children: 0.3mg/kg/day orally or IV	
<b>Tricyclic antidepressants</b>		
<b>Amitriptyline</b>	Adults: 10- 25mg (maximum dose 200mg)/day, orally at bed time	Drowsiness initially, postural hypotension, life-threatening cardiac toxicity with overdose
	Children: 0.5mg/kg once a day orally at bedtime. Increase as needed by 0.2-0.4mg/kg every 2-3 days to maximum of 5mg/kg/day.	
<b>Anticonvulsants</b>		
<b>Valproate</b>	15mg/kg/day in 3 divided doses	Causes drowsiness Do not use in patients with liver disease.

	Maximum: 60mg/kg/day	Reduce dose in old patients.
<b>Gabapentin</b>	<p>Adults: Start with 300mg at bed time. After 2 days, increase to 300mg twice daily, after 2 following days increase to 300mg three times a day. Continue to increase as needed and tolerated.</p> <p>Maximum dose 3600mg/day.</p> <p>Children: 5mg/kg once per day at bedtime. Increase as needed and as tolerated to 2-3 times per day, then by 2-5 mg/kg/day to a maximum of 2400mg/day.</p>	<p>Drowsiness initially with each increase of dose. Dizziness. Tremor.</p> <p>Reduce dose in renal failure.</p>
<b>Local anesthetics /antiarrhythmics</b>		
<b>Lidocaine</b>	Start with 1mg/kg IV as a loading dose, then 1 – 3 mg/min IV constant infusion.	Cardiac arrhythmia, delirium
<b>Antispasmodics</b>		
<b>Scopolamin (hyoscine) butylbromide</b>	10-20mg 3-4 times/day, orally; or 10mg SC 3-4 times/day, maximum 60mg/day. Can also give as SC infusion.	Anti-muscarinic effects including, constipation, dry mouth, tachycardia.
<b>Scopolamin (hyoscine) hydrobromide</b>	10-20mg, 3-4 times/day, orally; or 0.2-0.4mg, 3-4 times/day, SC; or 2mg/day continuous SC infusion; or 1.5-6mg/72 hours transdermal	Scopolamine hydrobromide also can cause drowsiness
<b>Phloroglucinol hydrat 80mg + Trimethylphloroglucinol 80 mg (Spasfon)</b>	4-6 tablets/day; or 1-3 vials IM or IV	
<b>Skeletal muscle relaxants</b>		
<b>Diazepam</b>	2-10mg, 2-3 times/day, orally or IV	Drowsiness, locomotor ataxia
<b>Baclofen</b>	Start with 5mg 3 times/day, orally, maximum dose 20mg x 3 times/day	

<b>Bisphosphonates (use for bone pain from bone metastases)</b>		
<b>Pamidronate</b>	60-90mg IV, every 4 weeks	Hypocalcemia. Brief (1-2 days) fever or flu-like symptoms (less often with acid Zoledronic)
<b>Acid Zoledronic</b>	4mg IV, every 4- 8 weeks	

**Table 4: Weak opioids**

<b>Analgesics, Route</b>	<b>Starting Dose</b>	<b>Duration</b>	<b>Comments</b>
<b>Codeine</b> (30mg tablet, or combined with non-opioid like aspirin, paracetamol)  Oral route	Adults: 30-60mg  Children: 0,5 – 1mg/kg	Every 3 – 4 hours	<ul style="list-style-type: none"> <li>- Maximum dose of 360mg per day; for children not excess 6 times per day</li> <li>- May cause constipation</li> <li>- Often cause nausea</li> <li>- Reduce dose in patients with renal failure.</li> </ul>
<b>Dextropropoxyphene</b> Oral route	Adults 65mg		

**Table 5: Stronger opioids**

<b>Analgesics, Route</b>	<b>Starting Dose</b>	<b>Duration</b>	<b>Comments</b>
<b>Morphine sulfate</b> immediate release  Oral route	Adults: start with 5 mg, re-assess after 30min, then can increase to 10mg  Children: start with 0,15mg/kg, then can increase to 0,3mg/kg	After proper dose is found, every 4 hours	May increase by 50 – 100% each day if pain is refractory
<b>Morphine sulfate</b> Long acting  Oral route	Adults: 15mg		

<b>Morphine</b> IV or SC	Adults: 2-5mg	Every 3-4 hours	
	Children: 0,05-0,1mg/kg		
<b>Oxycodone</b> immediate release  Oral route	Adults 5-10mg	Every 3-4 hours	More potent than morphine.
	Children: 0,1mg/kg		
<b>Oxycodone</b> long-acting (Oxycontin)  Oral route	Adults 10mg	Every 12 hours	
<b>Hydromorphone</b>  Oral route	Adults: 1 – 3mg	Every 3-4 hours	More potent than morphine.
	<b>Hydromorphone</b>  IM or SC		
<b>Fentanyl</b> Transdermal patch	Adults: 25mcg/h	Apply one patch every 72 hours on chest or thigh	<ul style="list-style-type: none"> <li>- Use only for chronic pain, not for breakthrough pain.</li> <li>- Do not prescribe for patients with fever, sweating, or cachexia.</li> <li>- Suitable to relieve pain in very weak patients who are unable to take oral medications or get injected regularly.</li> <li>- Provide other short-acting analgesics until the patch takes effect after 12-18 hours.</li> <li>- Very expensive, difficult to store in hot and humid condition.</li> </ul>

## Adverse Effects, Adjuvants, and Barriers to Pain Relief

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1



## Objectives

- Learn the adverse effects of analgesics and ways to limit such effects
- Learn use of adjuvant analgesic agents
- Learn barriers to pain relief and ways to overcome them



2



## Opioid adverse effects

### Common

Constipation  
Dry mouth  
Nausea / vomiting  
Sedation  
Sweats

### Uncommon

Bad dreams / hallucinations  
Dysphoria / delirium  
Myoclonus / seizures  
Pruritus / urticaria  
Respiratory depression  
Urinary retention



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## Constipation . . .

- Common to all opioids
- Easier to prevent than treat
- Encourage high fiber diet but, dietary measures usually not sufficient



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## . . . Constipation

- Bulk forming agents not recommended
- Stimulant laxative
  - Bisacodyl
- Osmotic laxative
  - Polyethylene glycol (Forlax)
  - Sorbitol
- Additional agents
  - Mineral oil
  - Oral naloxone



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## Nausea / vomiting . . .

- Onset usually with start of opioids
  - tolerance usually develops within days
- Prevent or treat with dopamine-blocking antiemetics
  - Haloperidol 0.5 - 1 mg every 6 – 8 hours
  - Prochlorperazine 5 - 10 mg every 6 hours
- If nausea is refractory to treatment, try a different opioid if possible



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## Sedation . . .

- Onset with start of opioid
- Distinguish from exhaustion due to pain
- Tolerance develops within days



7



## . . . Sedation

- If persistent, alternative opioid
- Psychostimulants may be useful
  - methylphenidate, 5 mg every morning and noon, titrate, maximum 60 mg/day



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## Delirium . . .

- Presentation
  - confusion, bad dreams, hallucinations
  - restlessness, agitation
  - myoclonic jerks, seizures
  - depressed level of consciousness



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## . . . Delirium

- Treat agitation with haloperidol 0.5-5 mg orally every 4 - 6 hours as needed
- For severe agitation, use chlorpromazine intramuscularly or IV (more sedating)
- Delirium sometimes improves with a slight reduction in the opioid



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## Respiratory depression . . .

- Pain is a potent stimulus to breathe
- Opioid respiratory depression
- It is always preceded depression is due to generalized CNS by somnolence



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## . . . Respiratory depression

- **Management**
  - identify, treat contributing causes
    - reduce opioid dose
    - observe
  - if unstable vital signs
    - dilute 0.4 mg naloxone into 9 ml saline and give 1 ml IV every 1-2 minutes
    - too much naloxone may cause pain crisis



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## Urticaria, pruritus

- Opioids can cause mast cell activation and histamine release
- Treat with antihistamines
  - Diphenhydramine 12.5 – 50 mg orally every 6 hours as needed
  - Others:
    - Hydroxyzine
    - Fexofenadine
    - Loratadine
    - Doxepin



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## Opioid allergy

- Anaphylactic reactions are rare
  - If bronchospasm occurs discontinue the opioid
- Adverse effects such as nausea / vomiting, constipation, drowsiness are not allergic reactions



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## Adjuvant analgesics

- Medications that supplement primary analgesics
  - may themselves be primary analgesics
  - use at any step of WHO ladder



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## Adjuvant analgesics

- Especially useful for
  - Neuropathic pain
    - Opioids usually not very effective
  - Pain from bony metastases
    - Opioids effective but often not needed



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## Case 1 . . .

- Anh Tuan, 40-year-old farmer
- AIDS, CD4 = 34
- Burning pain hands, feet
  - Treated initially with stavudine (d4T) + lamivudine (3Tc)
    - Symptoms disappeared when medication stopped



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## . . . Case 1

- Burning pain hands, feet returned and has persisted for 6 months
  - severe
  - keeps awake at night
  - numbness in feet
  - trouble buttoning shirt
  - not responsive to high doses of opioids
- How to manage Anh Tuan's pain?



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### Pain is seen frequently in patients with AIDS

Fatigue	48-77%
Weight loss/anorexia	31-91%
<b>Pain</b>	<b>29-76%</b>
Anxiety	25-40%
Insomnia	21-50%
Cough	19-36%
Nausea/ vomiting	17-43%
Depression/ sadness	15-40%
Dyspnea/ respiratory symptoms	15-48%
Diarrhea	11-32%
Constipation	10-29%

\*Based on several published descriptive studies of patients with AIDS, predominantly in patients with late-stage disease, Europe and North America, 1990-2002.



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### Medications for neuropathic pain

- Tricyclic antidepressants
- Gabapentin (anticonvulsants)
- Local anesthetics/anti-arrhythmics (lidocaine patch or IV lidocaine)
- Corticosteroids
- SSRIs if others not effective



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### Tricyclic antidepressants for neuropathic pain . . .

- Amitriptyline
  - most extensively studied
  - 10–25 mg orally at bedtime, titrate upward as needed every 4–7 days
  - takes days or weeks to work
  - usual effective dose 50-300 mg/day
  - side effects (anticholinergic):
    - drowsiness, constipation, dry mouth, orthostatic hypotension, tachycardia
  - overdose can be lethal



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### Gabapentin for neuropathic pain

- Anticonvulsant
  - Start with 300 mg orally at bedtime
  - titrate upward every 2 or 3 days (300 mg orally twice per day, then three times per day) until effective or side effects occur
  - usual effective dose 300–600 mg three times/day
  - Maximum 1200 mg three times / day
  - Main adverse effect is drowsiness
    - tolerance develops within days
  - decrease dose in renal insufficiency
- Valproate is an alternative



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### Bone pain . . .

- Pain usually is constant, worse with movement
- Typically caused by metastases and by pathologic fractures
  - Vertebral compression fractures are common
  - Rule out spinal cord compression



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### Case 2

- Chi Phuong, 73-year-old with breast cancer, metastases to bone
- Morphine does not provide adequate pain control
- How to relieve Chi Phuong's pain?



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## Bone pain

- Management
  - opioids
  - NSAIDs
  - corticosteroids
  - bisphosphonates
  - external beam radiation
  - orthopedic intervention
  - external bracing



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## Pain from bowel obstruction . . .

- Causes
  - Constipation
  - External compression or infiltration by tumor
  - Adhesions from previous surgery
  - Inflammation from ulceration (gastric outlet obstruction)
- Associated symptoms – vomiting with or without nausea



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## . . . Pain from bowel obstruction

- Management
  - Opioid for pain
  - Corticosteroid if cause is tumor
  - Treat constipation, if present
  - Anticholinergic medications such as scopolamine to treat cramping
  - Metoclopramide to promote motility for ileus or gastroparesis
- Invasive intervention
  - Venting gastrostomy tube to drain stomach if appropriate
  - surgical reduction or bypass if appropriate for goals of care



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## Case 3

- Anh Cong, 67-year-old farmer
- Colon cancer, metastases to liver
- Right upper quadrant pain
  - tender liver
  - no evidence of ascites
- How to manage Anh Cong's pain?



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## Corticosteroids . . .

- Many uses
  - Malignant bowel obstruction
  - Pain from liver capsule stretch due to expanding tumor
  - Neuropathic pain
  - Nausea/vomiting
  - Anorexia
  - Fatigue
  - Fever / sweats
- Dexamethasone
  - long half-life (>36 h), dose once / day
  - doses of 4–20 mg / day



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## . . . Corticosteroids

- Adverse effects
  - Hyperglycemia
  - Infection risk
  - Occasionally psychosis or agitation
- Long-term adverse effects
  - Proximal muscle weakness
  - Hypertension
  - Osteoporosis



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## Barriers to good pain treatment

- Among physicians:
  - Pain relief not considered important
  - Inadequate pain assessment
  - Lack of knowledge of pain treatment
  - Fear of
    - Causing addiction
    - Adverse effects
    - Regulatory oversight
- Among patients
  - Patients unwilling to report pain
  - Patients unwilling to take medicine



## The International Narcotic Control Board - INCB

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1



## THE INTERNATIONAL NARCOTIC CONTROL BOARD - INCB (1)

### 1. What is INCB?

INCB is the abbreviation of the International Narcotic Control Board

In Vietnamese: Ủy ban kiểm soát ma túy quốc tế

- Established in 1968.
- Is a fair and independent treaty-based international organization that monitor implementation of the UN drug control conventions



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## THE INTERNATIONAL NARCOTIC CONTROL BOARD - INCB (2)

### 2. Functions of INCB

Laid down in the following treaties:

- Single Convention on Narcotic Drugs 1961
- Convention on Psychotropic Substances 1971
- UN Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988



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## THE INTERNATIONAL NARCOTIC CONTROL BOARD - INCB (3)

### 2. Functions

#### a. Advocating for licit manufacture of, trade in and use of drugs

- **INCB endeavours, in cooperation with Governments, to ensure that adequate supplies of drugs are available for medical and scientific uses and that the diversion of drugs from licit sources to illicit channels does not occur.**
- **INCB also give guidance to governments for for assessing chemicals used in the illicit manufacture of drugs to assist governments in combating the use of illicit chemicals**



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## THE INTERNATIONAL NARCOTIC CONTROL BOARD - INCB (4)

### 3. INCB responsibilities

- a) **Administers a system of estimates for narcotic drugs and a voluntary assessment system for psychotropic substances and monitors licit activities involving drugs through a statistical returns system, with a view to assisting Governments in achieving, inter alia, a balance between supply and demand.**
- b) **Monitors and promotes measures taken by Governments to prevent the diversion of substances frequently used in the illicit manufacture of narcotic drugs and psychotropic substances and assesses such substances to determine whether there is a need for changes in the scope of control of Tables I and II of the 1988 Convention.**



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## THE INTERNATIONAL NARCOTIC CONTROL BOARD - INCB (5)

### 3. INCB responsibilities

- c) **Analyses information provided by Governments, United Nations bodies, specialized agencies or other competent international organizations, with a view to ensuring that the provisions of the international drug control treaties are adequately carried out by Governments, and recommends remedial measure.**
- d) **Maintains a permanent dialogue with Governments to assist them in complying with their obligations under the international drug control treaties and, to that end, recommends, where appropriate, technical or financial assistance to be provided**



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## THE INTERNATIONAL NARCOTIC CONTROL BOARD – INCB (6)

2. INCB functions
  - b. With regard to illicit production, trade, and use:
    - INCB identify weakness of the international and national drug control systems and recommend remedial measures
    - INCB also has the responsibility to assess chemicals used in illicit drug production to determine whether those chemicals are internationally controlled



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## INTERNATIONAL PAIN POLICY FELLOWSHIP

- Goal: To support nations in developing and implementing opioid policy in palliative care
- Providing training on opioid policy by Study Pain Policy Group- SPPG at the Madison –Wisconsin University, at USA
- The fellowship is provided by the Open Society Institute – OSI tại New York



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# WHO GUIDANCE

## ON OPIOID CONTROL

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## ACHIVING BALANCE IN NATIONAL OPIOIDS CONTROL POLICY (WHO)

1. How to conduct balance assesement?
2. Ensure the availability of opioids for medical purposes
3. What need to be changed in the Law on Drug Control and Combat, Regulations on Narcotic prescription, Regulations on Psychotropic Drugs, general prescription regulations to achieve the balance? To ensure:
  - Manufacture
  - Distribution
  - Prescription



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WHO/EDM/QSM/2004.4  
ENGLISH ONLY

NARCOTIC & PSYCHOTROPIC DRUGS

**ACHIEVING BALANCE  
IN NATIONAL  
OPIOIDS  
CONTROL POLICY**  
GUIDELINES FOR ASSESSMENT

WORLD HEALTH ORGANIZATION

WHO/EDM/QSM/2004.4  
CHỈ CÓ BẢN TIẾNG ANH

THUỐC GÂY NGHIỆN VÀ THUỐC HƯỞNG TÂM THẦN

**TIẾN TỚI CÂN BẰNG  
TRONG CHÍNH SÁCH  
QUỐC GIA VỀ KIỂM  
SOÁT OPIOID**  
HƯỚNG DẪN ĐÁNH GIÁ

TỔ CHỨC Y TẾ THẾ GIỚI

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## WHO CRITERIA TO ASSESS OPIOID POLICY

1. Review national policies
2. Opioids are absolutely necessary
3. Responsibility to ensure the availability of opioids
4. Appointment of a competent administrative authority
5. Concerns on legal negative disciplines
6. Cooperation to ensure the availability
7. Standard terms for opioids and dependence
8. Avoiding enacting regulations that impede patients' access to therapeutic drugs
9. Avoiding enacting regulations that impede the prescription



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### ISSUES TO BE DISCUSSED (WHO GUIDANCE)

1. Is "balance" a valid concept? Is this concept accepted in the country?
2. Which key policies need to be revised?
3. What is the opportunity to develop policy evaluation?
4. Challenges in future



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### Conventions on Drug Control and Combat

1. Single Convention on Narcotic Drugs 1961 (amended in 1972)
2. Convention on Psychotropic Substances 1971
3. UN Commitment on combating illegal trade, transportation narcotics and psychotropic substances 1988



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### Single Convention 1961

- Noting that that the use of narcotics for medical purposes is still needed to relieve pain and opioids need to be made available for the that purpose
- Noting that drug addiction is a serious problem for individuals, a socio-economic problem for the society
- Recognizing the responsibility to stop and combat this evil



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### Single Convention 1961 (con't)

- Articles 19,20,21: Nations shall submit annual report and estimation to the INCB on quantity of licit use of narcotics for medical and scientific purposes.
- Article 29,30: Manufacture, trade and distribution of drugs must be under license. However, this requirement need not to apply to such drugs as physicians may lawfully work with their duly authorized therapeutic functions.
  - It is required that written prescriptions must be used dispensing.
  - Prescription for drugs in Schedule I should be written on official forms to be issued in the form of counterfoil books by the competent governmental authorities...



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### Single Convention 1961 (con't)

- **Article 34: Measures of Supervision and Inspection:**
  - a) All persons who obtain license, or who have managerial or supervisory positions in an enterprise shall execute faithfully and effectively provisions of current laws and regulations.
  - b) Must keep records on all drugs manufacture, trade and use, such records shall respectively be preserved for a period of not less than two years. Where counterfoil books of official prescriptions are used, such books including counterfoil shell also be kept for a period of not less than two years.
- **Article 36: Penal provisions:** Any actions contrary to the provisions of this Convention shall be punishable offences (imprisonment or other penalties of deprivation of liberty).



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### Balance in opioids control policy (1)

1. The Central Principle of "Balance" of WHO
  - The Central Principle of "balance" represents a dual imperative of governments to establish a system of control to prevent abuse, trafficking, and diversion of narcotic drugs while, at the same time, ensuring their medical availability.
  - Opioid analgesics are controlled drugs, they are also essential drugs and are absolutely necessary for pain relief.
  - Must take steps to ensure the adequate availability of opioids for medical and scientific purpose.
  - A system of control is necessary to prevent abuse, trafficking, and diversion.



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## Balance in opioids control policy (2)

### 2. WHO guidelines

- Guideline 1: Governments should examine their drug control policies for the presence of overly restrictive provisions that may impact their health care system in the delivery of pain relief, and take corrective action as needed.

Vietnam has issued:

- Penal Code (Article 221).
- Illicit Drug Control and Combat Law: Chapter III, Articles 15-24
- Drug Law

...



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## WHO guidelines (con't)

- Guideline 2: National drug control policies should recognize that opioids are absolutely necessary for medical care, in particular for relief of pain and suffering.
- Guideline 3: National drug control policies should recognize the obligation of governments to ensure adequate opioid availability for all medical and scientific needs.
- Guideline 4: Governments should designate an authority for ensuring adequate availability of opioids for medical care.



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## WHO guidelines (con't)

- Guideline 5: Governments should develop, using information from relevant sources, a practical method to estimate realistically the medical and scientific needs for opioids.
- Guideline 6: Governments should furnish to the INCB annual estimates of the quantities of narcotic drugs needed for medical and scientific purposes for the following year.



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## WHO guidelines (con't)

- Guideline 7: Governments should furnish a supplementary estimate to the INCB if it appears that the availability of narcotic drugs will fall short of medical needs, or to meet emergency needs or exceptional medical demand.
- Guideline 8: Governments should submit annual statistical reports to the INCB on the production, manufacture, trade, use and stocks of narcotic drugs



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## WHO guidelines (con't)

- Guideline 9: Governments should establish a dialogue with health care professionals about the legal requirements for prescribing and dispensing narcotic drugs.
- Guideline 10: National drug control authorities and health care professionals should cooperate to ensure the availability of opioid analgesics for medical and scientific purposes, including for the relief of pain.



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## WHO guidelines (con't)

- **Guideline 11: Governments should ensure, in cooperation with licensees, that the procurement, manufacture, and distribution of opioid medications are accomplished in a timely manner so that there are no shortages of supply, and that such medications are always available to patients when they are needed.**
- **Guideline 12: Governments should permit and encourage the distribution and availability of opioid medications throughout the country, in order to maximize physical access of patients to pain relief medications while maintaining adequate controls to prevent diversion and abuse.**



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## WHO guidelines (con't)

- Guideline 13: Governments should establish and promote a national cancer control programme that includes cancer pain relief and palliative care as a priority for health care resources, including education about the WHO Analgesic Method and provision of pain relief and palliative care.
- Guideline 14: Terminology in national drug control policy should not have the potential to confuse the medical use of opioids for pain with drug abuse or drug dependence.



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## WHO guidelines (con't)

- Guideline 15: In their efforts to prevent diversion, governments should avoid undue restrictions impacting on patient care decisions which are ordinarily medical in nature. Such decisions as the amount of drug prescribed and duration of treatment should be made by the physician and be based on individual patient needs.
- Guideline 16: National drug control policy should avoid prescription requirements that may unduly restrict physician and patient access to pain relief.



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## Balance

Opioid  
CONTROL



PATIENTS'  
ACCESS TO  
opioid



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## NEEDS AND CURRENT STATUS OF OPIOID USE IN VIETNAM

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### I. OPIOID IS ABSOLUTELY NECESSARY FOR MEDICAL PURPOSES (1)

1. Both list of Essential Drugs (WHO, Vietnam) and list of drugs used in hospital settings have opioids for treatment of pain
2. Some finding in the Palliative Care Rapid Situational Analysis in 5 provinces of Vietnam  
*(MOH in collaboration with Family Health International, POLICY Project, CDC/VCHAP)*
3. MoH issued the National Palliative Care Guidelines for Cancer and AIDS patients.



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### I. OPIOID IS ABSOLUTELY NECESSARY FOR MEDICAL PURPOSES (2)

4. Numbers of cancer and HIV/AIDS patients increasing
    - a. Statistics from the National Cancer Institute:
      - 2006 (up to Sep 31, 2006): 200,000 newly diagnosed cases and 70,000 deaths
    - b. HIV/AIDS:
      - HIV/AIDS situation up to Oct 31, 2006 (*Source Vietnam Administration for AIDS Control, MoH*)
      - Number of reported HIV cases: 114,367
      - Number of AIDS cases: 19,695
      - Number of deaths: 11,468
- => Considerable number of patients in need of palliative care in Vietnam  
=> Needs for opioid used increasing



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## II. FACTORS AFFECTING OPIOIDS AVAILABILITY IN VIETNAM

1. Laws and Regulations.
2. Availability of opioids
3. Provision of opioids to patients
  - a) Manufacture
  - b) Distribution, reservation and selling
  - c) Prescription
4. Barriers to the availability of opioids



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## 1. LAWS AND REGULATIONS

a) 38 current legal documents related to opioid:

- Constitution, article 61.
- Law on Illicit drug Control and Combat.
- Penal Code
- Drug Law
- Other guidances under laws:

For the health system, key regulations are those for: narcotics management, psychotropic management, prescription and drugs must be sold with prescriptions.



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## 2. AVAILABILITY OF OPIOIDS

Strong opioids:

- Morphine 10mg (injection), cost of one 10mg vial is VND 4,200 (Commune Health Center can only use for emergency cases)
- Morphine 30mg (tablet) (10mg tablet not available), cost between VND 2,400 – 3,500  
Morphine is currently not enough in Vietnam and long-acting formulations are not available.
- Pethidine 100mg (injection)/ 2ml vial, cost VND 12,600 (at commune level, only used for emergency cases)
- Fentanyl 0,5mg (injection)/10ml vial, cost VND 16,800  
0,1 mg/2ml vial, cost VND 7,350
- Fentanyl (patch) 50 mcg cost VND 226,380  
one patch 25mcg cost VND 123,480  
Not very much available due to strict reservation conditions and expensive cost.
- Oxycodone, hydromorphone, hydrocodone, methadone and buprenorphine are not available in Vietnam

Mild opioids: No stand-alone codeine for pain relief



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## 3. PROVISION OF OPIOIDS TO PATIENTS

- 3.1. Procurement, manufacture
- 3.2. Supply, reservation
- 3.3. Prescription
- 3.4. Selling in retail



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## 1. PROCUREMENT, MANUFACTURE (1)

a. Opioid procurement

- The Drug Administration of Vietnam (Unit for Controlled Drugs) submit annual evaluation of drug use to the INCB. The evaluation based on consuming of opioids from the previous year.
- Regulations on staffing, reservation standard procedures, handling, transportation, estimation, and reporting on narcotics => high cost, reluctant to use



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## Narcotics use in Vietnam

Drug	2001	2002	2003	2004	2005
Morphine (kg)	4		4	8	12
Codeine (kg)	1 640	1 703	2 092	2 616	2 968
Dihydrocodeine (kg)	0	0	0	0	0
Pholcodine (kg)	0	0	0	0	0
Dextropropoxyphene	900	900	1 395	2 160	1 845
Methadone (kg)	0	0	0	0	0
Diphenoxylate (kg)	0	0	0	0	0
Fentanyl (g)	71,150	82,365	40,059	138,500	120,000
Pethidin (kg)	6	49	37	31	35

Total amount of opioids in Vietnam (statistics from INCB)

=> Very low in compare to the population and needs of patients



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**Narcotics use of vietnam and some other contries before 2004 (source: INCB)**

Drug	Việt Nam	Malaysia	Korea	Philippines
Morphine (kg)	8	33	97	18
Codeine (kg)	2 616	189	229	30
Dihydrocodeine (kg)	0	282	1720	0
Pholcodine (kg)	0	49	0	0
Hydrocodone (kg)	0	0	2	0
Oxycodone (kg)	0	0	13	5
Dextropropoxyphene	2 160	0	0	0
Methadone (kg)	0	4	0	0
Diphenoxylate (kg)	0	32	0	0
Fentanyl (g)	138,500	222,262	604,480	13,280
Pethidin (kg)	31	107	122	9

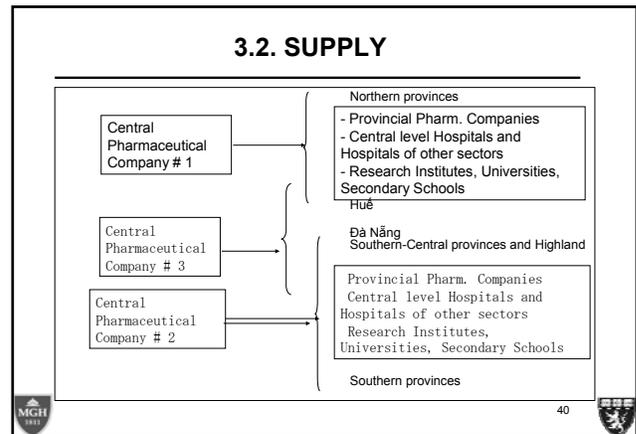
**Use by DDD/1,000,000 person/day**

	Codeine	Fentanyl	Morphine	Pethidine
China	1	13	7	5
Philippines	1	1	7	1
Indonesia	2	1	-	1
Việt Nam	-	5	1	3
Malaysia	-	41	22	30
Korea	40	93	77	17
Singapore	1	67	33	21

### 3.1. PROCUREMENT, MANUFACTURE (2)

b. Manufacture

- Material manufacture: 0 (import 100%)
- Product manufacture:
  - Morphine: 02 enterprises
  - Codeine : 40 (only in combination forms)
  - Dextropropoxyphene: 15 (only in combination forms)
  - Fentanyl: 0
  - Pethidine: 0
- Manufacturers and companies allowed to produce and sell narcotics are reluctant to produce narcotics. Mostly produce in combination forms below the controlled levels.



### 3.3. PRESCRIPTION

- Only doctors working at governmental health facilities are permitted by the hospitals directors to prescribe morphine. Private doctors, doctors working in private centers, and doctors working in governmental health facilities without permission of directors are not allowed to prescribe.
- Doctors signatures must be filled at pharmacies.
- Assistant doctors are not allowed to prescribe (except remote and mountainous areas)
- Morphine prescription limits: maximum 7 days. If dose at 30mg or above, only allowed to prescribe 5 days
- Can prescribe mild opioids for 10 days.
- Patients must show up for prescription (cancer and HIV patients at end stage staying at home and can not travel).
- Filling prescriptions for 5 years is too long (discourage drug dispensers/sellers)
- There still no commitment from patient family members on using opioid for the medical purpose and return when patients died and there still drugs not used up

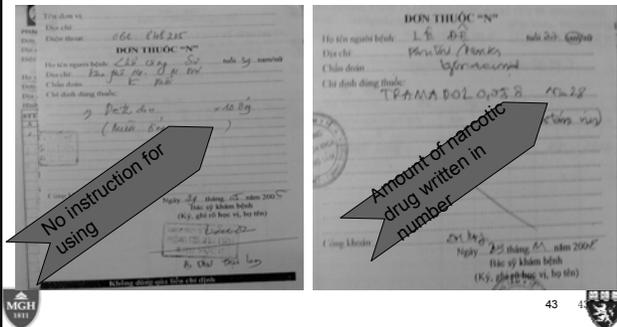
=> Barriers to access to opioids for patients

### PRESCRIPTION

Prescription for out-patients is still very low, may not responded to patients' needs

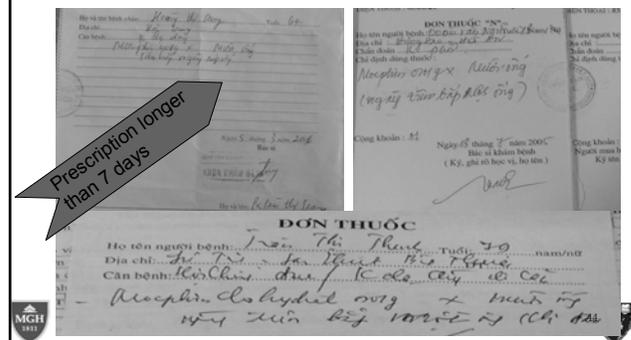
❖ Some prescriptions did not comply with Prescription Regulations and Drugs sold with Prescription Regulations: longer allowed duration

(=> Whether patient truly in need? Is number of days appropriate?)



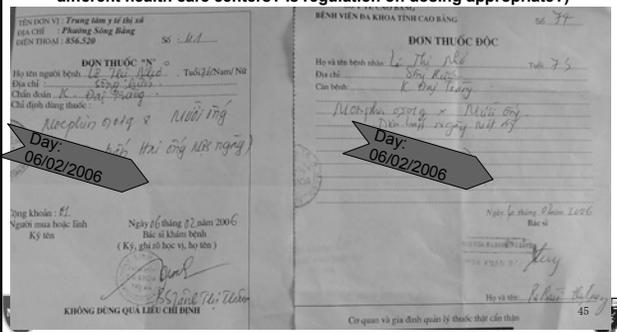
❖ Some prescriptions did not comply with Prescription Regulations and Drugs sold with Prescription Regulations: longer allowed duration

(=> Whether patient truly in need? Is number of days appropriate?)



Prescriptions for one patient at different health care centers in the same day

(abuse? Or patient really in need of high dose so that she went to different health care centers? Is regulation on dosing appropriate?)



3.4. SELLING IN RETAIL

- Number of drug stores allowed to sell opioids are different from province to province. Some provinces have only one place (Quang Ninh, Khanh Hoa)
- There is still no mandatory or support system for businesses to sell prescribed opioids for therapeutic purposes
- The current regulations (issued in 2003) do not allowed private businesses to sell narcotics (conflicted with Drug Law issued in Oct 2005). The provincial pharmaceutical company only sell narcotics in one place depending on the organization and scale of that company.
- Some provinces add one condition to request the opioid prescription must be approved by the director of the company

Inappropriate number of retail outlets

No.	Province	Population (in million)	No. of districts	No. of opioid retail outlets
1	Quảng Ninh	1,078	14	1
2	Nam định	1,961	14	12
3	Hải Dương	1,711	14	14
4	Khánh Hoà	1,122	8	1
5	Bình Thuận	1,115	8	8
6	Đàklak	1,710	13	14
8	Đồng Nai	2,193	11	8
9	Trà Vinh	1,028	8	8
10	TP HCM	5,891	24	2
11	Hà Nội	3,145	14	4

Population number from the 2005 Annual Statistics  
Data from MoH 2006 monitoring and Inspection 47

Some descriptions on opioid use

- Đồng Nai province has 8 retail outlets (7 outlets by the pharmaceutical company, 1 by the Provincial General Hospital)
  - At 6 outlets in 6 districts, in the first 6 months of 2006, only sold 16 vials of morphine and 5 vial of Dolacgan, when there is considerable number of cancer patients due to Dioxin leaving near by Biên Hoà airport.
  - Biên Hoà City General Hospital (place for cancer treatment of Đồng Nai province) have one counter for opioid, but there were 50 vials of morphines in 2006 and did not sell any single vial
- At Chợ rẫy hospital:
  - There is one division for pain relief and the need for tablets of morphine in 2006 is 8,000 pills, up to Oct 2006 the division could buy only 3,500 pills, and then couldn't buy more, so that met only 43.7% need of morphine tablets of patients.

### Retail

❖ The approval process for opioid buying is too complex (DoH adds more regulations?)

Prescription approval from Hospital Directory Board

Prescription approval from Directory Board of the Pharm. Company

❖ There is cases where prescription day happened after the day drugs sold (putting wrong date or because patient in severe pain, buying first and submitting prescription to the drug store after?)

Selling date: June 11, 2006

Prescribing date: June 12, 2006

### 4. BARRIERS TO THE AVAILABILITY OF OPIOID (1)

4.1. Legal documents

- Still using negative terms referring to opioids in the legal documents.
- Example "Controlled substances" including drugs can cause dependence and also essential drugs. Should not identify opioids with social evils, crimes and drug use.
- Should use more positive terms, for example: explaining that "opioids are addicting drugs" can be replaced by "opioids are drugs that may cause psychological dependence and can be diversified"
- Should not regulate to frame all opioid names to avoid the risk of opioid diversion
- Should confirm that opioids are essential drugs for pain relief.
- Should have change on assessment for patients' opioid need? Have clear regulations to submit supplement request or to reduction request for opioid need to INCB

### 4. BARRIERS TO THE AVAILABILITY OF OPIOID (2)

4.2. Opioid availability

- Low quantity produced (amount, various strengths...) low number of suppliers.
- Low number of drug stores allowed to sell (depends on each province)
- Limits on days and amount allowed to prescribe.
- The national opioid policy requests using opioid very prudently, which may leads to misunderstanding and reluctance to prescribe opioids
- Additional regulations by other levels of authorities:
  - DoHs request to add a regulation: pharm. companies have to approve all opioid prescriptions and collect used empty vials or packages => one more complex step for patients;
  - Hospitals or departments request to return used empty vials => physicians are reluctant to prescribe.

### 4. BARRIERS TO THE AVAILABILITY OF OPIOID (3)

4.3. Technical, knowledge and education aspects

- **Technical aspect:**
  - No long-acting morphine produced yet
  - Lack of formulations and strengths to choose between options (i.e.: only morphine 30mg tablet)
  - No stand-alone codeine for pain relief
- **Knowledge and education aspects:**
  - Reluctance of doctors to prescribe and of pharmacists to sell opioids
  - Lack of adequate knowledge on appropriate use of opioids for patients
  - No national palliative care training for health care workers.

**How to**

Minimize opioid diversion and inappropriate use?

**But still ensure**

Patients' access to opioids (quality of palliative care)

Develop and revise regulations

To ensure the availability of opioids (supply, manufacture, prescription, and selling)

**Doctors, pharmacists, managers need to**

Thank you



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## Adult Learning Theory

Ann Williams, RN, PhD  
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### OBJECTIVES

At the completion of this module the participant will be able to:

1. Conduct a needs assessment
2. Write appropriate learning objectives
3. Design a lesson plan
4. Conduct a training session
5. Evaluate a training program

### CONTENT

1. Definition of adult learning theory
2. Needs assessment
3. How to write objectives
4. Establish ground rules
5. Content
6. Teaching strategy
7. Special situations
8. Feedback

### I. DEFINITION OF ADULT LEARNING THEORY

Most physicians in Vietnam have acquired their professional knowledge through traditional learning methods in formal classroom settings. In this type of learning the students come with an expectation that the teacher has clinical experience and knowledge that the student does not. The usual style of teaching is that the teacher provides the student with some new knowledge and the student assumes that eventually that knowledge will be useful to them.

When teaching a group of adults who have a breadth of life, as well as work experience, it is useful to structure the learning differently. Most working adults are extremely busy with their jobs and families. It is important therefore to focus on teaching those things that are of importance to the participants. For this reason, it can be useful sometimes to do a **needs assessment** of the audience to make sure you have an idea of what they want to learn.

The adult learner brings to the class a wealth of experience they have gained while working and has had opportunities to apply some of the knowledge they acquired in their formal educational process. Within the adult classroom, all participants can be teachers as well as learners because all can learn from each other. It is useful to incorporate discussion and problem solving into the training so that all can benefit from the experience of others.

It can be helpful to think of oneself as a facilitator of the learning process rather than an expert. There may be many experts in the class in certain areas, and it makes the class more interesting when different people can speak about their “real world” experience with the concepts being taught.

## II. NEEDS ASSESSMENT

### A. Define the purpose of workshop

Example: Teach health care workers about opioid conversion.

### B. Selecting the target audience

- Who are the learners?
- How were they identified or selected?
- Were they assigned?
- Did they apply through a competitive process?
- Did they volunteer?

This information is useful because it is helpful to the instructor to know if the participants want to be there or not. The more information the teacher has about the audience the more specific he/she can be with the content.

## III. HOW TO WRITE EDUCATIONAL OBJECTIVES

The first thing that needs to be done when preparing to conduct a workshop is to describe what the participant will be able to do at the completion of the workshop. It is necessary to have the objectives clearly stated first because they will influence: the content of the workshop, the instructional materials, the methods, and the speakers.

Having a clearly defined set of objectives makes it possible to evaluate the workshop. The objectives provide us with something to measure to see if the educational program accomplished what we wanted it to. When the objectives are clearly stated it also helps the participants focus their energy toward the intended outcome. This is usually done by stating what the participant will be able to do at the end of the workshop. For example:

*The participant will be able to list 4 ways HIV is transmitted.*

*Vs.*

*The participant will learn how HIV is transmitted.* (Does not say what the participant will be able to do.)

*The participant will be able to describe ways to prevent HIV from being transmitted in the workplace.*

Vs.

*The participant will understand how to prevent HIV transmission in the workplace.*  
(Cannot measure this, does not say what the participant will be able to do.)

The objective is a statement describing an instructional outcome rather than an instructional process or procedure.

#### **IV. ESTABLISH GROUND RULES**

It is useful to establish “ground rules” to describe how the group will operate. Typical ground rules are:

- We will start and finish on time.
- An agenda will be announced or provided so that participants will know what is expected of them.
- Anything that is mentioned in the group is confidential and should not be repeated outside the group.
- One person speaks at a time and the others listen.
- All people are equal and all opinions are respected. There will be no criticism of another’s opinion.
- It is OK to disagree.

There are several ways to establishing ground rules. They may be written on a flip chart, and participants can be asked if there are any they wish to add. The group can then be asked if they can abide by the ground rules, and the list can be posted in the room. The list can be added to or altered by the group during the course of the workshop if they wish. Posting the ground rules reminds participants and allows the leader to point them out if it becomes necessary during the course of the workshop.

## V. STRUCTURE AND CONTENT

The structure and content evolves from the specific objectives that the planning committee agrees on. Based on the objectives, you can decide on:

- Key topics
- Method of teaching
- Time frame
- Any audiovisual aids or handouts

Remember that:

- Adults have a wealth of experience and often can teach each other if opportunities for discussion and sharing are made available to them.
- Adults want to learn things that are practical and can help them in their everyday life.
- Adults need to understand the point of the workshop and activities within the workshop.

## VI. TEACHING STRATEGY

- Providing new information to participants:

This is generally done by a lecture accompanied by some other teaching tools.

**People learn in various ways:**

- Some people learn by hearing
- Others by seeing
- Others by reading
- Many by a combination of all three.

It is wise therefore when giving a lecture to have visual aids to accompany the presentation as well as handout with a summary of the key points or an outline of the lecture.

- Provide opportunity for participants to apply new knowledge or skills:

In order to facilitate learning it is beneficial to have the participants use the new knowledge or skills as soon as possible. In a classroom setting this can be done with small group case discussions or role play (simulation of real situations). It also can be done by seeing patients with the group in the clinic or hospital and then discussing the cases. In each type of these situations, new behavior, information, skills, and procedures can be practiced and adjustments can be made with immediate feedback from the leaders and other participants.

## A TABLE OF TEACHING STRATEGIES

TEACHING STRATEGIES	OUTCOMES
Lecture	Lecture provides new information. It provides an opportunity for people to learn new knowledge or expand upon knowledge that they already have.
Leader Led Discussion	A leader led discussion allows people to ask questions and answers and clarify the new knowledge they may have just obtained. It provides an opportunity for participants to share some of their own experiences but the leader is in charge of the discussion and is in control of the direction of the discussion. This is sometimes a way for the leader to check to see if the participants are comprehending what has been covered in the lecture.
Small Group Discussion	In this modality usually the leader will assign a topic or task and then the small group discusses it. This is a good way to provide an opportunity for those who are shy or uncomfortable in a large group to speak in smaller group. It also allows the participants to learn from each other and share experiences.
Demonstration & Repeat Demonstration	This strategy is a way to try and provide an experience for the participants so they can apply the new knowledge. If the leader gives a demonstration and then asks the participants to repeat it, it allows the participants the opportunity to practice or experiment with new behaviors or skills in a place where guidance is still available.
Role-Play	This strategy attempts to create a “real life” situation so that the participant can have a chance to practice new behaviors or skills in an environment where they can receive feedback and make changes and adjustments and become more proficient.
Case Discussions	This is another teaching strategy that tries to create a situation that someone may see in the clinical setting and then has the participant think about management strategies or techniques they would use in a real life situation and analyze the results and outcomes of some decisions.
Learning Activities (Games, Forced Choice Activities, Values Clarification)	There are a variety of learning activities that can be used to address the affective learning domains. These activities are ways to get people to articulate their feelings and emotional responses they may encounter while doing the work. The purpose of these activities is to provide a safe and non emotional situation where people can talk about managing the emotions and reactions that often come up while doing the work.

## VII. SPECIAL SITUATIONS

There are a couple of special situations that a new teacher should be aware of:

- Answering difficult questions
  - It is almost inevitable that a participant will ask the teacher a question that s/he cannot answer. There is a misperception on the part of inexperienced teachers that they should know the answer to all questions posed. This is an unrealistic expectation. If a teacher does not know the answer, s/he should acknowledge this and offer to try to find the answer.
  - It is important that the teacher get back to the student with a response even if the response is that no definitive answer could be found.
- Problem participants

Sometimes, a learner may cause problems for the class:

- The non- participative learner

If a learner seems to not be participating this can have several causes. It may be that s/he is shy and will participate in a small group. Some participants will not raise their hand, but will participate if you call on them.

- The talkative or domineering learner

Sometimes a participant may be quite experienced and have a lot to share but also excludes others. One strategy is to thank him/her for all their comments and tell him/her you would like to give others an opportunity to speak.

## VIII. EVALUATION

Based on what they have learned, participants may revise their previous ways of doing things, or they may decide that the new information is not applicable in their situation. A follow-up meeting can be very useful to discuss what changes each participant made in his/her practice, what successes they had due to the new knowledge, skills or practice patterns, and what barriers they encountered in changing their practice.

Solicit feedback from the audience through discussion and questionnaires (see below).

**FEEDBACK**

**Observer Check List**

**Name of Presenter:**

**Topic:**

	<b>Excellent</b>	<b>Good</b>	<b>Changes needed</b>
<u>Opening remarks, greeting:</u> Eye contact, warmth, smile, established welcoming environment?			
<u>Explanation of purpose (objectives):</u> Clear, understandable, anticipated length of workshop			
<u>Presentation:</u> <ul style="list-style-type: none"> <li>• Use of visuals or handouts</li> <li>• Voice</li> <li>• Eye contact</li> <li>• Response to questions</li> <li>• Ability to assess audience understanding</li> <li>• Skill in speaking to entire room</li> <li>• Use of activities or encouragement of audience participation</li> <li>• Content</li> <li>• Content matched objectives</li> </ul>			
<u>Use of Teaching Aids:</u> <ul style="list-style-type: none"> <li>• Microphone</li> <li>• Transparencies</li> <li>• Powerpoint</li> <li>• Flipchart</li> <li>• Handouts</li> </ul>			
<u>Questions and Answer:</u>			

<ul style="list-style-type: none"> <li>• Time left for questions</li> <li>• Called on people from various places in room</li> <li>• Repeated the question</li> <li>• Said “I don’t know but will find out”</li> </ul>			
<p>Conclusion:</p> <ul style="list-style-type: none"> <li>• Summarized key points</li> <li>• Repeated the objectives</li> <li>• Gave referrals or a place for further information</li> </ul>			
Overall Presentation			
Comments			

Personal reflection: Possible questions to ask oneself after the talk.

1. What was successful?
2. Factors that facilitated success?
3. What did not work so well?
4. Factors that inhibited success/barriers?
5. What would you do differently next time?

## Adult Learning Theory

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## Objectives

- After completion of this module, the participant will be able to:
  - Conduct an assessment of learners' needs
  - Write appropriate learning objectives
  - Design a lesson plan
  - Conduct a training session
  - Evaluate a training session



2



## Adult learning theory

- Most adults are busy. Therefore, teaching should focus on subjects that are important to the participant
- Adults often have a lot of experience. Therefore, training sessions should include discussion and problem solving so all can benefit from the experience of others.
- The teacher should be a facilitator of the learning process rather than an expert.



3



## Effective strategies for teaching

### 1. Understanding the audience

- Who are the learners?
- How were they selected?
- Did they volunteer?
- Were they assigned?
- Helps the instructor know if the audience wants to be there
- Helps the instructor focus on the most relevant content.



4



## Effective strategies for teaching

### 2. Write appropriate learning objectives

- A clear set of objectives:
  - Makes it possible to evaluate the workshop
  - Helps the participant focus on achieving the intended outcome of the training



5



## Example of a learning objective

- **Clear learning objective**
  - The participant will be able to use the equianalgesic table to convert a codeine dose to a morphine dose
- **Unclear learning objective**
  - The participant will understand equianalgesic conversion



6



## Example of a learning objective

- **Clear learning objective**
  - The participant will be able to develop a differential diagnosis of pain in a patient with advanced AIDS or cancer
- **Unclear learning objective**
  - The participant will understand differential diagnosis



7



## Objectives

- After completion of this module, the participant will be able to:
  - Conduct an assessment of learners' needs
  - Write appropriate learning objectives
  - Design a lesson plan
  - Conduct a training session
  - Evaluate a training session



8



## Effective strategies for teaching

3. Establish ground rules
- Write a few ground rules on a flip chart and then ask the participants if there are any they want to add.

*Examples of ground rules:*

- We will start on time and finish on time
- One person speaks at a time
- An agenda will be announced
- Anything mentioned in the group is confidential
- All participants are equal
- It is OK to disagree, but all opinions will be respected



9



## Effective strategies for teaching

4. Teaching methods
- Provide new information to patients
    - Lecture
    - Visual aids (powerpoint slides, overhead projector, flip chart)
    - Handouts
  - Provide opportunity for participants to apply new knowledge
    - Small-group discussions
    - Role-play
    - Bedside teaching rounds



10



## Effective strategies for teaching

### Special situations

- Answering difficult questions
  - Teachers may not know the answers to all questions posed
  - Tell the student that you do not know but you will try and find the answer
- Problem Participants
  - Non participative
  - Over-talkative, domineering



11



## After the talk

- Evaluate the teaching session
  - Solicit feedback from:
    - Learners
      - Verbal
      - Written evaluation forms
  - Topics:
    - factors that facilitated success
    - factors that inhibited success
    - what worked well and what did not?
- Remain after the class for questions from individual learners



12



## Action plan

- **Describe the learners and their needs**
- **Write learning objectives**
- **Establish initial ground rules**
- **Determine teaching methods**
- **Enjoy helping others learn**



13





## Pain Case Discussions

Eric L. Krakauer, MD, PhD  
Harvard Medical School & Massachusetts General Hospital

### Case 1

Anh Son is a 58 year old father of 2 adult children now disabled from his job as a carpenter because of Stage IV metastatic non-small cell lung cancer that was diagnosed 6 months ago. Recently he has been complaining of increased chest pain. He is taking paracetamol/codeine (500mg/30mg) without significant improvement in his pain.

Anh Son has a history of IDU but has not used illicit drugs in 10 years. His doctor expresses frustration with Anh Son's continued pain and expresses doubts about how real the pain is given his history.

- 1. What is the differential diagnosis of his pain?**
- 2. What further assessment data is needed to develop a pain management plan?**
- 3. How does his history affect the pain management plan?**

Anh Son reports constant 6/10 pain in his right chest area, radiating to his back, and worsening over the last 2 weeks. He has no fever or dysphagia but mild dyspnea. He has been taking two paracetamol/codeine (500mg/30mg) tablets every six hours. The paracetamol/codeine gives him 50% relief that lasts only 3-4 hours. Anh Son asks if he can take the tablets every 4 hours around the clock.

- 4. How would you respond to Anh Son?**
- 5. How would you suggest changing the pain medications?**
- 6. If you decide to use morphine, what dose would you give?**
- 7. What other issues should be part of the pain management plan?**

Anh Son does well on this plan for the next 3 months but then develops increasing low back pain associated with pain radiating down the back of his right leg. He describes the pain as constant and throbbing with occasional electric-shock-like pains going down his leg. On motor exam, his right leg is slightly weaker than the left. You are concerned about metastatic disease of the spine, radiculopathy, and possible spinal cord compression. He is now taking morphine 20mg every 4 hours and an additional 15mg 5-6 times a day for breakthrough pain. Each dose of 20 mg morphine gives him 60% relief.

**8. How would you respond to this clinical situation?**

**9. How would you adjust his opioids?**

**10. What would you tell Anh Son to do at night before bed so that he does not wake up in the night with pain?**

Three weeks later, Anh Son is admitted to the hospital with increasing dyspnea, dysphagia, and delirium. He is found to have progressive spread of the cancer in his lungs, mediastinum and bones. He had been taking 35 mg morphine every 4 hours and 35 mg 1-2 times a day for breakthrough pain, dexamethasone 10 mg orally every morning and gabapentin 600 mg orally 3 times / day. He is volume depleted but his laboratory studies are otherwise within normal limits. His oxygen saturation is 98% on 2L/minute.

**11. How might his current condition affect the pain management plan?**

**12. What medications would you change or continue? What doses would you use?**

Anh Son becomes sedated on the SC morphine, and his respiratory rate decreases to 5 breaths per minute. Further discussion with his family reveals that he has only been able to swallow the morphine 2-3 times a day. He has decreased oxygen saturation and the decision is made to give him naloxone.

**13 How do you give the naloxone?**

**Case 2**

Chi Huong is a 64 year old woman with a history of thyroid cancer metastatic to the spine. In addition to direct invasion of thoracic and lumbar vertebral bodies, she has a 3x8 cm mass that is anterior to her lumbar and sacral spine. She has had maximal radiation doses to her spine. She has been admitted with recent worsening of her back pain. She is currently being treated with morphine 45mg every 4 hours and 30mg every 4 hours as needed (She has used 30mg of morphine in the past 24 hours for breakthrough pain), gabapentin 900mg three time per day, ibuprofen 800mg every 8 hours, ranitidine 150 mg orally twice per day, and senna 2 tablets twice per day.

You are called by the nurse because Chi Huong fell getting out of bed and now is complaining of severe pain in her low back radiating down her legs.

You arrive at the patient's bedside to find her crying and writhing in pain. It is impossible to examine her. She describes the pain as intense, shooting, and electric in nature and rates the pain as more than 10/10. She is begging that you make her pain better. You determine she is in an acute pain crisis.

**1. What do you think is the cause of her pain?**

**2. How would you treat her pain crisis?**

**3. You have given an initial dose of pain medication and now re-assess the patient. How will you decide what to do?**

She reports no improvement in the pain. You now give 20mg of morphine IV. You have also given her dexamethasone 20 mg IV as an adjuvant for her pain. Her pain is partially relieved with your intervention. But the following day she reports increased pain.

**4. What are other options for treating her pain?**

**Case 3**

Anh Duc is a 48 year old male with AIDS and chronic abdominal pain that he describes as constant and diffuse. It is unrelated to eating or bowel movements. You think the pain may be due to MAC, drug resistant TB, CMV colitis, or another undiagnosed OI. Anh Duc recently completed a standard 8-month treatment for TB. He is being treated for MAC with ethambutol and clarithromycin, and his ARV regimen is d4T / 3TC / nevirapine. His amylase is normal, and his liver transaminases are only slightly elevated. His pain had been fairly well controlled with a fentanyl patch 100 mcg/hour and a rescue dose of morphine 30 mg orally every 4 hours as needed. Recently, however, he has developed fever, persistent sweating, anorexia, frequent vomiting, and marked cachexia, and he has not been able to eat or take oral medications regularly. His abdominal pain is worsening rapidly.

- 1. What are the main contra-indications for use of the fentanyl transdermal patch?**
  
- 2. How would you suggest changing the pain regimen?**
  
- 3. How would you convert the fentanyl patch to IV / SC morphine?**
  
- 4. Why might the calculated morphine dose be too low?**
  
- 5. Why might the calculated morphine dose be too high?**

## Pain Case Discussions

Eric L. Krakauer, MD, PhD  
Harvard Medical School & Massachusetts General Hospital

### Facilitators Guide

#### Case 1

##### 1. What is the differential diagnosis of his pain?

Tumor invasion of the pleura or chest wall, pneumonia, pulmonary embolus, pleural effusion, bone metastases, cardiac ischemia, esophagitis, cardiac ischemia, zona, addiction.

##### 2. What further assessment data is needed to develop a pain management plan?

Location; severity (rating of pain on a scale from 1-10); onset (sudden or gradual); what makes it better or worse; effects of pain on activities of daily life; further description – does it feel sharp or dull, burning, shooting, crampy; associated symptoms such as fever, cough, dyspnea, dysphagia.

##### 3. How does his history affect the pain management plan?

The treatment should be planned based on the most likely diagnosis.

Review concepts of opioid tolerance, physical dependence, addiction. Describe how to assess for addiction, how to monitor patients with history of addiction, use of treatment agreements, urine toxicology tests.

##### 4. How would you respond to Anh Son?

Son already is already taking the maximum safe dose of paracetamol. A higher dose would put him at risk for liver toxicity.

Higher doses of codeine are unlikely to be effective.

Therefore, increasing the paracetamol/codeine dose is not a good idea.

##### 5. How would you suggest changing the pain medications?

Possibilities (depending on the most likely diagnosis):

- 1) Add NSAID and/or adjuvant: amitriptyline, gabapentin, corticosteroids (not with NSAID)
- 2) Switch to morphine

##### 6. If you decide to use morphine, what dose would you give?

30mg of codeine per tablet, patient is taking 2 tablets every 6 hours = 240 mg codeine/day

From the equianalgesic table:

200 oral codeine = 30 mg oral morphine, so

240mg oral codeine = X mg oral morphine

X = 36 mg oral morphine

Divide dose by 6 to calculate every 4 hour dosing = 6 mg of oral morphine

Incomplete cross tolerance: reduce dose by 33% = 4 mg

Add 1 mg per dose to replace the effect of the paracetamol = 5 mg

Use half of a 10 mg breakable tablet (if available) or 5 mg or oral solution every 4 hours.

### **7. What other issues should be part of the pain management plan?**

Constipation prophylaxis.

Additional rescue doses for breakthrough pain: ~ 10% of 24 hour dose every 2 – 4 hours as needed.

### **8. How would you respond to this clinical situation?**

- a) If feasible, obtain CT scan of back to evaluate for spinal metastases and spinal cord compression. If spinal metastases are present at site of pain, or if cord compression is present, order radiation therapy if possible.
- b) Add high-dose steroid if not already done
- c) Add adjuvant drug for neuropathic pain such as amitriptyline or gabapentin

### **9. How would you adjust his opioids?**

- a) Increase standing morphine dose:

Total morphine = standing morphine + rescue doses

Standing morphine = 20 mg x 6 doses = 120 mg

Rescue doses = 15 mg x 6 doses = 90 mg

Total morphine = 120 mg+ 90 mg = 210 mg/day

Divide by six to get the new 4-hour dose = 35 mg every 4 hours

b) Increase the rescue dose: 10% of 210 mg = 20 mg every 2 hours as needed for breakthrough pain.

**10. What would you tell Anh Son to do at night before bed so that he does not wake up in the night with pain?**

If the patient is having trouble sleeping at night, give double the regular dose at bedtime.

**11. How might his current condition affect the pain management plan?**

He is at risk for pain crisis if he becomes unable to take oral analgesics as prescribed.

**12. What medications would you change or continue? What doses would you use?**

Change to IV or SC opioid. Change to IV steroid if possible (same dose of dexamethasone). Treat delirium.

Total oral morphine dose/day = 35 mg x 8 doses = 280 mg  
To convert oral morphine to IV morphine, divide the dose by 3:  
 $280 \text{ mg} / 3 = 93 \text{ mg}$  of IV morphine per day

Convert to an hourly rate:  $93 \text{ mg} / 24 = \text{approx } 4 \text{ mg/hr}$  SC or IV.

Incomplete cross tolerance does not apply because the same drug is used (morphine).

**13. How do you give IV naloxone in palliative care?**

Dilute 0.4 mg naloxone into 9 ml of normal saline and administer 1 ml (0.04 mg) every 1-2 minutes until the respiratory rate is satisfactory.

**Case 2**

**1. What do you think is the cause of her pain?**

Bone metastases and possibly one or more compression fractures, new or old, with impingement on spinal nerve roots causing neuropathic pain. Possibly also spinal cord compression.

**2. How would you treat her pain crisis?**

Pain crisis always requires IMMEDIATE assessment and treatment. It also requires repeated re-assessment of the effect of treatment until the patient is comfortable.

**Step 1.** Review her total opioid requirements in the past 24 hours.

She has used  $45 \times 6 = 270 + 30 \text{ mg} = 300 \text{ mg}$  of oral morphine in the past 24 hours

**Step 2.** Decide whether to treat with oral or IV opioid.

Pharmacokinetics of morphine:

a) **IV**

Onset of action: rapid (~ 5 – 10 minutes)

Peak effect: 10 – 20 minutes

Duration of action: 2 – 7 hours

b) **Oral immediate release**

Onset of action: slower (20 – 60 minutes)

Peak effect: 60 minutes

Duration of action: 2 – 7 hours

If available ALWAYS use IV opioid in an acute pain crisis.

**Step 3.** Give 10-20% of daily opioid dose as a bolus.

300mg of oral morphine is equivalent to 100mg of IV morphine.

10-20 % is 10mg to 20mg of IV morphine

Re-assess after 15 minutes

NOTE: If she were opioid naïve, you would give 2 – 5 mg IV morphine (or 5 – 15 mg oral morphine).

**Step 4.** Stay at the bedside, provide emotional support, and RE-ASSESS 15 minutes after each IV dose or 30 minutes after each oral dose whether additional bolus doses are needed.

**3. You have given an initial dose of pain medication and now re-assess the patient. How will you decide what to do?**

Pain score unchanged:

DOUBLE the dose

Pain score decreased by <50%:

Repeat the SAME dose

Pain score decreased by >50%:

Consider this the effective dose and repeat as needed every 1 hour IV or every 2 hours orally

**4. What would be other options for treating her pain?**

Continuing to increase opioid dose based on previous use.

Continuing high-dose steroid.

Adding other adjuvants such as amitriptyline, gabapentin, carbamazepine, valproic acid, or lidocaine infusion.

In the most extreme cases of severe pain refractory to opioid, steroid and adjuvants: palliative sedation.

### Case 3

#### 1. What are the main contra-indications for use of the fentanyl transdermal patch?

Fever

Sweating

Cachexia

Acute or rapidly changing pain (fentanyl patch doses should be changed no more frequently than every 24 hours).

Poverty (it is very expensive)

#### 2. How would you suggest changing the pain regimen?

The fentanyl patch should be discontinued. Since Anh Duc cannot reliably take oral morphine, treatment with IV or SC morphine would be best. He should receive morphine either every four hours or as a constant infusion. He also should receive rescue doses as needed for breakthrough pain.

#### 3. How would you convert the fentanyl patch to IV / SC morphine?

Using the conversion table in the syllabus, fentanyl patch 100 mcg / hour = approximately 96 mg IV morphine.

Decrease by 33% for incomplete cross tolerance = 64 mg IV morphine.

$64 \text{ mg} / 6 = \text{approximately } 11 \text{ mg IV every } 4 \text{ hours}$

If a continuous IV or SC infusion is preferred:  $64 \text{ mg} / 24 \text{ hours} = \text{approximately } 3 \text{ mg} / \text{hour}$ .

Rescue dose (5% to 10% of total daily dose): approximately 5 mg IV every hour as needed.

Since the effect of the fentanyl usually diminishes gradually over 12 – 18 hours, the morphine can be started incrementally:

- Remove the fentanyl patch and start morphine infusion at 1 mg / hour.
- 4 hours after removing the patch, increase to 2 mg / hour
- 8 hours after removing the patch, increase to 3 mg / hour.

Observe the pain closely both for inadequate analgesia and for over-medication.

#### 4. Why might the calculated morphine dose be too low?

The patient's abdominal disease might be worsening causing increasing pain.

He may have been taking more rescue doses of morphine than we thought and have a higher than expected tolerance to morphine.

#### 5. Why might the calculated morphine dose be too high?

He may not have been absorbing the fentanyl because of his cachexia and sweating.



# Day 3



## Dyspnea Assessment and Treatment

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### Objectives

*After the lecture, the trainees will be able to:*

1. Understand the basic pathophysiology of dyspnea in HIV/AIDS and cancer patients.
2. Develop a differential diagnosis of dyspnea.
3. Prescribe the best treatment for dyspnea based on its likely cause and on the goals of the patient.
4. Assess and treat cough in HIV/AIDS and cancer patients.

### Contents

#### 1. Definition and Assessment:

- 1.1. Dyspnea is the subjective sensation of difficulty breathing or shortness of breath.
- 1.2. Dyspnea may be described as:
  - “an uncomfortable sensation of breathing,”
  - “breathlessness,”
  - “shortness of breath,”
  - “inability to get enough air,”
  - “the feeling of suffocation.”
- 1.3. The only reliable measure of dyspnea is the patient’s subjective report. Respiratory rate, pulse oximetry, and blood gas measurements do not necessarily correlate with dyspnea.
- 1.4. The prevalence of dyspnea in patients with life threatening illnesses is between 12-74%.

#### 2. Pathophysiology of Dyspnea (see Figure 1)

2.1 Sense of “respiratory effort” arises from a signal transmitted from the motor cortex to the sensory cortex, together with the outgoing motor command to the muscles of ventilation. Brain stem signaling to the sensory cortex may also contribute to the sense of respiratory effort.

#### 2.2. Chemoreceptors:

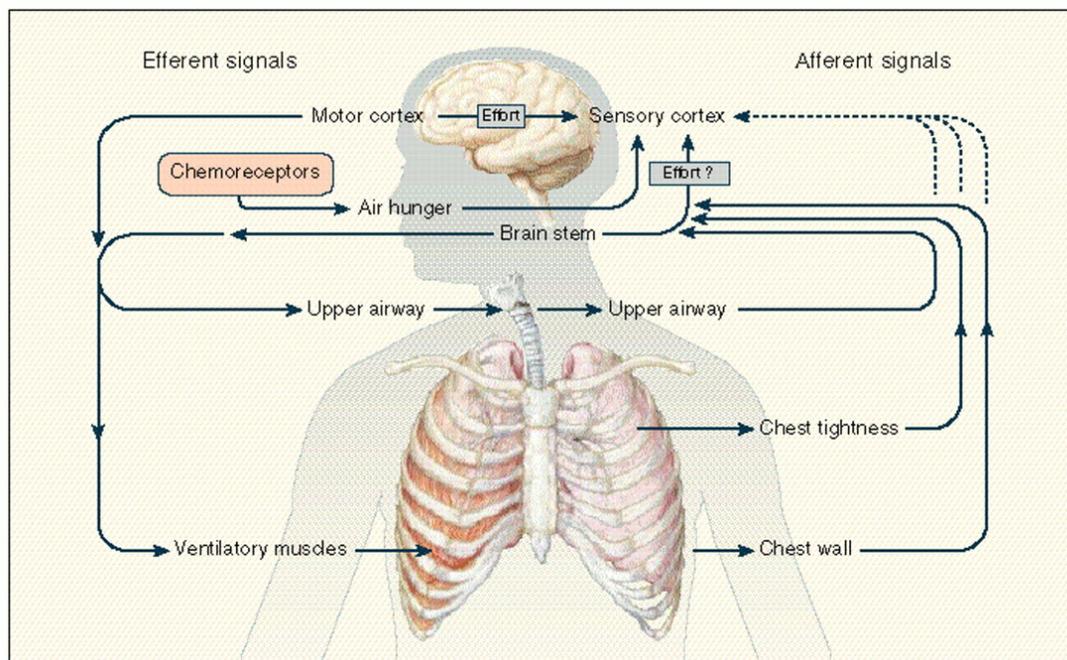
Receptors located in the brain stem detect *hypercapnia* and *hypoxia*. The sense of “air hunger” is thought to arise from stimulation of these receptors within the brain stem.

### 2.3. Mechanoreceptors:

- Upper-airway and facial receptors: These receptors appear to modify the sensation of dyspnea (e.g. receptors in the trigeminal-nerve distribution influence the intensity of dyspnea). This may explain why a cool breeze or a fan can reduce the sensation of dyspnea.
- Lung Receptors: Stimulation of vagal-irritant receptors probably results in the sensation of “chest tightness,” whereas stimulation of pulmonary stretch receptors probably decreases the sensation of dyspnea.
- Chest-Wall Receptors: Afferent information from the chest wall modifies the intensity of dyspnea

2.4. Afferent Mismatch: Mismatch between outgoing motor signals to the respiratory muscles and incoming afferent information. If information from chemoreceptors and mechanoreceptors indicates an inability to respond adequately to the outgoing (efferent) drive to breath, dyspnea results.

**Figure 1:** Pathophysiology of Dyspnea (from Manning H and Schwartzstein R. N Engl J Med 1995;333:1547-1553)



### 3. Etiology of Dyspnea

- Blood, pus, or fluid in the alveoli
  - Pulmonary edema
  - Pneumonia
  - Aspiration
  - Pulmonary hemorrhage
- Airway obstruction

- Bronchospasm
- Thick secretions
- Foreign body (such as food)
- Tumor
- Tumor
  - Replacing lung parenchyma
  - Lymphangitic spread in the inter-alveolar septa.
- Inability to expand lungs or chest
  - Pleural effusion
  - Pulmonary fibrosis
  - Chest muscle weakness from neurologic disease, infection (polio) or paralytic medications
- Pulmonary embolism
- Anemia
- Metabolic problems
  - Metabolic acidosis
  - Hypophosphatemia
- Psychosocial issues
  - Anxiety
  - Family problems
  - Financial problems
  - Legal problems
  - Spiritual or existential distress

**4. Assessment of dyspnea**

4.1. Effective treatment must be based on differential diagnosis to identify the most likely cause of dyspnea.

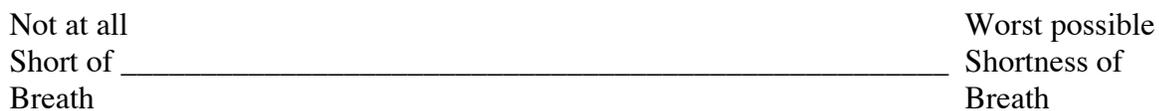
4.2. *Subjective assessment:* The degree of dyspnea can be rated accurately only by the person who is experiencing it. When taking the patient’s history ask about the minimum level of activity that causes shortness of breath.

4.3. A *Visual Analogue Scale (Figure 2)* is a vertical or horizontal line anchored at either end by descriptive words such as “not at all breathless” to “worst imaginable breathlessness”. The patient marks the line at the point representing the degree of dyspnea felt . It is important to specify the time frame you wish the patient to rate, such as “rate how short of breath you are right now” or “rate how short of breath you have been over the last 24 hours”. Changes in dyspnea can be assessed by administering the same scale at different times.

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**Figure 2: Visual Analogue Scale for Dyspnea**

To use the scale: Ask the patient to put a mark on the line to rate his or her shortness of breath from “not at all” to “worst possible”.



4.4. *Objective assessment*: Observable signs can provide additional indirect measures of dyspnea to compare with the subjective rating or to estimate shortness of breath if the patient is unable to communicate. Observable manifestations associated with dyspnea include:

- Increased respiratory rate (tachypnea). Often, 20 or more breaths per minute indicates dyspnea in an adult. However, sometimes patients will breath rapidly but shallowly and feel no dyspnea.
- Use of accessory respiratory muscles
- Labored breathing
- Diaphoresis
- Open mouth breathing
- Audible wheezing
- Gaspings breaths
- Coughing
- Interrupted or staccato speech
- Pursed lip breathing
- Pallor
- Restlessness

## 5. Treatment of Dyspnea (see Table 1)

5.1. If possible and appropriate for the patient's goals, treat the *underlying cause*. For example, if appropriate, pneumonia or pulmonary TB can be treated with antibiotics, severe anemia can be treated with blood transfusion, diuretics can be used for pulmonary edema, thoracentesis can reduce a pleural effusions, etc.

5.2. Dyspnea of any cause can be relieved with opioids. Sometimes, oxygen, anxiolytics and non-pharmacological interventions also are effective.

5.3. Use of opioids in the management of dyspnea

- Opioids relieve the distress of breathlessness in many patients without a measurable effect on the respiratory rate or blood gas concentrations.
- Opioids act both peripherally and centrally.
- In the opioid naïve patient, low doses used to relieve pain may be effective, e.g. morphine 2-4mg IV/SQ every 2-4 hours as needed.
- Opioid treatment for dyspnea (and likewise for pain), is consistent with good medical practice, and if used appropriately, is unlikely to hasten death or lead to addiction.

5.4. Sample opioid prescriptions

- Mild dyspnea (in opioid-naïve patient): morphine 5 mg tab orally every 4 hours as needed or around the clock if dyspnea is persistent. If given around the clock, a rescue dose also should be provided for breakthrough dyspnea: 5 mg orally every 2 hours as needed.
- Severe dyspnea (in opioid-naïve patient):
  - Morphine 5-10 mg orally or 2-4 mg IV/SC every 2-4 hours as needed. IV or SC opioid is preferred when dyspnea is severe because it takes effect more quickly than oral opioid.
  - If dyspnea is persistent, give around-the-clock every 4 hours with additional breakthrough dose of 5% to 10% of the total daily dose every 15 minutes as needed.

- Severe dyspnea (in patients receiving an opioid on a fixed schedule):
  - 5% to 10% of the total 24 hour opioid dose can be given every 15 minutes as needed until the dyspnea is controlled. Then increase the dose given around the clock by adding to the 24 hour total the amount of rescue medication needed to achieve relief.

#### 5.5. Use of anxiolytics in the management of dyspnea

- Anxiolytics such as benzodiazepines should not be the primary treatment for dyspnea. Usually the anxiety resolves once the dyspnea is relieved with opioid.
- Anxiolytics may be helpful when patients have an anxiety disorder that is distinct from the dyspnea and from the disease underlying the dyspnea.
- Anxiolytics can be used safely in combination with opioids, although this may increase sedation.
- Sample treatment regimen: Lorazepam 0.5-2mg orally, IV or SC every 1 hour as needed until calm, then dose routinely every 4-6 hours to maintain calm.

#### 5.6. Use of oxygen in the management of dyspnea

- Oxygen often relieves mild dyspnea of some types. However, oxygen rarely is completely effective for severe dyspnea, and it is not needed to relieve dyspnea in dying patients. Opioids are much more effective.
- Some patients and family members will request oxygen because it is a symbol of medical care even when it is not needed for symptom relief. Patients, family members, and some clinical staff may have inaccurate beliefs of many kinds about oxygen therapy. Some may request oxygen when it is not needed or refuse it when it could be beneficial. In these situations, we should explore the reasons for these requests and related cultural and religious beliefs.
- Pulse oximetry is not a useful indicator of dyspnea. Low measurements may excite staff and family but may not correlate with the patient's subjective experience. Normal measurements do not necessarily mean that the patient is not feeling dyspnea.

#### 5.7. Non-pharmacologic interventions for dyspnea

- An electric fan or cool breeze from an open window may provide symptomatic relief. Studies of induced dyspnea in normal subjects indicate that receptors in the trigeminal-nerve distribution influence the intensity of dyspnea.
- Reduce room temperature, if possible
- Limit the number of people in the room.
- Eliminate environmental irritants (such as smoke and dust) as much as possible.
- Maintain a line of sight to the outside, if possible
- Find the most comfortable position for each individual patient. Often, this is sitting upright. Some patients benefit from frequent re-positioning.
- Reassure the patient to alleviate anxiety.
- Behavior therapy: patients can learn relaxation techniques including distraction and hypnosis and relaxing breathing techniques.
  - *Relaxation techniques:*
    - In a quiet environment, wearing loose clothing, and in a comfortable position, the patient should select a personally soothing image or a word or to repeat, while taking slow abdominal deep breaths and with slow expirations.
  - *Breathing techniques:*

- A caregiver can coach the patient breath by breath, beginning by matching the patient’s rapid, panting breathes and then gradually extend the expirations, slowing the respiratory rate and calming the patient.
  - Pursed lip breathing: Breathe in normally through nose for a count of three. Purse lips as if to whistle and blow out slowly, for a count of 6 or 7. Expiration should take about twice as long as inspiration.
  - Paced breathing: coordinating breathing with activities. Breathe in at rest; exhale slowly while performing the activity (such as stair climbing, lifting an object). Be sure not to hold your breath.
- Use the interdisciplinary team to decrease loneliness, explore existential or spiritual issues, provide counseling, and to address family, financial or other issues that may be contributing to emotional distress and thus to dyspnea.

\*\*\*\*\*

**Table 1:** Causes of Dyspnea and Pharmacological Treatments (from the Vietnamese Ministry of Health Guidelines on Palliative Care for Cancer and AIDS Patients, 2006)

Causes of Dyspnea	Recommended Pharmacological Treatments
Pneumonia	<p>Treat with antimicrobial only if consistent with patient’s goals (may not be appropriate for dying patients).</p> <p>Opioid-naïve patient: Morphine 5-10 mg orally or 2-4 mg intravenously (IV) or subcutaneously (SC) every 2-4 hours as needed.</p> <p>If dyspnea is persistent, give by-the-clock every 4 hours with additional breakthrough dose of 5% of total daily dose every 15 minutes as needed. Increase dose as needed by 33% per dose.</p>
Cardiogenic pulmonary edema	<p>Diuresis with furosemide.</p> <p>Opioid-naïve patient: Morphine 2-4 mg every 2-4 hours IV/SC as needed.</p> <p>If dyspnea is persistent, give by-the-clock every 4 hours with additional breakthrough dose of 5% of total daily dose every 15 minutes as needed.. Increase dose as needed by 33% per dose.</p>
Non-cardiogenic pulmonary edema	<p>Opioid-naïve patient: Morphine 2-4 mg IV/SC every 2-4 hours as needed.</p> <p>If dyspnea is persistent, give by-the-clock every 4 hours with additional breakthrough dose of 5% of total daily dose every 15 minutes as needed.. Increase dose as needed by 33% per dose.</p>
Pulmonary	<p>Opioid-naïve patient: Morphine 2-4 mg every 2-4 hours</p>

hemorrhage	IV/SC as needed.  If dyspnea is persistent, give by-the-clock every 4 hours with additional breakthrough dose of 5% of total daily dose every 15 minutes as needed.. Increase dose as needed by 33% per dose.
Severe anemia	Transfuse only if consistent with patient's goals (may not be appropriate for dying patients).  Opioid-naïve patient: Morphine 5-10mg orally or 2-4 mg IV/SC every 2-4 hours as needed.  If dyspnea is persistent, give by-the-clock every 4 hours with additional breakthrough dose of 5% of total daily dose every 15 minutes as needed.. Increase dose as needed by 33% per dose.
Respiratory secretions / "death rattle"	Hyoscine butylbromide 20 mg every 2 hours orally or 0,4mg every 2 hours SC as needed.  Opioid-naïve patient: Morphine 2-4 mg every 2-4 hours IV/SC as needed.  If dyspnea is persistent, give by-the-clock every 4 hours with additional breakthrough dose of 5% of total daily dose every 15 minutes as needed.. Increase dose as needed by 33% per dose.
Reactive airway disease (asthma, chronic obstructive pulmonary disease)	Standard treatment

\*\*\*\*\*

### 5.8. Management of Dyspnea in Children

- Morphine 0.1 mg/kg orally (immediate release) or 0.05 mg/kg SC/ IV every 2-4 hours as needed.
- Lorazepam 0.025-0.1 mg/kg orally/SC/ IV every 2-4 hours as needed.

## 6. Cough Assessment and Treatment

6.1. Definition: The forceful expulsion of air from the lungs.

Stimulation of the cough reflex results in inspiration, glottic closure, and tightening of the abdominal and intercostal muscles. As a result, positive pleural pressures reach as high as 100 to 200 mmHg, producing the forceful exhalation.

6.2. Most common etiologies of cough in cancer and HIV/AIDS patients:

The major causes of cough in cancer and HIV disease are endobronchial and parenchymal tumor and infection and inflammatory processes in the airways caused by tumor or infection. Among infectious causes of cough, *Mycobacterium tuberculosis* is of particular concern in immunosuppressed patients. Aspiration is a common cause of cough in patients with late-stage disease or cancers of the mouth and neck.

### 6.3. Assessment of Cough:

- History: It is important to elicit the following information about the cough:
  - Onset
  - Precipitating events
  - Frequency
  - Sputum production
  - Hemoptysis
  - Fevers or night sweats
  - Weight loss
  - Dyspnea
  - Current and past treatments
  - History of respiratory illness
- Physical examination: Listen to the patient cough while examining the chest. Note the frequency and quality of the cough. Examine the upper airway including the nose for drainage, the throat for visible mucus, and the sinuses for tenderness. (Drainage from the nose and sinuses into the back of the throat is a frequent cause of cough and, if identified, directs treatment.) The presence of rales or rhonchi suggest that the etiology of the cough is a parenchymal lung process. Wheezing suggests airway obstruction or sometimes pulmonary edema. Decreased breath sounds may suggest parenchymal or pleural disease, lung collapse, or improper placement of an endotracheal tube. Stridor suggests obstruction of the trachea or pharynx.

### 6.4. Treatment of cough:

- When appropriate for the patient's goals, treat the underlying cause.
- Opioids such as codeine and morphine are effective for cough at the same doses used to treat dyspnea and pain.
- Non-pharmacologic interventions to relieve cough:
  - Chest physical therapy to loosen secretions
  - Postural drainage: positioning the patient so that gravity enhances the drainage of lung segments.
  - Suctioning of the mouth or posterior pharynx may be useful to remove secretions if it is not too uncomfortable for the patient.
  - Eliminate environmental irritants such as household smoke and fumes from cooking or heating stoves.
  - Discourage smoking on the part of the patient and family.
  - Maintain good ventilation in patient's room.
  - Use universal precautions when caring for a patient with cough and sputum production. Patients with active pulmonary TB, suspected or confirmed, should be placed in respiratory isolation if possible and staff and family members should wear an N-95 respirator mask whenever near the patient.

**Daily evaluation questions**

1. A patient with dyspnea who has not taken any opioid in the past should be given what dose?
  - a. 10 – 20 mg orally every 8 hours as needed
  - b. 10 – 20 mg orally every 4 hours as needed
  - c. 5 - 10 mg orally every 4 hours as needed**
  - d. 2 – 4 mg orally every 4 hours as needed
  
2. Dyspnea can be caused by:
  - a. Pulmonary edema
  - b. Psychosocial distress
  - c. Pneumonia
  - d. Muscle weakness
  - e. All of the above**
  - f. a and c only
  - g. a, c, and d only
  
3. Oxygen is essential for relieving all types of dyspnea.    Yes    **No**
  
4. The rescue dose of morphine for dyspnea should be \_\_\_\_% to \_\_\_\_% of the total daily morphine dose.            **5% to 10%**

**References (Suggested reading)**

Manning H, Schwartzstein R. Pathophysiology of dyspnea. *N Engl J Med* 1995;333:1547-1553.

Weil JV, McCullough RE, Kline JS, et al. Diminished ventilatory response to hypoxia and hypercapnia after morphine in normal man. *N Engl J Med* 1975;292:1103-1106.

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# Dyspnea Assessment & Treatment

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## Objectives

- To understand the basic pathophysiology of dyspnea in HIV/AIDS and cancer patients
- To learn to develop a differential diagnosis of dyspnea.
- To learn the best treatment for dyspnea based on its likely cause and on the goals of the patient.



2



## Definition

- **Dyspnea is a subjective feeling of shortness of breath**
  - “an uncomfortable sensation of breathing”
  - “breathlessness”
  - “shortness of breath”
  - “inability to get enough air”
  - “the feeling of suffocation”

(continued)



3



- **Prevalence:**

- In patients with life threatening illnesses the prevalence is between 12% and 74%

- **Assessment:**

- The only reliable measure is the patient's subjective report. Respiratory rate, pulse oximetry, and blood gas measurements do not necessarily correlate with dyspnea



4



## Pathophysiology of Dyspnea

- **Chemoreceptors**
  - Located in the brain stem
  - Detect hypercapnia and hypoxia
  - The sense of “air hunger” is thought to arise from stimulation of these receptors in the brain stem



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## Pathophysiology of Dyspnea

- **Mechanoreceptors**

- In the upper-airway and face
  - Modify the sensation of dyspnea
- In the lung
  - Stimulation of vagal-irritant receptors → “chest tightness”
  - Stimulation of pulmonary stretch receptors → ↓sensation of dyspnea
- In the chest-wall
  - Afferent information from the chest wall modifies the intensity of dyspnea



6



## Pathophysiology of Dyspnea

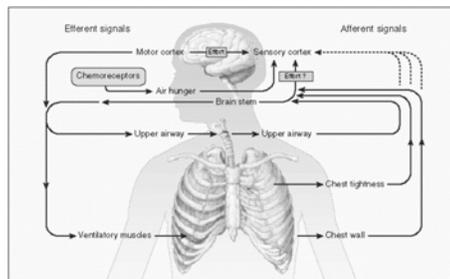
- **“Afferent Mismatch” Theory:**
  - Mismatch between outgoing (efferent) motor signals to the respiratory muscles and incoming (afferent) information. If information from chemoreceptors and mechanoreceptors indicates an inability to respond adequately to the outgoing drive to breath, dyspnea results.



7



## Efferent and Afferent Signals That Contribute to the Sensation of Dyspnea



Manning H and Schwartzstein R. N Engl J Med 1995;333:1547-1553



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## Differential Diagnosis of Dyspnea

- Blood, pus, or fluid in the alveoli
  - Pneumonia
  - Pulmonary edema
  - Pulmonary hemorrhage
  - Aspiration
- Airway obstruction
  - Bronchospasm
  - Thick secretions
  - Tumor
  - Foreign body (such as food)
- Tumor
  - Replacing lung parenchyma
  - Lymphangitic spread in inter-alveolar septa



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## Differential Diagnosis of Dyspnea

- Inability to expand lungs or chest
  - Pleural effusion
  - Ascites
  - Pulmonary fibrosis
  - Chest muscle weakness (neurologic disease, infection [polio], paralytic drugs)
- Pulmonary Embolism
- Anemia
- Metabolic problems
  - Metabolic acidosis
  - Hypophosphatemia
- Psychosocial Issues
  - Anxiety
  - Family problems
  - Financial problems
  - Legal problems
  - Spiritual distress



10



## Assessment of Dyspnea

- Treatment must be based of differential diagnosis
- Subjective assessment
  - Only accurate measure
  - Numeric or visual analogue scale
- Objective assessment (indirect measures)
  - Increased respiratory rate
  - Use of accessory respiratory muscles
  - Labored breathing
  - Gasping
  - Diaphoresis
  - Open mouth or pursed-lip breathing
  - Wheezing
  - Coughing
  - Interrupted speech



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## Treatment of Dyspnea

- Treat the underlying cause (if consistent with the goals of care). For example:
  - Treat pneumonia or pulmonary TB with antibiotics
  - Transfuse for severe anemia
  - Treat pulmonary edema with diuresis
  - Treat pleural effusion with thoracentesis
  - Et Cetera
- Symptomatic relief:
  - Opioids are the most effective treatment
  - Sometimes oxygen, anxiolytics, and non-pharmacological interventions also are effective.



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## Use of opioids in the management of dyspnea

- Opioids can relieve breathlessness without a measurable effect on the respiratory rate or blood gas concentrations
- Opioids act *both* peripherally and centrally
- In the opioid naïve patient, low doses may be effective. For example:
  - Morphine 5-10 mg orally or 2-4mg IV/SC every 2-4 hours as needed
- If dyspnea is severe and persistent, give by-the-clock and make available an additional rescue dose:
  - 5% of total daily dose every 15-30 minutes as needed
- When used properly, opioids for pain or dyspnea are unlikely either to hasten death or to lead to addiction.



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## Use of anxiolytics in the management of dyspnea

- Should not be the primary treatment for dyspnea
- May be helpful when patients demonstrate comorbid anxiety with dyspneic episodes (try opioid first)
- Safe in combination with opioids, although may increase sedation
- Example:
  - Lorazepam 0.5-2mg PO, IV, or SC every 1 hour as needed until calm, then dose routinely every 4-8 hours to keep calm



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## Use of oxygen in the management of dyspnea

- May relieve mild dyspnea in some situations
- Rarely completely effective for severe dyspnea
- Usually is not needed to relieve the dyspnea of a dying patient
- Expensive and may not be readily available, especially in the home setting
- Symbolized medical care – thus sometimes requested by families when not effective
- Pulse oximetry is not a useful indicator of dyspnea



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## Non-Pharmacological interventions for dyspnea

- An electric fan or cool breeze alone may provide symptomatic relief
  - Studies of induced dyspnea in normal subjects indicate that receptors in the trigeminal-nerve distribution influence the intensity of dyspnea
- Open window, keep line of sight to outside (if possible)
- Reduce room temperature, if possible
- Limit the number of people in the room
- Eliminate environmental irritants like smoke
- Find most comfortable position for the patient
- Behavioral approaches—relaxation, distraction, hypnosis
- Use interdisciplinary team to decrease loneliness, explore spiritual issues, provide counseling, and help with social problems that may contribute to distress



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## Specific palliative treatment of dyspnea based on cause

- Pneumonia
  - Treat with antimicrobial only if consistent with goals of care (may not be appropriate for dying patients)
  - Opioid-naïve patient:
    - Morphine 5-10 mg orally or 2-4 mg intravenously (IV) or subcutaneously (SC) every 2-4 hours as needed
  - If dyspnea is persistent, give by-the-clock every 4 hours and make available an additional rescue dose:
    - 5% of total daily dose every 15 minutes as needed.
  - Increase dose as needed by 33% per dose.



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## Specific palliative treatment of dyspnea based on cause

- Cardiogenic pulmonary edema
  - Diuresis with furosemide
  - If diuresis is ineffective or if dyspnea is severe, give morphine as per previous slide
- Severe anemia
  - Transfuse if consistent with goals of care (may not be appropriate for dying patients)
  - If transfusion not appropriate or if dyspnea is severe, give morphine as above.



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### Specific palliative treatment of dyspnea based on cause

- Respiratory secretions / “death rattle”
  - Hyoscine butylbromide 20 mg every 2 hours orally or 0,4mg every 2 hours SC as needed
- Reactive airway disease (chronic obstructive pulmonary disease)
  - Standard treatment: bronchodilators, steroids
  - Morphine if standard treatment ineffective and if consistent with goals of care



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### Specific palliative treatment of dyspnea based on cause

- Non-cardiogenic pulmonary edema, pulmonary hemorrhage, advanced cancer
  - Morphine as above



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## **Dermatology in Palliative Care**

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### **Objectives**

*After the lecture, the trainees will be able to:*

1. Describe common causes of pruritis in patients with AIDS and cancer.
2. Plan treatment of pruritis based on a differential diagnosis.
3. Recognize the 4 stages of pressure ulcers.
4. Prevent and treat pressure ulcers.
5. Provide palliative care for malignant and fungating wounds.

### **Contents**

#### **1. Pruritis**

- 1.1. Pruritis is the most common dermatological symptom experienced by patients with HIV/AIDS.
  - Pruritis in HIV/AIDS patients has many causes:
    - Dry skin (xerosis cutis)
    - Atopic dermatitis (eczema)
    - Fungal infections of the skin
      - Dermatophytes causing tinea pedis, tinea corporis, tinea cruris, tinea capitis, or onychomycosis
    - Parasites:
      - Skin: scabies, pediculosis
      - Systemic: Trichinosis
    - Virus: HIV
    - Bacteria: Syphilis
    - Folliculitis
      - Eosinophilic (no clear infectious agent)
      - Infectious
        - Bacterial (usually Staph. aureus)
        - Yeast (Pityrosporum ovale)
        - Mite (Demodex folliculorum)
    - Cholestasis
    - Liver failure

- Uremia / renal failure
- Adverse drug reactions
  - Usually with rash:
    - Antibiotics such as sulfonamides (cotrimoxazole) and beta-lactams
    - Anticonvulsants
    - Antiretrovirals;
      - NNRTIs
      - Fosamprenavir
      - Tipranavir
  - Often without rash
    - Opioids
- Insect bites
- Pruritis nodularis: itchy fibrotic nodules that result from scratching
- Lichen simplex chronicus
- Psoriasis
- Seborrheic dermatitis
- Iron deficiency
- Psychiatric causes (for example, hallucinations)

1.2. Pruritis is also common in patients with cancer or advanced systemic disease. Frequent causes in these populations include:

- Dry skin
- Adverse drug reactions (especially opioids)
- Uremia / renal failure
- Cholestasis
- Liver failure
- Diabetes mellitus
- Paraneoplastic syndromes (for example, polycythemia vera, carcinoid, solid tumors such as breast and gastric adenocarcinomas)
- Skin involvement with cancer (for example, cutaneous lymphomas)
- Iron deficiency
- Hyperthyroidism or hypothyroidism
- Psychiatric causes

1.3. Neurobiology of pruritis

- Many substances have been proposed as cutaneous mediators of pruritis:
  - Amines: histamine, serotonin, dopamine, adrenaline, noradrenaline, melatonin
  - Proteases: tryptases, chymases, carboxypeptidases, papain, kallikrein
  - Neuropeptides: Substance P, calcitonin gene-related peptide (CGRP), bradykinin, endothelin, neurokinin A, somatostatin, vasoactive intestinal peptide (VIP), cholecystokinin (CCK), neurotensin
  - Opioids
    - Endogenous:
      - met-enkephalin
      - leu-enkephalin

- B-endorphin
    - Exogenous:
      - morphine
    - Eicosanoids: prostaglandin E<sub>2</sub> (PGE-2), other prostaglandins, leukotriene B<sub>4</sub> (LTB<sub>4</sub>)
    - Growth factors
    - Cytokines: interleukins, tumor necrosis factors, eosinophil products
- Itch is mediated by a subset of unmyelinated C fibers called “C itch nociceptors” or “C itch fibers”.
  - These afferent fibers are stimulated by histamine and other pruritogens,
  - Their terminals are in the superficial layers of the skin.
  - They project to a distinct subpopulation of secondary neurons in the central nervous system (CNS).
  - If a stimulus causes both C itch fibers and other nociceptors to fire, more than one type of nociceptive dorsal horn neuron is activated. The result is pain, and itch may be blocked.

#### 1.4. Proposed pathophysiology of specific types of pruritis

- Chronic renal failure (uremic pruritis)
  - Dryness of the skin
  - Secondary hyperparathyroidism
  - Abnormal mast cell proliferation and histamine release in the skin of patients on hemodialysis.
  - Other possible mechanisms:
    - Increased vitamin A levels
    - Proliferation of non-specific enolase-positive sensory nerve endings in the skin
    - Peripheral neuropathy
    - Elevated serotonin
    - Pruritogenic drug metabolite.
- Cholestasis
  - Bile salts and/or unidentified pruritogenic intermediary in bile salt synthesis retained in the skin.
  - Activation of mast cells with histamine release.
  - Centrally acting pruritogenic endogenous opioids accumulating as a result of hepatocyte secretory failure
- Opioid-induced pruritis: occurs in 1% of patients after systemic administration and in 20-90% of patients receiving spinal opioids.
  - Opioids cause the release of histamine from mast cells, but this does not appear to be the main mechanism of itching.
  - Opioid antagonism of the inhibitory transmitters, glycine and GABA, may be responsible for itch.

#### 1.5. Treatment of pruritis

- General intervention:
  - Trim fingernails very short to minimize excoriations and the resulting risk of skin infection.
  - Treat any skin infection.

- Instruct the patient to avoid any soap, skin care product, or other material that may be causing an allergic reaction.
- If possible, change or stop any medications that may be causing pruritis.
- Treatment of specific causes of pruritis:
  - Dry skin
    - Emollient lotion
  - Atopic dermatitis (eczema)
    - Avoid any soap, skin care product, or other material that may be causing an allergic reaction.
    - High potency topical steroid.
      - Avoid putting high potency topical steroid on face and hands.
  - Eosinophilic folliculitis (HIV/AIDS patients)
    - Itraconazole 200 mg per day orally.
  - Cholestasis
    - Cholestyramine 4 gm mixed with water orally before and after breakfast with additional doses as needed before lunch and dinner. Maximum 16 gm per day.
    - Rifampin 150 mg twice daily orally. Before treating, it is essential to make sure the patient does not have tuberculosis.
    - Ondansetron 8 mg twice per day orally.
    - Antihistamine:
      - Diphenhydramine 12.5-50 mg every 4 hours orally or IV as needed, or
      - Hydroxyzine 10-50 mg every 6 hours orally or SC as needed.
    - Biliary stent if possible and if consistent with patient's goals.
  - Scabies
    - Permethrin 5% lotion. Apply from chin to toes, leave on 8-10 hours. Repeat in one week.
    - Lindane 1% lotion apply from chin to toes, wash off in 8 hours.
      - Do not use in pregnant women or young children.
    - For severe cases: Ivermectin 200 mcg / kg orally once. Repeat in two weeks.
    - If the above treatments are not available, use benzyl benzoate.
    - In addition to treating the patient with medications, all clothes and bedding must be washed in hot water and, if possible, dried by machine with high heat. This will prevent re-infection.
    - Antihistamine as above until scabies is cured and itch resolves.
  - Opioids
    - Change to a different opioid if possible.
    - Antihistamine as above.
  - Prurigo nodularis
    - High potency topical steroid under an occlusive dressing to prevent continued scratching.
    - Antihistamine as above.
  - Other causes: HIV, malignancy, uremia.
    - Antihistamine as above.
    - Steroid:
      - Prednisilone 20-80 mg per day orally, or
      - Dexamethasone 4-20 mg per day in one or two doses orally or IV.

- Many possible side effects. Avoid long-term steroid use unless pruritis is severe and/or patient is dying.)

## 2. Ulcers

### 2.1. Pressure ulcers (decubiti or bed sores).

- Stage 1: Non-blanching erythema of intact skin. In dark skin, the erythema may appear blue or purple. (**Figure 1**)



**Figure 1:** Stage 1 pressure ulcer.

- Stage 2: Partial-thickness skin loss involving epidermis, dermis, or both. The ulcer looks like an abrasion, shallow crater, or blister. (**Figure 2**)



**Figure 2:** Stage 2 pressure ulcer.

- Stage 3: Full-thickness skin loss involving subcutaneous tissue. May extend down to underlying fascia, but not through it. Looks like a deep crater. (**Figure 3**)



**Figure 3:** Stage 3 pressure ulcer.

- Stage 4: Extends through subcutaneous tissue and fascia to underlying muscle, bone, tendon, joint capsule, or other deep structures. Sinus tracts or fistula may be present. (**Figure 4**)



**Figure 4:** Stage 4 pressure ulcer.

- Treatment
  - Stage 1 or 2:
    - Relieve pressure on the ulcer:
      - Soft mattress
      - Reposition patient frequently
      - Heel pads or raise heels off bed
    - Keep patient dry.

- Avoid skin trauma from sliding.
- Cleanse intact skin with antibacterial agent such as povidine iodine.
- Cleanse wounds gently with saline.
- Treat pain using the WHO 3-step analgesic ladder.
- Semipermeable membrane dressing.
- Stage 3
  - Relieve pressure on ulcer.
  - Keep patient dry.
  - Avoid skin trauma from sliding.
  - Treat pain using WHO 3-step analgesic ladder
  - Cleanse wound gently with saline.
  - Use hydrocolloid dressing (Duoderm), calcium alginate dressing (especially if bleeding), or paraffin soaked gauze dressing.
- Stage 4
  - Relieve pressure on ulcer.
  - Keep patient dry.
  - Avoid skin trauma from sliding.
  - Treat pain using WHO 3-step analgesic ladder
  - Wet-to-dry dressing or alginate dressing until debridement is complete. Then sugar-povidine-iodine packing, honey, or powdered sugar to reduce risk of infection and promote healing.
  - For thick eschar or extensive necrosis, surgical debridement.
  - Malodorous wound (caused by superficial anaerobic wound infection):
    - Crush metronidazole pill (or open metronidazole capsule) and sprinkle powder on wound 2 – 3 times per day.
    - Activated charcoal dressing, if available.

## 2.2. Malignant wounds / fungating lesions

- Common causes:
  - Patient delays seeking medical care
  - Tumor is refractory to treatment
- Common types:
  - Primary skin cancers
  - Head and neck cancers
  - Locally invasive cancers such as breast cancers
  - Skin metastases
- Treatment
  - Pain relief using WHO 3-step analgesic ladder
  - Keep the wound clean
    - Gentle debridement if necessary (aggressive debridement can cause bleeding that is difficult to control)
    - Saline irrigation
    - Alginate dressing
  - Control bleeding
    - Radiation therapy can be used for hemostasis.
    - Silver nitrate

- Electrocautery
- Infection
  - Control odor caused by superficial anaerobic wound infection:
    - Crush metronidazole pill (or open metronidazole capsule) and sprinkle powder on wound 2 – 3 times per day.
    - If metronidazole is not available, honey or powdered sugar may be applied to the wound.
  - Use a systemic antibiotic only if there is infection in the surrounding tissues and if appropriate for the patient's goals of care.
    - For malodorous wounds with surrounding skin or tissue infection:
      - Metronidazole 250 – 500 mg orally every 8 hours.
      - Clindamycin 150 – 300 mg orally every 6 hours for up to 10 days.
- Dressing
  - Keep moist with hydrocolloid dressing (Duoderm), calcium alginate dressing (especially if bleeding), or paraffin soaked gauze dressing.
  - Wet-to-dry dressing should not be used because it will stick to the wound and is likely to cause bleeding when removed.

### 3. Other dermatologic problems in patients with advanced chronic diseases

#### 3.1. Side effects of cancer therapy

- Radiation dermatitis
- Adverse reactions to chemotherapy
- Graft versus host disease (bone marrow and stem cell transplant patients)

#### 3.2. Paraneoplastic syndromes

- Acanthosis nigricans
- Dermatomyositis
- Acquired ichthyosis

#### 3.3. Exacerbation of chronic skin diseases

- Psoriasis
- Seborrheic dermatitis

#### 3.4. Common skin problems in patients with HIV/AIDS and other immunocompromised patients

- Drug rashes
  - Especially sulfa drugs, beta-lactams, nevirapine
- Fungal infections:
  - *Penicillium marneffeii*
  - *Cryptococcus*
  - *Candida*
  - Histoplasmosis
  - Dermatophytes
    - *Tinea pedis*
    - *Tinea corporis*

- Tinea capitis
  - Tinea cruris
  - Onychomycosis
- Bacterial infections
  - Furunculosis (Staph. aureus)
  - Bacillary angiomatosis
  - Cellulitis
- Viral infections
  - Herpes simplex
  - Varicella zoster (shingles)
- Parasitic infections
  - Scabies
- Folliculitis
  - Eosinophilic (no clear infectious agent)
  - Infectious
    - Bacterial (usually Staph. aureus)
    - Yeast (Pityrosporum ovale)
    - Mite (Demodex folliculorum)
- Kaposi's Sarcoma
- Prurigo nodularis (see section on Pruritis above)
- Seborrheic dermatitis

### Daily evaluation questions

1. Many types of pruritis are caused by release of \_\_\_\_\_ from activated mast cells.  
**histamine**
2. One of the most important interventions for pruritis of any cause is to make sure the patient's fingernails are trimmed very short. **True** False
3. A pressure ulcer that extends through the skin and subcutaneous to underlying muscle or bone is classified as:
  - a. Stage 1
  - b. Stage 2
  - c. Stage 3
  - d. Stage 4**
4. Treatments for pressure ulcers of any stage include all of the following **except**:
  - a. Metronidazole powder**
  - b. Relieve pressure on the ulcer
  - c. Keep the patient dry
  - d. Avoid skin or wound trauma from sliding

5. Malodorous wounds can be treated by applying to the wound:
- a. Metronidazole powder
  - b. Honey
  - c. Powdered sugar
  - d. All of the above**
  - e. A and c only

**References (Suggested reading)**

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## Dermatology in Palliative Care

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1



## Pruritis



2



## Pruritis (Itching)

- Pruritis is the most common dermatological symptom experienced by patients with HIV/AIDS.
- Various etiologies may be responsible for causing pruritis in HIV/AIDS patients.
- Pruritis is also found in patients with cancer or advanced systemic disease.



3



## Causes of pruritis in HIV/AIDS

- Dry skin (xerosis cutis)
- Scabies
- Bites by mosquitoes or other insects
- Folliculitis (eosinophilic, bacterial)
- Cholestasis (obstructive biliary disease)
- Adverse drug reactions
- Uremia
- Liver failure
- Prurigo nodularis
- Psychiatric causes (somatic hallucinations)



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## Causes of pruritis in cancer or advanced systemic disease

- Dry skin
- Allergic reaction to drugs
- Uremia
- Cholestasis
- Opioids
- Paraneoplastic process
- Skin involvement with cancer (for example, Hodgkin's lymphoma and cutaneous lymphomas)
- Psychiatric causes
- Patients with myeloproliferative disorders, especially polycythemia vera



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## Why scratching probably helps decrease itch?

- Afferent nerve fibers mediating itch are a subset of the large population of polymodal C-nociceptors, which also mediate pain.
- If a stimulus recruits more nociceptors, including this population (polymodal C-nociceptors), more nociceptive dorsal horn neurons are activated to cause pain, and itch may be blocked.



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## Proposed pathophysiology for specific types of pruritis

1. Chronic renal failure (uremic pruritis)
  - Dryness of the skin
  - Secondary hyperparathyroidism
  - Abnormal mast cell proliferation in skin / increased histamine concentration in skin.
  - Increased vitamin A levels
  - Proliferation of non-specific sensory nerve endings in the skin
  - Peripheral neuropathy
  - Elevated serotonin levels in skin
  - Another unidentified pruritogenic metabolite



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## Specific etiologies and proposed pathophysiology

2. Cholestasis
  - Retained bile salts and/or unidentified pruritogenic intermediary in bile salt synthesis,
  - Activation of mast cells with release of histamine
  - Centrally acting pruritogenic endogenous opioids accumulating as a result of hepatocyte secretory failure



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## Specific etiologies and proposed pathophysiology

3. Opioid-induced pruritis
  - Occurs in 1% of patients receiving systemic opioid and 20-90% receiving intra-theal (spinal) opioid
  - Opioids cause release of histamine from mast cells, but this does not appear to be the main mechanism of itching
  - The dorsal horn of the medulla oblongata mediates itch and face-scratching behavior
    - Opioid antagonism of the inhibitory transmitters glycine and GABA may cause itch



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## Specific management of pruritis based on etiology

1. General Measure: Keep patient's fingernails trimmed short to minimize risk of excoriation and skin infection
2. Dry skin: emollient lotion
3. Contact dermatitis: high potency topical steroids
4. Prurigo nodularis:
  - High potency topical steroid under occlusive dressing
  - Oral antihistamine such as diphenhydramine



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## Specific management of pruritis based on etiology

5. Scabies
  - **Permethrin lotion apply from chin to toes, leave on 8-10 hours. Repeat in one week**
  - **Lindane 1% lotion, apply from chin to toes, leave on 8-10 hours. Do not use in pregnant women or young children.**
  - **Ivermectin 200mcg/kg orally once. Repeat in 2 weeks.**
  - **Benzyl benzoate**
  - **Antihistamine such as diphenhydramine for symptomatic relief until scabies cured**
  - **Very contagious: Treat all close contacts and wash all bedding and clothes in hot water**

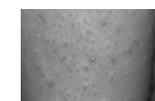


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## Specific management of pruritis based on etiology

6. Norwegian scabies
  - Permethrin or ivermectin as above
  - Extremely contagious: treat close contacts and wash clothes as above
7. Eosinophilic folliculitis (HIV/AIDS patients)
  - Itraconazole 200 mg per day orally until resolved
8. Bacterial folliculitis (usually *Staph aureus*)
  - Topical erythromycin or clindamycin or systemic anti-staphylococcal antibiotic



## Specific management of pruritis based on etiology

### 9. Cholestasis

- Cholestyramine 4 gm mixed with water before and after breakfast with additional doses as needed before lunch and dinner. Maximum 16 gm / day.
- Rifampin 150 mg twice daily orally (do not give if patient might have TB)
- Ondansetron 8 mg twice per day orally;
- Biliary stent if possible and if consistent with goals of care.

### 10. Opioids

- Opioid rotation if possible.
- Diphenhydramine 12.5-50 mg every 4 hours orally or IV dependent on patient's condition.
- Hydroxyzine 10-50 mg every 6 hours orally or SC dependent on patient's condition.



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## Specific management of pruritis based on etiology

### 11. Other causes: HIV, malignancy, uremia

- Diphenhydramine or hydroxyzine as above.
- Prednisilone 20-80 mg per day orally;
- Dexamethasone 4-20 mg per day in one or two doses orally or IV.



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## Management of Ulcers



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## Management of Decubitus Ulcers (Pressure Sores)

- Stage 1 or 2 Decubitus Ulcer
  - Relieve pressure on sore:
    - soft mattress
    - reposition patient frequently
    - heel pads or raise heels off bed
  - Keep patient dry
  - Avoid skin trauma from sliding
  - Treat pain (NSAIDs, opioids)
  - Semipermeable membrane dressing



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## Stage 1 Decubitus Ulcer



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## Stage 2 Decubitus Ulcer



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## Management of Decubitus Ulcers (Pressure Sores)

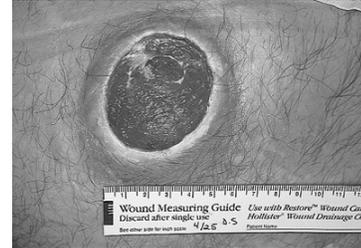
- Stage 3
  - Relieve pressure on sore
  - Keep patient dry
  - Avoid skin trauma from sliding
  - Treat pain
    - NSAIDs
    - Opioids—systemic or topical (morphine 1mg in 1gm hydrogel)
  - Avoid povidine-iodine 10%
    - may inhibit healing process by killing epithelial cells
  - Use hydrocolloid dressing (Duoderm), calcium alginate dressing, or paraffin soaked gauze dressings



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## Stage 3 Decubitus Ulcer



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## Management of Decubitus Ulcers (Pressure Sores)

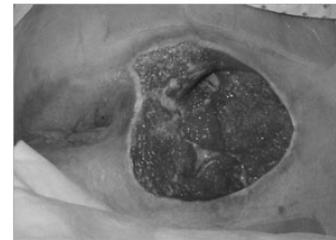
- Stage 4
  - Relieve pressure on sore
  - Keep patient dry
  - Avoid skin trauma from sliding
  - Treat pain
    - NSAIDs
    - Opioids—systemic or topical (morphine 1mg in 1gm hydrogel)
  - Wet-to-dry dressing or alginate dressing
  - For thick eschar or extensive necrosis, surgical debridement or sugar-povidine-iodine packing.
  - For malodorous wound, crush metronidazole pill (or open metronidazole capsule) and sprinkle powder on wound



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## Stage 4 Decubitus Ulcer



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## Malignant wounds/Fungating lesions

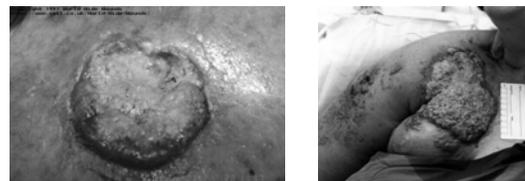
- Common causes
  - Primary skin cancers
  - Head and neck cancers refractory to chemotherapy and radiation
  - Skin metastases from breast cancer or other cancers



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## Malignant Wound/Fungating Wound



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## Management of malignant wounds

- Pain management
  - Systemic opioids for severe pain
  - Topical opioids (morphine 1mg in 1gm hydrogel = 0.1% conc.)
- Keep the wound clean
- Gentle debridement
- For malodorous wound, crush metronidazole pill (or open metronidazole capsule) and sprinkle powder on wound
- Control bleeding
  - If available, may use radiotherapy (e.g. linear accelerator with electron particle beam for hemostasis)
- Apply appropriate dressing (e.g., wet-to-dry, paraffin soaked gauze)



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## Infected ulcers

- Wounds may become malodorous
- Odors are usually the result of anaerobic infections and/or poor hygiene
  - For superficial infections: use topical metronidazole as above or silver sulfadiazine 2-3 times per day
  - For soft tissue infections give systemic metronidazole 250-500mg every 8 hours orally or IV in addition to topical management



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## Nausea / Vomiting Assessment and Treatment

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### Objectives

*After the lecture, the trainees will be able to:*

1. Understand the basic pathophysiology of nausea and vomiting.
2. Develop a differential diagnosis of nausea and vomiting.
3. Prescribe the best treatment for nausea and vomiting based on its likely cause.

### Contents

#### 1. Definitions:

- 1.1 Nausea is a subjective sensation that precedes vomiting.
- 1.2. Vomiting is the forceful expulsion of gastric contents due to a complex neuromuscular process with voluntary and involuntary components.

#### 2. Pathophysiology of nausea and vomiting

2.1. Nausea is caused by stimulation of one or more of four sites (see **Figure 1**):

- The gastrointestinal (GI) tract;
- The vestibular system;
- The chemoreceptor trigger zone (CTZ) in the area postrema of the floor of the fourth ventricle in the brain;
- Higher centers in the central nervous system (CNS) including the thalamus, hypothalamus, or cerebral cortex.

2.2. One or more of the four sites involved in nausea stimulates the *vomiting center* (VC) comprised of the nucleus of the tractus solitarius and the reticular formation of the medulla oblongata. The VC acts as the final common pathway for many types of vomiting by initiating parasympathetic and motor efferent activity that produces vomiting.

2.3. *The gastrointestinal tract:* The gastrointestinal tract (and heart) can activate the vomiting center by stimulation of mechanoreceptors or chemoreceptors on glossopharyngeal or vagal afferent fibers (cranial nerves IX and X) or by release of serotonin from gut enterochromaffin cells, which in turn stimulate **5-hydroxytryptamine type 3 (5-HT<sub>3</sub>) receptors** on vagal afferents.

2.4. *The vestibular system:* The vestibular system activates the vomiting center when stimulated by motion or disease such as labyrinthitis or, rarely, when sensitized by medications such as opioids.

**Histamine type 1 (H<sub>1</sub>)** and **acetylcholine muscarinic type 1 (Ach M<sub>1</sub>)** receptors are thought to exist on vestibular afferents.

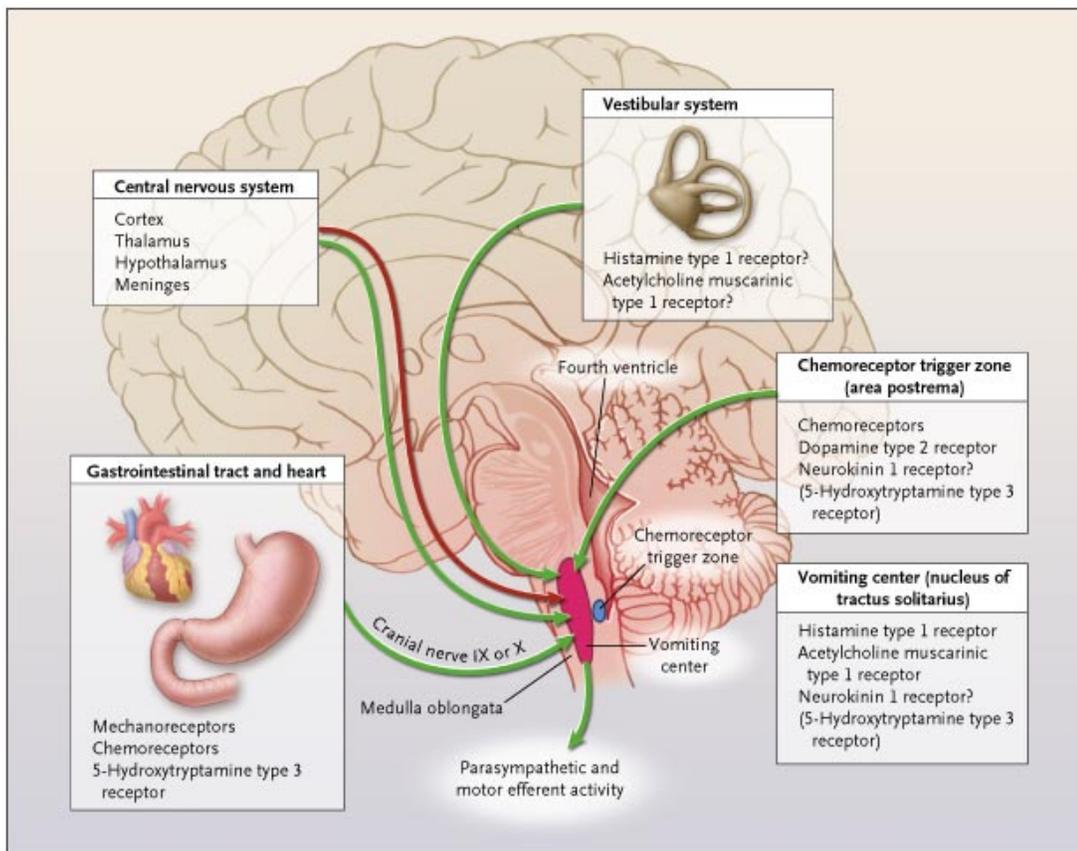
2.5. *The chemoreceptor trigger zone (CTZ) in the area postrema of the floor of the fourth ventricle:*

- The CTZ lacks the blood-brain barrier otherwise present throughout the central nervous system.
- Endogenous or exogenous blood-borne toxins stimulate chemoreceptors in the CTZ. The ensuing activation of the CTZ is mediated by **dopamine type 2 (D<sub>2</sub>) receptors**.
- Efferent activity from the CTZ then activates the VC.
- **Neurokinin 1 (NK<sub>1</sub>) receptors** for substance P also probably are present in the CTZ (and the VC) and also likely mediate nausea and vomiting.
- The **5-hydroxytryptamine type 3 (5-HT<sub>3</sub>) receptors** for serotonin in the CTZ and VC, unlike those in the GI tract, probably do not play a major role in nausea and vomiting.

2.6. *Higher centers in the central nervous system (CNS):* Higher CNS centers may either activate or inhibit the vomiting center. There may also be direct activation of **H<sub>1</sub> receptors** in the meninges by increased intracranial pressure.

\*\*\*\*\*

**Figure 1:** Pathophysiology of Nausea and Vomiting (from Krakauer et al. A 58-year-old man with esophageal cancer and nausea, vomiting, and intractable hiccups. N Engl J Med. 2005 Feb 24;352(8):817-25)



2.7. Activation of the vomiting center (VC) by one or more of the four pathways above leads to parasympathetic and motor efferent activity that produces vomiting.

- Activation of the vomiting center is mediated by **histamine type 1 (H<sub>1</sub>) receptors** or **acetylcholine muscarinic type 1 (ACh M<sub>1</sub>) receptors**, with subsequent parasympathetic and motor efferent activity resulting in vomiting.
- **Neurokinin 1 (NK<sub>1</sub>) receptors**, for which substance P is a ligand, are found both in the chemoreceptor trigger zone and the vomiting center and probably also are involved in mediating nausea and vomiting.

### 3. Differential diagnosis of nausea and vomiting in cancer and HIV/AIDS patients

Optimal palliation of any distressing symptom requires understanding of the symptom's cause.

Whenever this is not obvious, a thorough differential diagnosis should be performed.

#### 3.1. Stimulants of the chemoreceptor trigger zone (CTZ)

- Endogenous emetogenic toxins
  - Renal failure
  - Hepatic failure
  - Lactic acidosis (for example, from nucleoside reverse transcriptase inhibitors d4T, ddI, or less often AZT)
  - Hypercalcemia
  - Hyponatremia
  - Inflammatory mediators (emetogenic cytokines)
  - Tumor toxins (emetogenic factors produced by cancer cells)
  - Diabetic ketoacidosis
- Exogenous emetogenic toxins
  - Bacterial toxins (for example, staphylococcal food poisoning)
  - Medications
    - Opioids
    - Cytotoxic chemotherapeutic agents
    - Antibiotics (for example, erythromycin, doxycycline)
    - Antivirals (for example, AZT)
    - Digoxin

#### 3.2. Stimulation or sensitization of the vestibular system

- Injury to the vestibular apparatus or cranial nerve VIII (for example, by infection or tumor)
- Medications
  - Opioids (rare)

#### 3.3. Noxious stimulation of the gastrointestinal tract

- Stimulation of mechanoreceptors (stretch receptors) on vagal afferents
  - Constipation, which can be caused by:
    - Medications
      - Opioids
      - Anticholinergics (used to treat nausea)
      - 5-HT<sub>3</sub> receptor blockers
      - Calcium channel blockers
    - Dehydration
    - Lack of activity
  - Ileus

- Medications (as for constipation)
      - Ascites
      - Autonomic dysfunction
    - Obstruction of hollow viscus by tumor or inflammation
      - Small or large bowel
      - Gastric outlet
      - Ureters
    - Delayed gastric emptying
      - Medications (as for constipation)
      - Tumor infiltration of gastric wall (linitis plastica)
      - Inflammation
      - Ascites
      - Autonomic dysfunction
    - Tumor infiltration of visceral organs such as liver with capsular stretch
    - Congestive heart failure
      - Ventricular stretch
      - Liver congestion with capsular stretch
  - Stimulation of chemoreceptors on glossopharyngeal or vagal afferents (cranial nerves IX or X)
    - Mucosal irritation of the pharynx, esophagus, or stomach
      - Infection (candida, CMV, HSV, helicobacter pylori)
      - Medications (NSAIDS)
      - Ethanol
      - Gastro-esophageal reflux
      - Radiation therapy
    - Cardiac ischemia
  - Stimulation of 5-hydroxytryptamine type 3 (5-HT<sub>3</sub>) receptors on vagal afferents by release of serotonin (5-hydroxytryptamine) from enterochromaffin cells in the GI tract
    - Cytotoxic chemotherapeutic agents
    - Radiation therapy to abdominal area
    - Possibly surgery
- 3.4. Disease of the central nervous system (CNS)
- Increased intracranial pressure stimulating meningeal mechanoreceptors
    - Tumor (primary CNS tumor or metastasis)
    - Infection
      - Cryptococcal meningitis
    - Bleeding
  - Meningeal irritation
    - Meningitis
      - Infectious
      - Carcinomatous
  - Migraine
  - Psychogenic
    - Anxiety
    - Anticipation of emetogenic chemotherapy

#### 4. Approach to the patient with nausea and vomiting

4.1. Start with history of the present illness, history of the symptoms, and physical examination.

- If the patient's symptoms are severe, or if the history or physical examination might cause significant discomfort, both should be as directed and brief as possible and should be accompanied by immediate efforts to symptom relief.
- A thorough history and physical examination can be completed when the patient is more comfortable, and the differential diagnosis and treatment can then be adjusted if appropriate.

4.2. History of nausea and vomiting: important points

- Onset (when did it start?)
- Frequency
- Precipitating events
- Duration of episodes
- Severity
- Does vomiting occur without nausea?
- Relation to eating or drinking
- Presence of blood or "coffee ground" material in the emesis
- Associated symptoms (pain, fever, constipation, diarrhea, weight loss, dizziness, weakness)
- Possible consumption of contaminated food or water
- Urine output (reduced quantity?)
- Medications (modern and traditional)
- Affect of nausea or vomiting on daily activities

4.3. Physical examination

- Abdominal exam (Soft? Tender? Guarding? Rebound tenderness / peritoneal signs? Distention? Hepatomegaly? Splenomegaly? Bowel sounds?)
- Rectal examination (occult blood in the stool?)
- Neurologic examination (if any suspicion of CNS disease, disease of vestibular system, autonomic dysfunction)
- Orthostatic examination to assess for volume depletion
- In babies: assess for lack of tears when crying or no wet diapers for 3 or more hours

4.4. Diagnostic testing

- Testing should be directed by the history, physical examination, and resulting differential diagnosis. Possibly relevant tests might include:
  - Complete blood count (CBC) to assess for infection or anemia
  - Chemistries to assess for fluid or electrolyte derangements
  - Serum levels of potentially toxic drugs (such as digoxin)
  - Abdominal radiographs (including an upright or decubitus film) or abdominal CT scan (if available) to assess for bowel obstruction or severe constipation. CT to assess for tumor or metastatic disease. CT scan or abdominal ultrasound to assess for abscess, ascites, hydronephrosis.

#### 5. Treatment of nausea and vomiting (see Table 1 for doses)

5.1. If possible and appropriate for the patient's goals, identify and correct or remove the underlying cause (for example: constipation, metabolic derangements, gastritis due to NSAID therapy or ethanol, emetogenic medications).

5.2. Symptom relief should be based on a thorough differential diagnosis and clinical judgment about the most likely pathophysiology or cause.

5.3. Nausea and vomiting caused by endogenous or exogenous emetogenic toxins or metabolic derangements stimulating D<sub>2</sub> receptors in the CTZ:

- Butyrophenones are the most potent D<sub>2</sub> receptor antagonists.
  - Example: haloperidol
  - Start with 0.5 mg IV, SC, or orally as needed or every 8 hours around the clock if the nausea is constant.
  - If given around the clock, add a rescue dose for breakthrough nausea.
- Phenthiazines are less potent D<sub>2</sub> receptor antagonists but also can be used.
  - Examples: prochlorperazine (Compazine), chlorpromazine (Thorazine)
- Corticosteroid: useful for treating nausea of many causes. May be effective for this type of nausea for unclear reasons.

5.4. Nausea and vomiting caused by stimulation or sensitization of vestibular system:

- H<sub>1</sub> receptor antagonists such as diphenhydramine IV or orally, hydroxyzine IV or orally, promethazine IV or rectally.
  - Side effects include sedation, delirium.
- Ach M<sub>1</sub> receptor antagonists such as scopolamine IV, SC or transdermally.
  - Also relieve crampy abdominal pain.
  - Side effects include sedation, delirium, constipation.

5.5. Nausea and vomiting caused by chemotherapy or by radiation therapy to abdominal area:

- Antagonists of serotonin (5-HT<sub>3</sub>) receptors on vagal afferents
  - Examples: ondansetron, granisetron
- Steroid such as dexamethasone

5.6. Nausea and vomiting caused by increased intracranial pressure

- Steroid (high dose)

5.7. Nausea and vomiting caused by anxiety

- Benzodiazepines
  - Lorazepam (medium duration of action)
  - Diazepam or clonazepam (long duration of action)

5.8. Nausea and vomiting caused by mucosal irritation of stomach or esophagus:

- Cytoprotective agents
  - Proton pump inhibitors (PPI) such as omeprazole are the most effective drugs.
    - Recommended also for
  - Histamine type 2 (H<sub>2</sub>) receptor antagonists such as ranitidine
  - One of these drugs also is recommended for:
    - Any patient taking NSAID for pain
    - Any patient with symptoms of gastro-esophageal reflux disease
    - Any palliative care patient who has nausea or abdominal pain of uncertain cause

## 5.9. Nausea and vomiting caused by ileus or delayed gastric emptying without obstruction:

- Metoclopramide (prokinetic agent)
  - Works mainly in GI tract as D<sub>2</sub> receptor antagonist and 5-HT<sub>4</sub> receptor agonist that promotes peristalsis.
  - Very little D<sub>2</sub> receptor antagonist effect at the CTZ.
- Other prokinetic drugs: domperidone, cisapride (many drug interactions)

## 5.10. Nausea and vomiting caused by distension of liver due to neoplasm:

- Steroid (high dose)

## 5.11. Nausea and/or vomiting caused by bowel obstruction.

- If obstruction is due to tumor, can try high dose steroid.
- Venting gastrostomy tube for drainage.
- Palliative surgery to relieve or by-pass the obstruction (if appropriate for the patient's goals).

## 5.12. Adjuvants for nausea and vomiting of any cause that can be added to other anti-emetics to try to improve effectiveness:

- H<sub>1</sub> receptor antagonists such as diphenhydramine IV or orally, hydroxyzine IV or orally, promethazine IV or rectally (can cause sedation or delirium).
- Ach M<sub>1</sub> receptor antagonists such as scopolamine IV, SC or transdermally (can cause constipation, sedation, delirium).
- Steroid

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**Table 1:** Differential Diagnosis of Nausea and Vomiting and Recommended Pharmacological Treatments (from the Vietnamese Ministry of Health Guidelines on Palliative Care for patients with cancer, HIV/AIDS, and other life-threatening illnesses, 2006)

Differential Diagnosis	Treatment at Medical Settings (Normal Starting Dose)	Home-based Care
Nausea-induced by drug toxicity, inflammatory mediators, virus, bacterial toxicity, metabolic derangement	Haloperidol 0.5-2 mg two to four times per day orally, IV, or SC  Prochlorperazine: 5-10 mg three to four times per day orally or IV, or 25 mg suppository rectally two times per day  Dexamethasone 8-20 mg per day in one or two doses orally or IV	Consume soft and rich-in-energy food; offer smaller meals; encourage the patient to take ORS, or sip tea with sugar, rice water, or drinks that the patient likes.  Drugs taken with foods, if possible.

Stimulation/ sensitization of vestibular apparatus	Diphenhydramine 25-50 mg three to four times per day orally or IV  Scopolamine 1.5-6 mg by transdermal patch every 72 hours, or 0.1-0.2 mg every 6-8 hours SC	Chronic nausea/vomiting or accompanied by other symptoms such as fever, headache, psycho-disorder, blood in the vomit, jaundice, or abdominal pain should be attended by physicians.  Remove all sources of strong odors such as cooking, bedpans.  Provide mouth care with cleaning and rinsing after each episode of vomiting.
Chemotherapy, radiation therapy to abdominal area	Ondansetron 8 mg up to three times per day orally or IV  Dexamethasone 8-20 mg per day in one or two doses orally or IV	
Increased intra- cranial pressure	Dexamethasone 8-20 mg in one or two doses daily, orally or IV	
Anxiety	Diazepam 2-10 mg three times a day, orally, IV or SC  Lorazepam 0,5-2 mg 4-6 times a day, orally, IV or SC  Clonazepam 0,5-1 mg twice daily, orally	
Gastritis, peptic ulcer	Ranitidine 150 mg twice per day, orally, or 50 mg every 8 hours IV. Dosing frequency should be reduced for renal failure.  Omeprazole 20-40 mg once or twice per day, orally	
Ileus/ gastroparesis	Metoclopramide 10 mg four times per day orally or IV	
Constipation	See section on Constipation	
Distension of liver or of hollow viscus due to neoplasm	Dexamethasone 8-20 mg in one or two doses, orally or IV.  Venting gastrostomy tube for drainage.  Palliative surgery	

Adjuvants for nausea/vomiting of any cause	Diphenhydramine 25-50 mg three or four times per day/, orally or IV  Scopolamine 1.5-6 mg transdermal every 72 hours, or 0,1-0,3 mg SC every 6-8 hours	
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## 6. Management of nausea and vomiting in children (see Table 3)

**Table 3:** Management of Nausea and Vomiting in Children (from the Vietnamese Ministry of Health Guidelines on Palliative Care for patients with cancer, HIV/AIDS, and other life-threatening illnesses, 2006)

Causes	Drug	Dose
From emetogenic toxins such as drugs, inflammatory mediators, viruses, bacterial toxins, metabolic derangements	Diphenhydramine	1 mg/kg orally/IV every 6 hours as needed
	dexamethasone	0.3 mg/kg/day orally or IV
From stimulation or sensitization of vestibular apparatus	Diphenhydramine	1 mg/kg orally/IV every 6 hours as needed
	Scopolamine	Adolescents: 1.5 mg by transdermal patch every 72 hours
From chemotherapy or radiation therapy	Ondansetron	0.15 mg/kg orally every 8 hours as needed
	Dexamethasone	0.3 mg/kg/day orally or IV
From increased intracranial pressure	Dexamethasone	0.3 mg/kg/day orally or IV
From anxiety	Lorazepam	0.025-0.1 mg/kg orally/IV every 8 hours as needed
From ileus or gastroparesis	Metoclopramide	0.25 mg/kg orally every 8 hours as needed
From constipation	See section on constipation	
From distention of liver or other hollow viscus due to neoplasm	Dexamethasone	0.3 mg/kg/day orally or IV
From bowel	Dexamethasone	0.3 mg/kg/day orally or IV

obstruction	Venting gastrostomy Palliative surgery	
Adjuvants for nausea/vomiting of any cause	Diphenhydramine Scopolamine	1 mg/kg orally/IV every 6 hours as needed Adolescents: 1.5 mg by transdermal patch every 72 hours

### Daily evaluation questions

1. Opioid-induced nausea usually can be relieved by giving a low dose of haloperidol.   **Yes**   No
  
2. Haloperidol exerts its anti-emetic effect by blocking the \_\_\_\_\_receptors in the chemoreceptor trigger zone (CTZ) of the brain.   **Dopamine type 2 or D<sub>2</sub>**
  
3. It is recommended that all palliative care patients with abdominal pain or nausea of uncertain cause be treated with:
  - a. Ondansetron
  - b. Haloperidol
  - c. Codeine or morphine
  - d. Omeprazole or ranitidine**
  - e. Steroid
  
4. Possible treatments for nausea and vomiting due to malignant bowel obstruction include:
  - a. Haloperidol
  - b. Steroid
  - c. Venting gastrostomy tube
  - d. Palliative surgery
  - e. b, c, and d only**
  - f. All of the above
  
5. Likely causes of nausea and vomiting in a patient with AIDS who has been taking d4T/3Tc/NVP for one year but whose CD4 count is 20 include:
  - a. CNS infection

- b. Lactic acidosis
- c. Constipation
- d. a and b**
- e. All of the above

**References (Suggested reading)**

Krakauer EL, Zhu AX, Bounds BC, et al. A 58-year-old man with esophageal cancer and nausea, vomiting, and intractable hiccups. *N Eng J Med* 2005;352:817-825.

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## Nausea / Vomiting Assessment and Treatment

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## Nausea

- Nausea is a subjective sensation that precedes vomiting
- It is caused by stimulation of one or more of four sites:
  - The gastrointestinal tract
  - The vestibular system
  - The chemoreceptor trigger zone (CTZ) in the area postrema of the floor of the fourth ventricle
  - Higher centers in the central nervous system (CNS)



2



## Vomiting

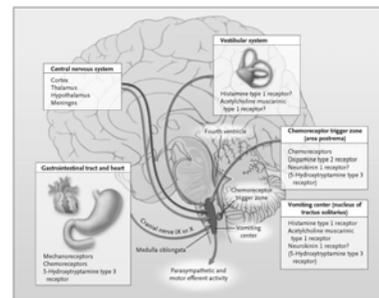
- Vomiting is the forceful expulsion of gastric contents
- Activation of the vomiting center (VC) by one or more of the four pathways above leads to parasympathetic and motor efferent activity that produces vomiting



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## The Pathophysiology of Nausea and Vomiting



Krakauer EL et al. N Engl J Med 2005;352:817-825



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## GI Tract

- Stimulation of chemoreceptors or mechanoreceptors on Cranial Nerves (CNs) IX or X
- Release of serotonin causing stimulation of 5-Hydroxytryptamine Type 3 (5-HT<sub>3</sub>) receptors on CN X.
- CNs IX & X stimulate Vomiting Center (VC)



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## Vestibular System

- Motion
- Labyrinthitis or other disease
- Opioid (rare)
- Histamine Type 1 (H<sub>1</sub>) and Acetylcholine Muscarinic Type 1 (ACh M<sub>1</sub>) receptors on CN VIII?
- CN VIII stimulates VC



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### Chemoreceptor Trigger Zone (CTZ)

- Lacks blood-brain barrier
- Endogenous & exogenous toxins stimulate chemoreceptors that activate CTZ
  - Mediated by Dopamine Type 2 (D<sub>2</sub>) receptors
- CTZ then activates VC
- Neurokinin Type 1 (NK<sub>1</sub>) receptors for Substance P also in CTZ
- 5-HT<sub>3</sub> receptors in CTZ probably not important



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### Central Nervous System (CNS)

- Can activate VC
- Can inhibit VC
- H1 receptors in meninges activated by increased intra-cranial pressure



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### Vomiting Center (VC)

- Activated by any of previous 4 pathways
- Mediated by Histamine Type 1 (H<sub>1</sub>) and Acetylcholine Muscarinic Type 1 (ACh M<sub>1</sub>) receptors
- Results in parasympathetic and motor efferent activity resulting in vomiting
- Neurokinin Type 1 (NK<sub>1</sub>) receptors for Substance P also in VC



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### Causes of nausea and vomiting

- Stimulants of CTZ
  - Endogenous
    - Renal failure
    - Liver failure
    - Lactic acidosis (eg. NRTIs: d4T, ddI, occasionally AZT)
    - Hypercalcemia
    - Hyponatremia
    - Inflammatory mediators (emetogenic cytokines)
    - Tumor toxins
    - Diabetic ketoacidosis



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### Causes of nausea and vomiting

- Stimulants of CTZ
  - Exogenous:
    - Bacterial toxins (eg. Staph)
    - Medications
      - Opioids
      - Cytotoxic chemotherapy agents
      - Antibiotics (eg. erythromycin, doxycycline)
      - Antivirals (eg. AZT)
      - Digoxin



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### Causes of nausea and vomiting

- Stimulation or sensitization of vestibular system
  - Injury (eg. infection, tumor)
  - Medication such as opioid (rare)



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## Causes of nausea and vomiting

- Noxious stimulation of GI tract
  - Stimulation of mechanoreceptors on CN X
    - Constipation
      - Medications
      - Dehydration
    - Ileus
      - Medications
      - Ascites
      - Autonomic dysfunction
  - Obstruction of hollow viscus by tumor or inflammation
    - Small or large bowel
    - Gastric outlet
    - Ureters



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## Causes of nausea and vomiting

- Noxious stimulation of GI tract (continued)
  - Stimulation of mechanoreceptors on CN X
    - Delayed gastric emptying
      - Medications
      - Tumor (linitis plastica)
      - Inflammation
      - Ascites
      - Autonomic dysfunction
    - Tumor infiltration of visceral organ with capsular stretch
    - Congestive heart failure



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## Causes of nausea and vomiting

- Noxious stimulation of GI tract (continued)
  - Stimulation of chemoreceptors on CNs IX or X
    - Mucosal irritation of pharynx, esophagus, stomach
      - Infection (Candida, CMV, HSV, H pylori)
      - Ethanol
      - GE reflux
      - Radiation therapy
    - Cardiac ischemia
  - Stimulation of 5-HT<sub>3</sub> receptors on CN X
    - Cytotoxic chemotherapy
    - Radiation therapy to abdomen
    - Possibly surgery



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## Causes of nausea and vomiting

- Disease of CNS
  - Increased ICP
    - Tumor
    - Infection (esp. cryptococcal meningitis)
    - Bleeding
  - Meningeal irritation
    - Meningitis
      - Infection
      - Carcinomatous
  - Migraine
  - Psychogenic
    - Anxiety
    - Anticipation of emetogenic chemotherapy



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## General management of nausea and vomiting

- If possible, identify and correct the underlying etiology
- Pharmacologic treatment should be rational and based on:
  - Thorough differential diagnosis
  - Clinical judgement about the most likely pathophysiology or etiology



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## General management of nausea and vomiting

- Empiric therapy with antiemetics should begin with a single agent targeting the presumed mechanism
  - The dose should be optimized before a second medication with a different mechanism is added
  - Sequential combination therapy may be required in some patients



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### Classes of medications used in the symptomatic management of nausea and vomiting

- Dopamine antagonists: haloperidol, prochlorperazine
- Antihistamines: diphenhydramine
- Anticholinergics: scopolamine, hyoscine butylbromide
- Serotonin antagonists: ondansetron
- Prokinetic agents: metoclopramide
- Antacids: ranitidine (H2 blocker), omeprazole (proton pump inhibitor)
- Other medications:
  - Steroid: dexamethasone
  - Anxiolytic: lorazepam



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### Specific management of nausea and vomiting based on etiology

#### 1) Endogenous or exogenous emetogenic toxins

- Haloperidol 0.5-2 mg as needed or two to four times per day orally, IV, or SC
- Prochlorperazine 5-10 mg as needed or three to four times per day orally or IV, or 25 mg suppository rectally as needed or two times per day
- Dexamethasone 8-20 mg per day in one or two doses orally or IV



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### Specific management of nausea and vomiting based on etiology

#### 2) Stimulation/ sensitization of vestibular apparatus

- Diphenhydramine 25-50 mg three to four times per day orally or IV
- Scopolamine 1.5-6 mg by transdermal patch every 72 hours, or 0.1-0.2 mg every 6-8 hours SC



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### Specific management of nausea and vomiting based on etiology

#### 3) Chemotherapy, radiation therapy to abdominal area

- Ondansetron 8 mg up to three times per day orally or IV
- Dexamethasone 8-20 mg per day in one or two doses orally or IV



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### Specific management of nausea and vomiting based on etiology

#### 4) Increased intra-cranial pressure

- Dexamethasone 8-20 mg in one or two doses daily, orally or IV

#### 5) Anxiety

- Diazepam 2-10 mg as needed or 2-3 times a day, orally, IV or SC
- Lorazepam 0.5-2 mg as needed or 3-6 times a day, orally, IV or SC
- Clonazepam 0.5-1 mg as needed or 1-2 times daily, orally



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### Specific management of nausea and vomiting based on etiology

#### 6) Gastritis/peptic ulcer

- Ranitidine 150 mg twice per day, orally, or 50 mg every 8 hours IV. Dosing frequency should be reduced for renal failure.
- Omeprazole 20-40 mg once or twice per day, orally

#### 7) Ileus/Gastroparesis

- Metoclopramide 10 mg four times per day orally or IV



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### Specific management of nausea and vomiting based on etiology

#### 8) Distension of liver due to neoplasm

- Dexamethasone 8-20 mg in one or two doses, orally or IV

#### 9) Bowel obstruction due to neoplasm

- Dexamethasone 8-20 mg in one or two doses, orally or IV
- Nasogastric tube or venting gastrostomy for drainage (if consistent with goals of care)
- Palliative surgery (if consistent with goals of care)



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### Specific management of nausea and vomiting based on etiology

#### 9) Constipation

- See treatment for constipation

#### 10) Adjuvants for nausea/vomiting of any cause

- Diphenhydramine 25-50 mg three or four times per day, orally or IV
- Scopolamine 1.5-6 mg transdermal every 72 hours, or 0,1-0,3 mg SC every 6-8 hours



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## Constipation / Diarrhea Assessment and Treatment

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### Objectives

*After the lecture, the trainees will be able to:*

1. Properly assess constipation and diarrhea in cancer and HIV/AIDS patients.
2. Develop a thorough differential diagnosis of constipation and diarrhea in cancer and HIV/AIDS patients.
3. Prescribe the best treatment for constipation and diarrhea in cancer and HIV/AIDS patients based on the most likely cause.

### Contents

#### 1. Constipation

##### 1.1. Definition:

- Discomfort associated with reduced frequency of bowel movements.
- Rome Criteria: 2 or more of the following:
  - straining at least 25% of the time
  - hard stools at least 25% of the time
  - incomplete evacuation at least 25% of the time
  - less than or equal to 3 bowel movements in a week.

##### 1.2. Differential Diagnosis of Constipation

- Medications:
  - Opioids (most common cause in cancer patients in rich countries)
  - Drugs with anticholinergic effects:
    - Anticholinergics like scopolamine
    - Anti-psychotics also used for nausea like haloperidol
    - Tricyclic anti-depressants also used for neuropathic pain like amitriptyline
  - Iron
  - Calcium channel blockers for hypertension
  - Antacids
  - Diuretics
  - Others
- Ileus
  - Recent surgery
  - Ascites
  - Medications

- Tumor infiltration of gut wall
- Mechanical obstruction
  - Tumor
  - Inflammatory bowel disease
  - Diverticulitis
- Metabolic abnormalities such as hypercalcemia
- Endocrine disease such as hypothyroidism or hyperparathyroidism
- Dehydration
- Immobility
- Spinal cord compression
- Autonomic dysfunction
  - Diabetes mellitus
  - Parkinson's disease
  - Multiple sclerosis
- Rectal or anal pain
  - Peri-anal abscess
  - Rectal fissure
  - Hemorrhoids

### 1.3. Approach to the patient with constipation:

- History:
  - Detailed bowel history, including correlation between bowel movements and medication changes
  - Diet and fluid intake
  - Medical history:
    - Medications
      - Opioids
      - Anticholinergic drugs
      - Other constipating drugs (see above)
    - Malignancy
    - Surgery
    - Pain in abdomen, rectum, anus
    - GI disease
    - Endocrine disease such as diabetes mellitus, thyroid or parathyroid disease
    - Nervous system disease
- Physical examination:
  - Rectal examination to rule out fecal impaction and assess for other rectal or anal pathology (abscess, fissure, external hemorrhoid)
    - **REQUIRED FOR ALL NEW PATIENTS WITH CONSTIPATION**
  - Abdominal exam to assess for bowel sounds, distention, tenderness, masses, ascites, surgical scars
  - Neurologic exam if disease of the central or peripheral nervous system is suspected
- Diagnostic testing:

- Testing should be directed by the history, physical examination, and resulting differential diagnosis. Possibly relevant tests might include:
  - Chemistries to assess for fluid or electrolyte derangements and for endocrine diseases such as diabetes and hypothyroidism
  - Abdominal radiographs (including an upright or decubitus film) or abdominal CT scan (if available) to assess for bowel obstruction, severe constipation or perforation (free air under the diaphragm). CT scan to assess for tumor or metastatic disease, diverticulitis, inflammatory bowel disease. CT scan or abdominal ultrasound to assess for ascites.
  - Colonoscopy is rarely needed.

#### 1.4. Treatment of Constipation (see **Table 1**)

- General measures
  - Establish what are “normal” bowel habits for a particular patient
  - Stop all unnecessary constipating medications
  - Treat any treatable underlying conditions as appropriate for the patient’s condition, prognosis, and goals of care. Possible interventions:
    - Hydrate if dehydrated
    - Correct metabolic derangements such as hypercalcemia
    - Treat endocrine disease such as hypothyroidism
    - Treat hemorrhoids, rectal fissure, or peri-anal abscess and any associated pain
    - Treat inflammatory bowel disease or diverticulitis
  - Encourage regular toileting
  - Increase activity, if appropriate and possible
  - Increased dietary fiber, if appropriate and possible
- Medications (see **Table 1** for doses)
  - Stimulant laxatives
    - Mechanism of action: irritation of the bowel resulting in increased peristaltic activity
    - Examples: senna, bisacodyl
  - Osmotic laxatives
    - Mechanism of action: water is drawn into the bowel lumen and/or held there, maintaining or increasing the moisture content and volume of stool. Larger stool volume stimulates peristalsis, and softer stool is easier to pass.
    - Requires good hydration.
    - Examples: lactulose, sorbitol, polyethylene glycol
  - Detergent laxatives (stool softeners)
    - Mechanism of action: facilitate the dissolution of fat in water and increase the water content of stool.
    - Examples: sodium docusate, sodium biphosphate enema
  - Prokinetic agents
    - Mechanism of action: stimulate the bowel’s myenteric plexus, and increase peristaltic activity and stool movement.

- Example: metoclopramide
- Lubricant stimulants
  - Mechanism of action: lubricate the stool and irritate the bowel, thus increasing peristaltic activity and stool movement.
  - Example: mineral oil (liquid paraffin)
- Large-volume enemas
  - Mechanism of action: soften stool by increasing its water content. They also distend the colon and induce peristalsis.
  - Example: warm water enemas
- Oral opioid receptor antagonists
  - Mechanism of action: reversal of effect of opioids on opioid receptors in the gut. Not well absorbed by the gut into the blood stream, so there usually is no effect on pain relief.
  - Example: oral naloxone

### 1.5. Constipation from opioids

- Occurs with all opioids
- Pharmacologic tolerance usually does not develop
- Dietary interventions alone are usually not sufficient
- Consider prescribing a bowel regimen for every patient taking an opioid frequently unless the patient has diarrhea that is not related to constipation.
- Typical treatment regimen:
  - Senna 1 tablet (or 8 ml of the liquid) orally twice per day for prophylaxis when initiating opioid therapy or for mild constipation.
  - If no bowel movement in any 48 hour period, increase senna to 2 tablets (or 15 ml) orally twice per day.
  - If no bowel movement in 24 hours, repeat rectal exam to rule out fecal impaction.
    - If impaction is present, manually disimpact as much as possible.
      - To soften stool to facilitate complete disimpaction, give mineral oil or paraffin enema.
      - If disimpaction is painful, stop and premedicate for pain before resuming disimpaction.
    - If no impaction is present, consider one or more of the following:
      - Mineral oil 10 – 30 ml orally at bedtime
      - Add an osmotic laxative such as lactulose 30 ml orally or per rectum 1 – 4 times per day.
      - Warm saline, sodium biphosphate, or paraffin oil enema once daily.
  - If still no bowel movement, consider an ORAL opioid antagonist such as naloxone. Starting dose is 1 mg orally 2 – 3 times per day. The dose may be doubled every 2 days up to a maximum dose of 12 mg/day in divided doses. Naloxone also can be given in a saline or tap water enema. **DO NOT GIVE IV OR SC.**

### 1.6. Management of Constipation in Children

- Children’s Senokot liquid:
  - 2-6 years: 2.5-3.75 ml once per day
  - 6-12 years: 5-7.5 ml once per day
- Glycerin suppository 1 suppository per rectum once per day
- Sorbitol 5-10 ml orally every two hours until stools
- Pediatric Fleets enema once per day as needed

\*\*\*\*\*

**Table 1:** Management of Constipation (from the Vietnamese Ministry of Health Guidelines on Palliative Care for patients with cancer, HIV/AIDS, and other life-threatening illnesses, 2006)

Causes	Treatment at Medical Settings (Normal Starting Dose)	Home-based Care
Opioid analgesic therapy	Assess for fecal impaction.  Manually disimpact as needed.  Senna 1-2 tablets or 15ml one to three times per day orally;  Bisacodyl 10 mg rectal suppository once or twice daily;  Sorbitol 15-30ml one to four times per day; or lactulose syrup 15-30ml one to four times per day  Mineral oil 5-30 ml at bedtime orally  Enema (sodium biphosphate or paraffin oil) once daily.  For severe cases: naloxone 1-2 mg every 8 hours orally.	Offer the patient fluids frequently.  Encourage the patient to eat a lot of vegetables and fruits, rich-fibre food such as sweet potatoes, pawpaw.  Drink one teaspoon of cooking oil before breakfast.  If it is hard for the patient to pass stool, apply grease or paraffin oil in the rectum. If the patient cannot do this, a caregiver can help (using gloves).  If the patient cannot pass stool for 5 days consecutively, a physician’s care is needed.
Other constipating medications: anticholinergics, iron, calcium channel blockers	Discontinue constipating drugs if possible.  Senna and/or sorbitol and/or cooking oil and/or bisacodyl and/or enema as above.	
Low-fiber diet	Bulk-forming agents and fluids	
Dehydration, inactivity	Rehydrate and mobilize only if consistent with patient’s goals	

## 2. Diarrhea

2.1. Definition: Increased frequency, liquidity, or volume of stools relative to the patient's usual bowel pattern.

2.2. Duration of diarrhea:

- Acute: 3 or more loose stools per day for 3 – 14 days
- Chronic: 3 or more loose stools per day for 14 days or more

2.3. Prevalence

- Infrequent among cancer patients except those receiving certain chemotherapy agents or radiation therapy to the abdomen. In either case, usually subsides within 1 – 2 weeks after therapy completed.
- Very common in HIV/AIDS patients (the most common gastrointestinal symptom).

2.4. Differential diagnosis of diarrhea

- General categories
  - Secretory diarrhea: excessive secretion of fluid into the gut lumen
    - Example: cholera
  - Osmotic diarrhea: abnormally high osmotic pressure in the gut lumen pulls in fluid
    - Examples: pancreatic insufficiency, celiac sprue, short-bowel syndrome, lactose intolerance, bacterial overgrowth, or osmotic laxative overuse
  - Mechanical diarrhea: mechanical forces generate excessively liquid or frequent stool
    - Partial bowel obstruction or fecal impaction
  - Diarrhea due to abnormally high motility: irritation of the gut causing excessive peristalsis
    - Example: irritant laxative overuse, bile acid diarrhea
  - Combination
- General causes
  - Gastrointestinal infections
  - Medications
  - Gastrointestinal bleeding
  - Bowel ischemia
  - Inflammatory bowel disease
  - Malabsorption syndromes
    - Pancreatic insufficiency
    - Short bowel syndrome (after surgical resection of stomach or bowel)
    - Enteropathy such as celiac disease (sprue)
    - Lactose intolerance
    - Bacterial overgrowth of small bowel causing fatty acid deconjugation and fat malabsorption
      - Diabetic autonomic neuropathy

- Scleroderma
- Partial bowel obstruction
- Constipation or fecal impaction (liquid stool is squeezed past immobile solid stool)
- Enteritis due to cancer therapy
- Malignancy
  - Bowel carcinoma
  - Villous adenoma
  - Islet cell tumors
  - Carcinoid
  - Bowel lymphoma
  - Kaposi's sarcoma of bowel
  - Bowel wall infiltration by tumor disrupting normal peristalsis
- Emotional stress
  - Anxiety
  - Irritable Bowel Syndrome
- Endocrine disease
  - Hyperthyroidism
  - Diabetes mellitus
  - Addison's Disease
- Pellagra (niacin deficiency)
- Alcoholism
- Bile acid diarrhea (after cholecystectomy or ileal resection)
- Cirrhosis
- Heavy metal poisoning (lead, mercury, arsenic)
- Infections responsible for diarrhea (especially in HIV disease)
  - Protozoa
    - Primarily in HIV infected patients:
      - Cryptosporidia: the most common pathogen and a major cause of morbidity with intractable watery diarrhea associated with malabsorption, profound weight loss, and malnutrition.
      - Entamoeba histolytica
      - Isospora belli
      - Cyclospora
      - Microsporidia
    - Giardia lamblia (due to drinking water tainted by sewage or stool)
  - Bacteria
    - Salmonella
    - Shigella
    - Campylobacter
    - Escherichia coli (including toxin-producing 0157:H7)
    - Vibrio cholerae
    - Other Vibrio species
    - Yersinia enterocolitica
    - Bacillus cereus

- Listeria
- Mycobacteria (primarily HIV infected patients)
  - Tuberculosis
  - Mycobacterium avium intracellulare (MAC)
- Bacterial toxins
  - Clostridium difficile causing pseudomembranous colitis
  - Clostridium perfringens
  - Staphylococcus aureus
- Viruses:
  - Enteric viruses such as rota, adeno, corona
  - Cytomegalovirus
  - Herpes Simplex
  - HIV
- Medications and other treatments that cause diarrhea
  - Antiretrovirals (ARVs):
    - All protease inhibitors (PIs), especially:
      - Nelfinavir
      - Lopinavir/ritonavir (Kaletra)
      - Saquinavir
    - Didanosine (ddI)
  - Antibiotics
    - Erythromycin (promotes GI motility)
    - Many antibiotics can cause *Clostridium difficile* colitis
  - Laxatives (when overused)
  - Caffeine
  - Quinidine
  - Cancer chemotherapeutic agents
    - Many cause enteritis. Diarrhea usually resolves within 1 – 2 weeks after treatment completed when mucosal surface of gut regenerates.
  - Radiation therapy to any body structure near the abdomen.
    - Causes enteritis. Diarrhea usually resolves within 1 – 2 weeks after treatment completed when mucosal surface of gut regenerates.

## 2.5. Approach to the patient with diarrhea

- History
  - Detailed bowel history, including:
    - Consistency, volume, frequency, color, and odor of stool
      - Examples:
        - Diarrhea due to fat malabsorption is greasy.
        - Cholera causes voluminous watery diarrhea.
        - Giardia diarrhea is particularly malodorous.
    - Presence of blood or black, tarry stool (melena)
    - Correlation between bowel movements and medication changes
    - Duration of diarrhea

- Diet
  - Food intolerances
  - Possible exposure to tainted water or food
  - Changes in diet
- Medical history:
  - Presence of abdominal pain, fever, bloating
  - Medications (including traditional medications)
  - History of surgery
  - History of malignancy
  - History of GI disease
  - History of endocrine disease
- Effect of diarrhea on the patient's daily activities
- Physical examination
  - Abdominal exam to assess for tenderness, distension, bowel sounds, masses, surgical scars
  - Rectal examination to rule out fecal impaction, assess for perineal pathology (per-anal abscess, anal fissure, external hemorrhoid, sacral decubitus), and check for occult blood
  - Assessment for volume depletion:
    - Orthostatic hypotension
    - Dry mucous membranes
    - Poor skin turgor
    - In babies: lack of tears when crying and no wet diapers for 3 or more hours.
- Diagnostic testing
  - Testing should be directed by the history, physical examination, and resulting differential diagnosis. Possibly relevant tests might include:
    - CBC with total lymphocyte count (or CD4 count if available)
    - Chemistries to assess for electrolyte derangements and volume depletion
    - Urine specific gravity to assess for volume depletion
    - Liver function tests
    - Fecal leukocytes
    - Stool fat
    - Stool ova and parasites
    - Stool AFB (BK)
    - If patient febrile, blood cultures from two sites
    - TB evaluation
    - Abdominal radiographs (including an upright or decubitus film) or abdominal CT scan to assess for bowel obstruction or severe constipation. CT to assess for tumor or metastatic disease, inflammatory bowel disease, bowel ischemia.
    - Colonoscopy, if available and appropriate for the patient's prognosis and goals, can enable diagnosis and effective treatment in some cases.

## 2.6. Treatment of diarrhea

- General interventions:
  - If possible and appropriate for the patient's goals, identify and remove or treat the underlying cause.
  - Stop all laxatives and any other medications that can cause diarrhea, if possible.
  - If the patient is volume depleted, and if appropriate for the patient's prognosis and goals, replace both fluids and electrolytes.
    - IV: normal saline or lactated Ringer's solution, any needed electrolytes
    - Oral: oral rehydration salts (ORS), porridge, fruit juice, soup in small amounts. Oral electrolytes as needed
  - Rule out a partial bowel obstruction or a fecal impaction before giving anti-motility medications.
  - Apply emollient ointment around anus to reduce damage to skin and mucous membranes.
  - Keep the patient clean including anal area and genitals.
  - Help the patient to maintain privacy and dignity.
  - Diet:
    - Do not force dying patients to eat if they have no appetite.
    - If patient wishes to eat, offer soft and rich-in-energy food in small amounts. Examples: rice and rice soup, peeled and cooked fruits, bananas, cooked cereals.
    - Avoid rough, fibrous, and high-fat food.
    - Avoid beverages that could exacerbate diarrhea such as alcohol and caffeine.
  - Instruct all caregivers to wash and disinfect hands after caring for the patient and after touching bed clothes.
- Specific interventions based on likely cause:
  - Bacterial or parasitic infection
    - Treat the underlying causes with appropriate antibiotics. This is one situation in which antibiotics may have a palliative use.
    - In patients with AIDS and CD4 count <100 with possible cryptosporidiosis or microsporidiosis, best treatment is ARV therapy. Diarrhea usually resolves when CD4 count exceeds 100.
    - Vietnam national guidelines for treatment of infectious diarrheas in HIV/AIDS patients is diagrammed in **Figure 1**.
  - Idiopathic, no response to antimicrobial treatment, radiation enteritis, cancer chemotherapy, short bowel syndrome, pancreatic insufficiency:
    - Make sure there is no fever, black or bloody stool, or mucous in stool, all of which could indicate infection.
    - Treat with an opioid:
      - Loperamide 4 mg orally, and then 2 mg after each loose stool up to a maximum of 16 mg per day.
        - Not well absorbed, so minimal drowsiness or pain relief.

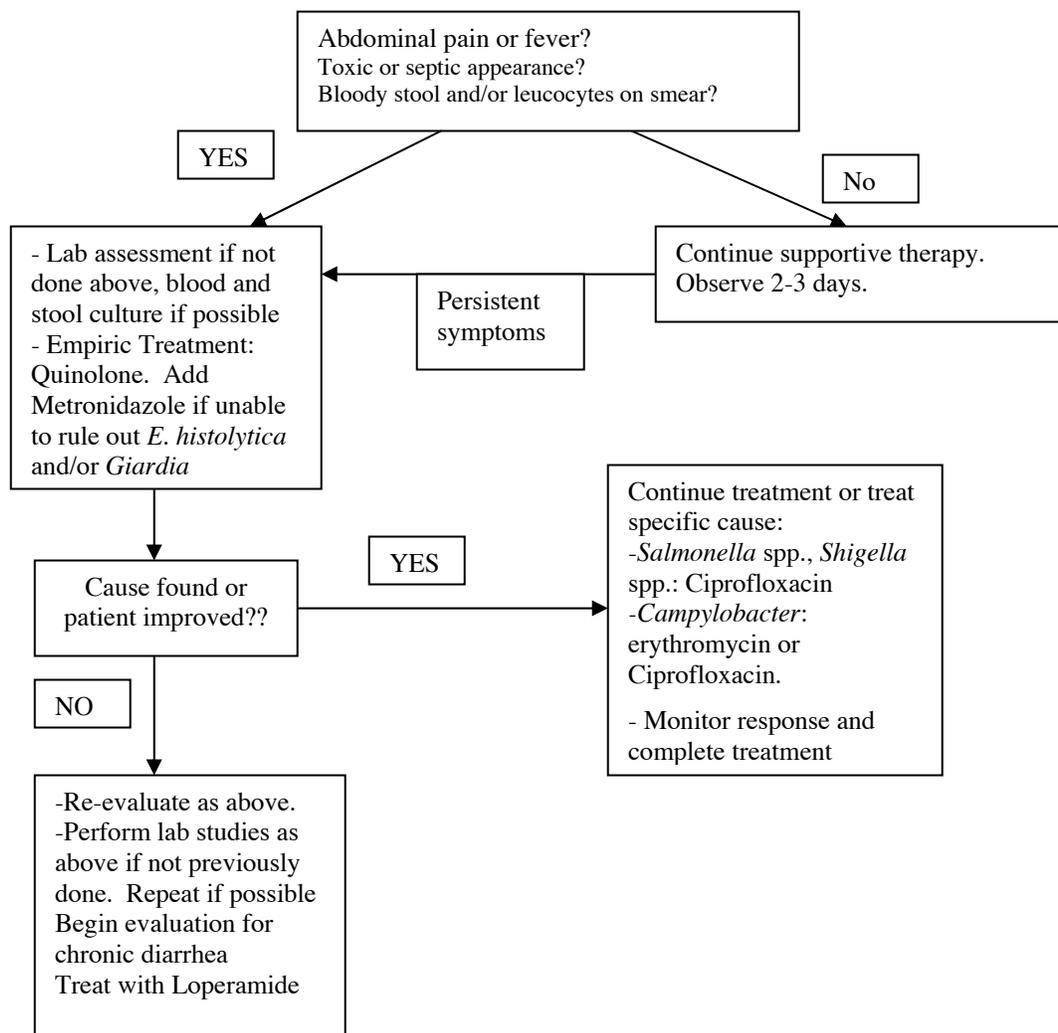
- Alternative opioids:
  - Diphenoxylate + atropine (5 mg + 0.05 mg) up to a maximum of four times per day as needed.
  - Paregoric (camphorated opium tincture) 5 – 10 ml orally up to a maximum of 4 times per day
  - Deodorized tincture of opium (10%) 0.3 – 0.6 ml orally up to a maximum of 4 times per day
  - Codeine (dose as for pain)
  - Morphine (dose as for pain)
- Other alternatives or adjuvants
  - Anticholinergics:
    - Scopolamine hydrobromide 3 – 6 mg by transdermal patch every 72 hours; or 0.8 mg orally every 8 hours; or 0.1 – 0.3 mg IV/SC up to every 4 hours as needed.
    - Hyoscyamine 0.125 – 0.25 mg orally or sublingually up to every 4 hours as needed.
  - Octreotide 100 – 200 mcg IV/SC every 8 hours (extremely expensive)
- Bile acid diarrhea
  - Cholestyramine 4 – 6 gm orally up to a maximum of 4 times per day
- Fecal impaction
  - Manual disimpaction and treatment for constipation
- Intermittent bowel obstruction due to tumor
  - Dexamethasone 8 – 20 mg per day in one or two doses orally or IV
- Laxative overuse
  - Stop or reduce dose of laxative
- Irritable bowel syndrome or mild medication-induced diarrhea
  - Bulk-forming agents such as psyllium
    - Use ONLY if patient able to drink lots of fluids
    - DO NOT USE if bowel obstruction or fecal impaction is possible or for severe diarrhea.
- Side effect of ARV therapy
  - If diarrhea is severe and infectious causes are unlikely, consider switching to a different ARV regimen, if possible.
- Management of diarrhea in children
  - Replete fluid and electrolytes with oral rehydration solution (ORS)
  - Loperamide
    - 13-20 kg: 1 mg three times per day orally as needed.
    - 20-30 kg: 2 mg two times per day orally as needed.
    - > 30 kg: 2 mg three times per day orally as needed.

**Figure 1:** Management of acute and chronic diarrhea in HIV/AIDS patients. From the Ministry of Health of Vietnam, Guidelines for Diagnosis and Treatment of HIV/AIDS (2005).

**Diarrhea**

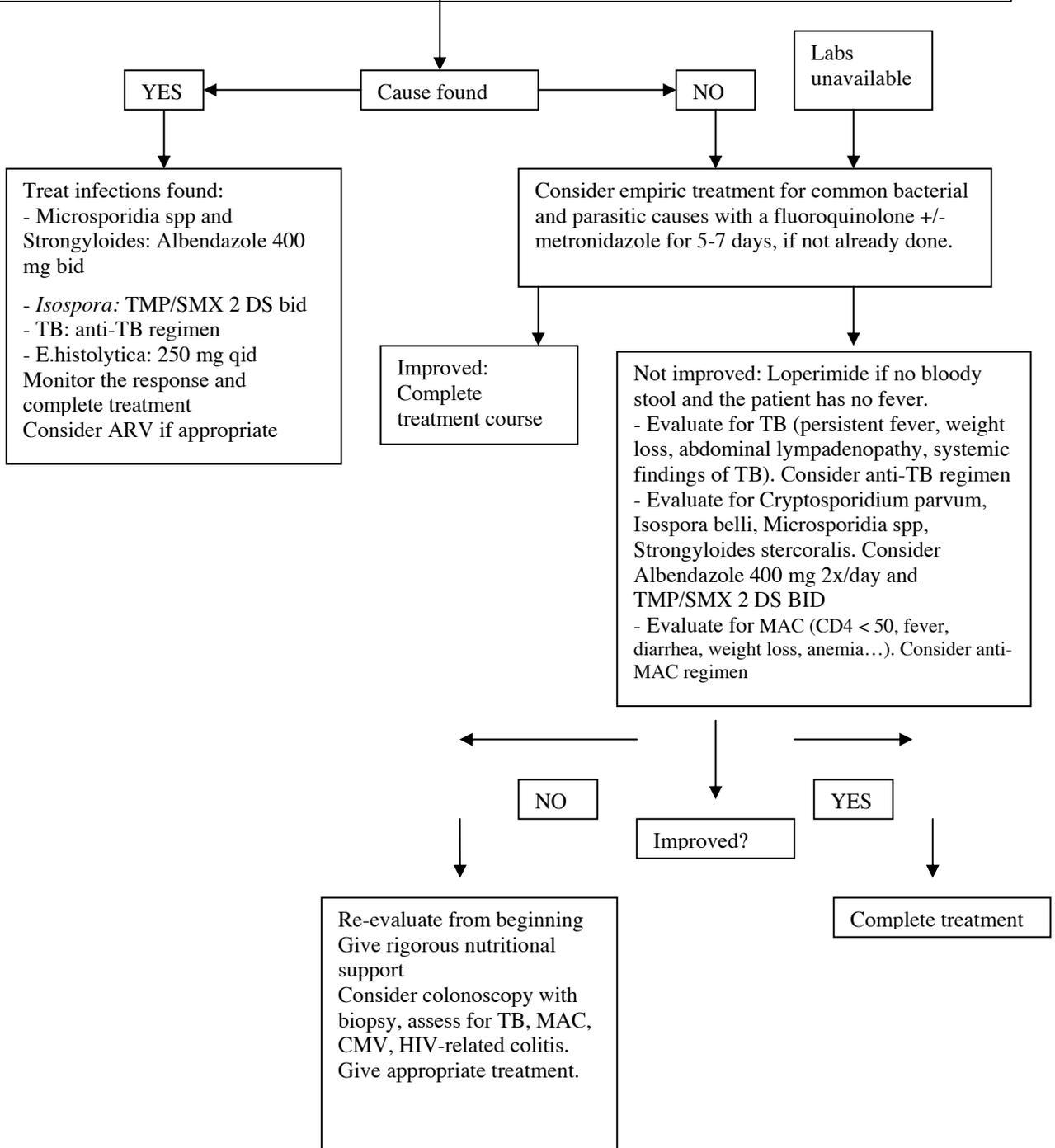
**a. Acute Diarrhea** (Presence of >3 loose stools/day < 14 days)

Common causes: *Salmonella*, *Campylobacter*, *Shigella*, *E.coli*, *Clostridium difficile*, *Giardia*, *Entamoeba histolytica*, medication side effect  
 History: Duration and severity of diarrhea, abdominal pain, presence of blood and mucous in stool, fever, weight loss, drugs administered before and after onset of diarrhea  
 Clinical exam: Fever, dehydration, nutritional status, other concurrent OIs, signs of abdominal perforation  
 Laboratory assessment CBC, stool evaluation for fecal leukocytes and erythrocytes, culture, ova and parasites (if possible)  
 Initial support: Give rehydration (oral and IV), nutritional support.



**b. Chronic Diarrhea** (Presence >3 loose stools/day  $\geq$  14 days)

Common causes: TB, Salmonella, Cryptosporidia, Microsporidia, Isospora, Cyclospora, MAC, HIV  
 History: Fever, abdominal pain, flatulence, anorexia, weight loss, character of stool.  
 Clinical exam: Dehydration, weight, nutritional status, immune status, other systemic signs.  
 Laboratory assessment: CBC with total lymphocyte count, stool evaluation for fecal leukocytes, ova and parasites, stool AFB, blood culture if fever, evaluation for TB  
 Initial support: Oral and IV hydration as needed, correct electrolyte imbalance, nutritional support



**Daily evaluation questions**

1. Which of the following drugs is NOT a common cause of constipation:

- a) Iron
- b) Drugs with anticholinergic effect
- c) Antiretroviral drugs**
- d) Opioids

2. Physical examination of every patient with constipation should include examination of the abdomen and of the \_\_\_\_\_ to rule out fecal impaction.                   **rectum**

3. For any patient taking an opioid who does not have diarrhea, consider giving a \_\_\_\_\_ to prevent constipation.                   **laxative or bowel regimen**

4. Constipation due to opioid therapy decreases with time as the patient becomes tolerant to opioid.                   **Yes    No**

5. Antiretroviral therapy may be both a cause and treatment for diarrhea in patients with AIDS.                   **Yes    No**

6. Constipation and fecal impaction can cause diarrhea.                   **Yes    No**

7. When a partial bowel obstruction has been ruled out and no other cause of diarrhea can be found, the most effective class of drug to treat diarrhea is \_\_\_\_\_.                   **opioids**

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## Constipation / Diarrhea Assessment and Treatment

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## Constipation



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## Constipation

- Definition
  - Constipation can be defined as “discomfort associated with reduced frequency of bowel movements.”
  - Rome Criteria: 2 or more of the following
    - straining at least 25% of the time
    - hard stools at least 25% of the time
    - incomplete evacuation at least 25% of the time
    - less than or equal to 3 bowel movements in a week



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## Causes of constipation

- Medications
  - Opioids
  - Anticholinergics
  - Iron
  - Calcium channel blockers
- Decreased motility
- Ileus
- Mechanical obstruction
- Metabolic abnormalities
- Spinal cord compression
- Dehydration
- Autonomic dysfunction



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## General management of constipation

- Determine what is “normal” for each individual patient
- Regular toileting
- Increase activity
- Good hydration
- Increased intake of dietary fiber



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## Pharmacological management of constipation

- Stimulant laxatives
  - Irritate the bowel and increase peristaltic activity
  - Examples: senna, bisacodyl
- Osmotic laxatives
  - Draw water into the bowel lumen, increase the moisture content of stool, increase stool volume.
  - Require good hydration
  - Examples: lactulose, sorbitol, polyethylene glycol (Forlax)
- Detergent laxatives (stool softeners)
  - Facilitate the dissolution of fat in water and increase the water content of stool
  - Examples: sodium docusate, sodium biphosphate enema



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## Pharmacological management of constipation

- Prokinetic agents
  - Stimulate the bowel's myenteric plexus and increase peristaltic activity and stool movement
  - Example: metoclopramide
- Lubricants
  - Lubricate the stool and irritate the bowel, thus increasing peristaltic activity and stool movement
  - Example: mineral oil (liquid paraffin)
- Large volume enemas
  - Soften stool by increasing its water content. They also distend the colon and induce peristalsis
  - Example: warm water enemas



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## Specific management of constipation based on etiology

1. Constipation secondary to opioids:
  - Assess for fecal impaction
  - Manually disimpact as needed
  - Senna 1-2 tablets or 15ml one to three times per day orally
  - Bisacodyl 10 mg rectal suppository once or twice daily



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## Specific management of constipation based on etiology

1. Constipation secondary to opioids: (cont'd)
  - Sorbitol 15-30ml one to four times per day orally or lactulose syrup 15-30ml one to four times per day
  - Mineral oil 5-30 ml at bedtime orally
  - Enema (sodium biphosphate or paraffin oil) once daily.
  - For severe cases: naloxone 1-2 mg every 8 hours orally.



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## Specific management of constipation based on etiology

2. Other constipating medications: anticholinergics, iron, calcium channel blockers
  - Discontinue constipating drugs if possible.
  - Senna and/or sorbitol and/or cooking oil and/or bisacodyl and/or enema as above.



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## Specific management of constipation based on etiology

3. Low-fiber diet
  - Bulk-forming agents and fluids
4. Dehydration, inactivity
  - Rehydrate and mobilize (if consistent with goals of care)



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## Diarrhea



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## Diarrhea

- Definition
  - Diarrhea can be defined as stools that are looser than normal and that may be increased in numbers
- Prevalence
  - Infrequent among cancer patients except those receiving chemotherapy or radiation to the abdomen
  - The most common gastrointestinal symptom in HIV/AIDS patients



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## Causes of diarrhea

- Infections
- Medications
- GI Bleeding
- Malabsorption
- Obstruction
- Overflow incontinence
- Stress



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## Pathogens responsible for diarrhea in HIV disease

- Protozoa (*Cryptosporidium*, *Giardia lamblia*, *Entamoeba histolytica*, *Isospora belli*, *Microsporidia*)
  - *Cryptosporidium* is the most common pathogen and a major cause of morbidity with intractable watery diarrhea associated with malabsorption, profound weight loss, and malnutrition.
- Bacteria (*Salmonella*, *Shigella*, *Campylobacter*, *E. coli*)
- Bacterial toxins (*Clostridium difficile*)
- Viruses (enteric viruses, CMV, HSV, HIV)
- *Mycobacterium avium intracellulare*



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## Treatments that cause diarrhea

- Antiretrovirals (ARVs): ddI, d4T, nelfinavir
- Antibiotics:
  - Macrolides (erythromycin)
  - Bacterial overgrowth
  - *Clostridium difficile*
- Laxatives (overuse)
- Cancer chemotherapy agents or radiation therapy to the abdomen
  - Causes enteritis that usually resolves 1 – 2 weeks after treatment stopped.



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## General management of diarrhea

- Counsel the patient or caregiver to:
  - Offer the patient ORS, porridge, soup in small amount
  - Offer soft and rich-in-energy food in small meals (if consistent with goals of care).
  - Avoid beverages that could exacerbate diarrhea such as alcohol or caffeine
  - Clean frequently, keep the genital and anal area clean.
  - Apply cream/ lotion around the anus to avoid damaging the skin.



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## General management of diarrhea

- Avoid drugs that increase peristalsis such as laxatives and metoclopramide
- Make sure the patient does not have partial obstruction or fecal impaction
  - Both can cause diarrhea
  - Both can occur in patients taking an opioid



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### Specific management of diarrhea based on etiology

1. Bacterial or parasitic infection
  - Treat the underlying causes with appropriate antibiotics.
    - This is one situation in which antibiotics may have a palliative use.
  - Replace fluids and electrolytes if this is consistent with the goals of care (may not be appropriate for dying patients)



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### Specific management of diarrhea based on etiology

2. Idiopathic, radiation enteritis, no response to antimicrobials, chemotherapy, surgical resection of bowel, pancreatic insufficiency
  - If no fever or blood or mucous in stool (which could indicate infection):
    - Loperamide 4mg orally, then 2 mg after each loose stool
    - Maximum of 16 mg per day
  - Alternative medications:
    1. Diphenoxylate + atropine (5 mg + 0.05 mg) up to a maximum of four times per day as needed.
    2. Paregoric (tincture of opium)
    3. May also consider bulking agents, cholestyramine, hyoscine, or octreotide.



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### Specific management of diarrhea based on etiology

3. Fecal impaction (causes repeated defecation)
  - Manual disimpaction and treatment for constipation
4. Intermittent bowel obstruction due to tumor
  - Dexamethasone 8-20 mg per day in one or two doses orally or IV



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### Specific management of diarrhea based on etiology

5. Laxative overuse
  - Stop or reduce dose of laxative
6. Side effect of ARV therapy
  - May require discontinuing or switching to a different ARV regimen, consult HIV specialist



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## Constitutional Symptoms Assessment and Treatment

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### Objectives

*After the lecture, the trainees will be able to:*

1. Develop a differential diagnosis and prescribe the best treatment for wasting.
2. Develop a differential diagnosis and prescribe the best treatment for fatigue.
3. Develop a differential diagnosis and prescribe the best treatment for fever and sweats

### Contents

#### 1. Introduction

1.1. Constitutional symptoms are a very common cause of discomfort and poor quality of life in patients with advanced HIV disease and cancer. They include:

- Weight loss and wasting (cachexia)
- Fatigue
- Fever and sweats

1.2. Efforts should be made to identify the cause of the symptom and to treat the underlying cause, if possible and if appropriate for the patient's goals.

1.3. Even when the underlying cause cannot be treated, it often is possible to relieve constitutional symptoms and thereby to improve the patient's quality of life.

#### 2. Wasting

2.1. Definitions:

- Anorexia: the loss of appetite.
- Wasting (cachexia): A state of general ill health characterized by malnutrition, body composition changes, weight loss, and weakness.
- Wasting syndrome associated with HIV (US CDC definition): Profound involuntary weight loss greater than 10% of baseline body weight plus either chronic diarrhea or chronic weakness and documented fever in the absence of concurrent illness or conditions other than HIV infection that could explain the findings.

2.2. Wasting syndromes:

- Often are accompanied by fatigue.

- Are associated with decreased quality of life and rapid disease progression.
- Occur frequently with:
  - Solid tumor malignancies
  - HIV/AIDS
  - Advanced heart, renal and hepatic failure
  - Advanced pulmonary disease

### 2.3. Differential diagnosis:

- Inadequate caloric intake due to:
  - Dysphagia or odynophagia due to:
    - Candida
    - CMV
    - HSV
    - Aphthous ulcers
  - Anorexia, nausea, or vomiting due to:
    - Infection
    - Malignancy
    - Medication side effect
    - Pain
    - Any other cause
  - Psychological problems
    - Depression
    - Anxiety
    - Grief
    - Loneliness
  - Social problems
    - Poverty (no enough money for food)
    - Alcohol or injection drug addiction
- Nutrient loss due to:
  - Chronic diarrhea
    - Infectious
    - Malabsorptive
    - Medication-related
    - Idiopathic (AIDS enteropathy)
- Metabolic dysregulation in setting of malignancy, infections (such as HIV and tuberculosis), chronic inflammation, or endocrine disease
  - Tumor factors such as LMF (lipid mobilizing factor), PIF (proteolysis inducing factor)
  - Host factors:
    - Secretion of cytokines such as TNF- $\alpha$ , IL-6
    - Changes in the neuroendocrine system
      - Reduced growth hormone secretion
      - Reduced testosterone secretion
      - Alterations in cortisol metabolism
  - Result is decreased protein synthesis, decreased lipogenesis, insulin resistance, muscle proteolysis, and other metabolic changes that cause wasting.

#### 2.4. Approach to the patient with wasting

- History: important points
  - Pattern of weight loss and gain over the past 6 months
  - Anorexia or early satiety
  - Difficulty with chewing or swallowing
  - Pain with chewing or swallowing
  - Nausea or vomiting
  - Diarrhea
  - Fever
  - Fatigue
  - Performance status (ability to work and to perform activities of daily living)
  - Financial problems (no money to buy food)
  - Psychological problems
  - Use of alcohol or injection drugs
  - Medications
  - Diet intake and patterns
    - Food diary
    - 24-hour recall
- Physical examination:
  - Weight
    - Unintentional weight loss of 5% over 1 month, 7.5% over 3 months, or 10% over 6 months is considered clinically significant.
    - Body Mass Index (BMI):  $\text{Weight (kg)} / \text{Height (m}^2\text{)}$ 
      - Patients with BMI < 20 are considered underweight
  - Fever
  - Evidence of vitamin deficiencies
  - Evidence of fat and muscle wasting
  - Hepatomegaly or splenomegaly
  - Edema
- Laboratory testing: Should be directed by symptoms such as odynophagia, vomiting, diarrhea, fever and by the effort to narrow the differential diagnosis.

#### 2.5. Treatment of wasting

- Assess for any reversible conditions (see Differential Diagnosis above) and treat or correct them if this is consistent with the patient's goals.
- Help the patient to increase caloric intake if this can be done comfortably and is consistent with the patient's prognosis and goals.
  - If the patient is very poor and cannot afford food or medication, seek social supports for the patient:
    - Clinics that provide free medications
    - Organizations that provide food
  - Encourage favorite foods
  - Nutritional supplements
  - Appetite stimulants
    - Corticosteroids:
      - Any benefit probably is temporary (up to a few months).

- Risk of serious side effects increases with time:
  - Increased immunosuppression and infection risk
  - GI bleeding
  - Adrenal insufficiency
  - Glucose intolerance
- Most useful in patients with a short prognosis, especially those who also have pain, nausea, fatigue, depressed mood, or other symptoms that steroids sometimes can relieve.
- Can be given just once per day in the morning to minimize sleep disturbance.
- Medications:
  - Prednisilone 20 – 80 mg orally in the morning
  - Dexamethasone 8 – 20 mg orally or IV once in the morning or in two divided doses
- Other drugs sometimes used:
  - Megestrol acetate (do not combine with steroid)
  - Testosterone (hypogonadism is common in men and women with HIV wasting, especially IDU)
- Occasionally artificial nutrition via nasogastric tube (temporary), tube gastrostomy or total parenteral nutrition.
  - Artificial nutrition rarely improves nutritional status in patients with advanced cancer or AIDS if disease-modifying treatment is ineffective or not available.

### 3. Fatigue (Asthenia)

3.1. Definition: the subjective perception of unusual or abnormal whole-body tiredness disproportionate to the level of activity or exertion, not relieved significantly by sleep or rest.

- Acute fatigue: Fatigue for < 1 month
- Chronic fatigue: Fatigue for  $\geq$  1 month

3.2. Fatigue affects up to 85% of AIDS patients and significantly limits activity and reduces quality of life.

3.3. Differential diagnosis

- AIDS (especially advanced disease)
- Other infections (especially tuberculosis and opportunistic infections)
- Malignancy
- Medication side effects (many classes including sedatives, antihistamines, anticholinergics, anticonvulsants)
- Dehydration
- Anemia
- Endocrine disease (such as hypothyroidism or hypogonadism)
- Major organ failure
- Metabolic derangements
- Malnutrition and wasting of any cause (see section on “Anorexia and Wasting” above)

- Depression
- Insomnia
- Multifactorial

#### 3.4. Approach to the patient with fatigue

- Remember that fatigue is a subjective sensation that is best rated by the person experiencing it.
- History:
  - Are you experiencing any unusual fatigue?
  - How intense is your fatigue on a scale of 0 – 10, if 0 is no fatigue and 10 is the most fatigue you can imagine?
  - Does your fatigue affect your daily activities and if so, how?
  - Are there activities you can no longer do because you are too tired?
  - When during the day is your fatigue worst?
- Physical examination and laboratory testing: Both should be directed at the most likely cause or causes of fatigue and by the effort to narrow the differential diagnosis. For example:
  - If you suspect HIV or TB or anemia, laboratory tests can be ordered.
  - If you suspect congestive heart failure, directed physical examination and tests such as echocardiogram can yield useful information.

#### 3.5. Treatment of Fatigue

- Treat underlying causes of weakness and fatigue as appropriate in light of the patient's goals. For example:
  - Blood transfusion and/or iron and/or B<sub>12</sub> and/or erythropoietin for anemia.
  - ARV therapy for AIDS
  - TB treatment for TB
  - Appropriate antibiotic for opportunistic infection
  - Thyroid hormone replacement for hypothyroidism
  - Antidepressant for depression
- Medications for fatigue of many causes:
  - Methylphenidate 2.5-5 mg orally at 8 AM and at lunch time. Doses can be increased as needed. Maximum 60 mg/day.
    - Watch for anxiety or agitation (psychostimulant).
    - Use with caution in patients with tachyarrhythmias.
    - Also can relieve depression much faster than selective serotonin re-uptake inhibitors (SSRIs) or tricyclic antidepressants (TCAs). Thus, very useful for depressed patients with short life expectancy (days or weeks).
    - Effective for relief of sedation due to opioid analgesics.
    - Do not give later than 2PM (interferes with sleep)
  - Prednisolone 20-80 mg orally in the morning
  - Dexamethasone 8 – 20 mg orally or IV once in the morning or in two divided doses

#### 3.6. Treatment of fatigue in children

- Treat underlying causes when appropriate
- Prednisolone 1 mg/kg once or twice per day orally with food

#### 4. Fever and Sweats

4.1. Fever and sweats are a common cause of discomfort and poor quality of life in patients with advanced cancers and AIDS.

4.2. Differential diagnosis of fever:

- In cancer patients:
  - Infection
  - Medication side effect
  - Directly related to the malignancy in 5-7% of patients
- In HIV-infected patients:
  - Opportunistic infections (such as TB or MAC)
  - HIV associated malignancies
  - Medication side effects. Examples:
    - Cotrimoxazole and other sulfa drugs
    - Abacavir and other ARVs
    - Amphotericin B
  - Endocrine disease
  - Autoimmune disorders
  - HIV virus itself

4.3. Differential diagnosis of sweats:

- Fever of any cause
- Sweats without fever:
  - Some infections
  - Malignancy
  - Endocrine disease
  - Medication side effect. Examples:
    - Opioids
    - Withdrawal from opioids

4.4. Treatment of fever and sweats:

- Treat the underlying cause of fever or sweats if possible and if consistent with the patient's goals.
- For fever:
  - Maintain body temperature within a comfortable range.
    - Not all fevers cause discomfort.
  - Paracetamol 500-1000 mg every 6 hours orally or suppository as needed. Do not exceed 4000 mg per day. Reduce the dose in patients with liver disease.
  - Alternatives or adjuvants to paracetamol:
    - Choline magnesium trisalicylate 500-1000 mg two or three times daily orally as needed
      - No effect on platelets and less GI toxicity than other NSAIDS
    - Ibuprofen 200-600 mg every 6 hours orally as needed
      - For severe, unremitting fever, can be given with paracetamol in a staggered fashion with the patient receiving one or the other every 3 hours.

- Give GI protection with proton pump blocker such as omeprazole or histamine type 2 blocker such as ranitidine when giving an NSAID frequently.
- For severe persistent fever in a dying patient: dexamethasone 4-20 mg per day orally or IV in the morning or in two divided doses.
  - Also can relieve fatigue, pain, and nausea and improve mood.
- Provide oral or intravenous hydration and electrolyte replacement if consistent with the goals of care.
- For sweats with or without fever:
  - Keep the patient warm and dry to prevent chills and shivering.
  - NSAIDS as above
  - Scopolamine 1.5 – 6 mg transdermal patch every 72 hours or 0.1 – 0.3 mg IV or SC every 4 hours as needed.
  - Cimetidine 400 – 800 mg orally twice per day

### Daily evaluation questions

1. Constitutional symptoms are an insignificant cause of discomfort in HIV/AIDS and cancer patients and do not require treatment.           **Yes    No**
2. The most common cause of wasting due to nutrient loss is \_\_\_\_\_.           **diarrhea**
3. Which of the following statements about corticosteroid therapy is true:
  - a. When it is effective against anorexia, fatigue, or fever, the good effect usually last for years if the patient survives that long.
  - b. Side effects may occur early but usually diminish with time.
  - c. It can relieve not only constitutional symptoms but also neuropathic pain, nauseas, and depressed mood.**
  - d. The best time to give it is at bedtime.
4. When a cancer or AIDS patient has discomfort from severe, unremitting fevers, an NSAID can be added to paracetamol therapy.           **Yes    No**

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## Constitutional Symptoms Assessment and Treatment

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## Constitutional Symptoms

1. Weight loss and wasting (cachexia)
2. Fatigue
3. Fevers and sweats



2



## Objectives

- To learn to develop a differential diagnosis of wasting, fatigue, and fever / sweats in HIV/AIDS and cancer patients.
- To learn the best treatments for wasting, fatigue, and fever /sweats based on the differential diagnosis.



3



## Weight Loss and Wasting (Cachexia)



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## Definitions

- Anorexia: the loss of appetite
- Wasting (cachexia): A state of general ill health characterized by malnutrition, non-intentional weight loss and weakness.
- Wasting syndrome associated with HIV (US CDC definition): Profound involuntary weight loss greater than 10% of baseline body weight plus either chronic diarrhea or chronic weakness and documented fever in the absence of concurrent illness or conditions other than HIV infection that could explain the findings.



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## Wasting Syndromes

- Frequently accompanied by fatigue
- Associated with decreased quality of life and rapid disease progression
- Occur often with:
  - Solid tumor malignancies
  - HIV/AIDS
  - Advanced heart, renal, and hepatic failure
  - Advance pulmonary disease



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## Differential Diagnosis

- Inadequate caloric intake due to:
  - Dysphagia
    - Candida
    - CMV
    - HSV
    - Aphthous ulcer
    - Head and neck cancer
  - Anorexia, nausea or vomiting due to:
    - Infection
    - Malignancy
    - Medication side effect
    - Pain
    - Any other cause
  - Psychological problems
    - Depression
    - Anxiety
    - Grief
    - Loneliness
  - Social problems
    - Poverty (not enough money for food)
    - Alcohol or injection drug use




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## Differential Diagnosis

- Nutrient loss due to:
  - Chronic diarrhea
    - Infectious
    - Malabsorptive
    - Medication-related
    - Idiopathic (AIDS enteropathy)




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## Differential Diagnosis

- Metabolic dysregulation in setting of malignancy, infection (eg. HIV, TB), chronic inflammation or endocrine disease
  - Tumor factors:
    - LMF (lipid mobilizing factor)
    - PIF (proteolysis inducing factor)
  - Host factors:
    - Cytokines such as TNF- $\alpha$ , IL-6
    - Changes in the neuroendocrine system such as reduced growth hormone or testosterone secretion and alteration in cortisol metabolism
  - Result is decreased protein synthesis, decreased lipogenesis, insulin resistance, muscle proteolysis, and other metabolic changes that cause cachexia.




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## Approach to the Patient with Wasting

- History:
  - Pattern of weight loss & gain over 6 months
  - Symptoms: Anorexia, difficulty or pain with eating, nausea, vomiting, diarrhea, fever
  - Psycho-social problems (poverty, EtOH, IDU)
  - Diet
- Physical Exam
  - Body Mass Index (BMI): weight (kg) / height (m)<sup>2</sup>
- Lab Testing:
  - Guided by symptoms and effort to narrow differential diagnosis




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## Treatment of Wasting

- Assess for and treat reversible conditions if consistent with goals of care
- Help patient to increase caloric intake if this can be done comfortably and if consistent with prognosis and goals of care:
  - If patient is poor
- Educate, provide emotional support
- Encourage favorite foods, nutritional supplements
- Steroids may stimulate appetite, but the effect is usually limited
- Artificial nutrition via nasogastric tube or gastrostomy rarely improves nutritional status in advanced cancer or AIDS if disease-modifying therapy is ineffective.




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## Fatigue




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## Fatigue (Asthenia)

- Definition:
  - The subjective perception of unusual or abnormal whole-body tiredness disproportionate to the level of activity or exertion, not relieved significantly by sleep or rest.
- Affects up to 85% of AIDS patients
  - Limits activity and reduces quality of life



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## Differential Diagnosis

- Malignancy
- Advanced AIDS
- Other infections (especially TB and OIs)
- Dehydration
- Anemia
- Major organ failure
- Endocrine disease (hypothyroidism, hypogonadism)
- Medications
- Wasting syndrome
- Depression
- Insomnia



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## Cancer-related fatigue

- Prevalence
  - Most surveys suggest prevalence of >50% among patients undergoing active chemotherapy
  - Prevalence can be >80% in some populations receiving chemotherapy, immunotherapy, and radiotherapy
  - Prevalence >75% in patients with advanced cancer



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## Approach to the Patient with Fatigue

- History:
  - Intensity (0 – 10 scale)
  - Effect on daily activities
- Physical exam & lab testing
  - Directed by most likely cause.
  - Example, if HIV, TB, anemia, or congestive heart failure suspected, rule out these diagnoses.



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## Treatment of fatigue

- Treat underlying causes of weakness and fatigue appropriate to patient's goals
- Symptomatic treatment:
  - Methylphenidate 2.5-5 mg orally at 8 AM and at lunch time.
  - Prednisilone 20-80 mg orally per day; or Dexamethasone 8-20 mg per day in one or two doses orally or IV.



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## Fevers/Sweats



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## Epidemiology

- Fever (pyrexia) is a common feature of terminal cancer and AIDS
- In cancer patients, fever is usually attributed to infection or drugs. It is directly related to the malignancy in only 5-7% of the cases.



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## Fever in HIV

- In HIV disease, fever may be due to:
  - Opportunistic infections such as TB or MAC
  - HIV associated malignancies
  - Drug side effects (for example, cotrimoxazole)
  - Endocrine dysfunction
  - Autoimmune disorders
  - HIV virus itself



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## Differential Diagnosis of Sweats

- Fever of any cause
- Sweats without fever:
  - Some infections
  - Malignancy
  - Endocrine disease
  - Medication side effect
    - Opioid
    - Withdrawal from opioid



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## Treatment of Fever & Sweats

- Treat the underlying cause of fever if possible and if consistent with the patient's goals.
- For fever:
  - Maintain comfortable body temperature (not all fevers are uncomfortable)
- For sweats with or without fever:
  - Keep patient warm and dry to prevent chills.



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## Pharmacological treatment of fever & sweats

- Paracetamol 500-1000 mg every 6 hours orally or per rectum as needed. Max: 4000 mg per day. Reduce the dose in patients with liver disease.
- Alternatives:
  - Choline magnesium trisalicylate 500-1000 mg two or three times daily orally;
  - Ibuprofen 200-600 mg every 6 hours orally as needed.
- For severe persistent fever in a dying patient: dexamethasone 4-20 mg per day in one or two doses orally or IV
- Oral or IV hydration only if consistent with goals of care.



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## Dyspnea Case Discussion

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### Objectives

*After the lecture, the trainees will be able to:*

1. Correctly apply principles for proper diagnosis and treatment of dyspnea.
2. Assist a dying patient to complete important tasks such as planning for the well-being and future of children and saying good-bye to family members.

### Contents

#### Dyspnea Case: Ms. Huyen

Ms. Huyen is a 32 year old woman with advanced AIDS. She is a widow who lives with her two young children and her elderly parents-in-law in Hanoi. Her parents and siblings live in Bac Giang Province and do not know that she has HIV.

Ms. Huyen took one or two antiretroviral drugs intermittently in 2004 and 2005. One year ago, she began taking a 3-drug ARV regimen prescribed at your hospital's OPC, but her CD4 count did not increase and now is falling. It is now 16. Six months ago, she developed cryptococcal meningitis and was treated successfully with fluconazole. She then developed a diffuse rash, and cotrimoxazole prophylaxis was discontinued. Her HIV appears to be resistant to all available ARVs. She is cachectic and weak and has begun to lose vision in her right eye.

Two months ago she began to have fever, cough, and worsening dyspnea. Chest radiograph at that time revealed patchy consolidation. Examination of her sputum smear revealed no AFB, but treatment for active pulmonary tuberculosis was started based on clinical suspicion. Her fever and shortness of breath did not improve. Treatment for pneumocystis jiroveci pneumonia with cotrimoxazole was then started, but her condition continued to worsen. She was admitted to the hospital, treated with prednisone 40 mg orally twice per day, and her cotrimoxazole was changed from oral to intravenous at the standard dose. Sputum cultures have not revealed a likely bacterial or fungal pathogen.

Currently, her vital signs are as follows:

Temperature 39. Heart rate 110. Blood pressure 92/65. Respiratory rate 36. Oxygen saturation 90% while receiving 5 l/minute of supplemental oxygen by nasal cannula.

She is able to speak only in short sentences and complains of distressing shortness of breath that prevents her from sleeping. She is extremely anxious.

Physical examination is remarkable for cachexia, sweating, reduced breath sounds and dullness to percussion over her left chest, tachycardia without murmurs and white retinal lesions consistent with CMV retinitis. When she gets out of bed to use the toilet, she becomes cyanotic.

Laboratory studies are as follows:

WBC 2.1

HCT 18

Creatinine 0.8

- 1. What is the differential diagnosis of her dyspnea?**
- 2. How would you treat her initially?**
- 3. Would it be equally effective to treat her dyspnea and anxiety with a benzodiazepine? Why or why not?**

After one dose of morphine 4 mg IV, Ms. Huyen's respiratory rate falls to 20. She says that she feels more comfortable and then immediately goes to sleep. Her blood pressure is 82/60.

- 4. Do you think you gave her too much morphine? Why or why not?**

Ms. Huyen feels much better on her morphine regimen. You ask her about her understanding of her illness and what she expects will happen in the future. She says that she knows she is dying and becomes tearful. She says she does not know what will happen to her young children since her parents-in-law are very old.

- 5. How might you respond?**

Ms. Huyen receives a blood transfusion and therapeutic thoracentesis. She continues to take a low dose of morphine around the clock that controls her dyspnea. Her parents come from Bac Giang, and she has a tearful reunion with them. They are shocked that she has AIDS and is dying, but after you explain that she badly needs their understanding and support, they focus on caring for their daughter. Arrangements are made for the children to live with Ms. Huyen's parents and brother's family who live together in Bac Giang after Ms. Huyen dies. Ms. Huyen asks that some photos and jewelry be put in two boxes, one for each of her children, and she writes a letter to each of them to be placed in the boxes. The children are brought to see her.

A few days later, Ms. Huyen suddenly develops severe respiratory distress. Her respiratory rate is 40 and she is unable to speak. You give morphine 4 mg IV, but it has no effect. You repeat the dose in 15 minutes and again in 30 minutes, but her condition does not change.

**6. How would you treat her now?**

You give 2 more morphine boluses of 4 mg and then 3 boluses of 8 mg at 15 minute intervals. Her respiratory rate then slows to 25. She is now quite sleepy but still opens her eyes when her name is called. After one more bolus of 8 mg, her respiratory rate is 18, and she seems comfortable. Her parents are very relieved that she is not suffering. One hour later, Ms. Huyen dies.

- 7. Do you think that you caused Ms. Huyen's death by giving morphine? If so, do you think it was wrong to give as much morphine as you did? Do you think that the morality of giving morphine depends on the physician's intention? For example, does it make any difference morally if a physician intends to hasten a patient's death or simply intends to relieve suffering with the knowledge that hastening death may be an unintended side effect?**



## Dyspnea Case Discussion

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### Facilitator's Guide

#### 1. What is the differential diagnosis of her dyspnea?

- Drug resistant TB
- Pneumocystis jiroveci pneumonia
- Unidentified bacterial, fungal or viral pneumonia
- Pleural effusion
- Severe anemia
- Pulmonary embolus

#### 2. How would you treat her initially?

- If she is opioid naïve, give morphine 5 – 10 mg orally every 30 minutes or 2 – 4 mg IV every 15 minutes until she is more comfortable.
- If she already is taking an opioid and probably has some tolerance to opioid, start with a higher dose and/or double the initial dose if it is not effective.
- Once she is more comfortable, give a dose every 4 hours around the clock with additional rescue doses for breakthrough dyspnea. For example, if he became comfortable after 1 or 2 doses of morphine 5 – 10 mg orally or 2 – 4 mg IV, give the same dose every 4 hours around the clock and 5% to 10% of the 24 hour dose as a rescue dose every 30 minutes to 3 hours as needed.
- Consider therapeutic thoracentesis if chest radiograph reveals a free-flowing pleural effusion.
- Consider transfusion of red blood cells

#### 3. Would it be equally effective to treat her dyspnea and anxiety with a benzodiazepine? Why or why not?

- No because benzodiazepines do not treat dyspnea. The most important cause of her anxiety probably is her dyspnea. Therefore, if you treat her dyspnea with an opioid, her anxiety probably will be relieved as well.
- For patients with chronic anxiety, a benzodiazepine can be added to the opioid regimen.

#### 4. Do you think you gave her too much morphine? Why or why not?

- If she is easily arousable and her respiratory rate is no lower than 15 breaths per minute, she has not received too much morphine. She is sleeping because she is exhausted.
- As the goal of care shifts toward comfort, the blood pressure becomes less relevant. In some cases, you could consider giving a blood transfusion (packed red blood cells) or intravenous fluid such as normal saline or lactated Ringer's solution to support the blood pressure.

**5. How might you respond?**

- Ask what she fears most.
- Regardless of her reply, assure her that any physical discomfort can be treated.
- Ask what she would like for her children.
- Ask if she would like to see her parents and siblings.
- Ask if you can help arrange for her parents or siblings to come and to explain the situation to them.
- Ask if she would like to leave a legacy such as a “memory box” for her children.
- Ask if there are other ways you might be helpful.

**6. How would you treat her now?**

- Continue giving intravenous morphine every 15 minutes until she is comfortable. If another 1 – 2 doses have no effect, double the dose and continue giving a dose every 15 minutes.
- In addition, begin a continuous intravenous infusion of morphine at ~ 2 mg/hour. The rate should be titrated to the patient’s comfort. However, breakthrough dyspnea (or pain) ALWAYS SHOULD BE TREATED WITH MORPHINE BOLUSES, NOT WITH AN ADJUSTMENT IN THE INFUSION RATE. If more than one rescue dose is needed in any 2-hour period, the second rescue dose should be given and the infusion rate increased by 33%.
- Inform the patient’s family and the nursing staff that Ms. Huyen may be dying and that treatment now is focused on making her comfortable.

**7. Do you think that you caused Ms. Huyen's death by giving morphine? If so, do you think it was wrong to give as much morphine as you did? Do you think that the morality of giving morphine depends on the physician's intention? For example, does it make any difference morally if a physician intends to hasten a patient's death or simply intends to relieve suffering with the knowledge that hastening death may be an unintended side effect?**

- Ms. Huyen’s disease killed her, not you. Studies have revealed no evidence that aggressive symptom management hastens death.
- As long as it is agreed that the goal of care is comfort and the physician’s intention is only to make the patient comfortable, it is not immoral to provide morphine or other medications for comfort even at the risk of foreseeable but unintended side effects such as sedation, respiratory depression, and a hastening of death.

## Gastro-intestinal Symptom Case Discussion

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### GI Case: Mr. Binh

Mr Binh is a 52-year-old delivery man. He has been healthy except for dyspepsia for many years. About six months ago, he began losing weight and noticing that he could not eat as much as previously. He now has lost 7 kg. Mr. Binh also began to tire easily, to become breathless when lifting boxes of electrical goods he is delivering, and to appear pale. Recently, he developed constant, aching epigastric abdominal pain. He went to the outpatient clinic at the hospital where it was found that his hemoglobin was 7.4, his MCV was 71, and his SGPT was slightly elevated. A stool test revealed occult blood. Mr Binh was admitted to the hospital for further evaluation and given paracetamol with codeine for pain with fair relief.

Gastroscopy revealed an ulcerated mass in the gastric antrum that was biopsied. The pathology result was poorly differentiated adenocarcinoma in the setting of atrophic gastritis and intestinal metaplasia. A CT scan showed the gastric mass, enlarged lymph nodes around the stomach, and multiple metastases in the liver. The largest live metastasis was 4 x 3 cm. The cancer was determined to be inoperable (Stage IV).

Mr. Binh was treated with a blood transfusion, and he continued taking paracetamol with codeine around the clock and as needed for pain. During his time in the hospital, he became nauseated and vomited his food occasionally. He was sent home and began palliative chemotherapy with 5-FU every two weeks as an outpatient.

Over the next four weeks, Mr. Binh's nausea did not improve. He vomited once or twice a day and sometimes was unable to eat.

### 1. What is the differential diagnosis of Mr. Binh's nausea and vomiting?

### 2. What aspects of the history, physical examination, or test results would help you to distinguish between the possible diagnoses and to choose the most likely one or ones?

Mr. Binh reports that his nausea has been constant but becomes worse for the 48 hours after chemotherapy. He vomits mostly food and usually after forcing himself to eat. He reports only mild constipation and anxiety and no change in his pain. He denies taking an NSAID or drinking alcohol recently. Neurologic examination is unremarkable. Basic blood chemistry studies are normal.

You treat him with haloperidol 0.5 mg orally every 8 hours and 0.5 – 1 mg orally every 4 hours as needed for breakthrough nausea. On this regimen his nausea resolves. You also prescribe ondansetron 32 mg IV and diphenhydramine 50 mg IV with his next chemotherapy and ondansetron 8 mg orally every 8 hours for 48 hours after chemotherapy. You also advise him to take senna 2 tablets orally at bedtime.

**3. What do you think was the main cause or causes of his nausea?**

When Mr. Binh comes for his next chemotherapy, he reports that he has minimal nausea but continues to vomit after every attempt to eat. His emesis is now sometimes bilious. He is able to keep down most clear liquids and his pills. He has not taken the senna. He also reports worsening diffuse abdominal pain that interrupts his sleep and that is no longer relieved by the maximum daily dose of paracetamol with codeine. In addition, he complains of new abdominal distention. His only bowel movements in the past two weeks have been three episodes of watery diarrhea that he was unable to control and that caused him to soil his pants. He is very upset about this.

On exam, his belly is soft but tender primarily in the epigastric area, right upper quadrant, and left lower quadrant. There is no rebound tenderness or guarding. His abdomen is moderately distended. There are normal bowel sounds. Neurologic examination is again unremarkable. CT scan of the abdomen reveals liver metastases that are increasing both in size and number, little change in the gastric mass, a large distended stomach containing fluid, thickening of the stomach wall, a small amount of ascites, and a large amount of stool in the colon and rectum.

**4. What is your diagnosis (or diagnoses), and how would you respond?**

**5. What is the relative contra-indication to giving metoclopramide with haloperidol?**

Mr. Binh's pain is relieved quickly with IV morphine. Rectal examination reveals impacted stool, and this is removed manually. He has several large bowel movements over the next two days and feels much better. However, he continues for two days to vomit food and bilious material frequently after eating. Both Mr. Binh and his family are very concerned that he is losing weight and becoming very weak because he is not receiving any nutrition.

**6. How would you treat Mr. Binh in this situation, and what would you tell him and his family?**

## Gastro-intestinal Symptom Case Discussion

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### Facilitator's Guide

#### 1. What is the differential diagnosis of Mr. Binh's nausea and vomiting?

- Endogenous or exogenous toxins stimulating the CTZ:
  - o Chemotherapy (5-FU)
  - o Opioid (codeine)
  - o Tumor toxins
  - o Metabolic derangement such as hyponatremia
- Sensitization of the vestibular system
  - o Opioid
- Noxious stimulation of the GI tract (Cranial Nerves IX or X)
  - o Mediated by 5-HT<sub>3</sub> receptors on vagal afferents
    - Serotonin release due to chemotherapy
  - o Mediated by mechanoreceptors
    - Constipation from:
      - Opioid analgesic
      - 5-HT<sub>3</sub> receptor blocker (ondansetron) given with chemotherapy
      - Dehydration
    - GI tract obstruction
      - Mechanical obstruction:
        - o Gastric outlet obstruction due to tumor
        - o Small bowel obstruction due to tumor
        - o Large bowel obstruction due to tumor
        - o Squashed stomach syndrome (mechanical compression and obstruction of the stomach)
        - o Severe constipation / obstipation
      - Functional obstruction
        - o Linitis plastica with gastroparesis
    - Liver capsule stretch due to tumor
  - o Mediated by chemoreceptors
    - Mucositis from chemotherapy
    - Gastritis from ethanol or NSAID
    - Cardiac ischemia
- CNS problems
  - o Brain metastasis with increased intracranial pressure
  - o Carcinomatous meningitis
  - o Anxiety
  - o Severe pain

**2. What aspects of the history, physical examination, or test results would help you to distinguish between the possible diagnoses and to choose the most likely one or ones?**

- If the nausea occurs only at the time of chemotherapy or within a few days afterwards, this might indicate a side effect of chemotherapy.
- If the nausea began when he started taking codeine, this might indicate a side effect of the opioid.
- If he is hyponatremic or hypercalcemic or has renal or hepatic failure, these might be at least a partial cause of the nausea.
- If the patient has not moved his bowels well or at all for days, constipation probably is part of the problem.
- If he vomits shortly after eating without nausea, this might indicate a gastric outlet obstruction, “squashed stomach syndrome,” proximal small bowel obstruction, or linitis plastica with gastroparesis.
- If he vomits bile, this might indicate a small bowel obstruction or linitis plastica with gastroparesis.
- If he vomits fecal matter, this might indicate large bowel obstruction.
- If a repeat CT scan shows that the liver metastases are growing rapidly, or if there is right upper quadrant pain or a large and tender liver, this might indicate that liver capsule stretch is causing or contributing to the problem.
- If the patient is drinking alcohol or taking NSAIDS, these might be causing or exacerbating gastritis.
- If neurological examination reveals new focal deficits, or if a CT scan reveals brain metastases, these are likely contributing to the problem.
- If the patient appears very anxious or reports severe pain, this may be contributing to the problem.

**3. What do you think was the main cause or causes of his nausea?**

- Opioid
- Possibly emetogenic factors produced by the tumor or by an inflammatory response to the tumor.

**4. What is your diagnosis (or diagnoses), and how would you respond?**

Likely diagnoses:

- Chemotherapy treatment failure.
- Increasing pain likely due to:
  - o Enlarging liver metastases
  - o Constipation
  - o Inability to adequately absorb oral medications
  - o A combination of the above
- Gastroparesis due to linitis plastica or possibly gastric outlet or proximal small bowel obstruction.
- Constipation and possible fecal impaction with resultant diarrhea.

## Treatment:

- Admit to the hospital.
- Discontinue chemotherapy.
- Discontinue paracetamol and codeine.
- Morphine 2 mg IV or SC every 4 hours AND 2 mg IV or SC every 2 hours as needed for breakthrough pain.
- Dexamethasone 20 mg IV every morning and metoclopramide 10 mg IV four times per day before meals and at bedtime to treat presumed linitis plastica. Steroid also may help to reduce malignant bowel obstruction.
- Rectal examination with manual disimpaction if needed.
- Bisacodyl 10 mg suppository rectally twice per day in the morning and afternoon. Aim for 2 – 3 bowel movements per day for two days. Once constipation resolves, decrease dose to once per day in the morning.
- Sodium biphosphate or paraffin oil enema every day as needed.
- Continue haloperidol at same dose IV. Once pain and constipation are relieved, and if there is no nausea, consider stopping haloperidol to assess whether nausea returns (previously, nausea appeared to have been caused by codeine).

**5. What is the relative contra-indication to giving metoclopramide with haloperidol?**

Because metoclopramide is a dopamine receptor antagonist like haloperidol (although a much weaker antagonist than the anti-psychotics), simultaneous treatment with both can cause Parkinsonian symptoms in elderly patients or those with Parkinson's Disease.

**6. How would you treat Mr. Binh in this situation, and what would you tell him and his family?**

- Continue the current anti-emetic regimen of steroid, metoclopramide, and low-dose haloperidol for a few more days (sometimes the steroid may take a few days to work fully).
- Consider adding octreotide, if available (extremely expensive).
  - If the vomiting resolves, switch the morphine, metoclopramide, steroid, and bisacodyl to the oral forms. Also, consider stopping the haloperidol or switch it to the oral form. If the nausea, vomiting, and pain remain under control, the patient can be discharged.
  - If the vomiting does not resolve or improve after 4 – 5 days:
    - Consider stopping the metoclopramide (it is not helping).
    - Do not stop the steroid: it is not helpful for the vomiting, but it may be helping to relieve pain from liver capsule stretch.
    - Consider a gastric drainage tube, if available.
      - Venting gastrostomy tubes often cannot be placed in patients with linitis plastica because the gastric wall infiltrated by tumor will not heal around the tube. As a result, leakage into the peritoneal cavity can occur and the tube may become displaced from the stomach.
      - A nasogastric tube for nasogastric suctioning usually is not placed in this situation because it usually is uncomfortable for the patient. The exception is when the vomiting is very frequent or very distressing to the patient.
    - Discuss with the patient and/or family their concerns about nutrition.
      - Listen carefully and patiently to their concerns.

- Explain gently that there is no more treatment available for the cancer and that the best that doctors can do in this situation is to try to relieve uncomfortable symptoms.
- Explain gently that the patient can eat whatever he wishes to eat but that he probably will continue to vomit and should not be pressured to eat if he is not hungry.
- If artificial nutrition is available, consider NOT offering it, even if the family can afford it, because it usually does not help the patient's nutritional status and can have bad side effects including:
  - Maintaining gastro-intestinal secretions at a normal level, thereby continuing the stimulus to vomit;
  - Worsening of respiratory secretions and lung congestion with resultant dyspnea when the patient is dying;
  - Line sepsis.
- If the family specifically asks about artificial nutrition, explain gently that providing it to advanced cancer patients usually does not help because “it feeds the cancer but not the patient” and that it can cause discomfort (as described above).
- Consider suggesting gently to the patient or family that the patient may not have much more time to live and exploring with them whether there are tasks the patient would like to complete or people he would like to see or speak with while he remains able to do so. Help the patient and family to complete important tasks such as:
  - Preparing a will.
  - Leaving a legacy for children or grandchildren.
  - Reconciling with family members or friends with whom there has been conflict.
  - Saying good-bye to family and friends.

# Day 4



## **Psychological Distress in the Terminally Ill: Depression and Anxiety**

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### **I. Rationale: Psychological distress in the terminally ill**

- A) Some distress may be appropriate and inevitable
- B) Severe disturbance can lead to unnecessarily poor quality of life
  - 1) Amplifies pain
  - 2) Impairs ability to connect with others, make meaning of the situation, and say good-bye
  - 3) Causes anguish in family members and friends
  - 4) Increases risk of suicide
- C) Physicians should be able to distinguish between appropriate distress and severe disturbance
- D) Treating psychological disturbance can improve quality of life for patients and their families.

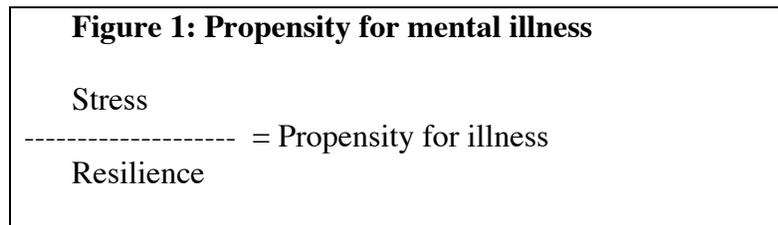
### **II. Prevalence of psychological distress in the terminally ill**

- A) Psychological distress is common among cancer and HIV/AIDS patients
  - 1) In the United States research has shown that 35-50% of cancer patients have psychiatric disorders
    - a) About 66% have reactive anxiety and depression (adjustment disorder with depressed or anxious mood)
    - b) About 15% have major depression
    - c) The rest are divided into organic disorders, personality disorders, and pre-existing mood, anxiety, and psychotic disorders
  - 2) Among poor people receiving government health insurance in the US, HIV-infected people were three times more likely to have a psychiatric illness than non-HIV-infected people. Likely reasons:
    - a) People with psychiatric illnesses are at higher risk for acquiring HIV infection than people without psychiatric illness.
    - b) People with HIV infection are at higher risk of developing psychiatric illness than non-HIV-infected.

- 3) Among people with AIDS in the US:
  - a) 9% are referred for psychiatric evaluation of bipolar disorder
  - b) 20% are referred for psychiatric evaluation of demoralization
  - c) 20% are referred for psychiatric evaluation of major depression
  - d) Anxiety disorders also very common
  - e) Dementia occurs often with advanced disease

### III. Depression, Anxiety, Adjustment Disorder

- A) A model for mental distress in the medically ill



- A) Adjustment disorders: reacting to illness
  - 1) Definition: A maladaptive reaction to an identifiable stressful life event
    - a) Symptoms must occur within three months of the stressor and persist for no longer than six months
    - b) The behavioral or emotional symptoms seem in excess of what would be normally expected.
    - c) Impairment of social or occupational functioning
  - 2) Symptoms of depression, anxiety, and disturbed behavior are most common
- B) Depression: A word and a disease
  - 1) A term used to describe clinical signs and symptoms ranging from transient feelings of discouragement, disappointment, sadness, grief, or despondency to a disorder with neuron-vegetative symptoms
- C) Major Depressive Episode can be due to
  - a) A manifestation of a primary affective disorder
  - b) A mood disorder associated with specific organic pathology or use of medications
  - c) A result of the confusing overlap of somatic symptoms of depression and symptoms of medical illness

D) Criteria for Major Depression

- 1) Depressed mood or anhedonia for > 2 weeks along with four or more of the symptoms listed below (English acronym: SIG E CAPS):
  - a) Sleep disturbance (increased or decreased)
  - b) Interests (diminished)
  - c) Guilt (or preoccupation of thought)
  - d) Energy (decreased)
  - e) Concentration (decreased)
  - f) Appetite disturbance (increased or decreased)
  - g) Psychomotor (agitation or retardation)
  - h) Suicidal thoughts (or thoughts of death)

E) Depression in the Medically Ill

- 1) Physical symptoms of medical illness overlap with neuron-vegetative symptoms of depression
- 2) Psychological stressors include loss of self-esteem, or the loss of a sense of control or power
- 3) Physical stressors include the illness (for example, HIV/AIDS or cancer), their sequelae (for example, opportunistic infection or paraneoplastic syndrome), or some treatments (for example, efavirenz, corticosteroids).

**Figure 2: The “ABCs of Depression” in the Medically Ill: Affect, Behavior, and Cognition**

<u>Affective symptoms</u>	Noncompliance
Depressed mood	Social withdrawal
Lack of pleasure	Psychomotor retardation
Crying	
Irritability	<u>Cognitive symptoms</u>
Hopelessness	Decreased concentration
Worthlessness	Suicidal ideation
Guilt	Pseudodementia
	Intractable pain
<u>Behavioral symptoms</u>	Excessive somatic preoccupation
Apathy	

F) Risk Factors for Depression

- 1) Personal or family history of substance abuse, depression, or bipolar illness
- 2) Pancreatic cancer, carcinoid cancer
- 3) HIV/AIDS
- 4) Being female: depression is twice as likely to occur in women

- 5) Having a chronic illness
- 6) Having specific personality styles (for example, attention-seeking, controlling, perfectionistic)

#### G) Somatic Effects of Depression

- 1) Pts with untreated major depression are 6-7 times more likely to die than are those in the general population
- 2) Depressed patients have increased cardiac beat-to-beat variability increasing risk of arrhythmia.
- 3) Depressed pts have altered hypothalamic-pituitary-adrenal axis functions, an increased number and frequency of cortisol bursts, and an increased cortisol level

#### H) Drugs Commonly Associated with Depressive Symptoms

##### Alcohol

##### *Antihypertensives*

reserpine  
methyldopa  
clonidine

##### *Cardiac medications*

digitalis  
diltiazem  
prazosin  
procaine derivatives

##### *Antiparkinson agents*

levodopa

##### Cimetidine

Cycloserine

Oral contraceptives

Corticosteroids

##### *Beta-blockers*

propranolol

#### I) Anxiety: Overview

1. Anxiety is common in terminal illness.
  - a. Over half of patients report significant anxiety
  - b. For most patients anxiety is a reaction to:
    1. Cancer or its treatments
    2. HIV/AIDS or its social consequences
  - c. About 20% meet criteria for formal anxiety disorders (similar rate to general population in the US).
2. Symptoms of anxiety and depression are more likely to run together than either alone.
  - a. In other words: negative affect is common in terminally ill patients.

#### J) Anxiety: Definition

1. A sense of dread and foreboding with a variety of autonomic (primarily sympathetic) symptoms
2. Symptoms:

- a. Sympathetic: diaphoresis, dizziness, dyspnea, dry mouth, headache, hyperventilation, muscle tension, nausea, palpitations, shortness of breath, tachycardia, tremulousness, urinary frequency, vomiting
  - b. Cognitive:
    - i. Recurrent, unpleasant thoughts about illness along with fears of death, disfigurement
    - ii. Cognitive styles that feature overgeneralization and expectation of catastrophe
  - c. Behavioral:
    - i. Perceive environment as hostile and therefore want to flee/avoid treatment
    - ii. Non-adherence to treatment
3. The entire spectrum of anxiety disorders can be seen in terminal illness:
- a. Phobia
  - b. Panic disorder
  - c. Post traumatic stress disorder
  - d. Others

#### K) Anxiety: Differential Diagnosis

- |                           |                                |
|---------------------------|--------------------------------|
| 1) Endocrine dysfunction  | 6) Metabolic disorder          |
| 2) Drug-related           | 7) Neurologic disease          |
| 3) Cardiovascular disease | 8) Gastrointestinal disease    |
| 4) Respiratory disease    | 9) Infection (for example, TB) |
| 5) Immunologic disease    | 10) Miscellaneous              |

#### IV. Insomnia

##### A) Types of Sleep Disorders

- 1) Primary Sleep Disorders: Sleep disturbance is the primary or only manifestation of the problem
- 2) Secondary Sleep Disorders: Sleep disturbance is part of a larger symptom complex
- 3) Parasomnias: Activities that would be more or less normal if performed during wakefulness, but are performed during sleep

##### B) Types of Insomnia

- 1) Primary or idiopathic
- 2) Psychiatric disorders
- 3) Environmental problems
- 4) Phase shifts
- 5) Dream related
- 6) Sleep apnea
- 7) Restless legs syndrome
- 8) Insomnia
- 9) Nocturnal myoclonus

- 10) Oversleeping
- 11) Drug-related
- 12) Neurological
- 13) Medical

C) Checklist for Work-up of Insomnia

- 1) Are there medical problems?
- 2) Are there psychiatric problems?
- 3) Are there behavior problems?
- 4) Does insomnia really exist?
- 5) Has the problem always existed?

D) Secondary Sleep Disorders: Medical Disorders

- 1) Neurological disorders: disruption of the sleep/wake/REM systems
- 2) Thyroid disorders:
- 3) Hyperthyroid - fragmented sleep
- 4) Hypothyroid - increased sleepiness and decreased delta sleep
- 5) Renal insufficiency: short, fragmented sleep
- 6) Stimulants: insomnia
- 7) Starvation: insomnia
- 8) Pain: insomnia
- 9) Sleep-exacerbated disorders: for example, paroxysmal nocturnal dyspnea
- 10) Iatrogenic problems: use of hypnotics

E) Factors that Destroy Sleep

- 1) Excessively noisy surroundings
- 2) Excessively hot rooms
- 3) Chronic use of hypnotics
- 4) Caffeine in the evening
- 5) Alcohol before bedtime
- 6) Chronic use of tobacco

F) Habits to Improve Sleep

- 1) Sleep only until refreshed
- 2) Establish regular arousal time
- 3) Maintain steady, daily exercise
- 4) Eat light bedtime snack
- 5) Read in bed instead of brooding

G) Sleep Medications

- 1) Benzodiazepines
  - a. Effective
  - b. Fatal overdose is rare
  - c. Can be habit-forming

- d. Can cause delirium and agitation, especially in the elderly and medically ill
- 2) Nonbenzodiazepine hypnotics
  - a. Effective
  - b. Generally not habit-forming
  - c. Can cause delirium and agitation, especially in the elderly and medically ill
- 3) Antihistamines:
  - a. Potentiate anticholinergic agents
  - b. Relatively safe (fatal overdose is rare)
  - c. Can cause delirium and agitation, especially in the elderly and medically ill
- 4) Chloral hydrate:
  - a. Affects protein binding
  - b. Can cause delirium and agitation, especially in the elderly and medically ill
- 5) Tricyclic antidepressants:
  - a. Non-specific agent for sleep
  - b. Low margin of safety, overdose can be lethal
- 6) Antipsychotics:
  - a. Risk of tardive dyskinesia with prolonged use

## V. Treatment of Mood Disorders

### A) Treatment of Depression and Adjustment Disorder

- 1. Pharmacotherapy
  - a. Tricyclic antidepressants
  - b. Selective Serotonin Reuptake Inhibitors (SSRIs)
  - c. Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)
  - d. Atypical antidepressants
  - e. Psychostimulants
- 2. Electroconvulsive therapy
- 3. Psychotherapy

### B) Tricyclic Antidepressants (TCAs):

- 1. Common TCAs:
  - a. Tertiary - Amitriptyline, Imipramine
  - b. Secondary – Nortriptyline, Desipramine
- 2. Useful in the treatment of certain pain syndromes (neuropathic pain)
- 3. Side-Effect Profile
  - a. Orthostatic hypotension (OH)
  - b. Anticholinergic effects
    - i. Anhydrosis, myosis, mental status changes
    - ii. Tertiary agents > secondary agents

- c. Conduction system effects
  - i. Prolong cardiac depolarization and increase the PR, QRS, and QTc
  - ii. Increased risk of complete heart block when used in patients with pre-existing bundle branch blocks.
  - iii. Sudden death may occur with QTc > 440msec

C) Selective Serotonin Reuptake Inhibitors (SSRIs)

- 1. Compared to TCAs are significantly less anticholinergic, antihistaminic, and alpha-adrenergic
- 2. Well-absorbed from the GI tract
- 3. Extensively metabolized in the liver
- 4. Half-life:
  - a. sertraline, paroxetine, fluvoxamine: 1 day
  - b. fluoxetine: 2-3 days
- 5. Non-Cardiac SSRI Side Effects
  - i. Tremor
  - ii. Agitation
  - iii. Irritability
  - iv. Anorexia
  - v. GI distress
  - vi. Insomnia
  - vii. SIADH
  - viii. Anorgasmia
  - ix. Potentially fatal serotonin syndrome in combination with Monoamine Oxidase Inhibitors (MAOIs)
- 6. Cardiac Effects of SSRIs
  - i. May raise TCA levels and increase conduction delays
  - ii. Rarely can cause bradycardia and syncope

D) Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)

- 1. Combine features of both TCAs and SSRIs
- 2. Some evidence shows more efficacy in treatment of depression
- 3. Have a role in the treatment of neuropathic pain
- 4. Have similar side effect profile as SSRIs, but also have more cardiac effects (for example, hypertension) and a significant withdrawal syndrome.
- 5. Examples:
  - a. Venlafaxine
  - b. Nefazodone

E) Atypical Antidepressants and their side effects

- 1. Trazodone
  - a. Weak antidepressant

- b. Sedating, often used as a sedative for sleep
- c. Causes significant OH and is associated with priapism
- 2. Bupropion
  - a. Low risk of cardiac toxicity
- 3. Mirtazepine
  - a. Serotonin and histamine agonist -- mild weight gain and sedation

F) Psychostimulants

- 1. Used to treat medically-ill, apathetic, anorexic, and geriatric depressed patients
- 2. Appears to work through release of dopamine and norepinephrine
- 3. Primarily renally excreted
- 4. Rarely cause tachycardia, hypertension, or arrhythmia
- 5. Relatively contraindicated with hypertension, pregnancy, seizures, delirium, psychosis, angina, or with monoamine oxidase inhibitors (MAOIs)

G) Electroconvulsive Therapy

- 1. The most effective treatment for major depression
- 2. Associated with exaggerated increases in BP, circulatory collapse, MI, EKG changes (ST depressions and repolarizations), and arrhythmias
- 3. Does not effect serum cardiac enzymes
- 4. Can be used safely, even in those with cardiac disease, if good anesthesia care is available if needed

H) Psychological Management

- 1. Provide information, clarifications, reassurance, and support
- 2. Ask specific questions about how patients believe their illness will affect daily life
- 3. Demonstrate interest in who they are and what is important to them
- 4. Can be stressful for staff, watch for and address staff demoralization
- 5. Refer for formal psychotherapy, if available. Types:
  - a. Cognitive Behavioral Therapy
  - b. Psychodynamic Therapy
  - c. Group therapy

**V. Treatment of Anxiety**

A) Psychological interventions

- 1) Reassurance
  - a) Provide information and emotional support
  - b) Explore patient's fears about illness and procedures
  - c) Clarify misconceptions
  - d) Be calm
- 2) Short term psychotherapy
- 3) Behavioral therapy

- B) Pharmacotherapy
  - 1) Benzodiazepines
  - 2) Neuroleptics
    - a) If fear impairs reason
  - 3) Anticholinergics
  - 4) SSRIs

## **VI. Conclusions**

- A) Be prepared to make the diagnosis of mood and anxiety disorder
- B) Treat depression when you encounter it: do not assume it is an appropriate reaction to a stressful situation
- C) Consider combination therapy: pharmacotherapy and psychotherapy
- D) Consider psychiatric consultation

<b>Figure 3: Antidepressant medications used in terminal illness*</b>			
<b>Drug</b>	<b>Starting Daily Dosage mg (orally)</b>	<b>Therapeutic Daily Dosage, mg (orally)</b>	<b>Comments</b>
<b>Serotonin reuptake inhibitors</b>			
Fluoxetine	5-10	20-60	Stimulating; long half-life
Sertraline	25	50-200	Relatively few drug interactions
Paroxetine	5-10	10-60	More anticholinergic side effects
Citalopram	10	10-60	Relatively few drug interactions
<b>Others</b>			
Trazodone	25-50	150-300	Sedating, orthostatic hypotension, rare priapism
Bupropion	75-100	150-450	Stimulating, risk for seizures, minimal effect on weight and sexual functioning; useful for smoking cessation
Venlafaxine	18.75-37.5	75-300	Treats neuropathic pain; causes elevated BP at higher doses
Mirtazepine	15	15-45	Sedating, anxiolytic, antiemetic, appetite stimulating
<b>Tricyclic antidepressants</b>			
Amitriptyline	10-25	50-150	Sedating
Imipramine	10-25	50-200	
Desipramine	10-25	50-150	Least sedating TCA
Nortriptyline	10-25	50-150	Least anticholinergic TCA; blood levels must be checked
<b>Psychostimulants</b>			
Methylphenidate	2.5 at 8 a.m. and noon	5-60	Insomnia, anxiety, tremor, tachycardia, hypertension, seizures, confusion, delirium
Modafinil	50-100 a.m.	100-400	Better tolerated than other stimulants; more costly.

\* Adapted from Miller K, Massie MJ. Depression and anxiety. Cancer J. 2006 Sep-Oct;12(5):388-97.

<b>Figure 4: Antianxiety and Hypnotic Medications Used in Cancer Patients*</b>			
<b>Drug</b>	<b>Approximate Dose Equivalent</b>	<b>Starting Daily Dose, mg (oral)</b>	<b>Comments</b>
<b>Benzodiazepines</b>			
Temazepam	15	15-30 at bedtime	Short acting, Safer in hepatic disease
Oxazepam	10	10-15 three times / day	Short acting, Safer in hepatic disease
Alprazolam	0.25	0.25- 1 three times / day	Useful for nausea, short acting
Lorazepam	1	0.5-2 three times / day	Useful for nausea, short acting, preferred in hepatic disease
Diazepam	5	2.5-10 two times / day	Longer half-life
Clonazepam	0.5	0.25-1 two times / day	Longer half-life, mood stabilizer
<b>Antihistamines</b>			
Hydroxyzine	10	10-50 three times / day	Sedating, may cause confusion
Diphenhydramine	25	25-50 three times / day	Sedating, may cause confusion
<b>Neuroleptics</b>			
Chlorpromazine	12.5	25 two times / day	Sedating anticholinergic; lowers seizure threshold
Haloperidol	0.5	0.5-2 three times / day	More EPS, not sedating
Olanzapine	2.5	2.5-10 once or twice / day	Sedating, appetite stimulation, weight gain, hyperglycemia
Risperidone	0.5	0.5-2.0 two times / day	Not sedating, some EPS > 6 mg daily dose
Quetiapine	25	25-100 at bedtime	Sedating, orthostatic hypotension

\* Adapted from Miller K, Massie MJ. Depression and anxiety. Cancer J. 2006 Sep-Oct;12(5):388-97.

**Figure 5: Suicide Risk Factors in Cancer Patients\***

**Related to mental status**

- Suicidal ideation
- Lethal plans
- Depression and hopelessness
- Delirium and disinhibition
- Psychotic features
- Loss of control and impulsivity
- Irrational thinking

**Related to cancer**

- Uncontrolled pain
- Advanced disease and poor prognosis
- Exhaustion and fatigue
- Site of cancer (oropharyngeal, lung, GI, GU, breast)
- Medication effects (steroids)

**Related to history**

- Previous suicide attempts
- Psychopathology
- Substance abuse (alcohol)
- Recent loss (spouse or friends)
- Poor social support
- Older male
- Family history of suicide

\* Adapted from Miller K, Massie MJ. Depression and anxiety. *Cancer J.* 2006 Sep-Oct;12(5):388-97.

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## Psychological Distress in the Terminally Ill Patient: Depression and Anxiety

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## Psychological distress in the terminally ill

- Some distress may be appropriate and inevitable
- Severe disturbance can lead to unnecessarily poor quality of life
  - **Amplifies pain**
  - **Impairs ability to connect with others, make meaning of the situation, and say good-bye**
  - **Causes anguish in family members and friends**
  - **Increases risk of suicide**
- Physicians should be able to distinguish between appropriate distress and severe disturbance
- Treating severe psychological disturbance can improve quality of life for patients and their families.




## Prevalence of psychological distress in the terminally ill

- Psychological distress is common among cancer and HIV/AIDS patients
  - In the United States 35 to 50% of cancer patients have psychiatric disorders
    - About 66% have reactive anxiety and depression (adjustment disorder with depressed or anxious mood)
    - About 15% have major depression
    - The rest are divided into organic disorders, personality disorders, and pre-existing mood, anxiety, and psychotic disorders (continued)




- In US, people with HIV are 3 times more likely to have psychiatric illness than people without HIV
  - People with HIV infection are at higher risk of developing psychiatric illness
  - People with psychiatric illness are at higher risk for acquiring HIV infection
- Among US HIV/AIDS patients:
  - 9% bipolar disorder
  - 20% demoralization
  - 20% major depression (more than cancer patients)
  - Anxiety disorders very common
  - AIDS dementia common in advanced disease




## A model for mental distress in the medically ill:

**Figure 1: Propensity for mental illness**

Stress  
----- = Propensity for illness  
Resilience




## Adjustment disorders: reacting to illness

- Definition: A maladaptive reaction to an identifiable stressful life event
  - Symptoms must occur within three months of the stressor and persisted for no longer than six months
  - The behavioral or emotional symptoms seem in excess of what would be normally expected.
  - Impairment of social or occupational functioning
- Symptoms of depression, anxiety, and disturbed behavior are most common




## Quote

Alone, she felt a hundred stabs of pain –  
She would destroy herself and end it all.

Một mình cay-đắng tram đường,  
thôi thì nát ngọc tan vàng thì thôi.

Truyện Kiều, 2615-2616



7



## Major Depression

- Major depression can be:
  - A manifestation of a primary affective disorder
  - A mood disorder associated with specific organic pathology or use of some medications
  - A result of the confusing overlap of somatic symptoms of depression and symptoms of medical illness



8



## Criteria for Major Depression

- Depressed mood or anhedonia for > 2 weeks with 4 or more of the following symptoms:
  - Sleep disturbance (increased or decreased)
  - Interests (diminished)
  - Guilt (or preoccupation of thought)
  - Energy (decreased)
  - Concentration (decreased)
  - Appetite disturbance (increased or decreased)
  - Psychomotor (agitation or retardation)
  - Suicidal thoughts (or thoughts of death)



9



## Depression in the Medically Ill

- Physical symptoms of medical illness overlap with neurovegetative symptoms of depression
- Physical stressors include the illness (HIV/AIDS or cancer), its sequelae (opportunistic infection, paraneoplastic syndromes), or its treatment (efavirenz, corticosteroids).
- Psychological stressors include loss of self-esteem, or the loss of a sense of control or power.



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## The “ABCs of Depression” in the Medically Ill: Affect, Behavior, and Cognition

- Affective symptoms
  - Depressed mood
  - Lack of pleasure
  - Crying
  - Irritability
  - Hopelessness
  - Worthlessness
  - Guilt
- Behavioral symptoms
  - Apathy
- Noncompliance
- Social withdrawal
- Psychomotor retardation
- Cognitive symptoms
  - Decreased concentration
  - Suicidal ideation
  - Pseudodementia
  - Intractable pain
  - Excessive somatic preoccupation



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## Risk Factors for Depression

- Personal or family history of substance abuse, depression, or bipolar illness
- Pancreatic cancer, carcinoid cancer
- HIV/AIDS
- Being female: depression is twice as likely to occur in women
- Having a chronic illness
- Having specific personality styles (e.g., attention-seeking, controlling, perfectionistic)



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## Somatic Effects of Depression

- Patients with untreated major depression are 6-7 times more likely to die than are those in the general population
- Depressed patients have increased risk cardiac of arrhythmia.
- Depressed patients have altered Hypothalamic-Pituitary-Adrenal axis functions and an increased cortisol level



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## Anxiety: Overview

- Anxiety is common in terminal illness.
  - Over half of patients report significant anxiety
  - For most patients anxiety is a reaction to:
    - HIV/AIDS and its social consequences
    - Cancer and its treatments
  - About 20% meet criteria for formal anxiety disorders (similar rate to general population in the US).
- Symptoms of anxiety and depression are more likely to be found together than either alone.
- The entire spectrum of anxiety disorders can be seen in terminal illness:
  - Phobia, Panic disorder, Post traumatic stress disorder, etc.



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## Anxiety: Definition

- A sense of dread and foreboding with a variety of autonomic (primarily sympathetic) symptoms
- Symptoms:
  - **Sympathetic:**
    - diaphoresis, dizziness, dyspnea, dry mouth, headache, hyperventilation, muscle tension, nausea, palpitations, shortness of breath, tachycardia, tremulousness, urinary frequency
  - **Cognitive:**
    - Recurrent, unpleasant thoughts about illness along with fears of death, disfigurement
    - Overgeneralization and expectation of catastrophe
  - **Behavioral:**
    - Perception of environment as hostile and therefore need to flee / avoid treatment
    - Non-adherence to medications



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## Anxiety: Differential Diagnosis

- Endocrine dysfunction
- Drug-related
- Cardiovascular dz
- Respiratory dz
- Immunologic dz
- Metabolic disorder
- Neurologic dz
- Gastrointestinal dz
- Infectious dz
- Miscellaneous



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## Insomnia: Types

- Primary Sleep Disorder (idiopathic)
- Secondary Sleep Disorder: due to medical or neuro-psychiatric disorder
- Environmental disturbances
- Phase shifts
- Dream related
- Sleep apnea
- Restless legs syndrome
- Nocturnal myoclonus
- Oversleeping
- Drug-related



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## Checklist for Work-up of Insomnia in Cancer & HIV/AIDS Patients

- Are there correctable medical problems (for example, pain or dyspnea)?
- Are there undiagnosed or untreated psychiatric problems (for example, anxiety or depression)?
- Are there behavior problems (for example, bad sleeping habits)?
- Is there an environmental problem (no decent place to sleep)?
- Is the problem due to medication or other substances (for example, efavirenz, overuse of benzodiazepine, steroid use in the evening, caffeine, alcohol, tobacco)?
- Is insomnia really present?
- Has the problem always existed?



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### Sleep Medications

- Benzodiazepines
  - Effective, fatal overdose is rare
  - Can cause delirium and agitation especially in elderly
- Nonbenzodiazepine hypnotics
  - Effective, generally not habit-forming
  - Can cause delirium and agitation
- Antihistamines:
  - Potentiates anticholinergic agents
  - Relatively safe (fatal overdose rare)
  - Can cause delirium and agitation
- Chloral hydrate:
  - Affects protein binding
  - Can cause delirium and agitation
- Tricyclic antidepressants:
  - Non-specific, low margin of safety (overdose can be lethal)
- Antipsychotics:
  - Often best choice for elderly



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### Treatment of Depression and Adjustment Disorder

- Pharmacotherapy
  - Tricyclic antidepressants
  - Selective serotonin reuptake inhibitors (SSRIs)
  - Serotonin & norepinephrine reuptake inhibitors (SNRIs)
  - Atypical antidepressants
  - Psychostimulants
- Electroconvulsive therapy
- Psychotherapy



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### Tricyclic Antidepressants (TCAs):

- Effective, but takes weeks to work
- Also useful in the treatment of neuropathic pain
- Side-Effect Profile:
  - Orthostatic hypotension (OH)
  - Anticholinergic effects
    - Anhidrosis, mental status changes, constipation
    - Tertiary agents (amitriptyline) > secondary agents (nortriptyline)
  - Cardiac toxicity
    - Prolongation of PR, QRS, and QTc intervals
    - Sudden death may occur with QTc > 440msec
    - Increased risk of complete heart block when used in patients with pre-existing bundle branch blocks.



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### Selective Serotonin Reuptake Inhibitors (SSRIs)

- Like TCAs, effective but take weeks to work
- Significantly less anticholinergic, cardiac, and hemodynamic effects than TCAs
- Well-absorbed from the GI tract
- Extensively metabolized in the liver
- Half-life:
  - sertraline, paroxetine, fluvoxamine: 1 day
  - fluoxetine: 2-3 days
- Side effects: Tremor, Agitation, Irritability, Anorexia, Nausea, Insomnia, SIADH, Anorgasmia
- Do not use in combination with Monoamine Oxidase Inhibitors (MAOIs)



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### Atypical Antidepressants and their side effects

- Trazodone
  - Weak antidepressant, but useful as a sedative (for insomnia)
  - Causes significant OH
  - Associated with priapism
- Bupropion
  - Effective, takes weeks to work
  - Low risk of cardiac toxicity
- Mirtazepine
  - Effective, takes weeks to work
  - Appetite enhancing and sedating (can be useful effects)



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### Psycho-stimulants

- Used to treat depression in medically-ill patients
- Effect is immediate (can use in combination with SSRI)
- Appears to work through release of dopamine and NE
- Primarily renally excreted
- Rarely cause tachycardia, HTN, or arrhythmia
- Relatively contraindicated in setting of hypertension, pregnancy, seizures, anxiety, delirium, psychosis, angina, or with MAOIs
- Example: methylphenidate



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## Electroconvulsive Therapy

- The most effective treatment for major depression
- Side effects may include large increases in BP, circulatory collapse, MI, EKG changes (ST depressions and repolarizations), and arrhythmias
- However, can be used safely, even in patients with cardiac disease if good anesthesia care is available



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## Psychological Management

- Provide information, clarifications, reassurance, and support
- Ask specific questions about how patients believe their illness will affect daily life
- Demonstrate interest in who they are and what is important to them
- Refer for psychotherapy, if available:
  - For example: group therapy / peer counseling



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## Treatment of Anxiety

- Psychological interventions
    - Reassurance / short term psychotherapy
      - Provide information and emotional support
      - Explore patient's fears about illness and procedures
      - Clarify misconceptions
      - Be calm
  - Pharmacotherapy
    - Benzodiazepines
    - Neuroleptics (if fear impairs reason)
    - Tricyclic Antidepressants
    - SSRIs
- (See syllabus for doses)



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## Conclusions

- Be prepared to make the diagnosis of mood and anxiety disorder
- Treat depression when you encounter it: do not assume it is an appropriate reaction to a stressful situation
- Consider combination therapy
  - Pharmacotherapy and psychotherapy
- Consider psychiatric consultation, if available



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## Altered Mental Status: Delirium and Dementia

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### I. Delirium

#### A) Delirium Overview

- 1) Delirium is a serious medical condition that requires immediate and thorough evaluation.
- 2) Delirium is often unrecognized or misdiagnosed as depression, personality disorder, or “difficult patient.”
- 3) Pathology in every organ system can cause delirium...
- 4) Delirium often has *multiple* causes.
- 5) Treatment entails treating the underlying condition.

#### B) Definition of Delirium

- 1) A disturbance of consciousness accompanied by cognitive deficits that cannot be accounted for by past or evolving dementia. It must include:
  - a. A disturbance of consciousness (i.e. reduced clarity of awareness of the environment)
  - b. A change in cognition
  - c. Develops over a short period (hours to days) and has a fluctuating course
  - d. Evidence that the disturbance is caused by the physiological consequences of a general medical condition

#### C) Delirium is a common and serious condition

- 1) Present in >30% of older medical inpatients and in 10-60% of surgical inpatients in the USA.
- 2) The more complicated the medical problem or the more frail the patient, the greater the likelihood of delirium.
- 3) Present in 70% of ICU patients, 10% of Emergency Department patients, and 42% of hospice patients
- 4) In the USA, delirious patients have longer hospital stays, greater functional decline, and increased risk of being confined to an institution instead of going home.
- 5) Associated with significantly increased mortality at 1 month and 6 months as compared to patients without delirium
  - a. One report of pooled results showed a 14% mortality rate at one month and 22% mortality rate at 6 months for patients with delirium (over twice the rate of non-delirious patients).

D) Common signs & symptoms

- 1) Prodrome (restlessness, anxiety)
- 2) Rapidly fluctuating mental status with lucid intervals
- 3) Disorientation (to time and place – almost never to self)
- 4) Increased or decreased psychomotor activity
- 5) Decreased attention
- 6) Disturbed sleep-wake cycle
- 7) Impaired memory
- 8) Disorganized thinking
- 9) Altered perceptions – misperception, visual hallucinations.
- 10) Emotional lability
- 11) Dysgraphia / dysnomic aphasia
- 12) Motor abnormalities

E) General Principles

- 1) Recognize that the disorder is present
  - a. It goes unrecognized or is misattributed to age, dementia, or other mental disorder in up to 70% of cases.
- 2) Don't assume psychiatric symptoms are due to a long-standing psychiatric disorder
- 3) Don't assume that psychiatric symptoms are a reaction to being in a critical care environment
- 4) Initiate a search for the underlying cause of the symptoms
- 5) Identify the symptoms that require treatment
- 6) Treat symptoms as specifically as possible

F) Evaluation of the Possibly Delirious Patient

- 1) The Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) criteria provide a practical framework for evaluation:
  - a. Consciousness
  - b. Cognition
  - c. Course
- 2) Sources of information:
  - a. History
  - b. Mental status examination
  - c. Relevant physical exam
  - d. Relevant laboratory studies
  - e. Medications
  - f. Outside sources of information (primary team, nurses, sitters, family, friends).
- 3) If the diagnosis is not certain, use the Mini-Mental State Exam (MMSE) and the draw-a-clock test.

G) Assessment of Mental Status

- 1) Evaluate the ABCs:
  - a. affect
  - b. behavior
  - c. cognition
- 2) The Mental Status Examination
  - a. Appearance & behavior
    - i. Hypervigilant?
    - ii. Frightened?
    - iii. Poor eye contact?
    - iv. Agitated?
    - v. Psychomotorically retarded?
  - b. Speech
    - i. Rambling?
    - ii. Rapid?
    - iii. Incoherent?
    - iv. Fluent?
  - c. Mood
    - i. Depressed?
    - ii. Fearful?
    - iii. Tearful?
    - iv. Irritable?
    - v. Anxious?
    - vi. Angry?
    - vii. Apathetic?
  - d. Affect
    - i. Despondent?
    - ii. Anxious?
    - iii. Perplexed?
    - iv. Blunted?
  - e. Thought
    - i. Paranoid?
    - ii. Loose associations?
    - iii. Hallucinating?
  - f. Cognition
    - i. Disoriented?
    - ii. Decreased concentration?
    - iii. Confused?
    - iv. Impaired memory?

**Figure 1: Delirium: Emergent Causes**

<b>Diagnosis</b>	<b>Key Clinical Questions</b>
<b>Wernike's Encephalopathy</b> - nystagmus, confusion, ataxic	Ataxia? Nystagmus?
<b>Withdrawal</b> - Alcohol, benzodiazepines	Drug or alcohol history? Increased sympathetic activity?
<b>Hypoxemia</b>	Arterial blood gas? Pulmonary disease?
<b>Hypertensive crisis/ encephalopathy</b>	Blood pressure (BP)? Papilledema?
<b>Hypoglycemia</b>	Diabetes history? Blood glucose?
<b>Hypoperfusion of CNS</b>	Cardiac history? Low BP? Low Hematocrit?
<b>Infection</b>	Fever? Increased WBC count? Source?
<b>Intracranial</b> - bleed, trauma	History of head trauma? Loss of Consciousness? Focal neurologic signs
<b>Meningitis/encephalitis</b>	Meningeal signs? Fever/WBC count? Viral prodrome?
<b>Poisons or medications</b>	Toxicology screen? Iatrogenesis (i.e. anti-cholinergics, benzos, steroids, opiates).

**Figure 2: Causes of Delirium**

<b>Infection</b>	HIV, sepsis, Pneumonia
<b>Withdrawal</b>	Alcohol, barbiturate, sedative-hypnotic
<b>Acute metabolic</b>	Acidosis, alkalosis, electrolyte disturbance, hepatic failure, renal failure
<b>Trauma</b>	Closed-head injury, heat stroke, postoperative, severe burns
<b>CNS pathology</b>	Abscess, hemorrhage, hydrocephalus, subdural hematoma, Infection, seizures, stroke, tumors, metastases, vasculitis, Encephalitis, meningitis, syphilis
<b>Hypoxia</b>	Anemia, carbon monoxide poisoning, hypotension, Pulmonary or cardiac failure
<b>Deficiencies</b>	Vitamin B12, folate, niacin, thiamine
<b>Endocrinopathies</b>	Hyper/hypoadrenocorticism, hyper/hypoglycemia, Myxedema, hyperparathyroidism
<b>Acute vascular</b>	Hypertensive encephalopathy, stroke, arrhythmia, shock
<b>Toxins or drugs</b>	Prescription drugs (i.e. antihistamines, H2-blockers, beta-blockers, opioids, benzodiazepines), illicit drugs, pesticides, solvents
<b>Heavy Metals</b>	Lead, manganese, mercury

## H) Treatment of Delirium

- 1) First and foremost: Treat any and all reversible medical causes.
  - a. Correct metabolic and systemic abnormalities
    - i. For example, treat infection or constipation, correct hypercalcemia or hyperammonemia.
  - b. Eliminate drug toxicity, remove the offending agent(s)
  - c. Administer appropriate antidote(s)
    - i. For example, naloxone (if patient does not have severe pain), flumazenil (for benzodiazepine overdose)
- 2) Control agitation, confusion, and psychotic symptoms.

## I) Treating the underlying cause

- 1) Treat Drug Withdrawal Syndromes
  - a. Alcohol and sedative-hypnotic (benzodiazepine, barbiturate) withdrawal can be lethal if untreated
    - i. Treat with benzodiazepines, neuroleptics
    - ii. Symptom-onset is a function of half-life -- the longer the half-life, the later the onset
    - iii. Treatment is best with a drug from same class, but with a longer half-life
  - b. Opioid withdrawal is uncomfortable but not lethal

## J) Obstacles to prompt treatment of drug withdrawal

- 1) Emergent admissions may result in sudden discontinuation of abused or prescription drugs
- 2) History of use may be difficult to establish in intubated or unconscious patients
- 3) Physical signs of withdrawal are non-specific
- 4) No laboratory tests can confirm the diagnosis

## K) Controlling the behavior of the delirious patient: Non-pharmacologic methods

- 1) Control agitated and confused behavior while searching for or treating the underlying cause.
- 2) Start with psychosocial measures, especially if the underlying cause is known
  - a. For example, make sure the patient's room has a calendar and clock, windows, a low noise level, dim lighting
  - b. Facilitate the presence of reassuring relatives.
- 3) Use restraints as a temporary measure to prevent the patient from harming himself or others.

## L) Controlling the behavior of the delirious patient: Pharmacologic methods

- 1) Many drugs can be used in delirium depending on its cause:
  - a. For example: neuroleptics, neuromuscular blockers, opioids (for pain), benzodiazepines (for agitation), anesthetics (inhaled or parenteral), and others (ketamine, clonidine)

- 2) Neuroleptics are agents of choice
  - a. Sedative, anxiolytic, and anti-psychotic properties.
  - b. Usually do not *cause* delirium.

M) Haloperidol is often the preferred drug

- 1) High potency neuroleptic
- 2) Minimal effects on blood pressure, heart rate, and respiratory drive
- 3) No anti-cholinergic properties
- 4) Can be administered parenterally.
  - a. Precipitates with phenytoin and heparin -- flush the IV line first
- 5) Onset of action: 10-30 minutes
- 6) High-dose associated with QTc prolongation and Torsades de Pointes
- 7) Extrapyramidal side effects are rare with IV use

N) Haloperidol Dosing

- 1) Titrate the dose to the symptoms
  - a. if mild, use 0.5-2 mg
  - b. if moderate, use 5-10 mg
  - c. if severe, use 10 mg or more
- 2) Repeat doses when necessary, every 15-30 minutes
- 3) Adjust dose to clinical course
- 4) Check ECG for QTc if appropriate based on goals of care

O) Other Neuroleptics

- 1) Chlorpromazine
  - a. More anticholinergic than haloperidol
  - b. More sedating than haloperidol
  - c. More apt to induce hypotension than haloperidol
  - d. More likely to induce arrhythmias than haloperidol
  
- 2) Atypical Antipsychotics
  - a. Olanzapine
  - b. Quetiapine
  - c. Risperidone
  - d. Clozapine
  - e. Ziprasidone

P) Alternative Agents for Agitation

- 1) Benzodiazepines
  - a. Lorazepam
    - i. Used orally, sublingually, and intravenously
    - ii. No active metabolites
  - b. Midazolam
    - i. Rapidly-acting; causes amnesia and respiratory depression
- 2) Propofol

- 3) Opioids
  - a. morphine typically used
- 4) Paralytics
  - a. if used, sedation required

## II. Dementia

### A) Dementia: Overview

- 1) A syndrome characterized by clinically significant decline in memory and at least one other area of cognitive function
- 2) Usually develops over months or years as opposed to delirium which has acute onset
- 3) More than 80 specific disorders can cause dementia
- 4) Some are common; some are rare
- 5) Not all dementias are progressive

### B) Dementia: Criteria

- 1) An acquired decline in memory
- 2) Impairment in social or occupational functioning
- 3) Impairment in at least one other area of higher cortical function
  - a. Aphasia: difficulty with language (speaking, reading, repeating)
  - b. Apraxia: inability to carry out motor tasks despite intact motor function
  - c. Agnosia: failure to recognize a familiar object despite intact sensory function
  - d. Executive dysfunction: problems with planning, abstraction, sequencing

### C) Dementia: Epidemiology

- 1) Advanced age is a risk factor
- 2) Prevalence is 1% at age 60 and doubles every 5 years afterwards
- 3) At age 85 prevalence is 50%
- 4) Most common types of dementia in the elderly:
  - a. Dementia of the Alzheimer's Type or DAT (60-80%)
  - b. Vascular Dementia (10-20%)
  - c. Lewy body disease (*at least* 5-10%)
  - d. Dementia of Parkinson's Disease
  - e. Frontotemporal dementia
  - f. Reversible dementias

### D) Dementia: Evaluation

- 1) Much can be done to help afflicted patients and their families even if the dementia is not curable
- 2) Gather a complete history

- a. Include a family history as certain types of dementia are heritable (For example, Huntington’s Disease and early-onset DAT).
- 3) Complete a medical and neurological examination
- 4) Order appropriate laboratory testing to help determine the cause
  - a. CT scan to assess for strokes
  - b. Vitamin B12, thyroid stimulating hormone, and test for syphilis to assess for potentially reversible causes of dementia

E) Dementia: History

- 1) Often best obtained from family members or friends
- 2) Determine course of illness
  - a. Gradual or abrupt onset (e.g., Dementia of the Alzheimer’s Type vs. vascular dementia)
  - b. Gradual decline or stepwise progression
- 3) Inquire about functional status
  - a. Ask about a patient’s typical day (work and leisure)
  - b. Ask about Activities of Daily Living (ADLs)
    - i. Capacity to perform basic tasks of self care (for example: bathing, dressing, toileting, feeding, continence, transferring)

**Figure 3: Distinguishing Dementia from Depression & Delirium†**

	<b>DAT*</b>	<b>Depression</b>	<b>Delirium**</b>
<i>Onset</i>	Insidious	Relatively rapid	Abrupt
<i>Initial Symptoms</i>	Memory deficits – verbal/spatial	Dysphoric mood or anhedonia	Difficulties with attention and disturbed consciousness
<i>Course</i>	Gradual, progressive – years	Persistent – lasts months if untreated	Fluctuating over days to weeks
<i>Family history</i>	May be present for DAT	May be present for depression	Not contributory
<i>Memory</i>	Recent memory worse than remote	Patchy/ Inconsistent	Poor registration
<i>Memory Complaints</i>	Variable – usually absent	Present	Absent
<i>Language Deficits</i>	Naming problems	Speech latency	Dysgraphia
<i>Affect</i>	Variable – may be neutral	Depressed/ irritable	Labile

† Adapted from the MGH Handbook of General Hospital Psychiatry 5<sup>th</sup> Edition. Stern TA, Fricchione GL, Cassem NH, Jellinek MS, Rosenbaum JF, eds. Mosby: 2004. p 138.

\*DAT – Dementia of the Alzheimer’s Type

\*\*Delirium is more common in patients with dementia. As a rule of thumb, dementia should be assumed to exist in an elderly patient with delirium until proven otherwise.

## F) Dementia: Causes (with representative examples):

- 1) *Irreversible Dementias*
  - a. Degenerative (e.g. DAT, Lewy body disease, Huntington's disease, Wilson's disease)
  - b. Vascular (e.g. Vascular dementia, strokes)
  - c. Traumatic (e.g. Chronic subdural hematoma)
- 2) *Potentially Reversible Dementias*
  - a. Psychiatric (e.g. Depression)
  - b. Neoplastic (e.g. Tumor-related, paraneoplastic)
  - c. Infections (e.g. HIV dementia, neurosyphilis, Lyme encephalopathy, Subacute sclerosing panencephalitis, Creutzfeldt-Jakob disease)
  - d. Obstructive (e.g. Normal Pressure Hydrocephalus)
  - e. Drugs/toxins (e.g. Korsakoff's from alcohol)
  - f. Metabolic (e.g. Thyroid abnormalities, B<sub>12</sub> deficiency)
  - g. Demyelinating (e.g. Multiple Sclerosis)
  - h. Autoimmune (e.g. Systemic Lupus Erythematosus)

## G) HIV Infection and the Central Nervous System

- 1) Within days of infection, HIV is transported to brain by monocytes
- 2) Monocytes differentiate into macrophages
  - a. Macrophages become activate randomly over time causing cell death
- 3) CNS is an independent reservoir of HIV
- 4) Antiretrovirals have variable blood-brain-barrier penetrance
- 5) HIV preferentially infects subcortical structures (hippocampus, basal ganglia, cerebellum, mid-frontal cortices)

## H) HIV-Associated Dementia

- 1) A subcortical dementia
- 2) An AIDS-defining condition.
- 3) US prevalence 21-25% in HIV patients prior to highly active antiretroviral treatment (HAART) and 7-10% since its the introduction
- 4) Characterized by
  - a. Slowed information processing
  - b. Attention and memory deficits
  - c. Impairments in abstraction and fine motor skills
- 5) A diagnosis of exclusion (no specific test)

## I) Physical and Neurological Exam

- 1) Carry out a careful medical assessment
  - a. Search for focal neurologic abnormalities
  - b. Assess vision and hearing
- 2) Assess abnormal and primitive reflexes
- 3) Conduct a mental status examination

**Figure 4: Neurologic Findings & Symptoms Associated with Types of Dementia**

Mood changes -- Depressive dementia, Depression combined with DAT
Headache, malaise -- Vasculitis, or systemic disease with cognitive changes
Release phenomena – DAT, Pick’s disease
Long tract and focal findings -- Vascular, Binswanger’s, Multiple Sclerosis, HIV, infections, tumors
Extrapyramidal symptoms -- Parkinson’s, Huntington’s, progressive supranuclear palsy, Wilson’s, Dementia with Lewy Bodies, late-stage DAT
Motor neuron disease – Fronto-temporal dementias
Prominent early-onset apraxia -- Corticobasal degeneration
Incontinence/ataxia – Normal pressure hydrocephalus (NPH)

J) Cognitive Testing

- 1) Mini-Mental State Examination (MMSE)
- 2) Draw a clock face
- 3) Copy simple designs or patterns
  - a. 0+0++0+++0++++
- 4) Perform simple acts to assess praxis
  - a. For example, comb hair, brush teeth
- 5) Consider formal neuropsychiatric testing, if possible

K) Laboratory Testing

- 1) No definitive laboratory studies are currently available to diagnose dementia
- 2) Routine hematologic and urine lab studies may guide one to a specific etiology for cognitive impairment
- 3) Allow the history along with the physical and psychiatric examinations to guide further evaluation.

L) Care of the dementia patient: Treating behavioral symptoms

- 1) Educate patient and family
- 2) Reorient to the environment gently and frequently
- 3) Communicate effectively
- 4) Speak just loudly enough
- 5) Keep content simple
- 6) Reassure and distract when distressed or paranoid

## M) Care of the Demented Patient: Medical interventions

- 1) General Principles
  - a. Treat reversible conditions
  - b. Reduce or eliminate drugs that affect the CNS
  - c. Identify and treat co-morbid medical conditions

## N) Pharmacotherapy of dementia

- 1) Weigh the benefits and risks of each drug
- 2) Start low and adjust doses slowly
- 3) Keep the regimen simple
- 4) After starting a drug, monitor for improvement or decline in function
- 5) Disease modifying medications:
  - a. Cholinesterase inhibitors
    - i. Donepezil 2.5-10mg per day orally
    - ii. Rivastigmine 1.5-6mg per day orally
  - b. NMDA-receptor modifiers
    - i. Memantine 5-10mg twice per day orally
    - ii. Used in advanced disease
- 6) Treat specific symptoms such as hallucinations, delusions, agitation, or depression with the appropriate medications

## O) Summary

- 1) Dementias are common in the elderly
- 2) Determine the cause of the impairment and treat reversible conditions
- 3) Dementia, Delirium, and Depression should be distinguished from one another, but they can coexist in the same patient
- 4) Family members are the hidden victims of progressive dementia
- 5) Take care of the caregivers
- 6) Consider psychiatric consultation, if available

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## Altered Mental Status: Delirium and Dementia

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1

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## Delirium Overview

- Delirium is a serious medical condition that requires immediate and thorough evaluation and intervention.
- Delirium is often unrecognized or misdiagnosed as depression, personality disorder, or “difficult patient.”
- Pathology in every organ system can cause delirium
- Delirium often has multiple causes.
- Treatment entails treating the underlying condition.



2



## Delirium Definition

- A disturbance of consciousness accompanied by cognitive deficits that cannot be accounted for by past or evolving dementia. It must include:
  - A disturbance of consciousness (reduced clarity of awareness)
  - A change in cognition
  - Develops over a short period (hours to days) and has a fluctuating course
  - Evidence that the disturbance is caused by the physiological consequences of a general medical condition



3



## A common and serious condition

- Seen in >30% of older medical inpatients.
- The more complicated the case or the more frail the patient, the greater the likelihood of delirium.
- Seen in 70% of ICU patients, 10% of emergency patients, and 42% of hospice patients
- Delirious patients have longer hospital stays and greater functional decline
- Associated with significantly increased mortality at 1 month and 6 months as compared to patients without delirium



4



## General Principles

- Don't assume psychiatric symptoms are due to a long-standing psychiatric disorder
- Don't assume that psychiatric symptoms are a reaction to being terminally ill
- Initiate a search for the underlying cause of the symptoms
- Identify the symptoms that require treatment
- Treat symptoms as specifically as possible



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## Delirium: Common signs & symptoms

- Prodrome (restlessness, anxiety)
- Rapidly fluctuating mental status with lucid intervals
- Disorientation (to time and place – almost never to self)
- Increased or decreased psychomotor activity
- Decreased attention
- Disturbed sleep-wake cycle
- Impaired memory
- Disorganized thinking
- Altered perceptions – misperception, visual hallucinations.
- Emotional lability
- Dysgraphia / dysnomic aphasia
- Motor abnormalities



6



## Assessment of Mental Status

- Perform a thorough evaluation including:
  - Medical and psychiatric history, mental status examination, relevant physical exam, relevant laboratory studies, medications, and outside sources of information (primary team, nursing, sitters, family, friends).
- The Mental Status Examination
  - Appearance & behavior
  - Speech
  - Mood
  - Affect
  - Thought
  - Cognition



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Figure 1: Emergent Items in the Differential Diagnosis

Diagnosis	Key Clinical Questions
Wernicke's - nystagmus, confusion, ataxic	Ataxia? Nystagmus?
Withdrawal - Alcohol, benzodiazepines	Drug or alcohol history? Increased sympathetic activity?
Hypoxemia	Arterial blood gasses? Pulmonary disease?
Hypertensive crisis/ encephalopathy	Blood Pressure (BP)? Papilledema?
Hypoglycemia	Diabetes history? Blood glucose?
Hypoperfusion of CNS	Cardiac history? Low BP? Low Hematocrit?
Infection	Fever? Increased White blood cell count (WBC)? Source?
Intracranial - bleed, trauma	History of head trauma? LoC? Focal neurologic signs
Meningitis/encephalitis	Meningeal signs? Fever/WBC count? Viral prodrome?
Poisons or medications	Toxicology screen? Iatrogenesis (i.e. anti-cholinergics, benzos, steroids, opiates).



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Figure 2: Differential Diagnosis

Infection	HIV, sepsis, Pneumonia
Withdrawal	Alcohol, barbiturate, sedative-hypnotic
Acute metabolic	Acidosis, alkalosis, electrolyte disturbance, hepatic failure, renal failure
Trauma	Closed-head injury, heat stroke, postoperative, severe burns
CNS pathology	Abscess, hemorrhage, hydrocephalus, subdural hematoma, Infection, seizures, stroke, tumors, metastases, vasculitis, Encephalitis, meningitis, syphilis
Hypoxia	Anemia, carbon monoxide poisoning, hypotension, Pulmonary or cardiac failure
Deficiencies	Vitamin B12, folate, niacin, thiamine
Endocrinopathies	Hyper/hypoadrenocorticism, hyper/hypoglycemia, Myxedema, hyperparathyroidism
Acute vascular	Hypertensive encephalopathy, stroke, arrhythmia, shock
Toxins or drugs	Prescription drugs, illicit drugs, pesticides, solvents
Heavy Metals	Lead, manganese, mercury



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## Treatment of Delirium

- Treat any and all reversible medical causes.
- Treat agitation, confusion, and psychotic symptoms.



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## Treating the underlying cause

- Correct metabolic and systemic abnormalities
  - For example, treat infection or constipation, correct hypercalcemia or hyperammonemia if appropriate for goals of care
- Eliminate drug toxicity
  - Discontinue the offending agent(s) if possible
  - Administer appropriate antidote(s)



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## Treating the underlying cause

- Treat Drug Withdrawal
  - Alcohol and sedative-hypnotic (benzodiazepine, barbiturate) withdrawal can be lethal if untreated
    - Treat with benzodiazepines, neuroleptics
    - Symptom-onset is a function of half-life -- the longer the half-life the longer the onset
    - Treatment best with drug from same class, but with a longer half-life
  - Opioid withdrawal is uncomfortable but not lethal
- Obstacles to prompt treatment of drug withdrawal
  - Emergent admissions may result in sudden discontinuation of abused or prescription drugs
  - History of use may be difficult to establish in unconscious patients
  - Physical signs of withdrawal are non-specific
  - No laboratory tests can confirm the diagnosis



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## Managing the behavior: Non-pharmacologic methods

- Control agitated and confused behavior while searching for or treating the underlying cause.
- Start with psychosocial measures, especially if the underlying cause is known
  - Calendars & clocks
  - Windows
  - Low noise level
  - Presence of reassuring relatives.
- Use restraints as a temporary measure to prevent the patient from harming himself or others.



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## Managing the behavior: Pharmacologic methods

- Many drugs can be used in delirium depending on its cause:
  - Neuroleptics, neuromuscular blockers, opioids (for pain), benzodiazepines (for agitation), anesthetics (inhaled or parenteral), and others (ketamine, clonidine).
- Neuroleptics are agents of choice
  - Sedative, anxiolytic, and anti-psychotic properties.
  - Usually do not *cause* delirium.



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## Managing the behavior: Pharmacologic methods

- Haloperidol is often the preferred drug
  - High potency neuroleptic
- Minimal effects on blood pressure, heart rate, and respiratory drive
- No anti-cholinergic properties
- Can be administered parenterally.
- Onset of action: 10-30 minutes
- High-dose associated with QTc prolongation and Torsades de Pointes (often irrelevant in palliative care when goal is comfort)
- Extrapyramidal side effects are rare



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## Managing the behavior: Pharmacologic methods

- Haloperidol Dosing
  - Titrate the dose to the symptoms
    - Mild -- use 0.5-2 mg
    - Moderate -- use 5-10 mg
    - Severe -- use 10 mg or more
  - Repeat doses when necessary, every 15-30 minutes
  - Adjust dose to clinical course
  - Check ECG for QTc if appropriate based on goals of care



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## Managing the behavior: Pharmacologic methods

- Alternative Agents for Agitation
  - Other neuroleptics such as chlorpromazine
  - Atypical neuroleptics such as olanzapine
  - Benzodiazepines
    - Lorazepam:
      - Used orally, sublingually, intravenously
      - No active metabolites
    - Midazolam:
      - Rapid onset of action
      - Causes amnesia and respiratory depression
  - Propofol
  - Opioids (morphine)
  - Paralytics: If used, sedation required



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## Dementia: Overview

- A syndrome characterized by clinically significant decline in memory and at least one other area of cognitive function
- Usually develops over months or years
  - Unlike the acute onset of delirium
- More than 80 specific disorders can cause dementia
- Not all dementias are progressive



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## Dementia: Criteria

- An acquired decline in memory
- Impairment in social or occupational function
- Impairment in at least one other area of higher cortical function:
  - **Aphasia**: Difficulty with language (speaking, reading, repeating)
  - **Apraxia**: Inability to carry out motor tasks despite intact motor function
  - **Agnosia**: Failure to recognize a familiar object despite intact sensory function
  - **Executive dysfunction**: Problems with planning, abstraction, sequencing



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## Dementia: Epidemiology

- Major risk factors:
  - AIDS
  - Advanced age
    - Prevalence 1% at age 60 and doubles every 5 years afterwards
    - At age 85 prevalence is 50%
  - Most common types of dementia in the elderly:
    - Dementia of the Alzheimer's Type (60-80%)
    - Vascular Dementia (10-20%)
    - Lewy body disease (*at least* 5-10%)



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## Dementia: Evaluation

- Much can be done to help afflicted patients and their families even if the dementia is not curable
- Gather a complete history
  - Including a family history as certain types of dementia are heritable (early-onset Alzheimer's).
- Complete a medical and neurological examination
- Order appropriate laboratory testing
  - CT scan to assess for strokes
  - Vitamin B12, thyroid stimulating hormone, syphilis
- It is crucial to distinguish dementia from delirium (see syllabus Figure 3)



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## Dementia: History

- Best obtained from family members or friends
- Determine course of illness
  - Gradual or abrupt onset (Dementia of the Alzheimer's Type vs. vascular dementia)
  - Gradual decline or stepwise progression
- Inquire about functional status
  - Ask about a patient's typical day (work and leisure)
  - Ask about Activities of Daily Living
    - Capacity to perform basic tasks of self care (bathing, dressing, toileting, feeding, continence, transferring)



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## Dementia: Differential diagnosis

### *Irreversible Dementias*

- Degenerative (e.g. DAT, Lewy body disease, Huntington's disease, Wilson's disease)
- Vascular (e.g. Vascular dementia, strokes)
- Traumatic (e.g. Chronic subdural hematoma)

### *Potentially Reversible Dementias*

- Psychiatric (e.g. Depression)
- Neoplastic (e.g. Tumor-related, paraneoplastic)
- Infections (e.g. HIV dementia, neurosyphilis, Creutzfeldt-Jakob disease)
- Obstructive (e.g. Normal Pressure Hydrocephalus)
- Drugs/toxins (e.g. Korsakoff's from alcohol)
- Metabolic (e.g. Thyroid abnormalities, B12 deficiency)
- Demyelinating (e.g. Multiple Sclerosis)
- Autoimmune (e.g. Systemic lupus erythematosus)



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## HIV Infection and the Central Nervous System

- Within days of infection, HIV is transported to brain by monocytes
- Monocytes differentiate into Macrophages
  - Activate randomly over time causing cell death
- CNS is an independent reservoir of HIV
- Antiretrovirals have variable blood-brain-barrier penetrance
- HIV preferentially infects subcortical structures (hippocampus, basal ganglia, cerebellum, mid-frontal cortices)



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## HIV-Associated Dementia

- A subcortical dementia
- An AIDS-defining condition.
- US prevalence 21-25% in HIV patients prior to highly active antiretroviral treatment (HAART) and 7-10% since its the introduction
- Characterized by
  - Slowed information processing
  - Attention and memory deficits
  - Impairments in abstraction and fine motor skills
- A diagnosis of exclusion



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## Physical and Neurological Exam

- Carry out a careful medical assessment
- Search for focal abnormalities
  - Assess vision and hearing
  - Assess abnormal and primitive reflexes
- Conduct a mental status examination



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## Neurologic Findings & Symptoms Associated with Types of Dementia

- Mood changes -- Depressive dementia, depression combined with DAT
- Release phenomena – DAT, Pick's disease
- Long tract and focal findings -- Vascular, Multiple Sclerosis, HIV/AIDS, infections, tumors
- Extrapyrimal symptoms -- Parkinson's, progressive supranuclear palsy, Wilson's, Dementia with Lewy Bodies, late-stage DAT
- Incontinence/ataxia – Normal pressure hydrocephalus (NPH)



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## Cognitive Testing

- Mini-Mental State Examination (MMSE)
- Draw a clock face
- Copy simple designs or patterns
  - e.g. 0+0++0+++0++++
- Perform simple acts to assess praxis
  - e.g., comb hair, brush teeth
- Consider formal neuropsychiatric testing



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## Care of the dementia patient: Treating behavioral symptoms

- Educate patient and family
- Reorient to the environment gently and frequently
- Communicate effectively
- Speak just loudly enough
- Keep content simple
- Reassure and distract when distressed or paranoid



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## Care of the demented patient: Medical interventions

- General Principles
  - Treat reversible conditions
  - Reduce or eliminate drugs that affect the CNS
  - Identify and address co-morbid medical conditions



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## Pharmacotherapy of dementia

- Weigh the benefits and risks of each drug
- Start low and adjust doses slowly
- Keep the regimen simple
- After starting a drug, monitor for improvement or decline in function
- Disease modifying medications:
  - Antiretrovirals for HIV dementia
  - Cholinesterase inhibitors
    - e.g. Donepezil (2.5-10mg daily), Rivastigmine (1.5-6mg daily)
  - NMDA-receptor modifiers
    - Memantine (5-10mg twice daily)
    - Used in advanced disease
- Target specific symptoms (hallucinations, delusions, agitation, depression) with the appropriate medications



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## Summary

- Dementias are common in AIDS patients and the elderly
- Determine the cause of the impairment and treat reversible conditions
- Dementia, Delirium, and Depression should be distinguished from one another, but they can coexist in the same patient
- Family members are the hidden victims of progressive dementia
- Take care of the caregivers
- Consider psychiatric consultation



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## Grief and Bereavement

Guy Maytal, MD

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### I) The experience of grief

- A) Grief is a painful, but nearly universal experience.
- B) There is a great variety in the content, quality, intensity, and duration of the grief experience among individuals and among cultures.
- C) Terminology
  - 1) Bereavement: The state of having lost someone close
  - 2) Grief: A mental state, activated by the death of a close friend or relation that facilitates the dual tasks of coping with the death
    - a. Adjustment of the relationship to the deceased
    - b. Full engagement in life without the loved one
  - 3) Mourning: The behavioral manifestations of grief
- D) Grief Contains a Mix of Emotions
  - 1) Painful
    - a. Sadness about the loss
    - b. Anxiety about how the person will manage
    - c. Guilt about not doing enough and about surviving
    - d. Anger about others not doing or caring enough
    - e. Shame about sense of vulnerability and uncontrollable emotionality
  - 2) Pleasurable
    - a. Enjoyment in recalling happy times or funny anecdotes
    - b. Pride in honoring the deceased
    - c. Warmth in recollecting closeness
    - d. Relief from burden
- E) Anticipatory grief
  - 1) Grieving begins with the knowledge of impending death
  - 2) Individuals grieving their own death feel a range of emotions (e.g. sadness, anxiety, anger), and engage in new behaviors (e.g. attempt to improve relationships and to be closer to loved ones).
  - 3) Anticipation of the death of another allows loved ones to prepare psychologically for the death and may ease their adjustment after the actual death.

- a. Caregiving behavior is one way for loved ones to express respect, affection, and attachment to the dying.

## II) Normal Grief Reaction

### A) Primary Phase of Grief

- 1) Transient: variable in duration: days – months
- 2) Characteristics
  - a. Sense of disbelief, difficulty accepting the death
  - b. A mix of emotions, often intense and unfamiliar
  - c. Preoccupation with thoughts and memories of the deceased
  - d. Relative disinterest in the rest of the world

### B) Bereavement over time

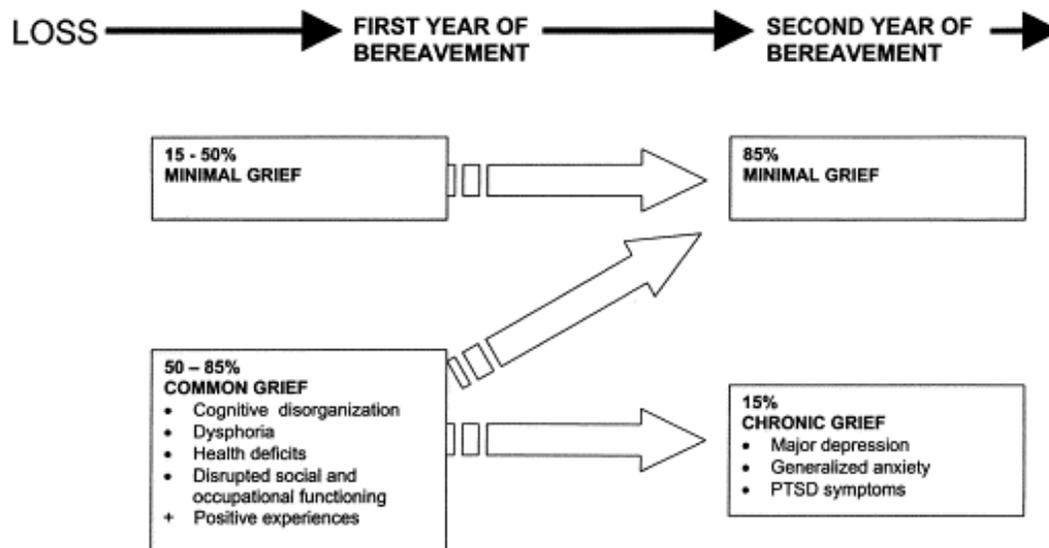
#### 1) Elizabeth Kubler Ross – Stage theory

- a. Five Stages:
  - i. Denial
  - ii. Anger
  - iii. Bargaining
  - iv. Depression
  - v. Acceptance
- b. Initially applied to dying individuals but later expanded to their relatives and to anyone experiencing catastrophic loss.
- c. An observational model with little quantitative validation

#### 2) Bereavement research

- a. No clear-cut stages.
- b. The bereaved initially experience intense distress in a variety of ways (yearning, disbelief, anger, depressed mood)
- c. Distress usually declines over time
- d. Individuals vary greatly in their need to feel and express intense feelings after a death.

### C) A working model for bereavement\* (*next page*)



\*Bonanno & Kaltman, Clin Psychol Rev. 2001 .

#### D) Characteristics of normal bereavement

- 1) 80-90% of individuals have a normal experience
- 2) Distress declines over time
- 3) The griever
  - a. gradually accepts the loss
  - b. reconnects with life in the absence of the bereaved
  - c. sustains self-esteem and sense of purpose
  - d. continues to be productive
  - e. continues to experience waves of sadness – especially around anniversaries and other reminders of the deceased.
    - i. These diminish in intensity and frequency over time.

### III) Abnormal bereavement

- Lack of adjustment to the loss
- Lack of reconnection with life
- Increased risk of developing complicated grief, major depression, suicidal thinking, and medical problems.

#### A) Risk factors for abnormal bereavement

- 1) Poor social supports
- 2) Past history of psychiatric problems
- 3) Past history of separation anxiety
- 4) High initial distress at the time of the death
- 5) Unanticipated death – lack of preparation
- 6) Other major current stressors
- 7) History of abuse/neglect as a child

## 8) Death of a child

## B) Depression in bereavement

- 1) Markedly increased incidence of depression in first year after death of spouse (4-9 times the rate in the general population)
- 2) Sad feelings are a normal part of bereavement, but an episode of Major Depression is not.
- 3) Can lead to significant morbidity and even suicide.
- 4) Should be treated as any other depressive episode – with medication and, if possible, with psychotherapy

## C) Medical sequelae associated with bereavement

- 1) Increased rates of mortality (especially older men), healthcare utilization, consumption of alcohol and tobacco.
- 2) Increased substance abuse can contribute to disease-related mortality and suicide

## D) Complicated grief

- 1) Definition: Persistence for at least 6 months of symptoms in two basic symptom clusters: separation distress and traumatic distress.
  - a. Separation Distress: The core phenomenon.
    - i. Death of a significant other.
    - ii. Intrusive, distressing preoccupation with the deceased person.
    - iii. Loneliness associated with impairments in social functioning and physical health.
  - b. Traumatic distress: Bereavement-specific manifestations of being traumatized by the death.
    - i. Feelings of purposelessness about the future, feeling shocked, difficulty acknowledging death, feeling that life is empty, fragmented sense of trust, security, and control, feeling numb.
- 2) Complicated grief has been shown to predict serious long-term mental and physical dysfunction independent of other mood or anxiety disorders.

**IV) Treatment of the bereaved**

## A) Before the death

- 1) Attend to the coping resources and vulnerabilities of loved ones
  - a. Provide those more vulnerable with psychosocial support.
- 2) The perceived quality of the patient's death affects bereavement of family

- a. Families of patients who “die well” have less of a burden during bereavement
  - b. “Dying well” means different things to different families.
- 3) Communication between the patient, family, and medical caregivers is central

#### B) After the death

- 1) Do what is appropriate in a given culture and for a particular family
- 2) Most grieving individuals do not want or need professional help, usually turning to friends, family, or religious institutions
- 3) Certain symptoms are amenable to treatment if they interfere with functioning
  - a. These include short-term treatment of sleep disturbance and anxiety symptoms.
- 4) Support groups can be helpful to some bereaved individuals – especially those that focus on a specific type of death (e.g. HIV/AIDS, suicide, death of child, violent crime).

#### C) Treatment of bereavement-related depression

- 1) Treat individuals who have symptoms of depression 6-8 weeks after a major loss.
- 2) Treatment is identical to other episodes of depression: anti-depressants and psychotherapy (if available)
- 3) Treatment improves depressive symptoms but does not affect intensity of grief

#### D) Treatment of complicated grief

- 1) Should focus on both understanding the loss and restoring a satisfying life.
- 2) Symptoms have been shown to improve with support groups, treatment of depression, brief psychotherapy, and crisis intervention.

### V) Conclusions

- A) Grief is a painful, but nearly universal experience.
- B) There is a great variety in the content, quality, intensity, and duration of the grief experience among individuals and among cultures.
- C) Normal bereavement can manifest as intense symptoms that slowly subside and cause little impairment by 6 months.
- D) Abnormal grieving can lead to major depression, medical sequelae, and complicated grief.
- E) Physicians should be alert to risk factors and signs of abnormal grieving both during and after the death. They should intervene and refer if appropriate and possible.

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## Loss, Grief, and Bereavement

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## The experience of grief

- Grief is a painful, but nearly universal experience.
- There is a great variety in the content, quality, intensity, and duration of the grief experience among individuals and among cultures.
- A conversation about grief and support for the grieving in Vietnam




## Terminology

**Bereavement:** The state of having lost someone close

**Grief:** A mental state, activated by the death of a close friend or relation that facilitates the dual tasks of coping with the death

- Adjustment of the relationship to the deceased
- Full engagement in life without the loved one

**Mourning:** The behavioral manifestations of grief




## Grief Contains a Mix of Emotions

- Painful
  - Sadness about the loss
  - Anxiety about how the person will manage
  - Guilt about not doing enough and about surviving
  - Anger about others not doing or caring enough
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  - Pride in honoring the deceased
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## Anticipatory Grief

- Grieving begins with knowledge of the impending death
- Individuals grieving their own death feel a range of emotions and engage in new behaviors
- Anticipation of the death allows loved ones to prepare psychologically and may ease adjustment after the actual death.
  - Caregiving behavior is one way for loved ones to express respect, affection, and attachment to the dying.




## Normal Grief Reaction




## Primary Phase of Grief

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- **Characteristics**
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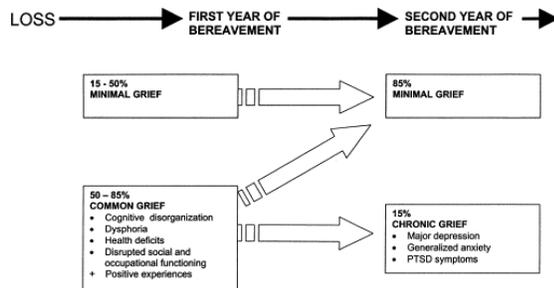
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  - An observational model with little quantitative validation
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  - No clear-cut stages.
  - The bereaved initially experience intense distress in a variety of ways (yearning, disbelief, anger, depressed mood)
  - Distress usually declines over time
  - Individuals vary greatly in their need to feel and express intense feelings after a death.



8

## A working model for grief reactions\*



\*Bonanno & Kaltman, Clin Psychol Rev. 2001.



9

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  - Reconnects with life in the absence of the bereaved
  - Sustains self-esteem and sense of purpose
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*(continued)*

15



- Complicated grief has been shown to predict serious long-term mental and physical dysfunction independent of other mood or anxiety disorders.



16



## Treatment of the bereaved



17



## Before the death

- Evaluate the coping resources and vulnerabilities of loved ones
  - Provide those more vulnerable with psychosocial support.
- The perceived quality of the patient's death affects bereavement of family
  - Families of patients who "die well" have less of a burden during bereavement
  - "Dying well" means different things to different families.
- Good communication between the patient, family, and medical caregivers is very important



18



## After the death

- Do what is appropriate in a given culture and for a particular family
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- Symptoms have been shown to improve with support groups, treatment of depression, brief psychotherapy, and crisis intervention.



21



## Conclusions

- Grief is a painful, but nearly universal experience.
- There is a great variety in the content, quality, intensity, and duration of the grief experience among individuals and among cultures.
- Normal bereavement can manifest as intense symptoms that slowly subside and cause little impairment by 6 months.
- Abnormal grieving can lead to major depression, medical sequelae, and complicated grief.
- Physicians should be alert to risk factors and signs of abnormal grieving both during and after the death. They should intervene and refer as appropriate.



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23



# Psychosocial Support in Palliative Care

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1

## Overview

- What is psychosocial support
- The importance psychosocial support
- National palliative care guidelines





2

## What is psychosocial support?

- A range of interventions that enable individuals and their caregivers to cope with the overwhelming distress that results from long term disease and death




3

## What is psychosocial support?

- The underlying principles:
  - To achieve a good quality of life people need to feel good about themselves and about the interactions they have with others
  - Social relationships, emotional well-being, and spiritual health all affect one another.
- “Simple Truth: We need love and connection to others in order to feel good about ourselves”




4

## What is psychosocial support?

- Addresses social, emotional, and spiritual needs/suffering of patients and families
  - Emotions: guilt, sadness, worry, shame, anger
  - Social
    - Support of family and friends
    - Access to basic needs – housing, food
  - Spiritual: Understanding life in view of ultimate meaning and value (Have I lived a worthwhile life?)
    - Provides hope
    - Connecting to greater reality – ancestors, spirituality, organized religion.




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## What is psychosocial support?

- Providing psychosocial support can include:
  - Counseling (disclosure, depression, grief)
  - Building self-confidence and self-efficacy (belief of individual to have control over life)
  - Increasing ability to see meaning in life
  - Social functioning and relationships (love, companionship, support from friends, family and peers; sense of belonging)
  - Addressing practical aspects of care (finances, housing, food)
  - Assisting with future planning (making a will, planning for children’s future)






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### Why is psychosocial support such an important part of palliative care?

- Patients experience suffering from emotional distress and social problems related to disease
  - E.g. guilt, reduced self-confidence, fear of isolation, loneliness, reduced desire to live, fear of death, anxiety about future and family, fear of loss in income, social status.
- Responds to the emotional and social needs of the whole family from diagnosis through bereavement
- Caregivers of family members or loved ones often face many difficulties in providing care
  - E.g. sadness of losing their loved one, lack of training and skills in providing care, worry related to financial concerns.



### Why is Psychosocial Support important: Needs in Viet Nam

- MoH Palliative Care Needs Assessment Findings (2005)
- PLHA and people with cancer reported significant emotional suffering:
  - 48% felt completely or mostly dissatisfied with their life
  - 79% of people with HIV and 87% of those with cancer said that they were either sad or very sad
  - 64% of family caregivers indicated they were spending more than 10 hours a day providing care to their family member with HIV or cancer.
  - Bereaved caregivers (44%) provided care 20-24 hrs a day
  - Caregivers reported being worried and depressed



### Role of palliative care worker in providing psychosocial support

- To assist patients and families:
  - Strengthening healthy coping mechanisms
  - Providing emotional support and improving self-confidence and self-reliance
  - Helping to improve relationships between patient, family, friends and peers.
  - Referring to social and economic support services
    - I.e. Support group, specialized clinic/hospital, home-based care, hospice care, spiritual leaders, housing aid, child protection and care, economic support, legal agencies
  - Caring for the patient's caregivers – family, friends, and others



### Key Qualities of Psychosocial Support Providers

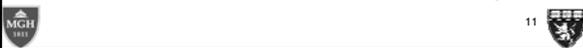
- Trustworthiness
- Self-Awareness
- Acceptance / Being Non-Judgmental
- Professional
- Ethical
- Empathetic
- Knowledgeable
- Culturally Competent



### National Palliative Care Guidelines: Psychosocial Support Contents

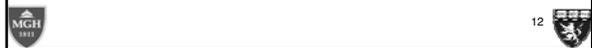
- Caregiver Roles, Qualities and Skills
- Psychosocial support for children
- Psychosocial needs assessment
- Counseling
- Referrals
- Caring for caregivers and managing burnout

(Section III; page 30)



### Making Referrals

- Appropriate referral points: Referral points depend on the level and type of care or service required. They may include:
  - PLHA or cancer support group
  - Specialized clinics or hospitals
  - Home-based care
  - Hospice care
  - Spiritual leaders
  - Housing aid
  - Child protection and care
  - Economic support
  - Legal agencies or local administration



## Plan for the Psychosocial Module

- Presentations of Dr. Ban and Dr. Guy
- Two panel discussions
- Loss/Grief
- Self care and memorial service
- Role play (tomorrow)



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**Thank You!**



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## Psychosocial Assessment Role Plays

Eric L. Krakauer, MD, PhD  
Harvard Medical School and Massachusetts General Hospital

### Case #1: Mr. Tho, a patient with HIV seen in clinic

#### Patient Mr. Tho

You are a 43 year old male construction worker with AIDS who has come to the doctor for a follow-up appointment. Recently, you have not been able to sleep well at night in part because of burning pain in your feet and legs. Last week you borrowed more money from your brother to buy the medication (gabapentin) prescribed by your doctor for the pain, and the burning has improved.

You were diagnosed with HIV at a VCT clinic two years ago, and you bought two ARVs that you took inconsistently at that time. You began taking a 3-drug regimen provided free of charge last year, but you think you are getting sicker despite the medicine. Your father has refused to see you or speak with you since he learned of your diagnosis several months ago. You have experienced a lot of fatigue and weight loss over the last three months and you are worried that you will die soon. You have seen many friends die with AIDS and are afraid of dying in pain. You feel ashamed that you acquired HIV from drug use, and you worry that you may have given HIV to your wife. You wonder what will happen to your wife and children now that you can no longer provide for them. You would like to talk with your brother to tell him how grateful you are for all his financial and emotional support over the last few years, but you have not been able to find the right words and you are afraid of upsetting him. In addition, you worry that your spirit may be restless and separated forever from the ancestors. These worries make you feel sad all the time and also disturb your sleep.

#### Mr. Tho's wife Phuong

You are very concerned about your husband who is getting visibly more sick each day. He has been unable to work for several weeks due to his weakness and foot pain, and your family is now suffering financially. You have three children ages 3, 4, and 7 and are no longer able to pay their school fees. You have never been tested for HIV because you are too afraid.

#### Dr. Hung

You are a busy physician working in an HIV outpatient clinic and you are seeing a follow-up patient with HIV on ARVs. Last week you prescribed gabapentin for his neuropathic foot pain. He is not taking stavudine, so you believe the neuropathy is due to HIV, and not from ARV side effects. You discover that the foot pain has improved with gabapentin therapy and you would like to take some time to do a proper psychosocial assessment.

You are worried that this patient is progressing to end-stage AIDS. He has lost a lot of weight and you suspect that his HIV is resistant to the ARVs that he is taking. There are no other ARVs available. You do not know how much this patient understands about his illness.

You notice that his wife has come with him to the appointment and you wonder how his illness is affecting the family. He looks sad and too weak to work. You would like to take some time to help this patient and his family understand the likely course of his illness and make appropriate plans for the future.

### **Dr. Loc**

You are a doctor in a busy HIV outpatient clinic. Your colleague, Dr. Hung, has just returned from a palliative care course and has just told you that he will need extra time with some of his patients so that he can do a psychosocial assessment. You are concerned that there is not enough time in the clinic schedule for extra talking. You do not understand the importance of the psychosocial assessment and would prefer that your colleague stay on schedule.

\*\*\*\*\*

## **Case #2: Mr. Thieu, a hospitalized patient with lung cancer**

### **Patient Mr. Thieu**

You are a 56 year old veteran of the American War with lung cancer metastatic to bone, liver, and lymph nodes who was hospitalized for severe pneumonia. After seven days of antibiotics, your fever has resolved and you are feeling better. You would like to talk with your doctor about how to cure your cancer.

You are a charming, successful businessman who has been able to avoid serious discussions of your illness by changing the subject and focusing on the big plans that you have made for the next three years. Your restaurant business has been going very well and you plan to open two new restaurants. You are aware that you have been losing weight and are more short of breath over the last few months, but you have attributed this to fatigue from your grueling work schedule.

### **Dr. Oanh**

You are a doctor in an urban cancer center. You are taking care of a 56 year old man with metastatic lung cancer who was recently hospitalized for post-obstructive pneumonia. The patient has improved with antibiotics, but you do not think that the patient, a successful businessman, understands the severity of his disease.

Your patient has been able to avoid serious discussion of his illness by changing the subject and focusing on his business plans. He often talks about being “cured” of his

illness and does not understand that his recent weight loss and shortness of breath mean that he has only weeks or months to live.

You are concerned that this patient's denial of his illness is preventing him from making important plans for the future. You do not know what the patient's family understands about his illness, but you suspect that he has not told them about the cancer. You wonder if the patient would want to make arrangements for his business or financial plans for his family before his death.

**Ms. Lien, Mr. Thieu's wife**

You are the wife of a successful businessman. Your husband is hospitalized with pneumonia but is now recovering.

You are worried about your husband because he has recently lost weight and appears to get tired quickly. When you have asked him how he is doing, he always says that he is fine and makes jokes.

You know that he has been seeing the doctor frequently and this makes you worried.



## Social Suffering Discussion

Guy Maytal, MD & Eric L. Krakauer, MD, PhD  
Harvard Medical School & Massachusetts General Hospital

### Premise:

Physicians regularly encounter patients who are suffering emotionally, socially and spiritually as a result of terminal illness. These same patients are often stigmatized or discriminated against due to their disease. However, many physicians do not have opportunities to talk to their patients about these important sources of suffering to better understand them. Physicians also rarely have the opportunity to talk to colleagues about these issues and specifically about ways to help relieve the social and spiritual suffering of their patients.

### Objectives:

- 1) To provide clinicians with an opportunity to hear from **patient-faculty** about their emotional, social, and spiritual problems and the ways in which these problems affect their lives.
- 2) To provide clinicians with an opportunity to share experiences and exchange ideas about the suffering of their patients and how best to address it.

Today we plan to have two conversations about these concerns. In the first conversation we will focus on the social suffering of people living with HIV/AIDS (PLHA). We will focus on the many types of stigma directed at PLHA (HIV/AIDS patient, TB patient, IDU, sex worker, MSM) and the ways in which stigma causes suffering among PLHA. In the second we will discuss the spiritual impact of life-threatening illness on patients. We hope that these conversations will promote open and ongoing discussion about these neglected sources of suffering and about ways to respond.

### Suggested questions for Social Suffering Discussion:

- What is stigma? How are PLHA stigmatized?
- Do you think that PLHA are stigmatized differently depending on the way they became infected (blood transfusion or medical accident, from a spouse, drug use, sex work)? If so, what are the differences in stigmatization?
- How aware of your diagnosis of HIV/AIDS are your family members? Your friends? Your neighbors? Your work colleagues?
- How has HIV affected your family ties? Friendships? Children? Work? Financial situation? Living situation?
- How has HIV affected these things among friends or acquaintances with HIV?
- Do you think that physicians and nurses treat PLHA differently than other patients? In what ways?
- How do PLHA cope with the stigma and its harmful results?

- Whom can you or other PLHA speak with about your HIV-related social problems?
- How could doctors (or nurses, or OPCs, or hospitals, or Health Departments) help PLHA with their social problems?

## Spiritual Suffering Discussion

Guy Maytal, MD & Eric L. Krakauer, MD, PhD  
Harvard Medical School & Massachusetts General Hospital

### Premise:

Physicians regularly encounter patients who are suffering emotionally, socially and spiritually as a result of terminal illness. These same patients are often stigmatized or discriminated against due to their disease. However, many physicians do not have opportunities to talk to their patients about these important sources of suffering to better understand them. Physicians also rarely have the opportunity to talk to colleagues about these issues and specifically about ways to help relieve the social and spiritual suffering of their patients.

### Objectives:

- 1) To provide clinicians with an opportunity to hear from **patient-faculty** about their emotional, social, and spiritual problems and the ways in which these problems affect their lives.
- 2) To provide clinicians with an opportunity to share experiences and exchange ideas about the suffering of their patients and how best to respond to it.

In our first conversation today, we focused on stigmatization of people living with HIV/AIDS (PLHA) and the social suffering it causes. Now, we will discuss the spiritual impact of life-threatening illnesses such as AIDS and cancer on patients. We will loosely define the spiritual as the sense of connection to something larger or more enduring than oneself. We hope that these conversations will promote open and ongoing discussion about this neglected source of suffering and about ways to respond.

Suggested questions for Spiritual Suffering Discussion:

- Do you think that people living with HIV/AIDS (PLHA) feel responsible for their illness? Feel guilty or ashamed about their illness? Why or why not?
- Do you think that people cancer feel responsible for their illness? Feel guilty or ashamed about their illness? Why or why not?
- Do you think that a diagnosis of HIV/AIDS or cancer can worsen or destroy:
  - o The sick person's relationship to living family members?
  - o The sick person's relationship to the ancestors?
  - o The sick person's relationship to her/his friends?
  - o The sick person's relationship to the community (neighborhood, hometown, country)?
  - o The sick person's self-esteem or sense of personal worth?
  - o The sick person's sense of identity?

- The sick person's understanding of the meaning of life or of having a place in the world?
- If people with HIV/AIDS or cancer feel ashamed or isolated, how might these feelings affect:
  - Their desire to live?
  - Their beliefs about death?
  - Their ability to prepare for death?
- How might doctors or nurses help HIV/AIDS or cancer patients to feel valued or respected? To find some meaning in their illness and suffering?
- How might doctors, nurses, or community health programs help HIV/AIDS or cancer patients to feel integrated into family and community life?
- How might doctors and nurses help terminally ill patients prepare for death?

## Teaching Clinicians about Professional Bereavement

Anthony Back, MD  
University of Washington School of Medicine

### Objectives:

1. Demonstrate a brief clinic routine for discussion of clinician reactions to the death of individual patients.
2. Understand personal reactions to death of a patient.

### Structure:

1. Introduction: 5 min
  - a. Explain rationale and objectives for session. The rationale: Clinicians who care for patients with life-threatening illnesses experience multiple losses. These losses can create emotional barriers to caring for future patients. Dealing with professional losses contributes to professional resiliency and well-being for clinicians. Ground rules for this exercise involve confidentiality.
2. Reflection 7 minutes (2 for instructions, 5 for writing)
  - a. Participant instructions: Write for 5 minutes about a patient death that was emotionally powerful for you. These notes are just for you. You will not be asked to read or share them. What happened? What was your reaction? What were your emotions at the time, and now? What did you learn or take away from this experience?
3. Pairs Discussion 6 minutes
  - a. Participant instructions: Find a partner. Talk to your partner about your reactions for 3 minutes. Share the aspects of your experience that you are comfortable with sharing. Partners should listen deeply but should not attempt to fix, modify, or contradict the person's experience.
4. Large group discussion 20 minutes
  - a. Facilitator question to group: What did you experience as you told your story, and as you listened to your partner's story?
5. Legacy writing 5 minutes
  - a. Participant instructions: Write a message to the patient on a small piece of paper. Fold the paper; it will be collected. These messages will be burned at the end of the session.

**Total time: 50 minutes**



# Day 5



## **Palliative Care for Patients with History of Opioid Dependence**

Eric L. Krakauer, MD, PhD  
Harvard Medical School & Massachusetts General Hospital

Peter Selwyn, MD, MPH  
Albert Einstein College of Medicine & Montefiore Medical Center  
New York

### **I. Introduction**

- A. Illicit drug users with HIV are at risk not only for the standard HIV/AIDS-related complications, but also for multiple medical and social problems secondary to illicit drug use and use of non-sterile injection equipment.
- B. These problems can cause severe suffering and may include:
  - 1. Infections such as hepatitis b and c, bacterial endocarditis with septic emboli, and skin infections, and septic arthritis.
  - 2. Sequelae of bacterial endocarditis including heart failure, stroke, and gangrenous extremities.
  - 3. Sequelae of hepatitis b or c including cirrhosis, liver failure, and hepatocellular carcinoma.
  - 4. Pain, dyspnea, weakness, and other symptoms caused by these conditions.
  - 5. Opioid-induced hyperalgesia that causes an increased susceptibility to pain.
  - 6. Loss of employment, family, and home.
- B. C. Effective intervention for this population requires integration of disease-modifying therapy for AIDS and AIDS-related conditions, treatment of addiction, and palliative care including treatment of pain and psychosocial interventions.

### **II. Disease-Modifying Treatment of HIV-Infected Drug Users**

- A. Clinical experience and comparative studies have indicated that drug users with HIV respond as well to HIV-specific treatment as do other patient groups.
  - 1. Drug users in some countries have been less likely to receive antiretroviral and other HIV-specific therapies when compared with other groups.
    - a. This may reflect a lack of access to medical care services, a failure to follow-up with ongoing care, or reluctance of medical providers to prescribe HIV therapies due to concerns about lack of adherence.
  - 2. In order to treat drug users effectively, it is important to identify the barriers to treatment and develop a plan to treat both the HIV infection and the drug abuse: otherwise any treatment is guaranteed to fail.
  - 3. Drug users who are in drug treatment programs have been found to be very adherent with HIV therapy.
- B. The leading current model for care of drug users with HIV is to combine treatment for HIV with drug addiction treatment services, such as methadone maintenance programs, either through combined programs or close coordination between medical and drug abuse

treatment providers. (See below for discussion of methadone maintenance).

1. When rehabilitation for drug addiction is combined with HIV treatment services, patients have a very good prognosis for improvement in physical health as well as recovery from drug addiction.
- C. Strategies for Accessing Drug Users in the United States
1. Close partnerships between health care providers, public health authorities, community-based agencies, and governmental agencies including law enforcement.
  2. Street outreach workers
    - a. Outreach workers are frequently former drug users who are in recovery from drug use, but who are close enough to the drug-using milieu and population to establish the necessary trust and credibility.

### III. Treatment for Drug Addiction in HIV-Infected Patients

- A. Most HIV-related drug use involves opioid drugs such as heroin.
- B. Depending on the local prevalence of other illicit drug use, HIV and palliative care providers will need to be familiar with recognition and treatment of patients who misuse these other substances.
- C. Methadone Maintenance
  1. Methadone maintenance is the most widespread specific treatment modality for opioid addiction, and it has been used extensively among drug users with and without HIV infection in North America, Europe, and Australia.
  2. Methadone is a long-acting opioid agonist used orally for opioid substitution therapy.
    - a. Methadone is also an analgesic but is dosed differently when used for treating chronic pain.
    - b. In Viet Nam, methadone will be used only to treat addiction.
  3. Methadone maintenance has been found to be effective in decreasing illicit opioid use and drug-related criminal activity, as well as reducing the risk of acquisition and transmission of HIV, and facilitating the delivery of HIV treatment for drug users.
  4. Methadone “maintenance” or substitution therapy, is appropriate for individuals who have developed both psychological and physical dependence on opioids, and who use opioids on a frequent or daily basis.
  5. In the United States, entry into methadone maintenance, which is intended as long-term treatment, is meant to be restricted to individuals who have a history of at least one year of regular opioid use, along with the presence of opioid dependence as evidenced by withdrawal or abstinence symptoms if they suspend use of the drug.
  6. In the United States over 90% of chronic opioid addicts who undergo short-term detoxification which is not followed up by long-term treatment such as methadone maintenance will relapse to illicit opioid use within the first year.
  7. Abstinence / withdrawal symptoms
    - a. The common self-reported abstinence symptoms experienced by opioid addicts generally include:
      - i. Musculoskeletal aches and pains
      - ii. Coryza and lacrimation
      - iii. Chills

- iv. Cutaneous pilo-erection
  - v. Diarrhea
  - vi. Nausea
  - vii. Malaise
- b. Symptoms generally occur within 24 hours after the last use of opioid
  - c. On physical examination, pertinent signs can include:
    - i. Tachycardia
    - ii. Lacrimation
    - iii. Cutaneous pilo-erection
    - iv. Hyperactive bowel sounds
  - d. These symptoms and signs are used to substantiate the history of opioid dependence in order to qualify for methadone maintenance treatment.
8. In other countries, including parts of Western Europe, a more “low threshold” approach to methadone maintenance has been employed, without the need to demonstrate symptoms and signs of physical dependence. This low threshold strategy has been intended specifically as a strategy to help decrease the spread of HIV infection among drug users.
9. Methadone dosing
- a. Methadone is administered as a single daily dose, generally in liquid form.
  - b. Dispensed on a daily basis to drug users at methadone maintenance clinics. These are typically brief visits in the early morning when patients stop at the clinic to receive their daily dose of medicine.
  - c. With its long half-life (close to 24 hours) and the single daily dosing schedule, methadone is an effective means of decreasing illicit opioid use, decreasing the use of unsterile needles for injection of heroin, and treating the abstinence symptoms and drug craving. These symptoms are otherwise very difficult to treat and result in high rates of relapse for opioid addicts who undergo acute detoxification.
  - d. Pharmacologic tolerance
    - i. In addition to physical dependence, opioid addicts also exhibit pharmacologic tolerance, meaning that they are able to metabolize opioids at a faster rate than non-tolerant individuals.
    - ii. Doses of opioids that they need to treat withdrawal symptoms and craving are higher than would be expected in a non-tolerant individual.
  - e. When starting methadone maintenance, once-daily doses are generally started at 20 to 30 mg per day, and then increased by 10 mg every 2 to 3 days until an adequate level is reached to treat withdrawal symptoms, eliminate drug craving, and improve daily functioning.
  - f. The effective dose of methadone to accomplish these objectives is lower than what would cause sedation or euphoria in an opioid-tolerant individual. Most patients receiving effective methadone maintenance treatment are able to continue normal, productive lives with no interference or noticeable effect on their daily activities.
  - g. In most patients, the effective dose of methadone for maintenance is usually in the

range of 60 to 100 mg per day.

10. Treatment is combined with ongoing counseling and other psychological care as needed to treat addictive behaviors and promote recovery.
11. Methadone maintenance treatment can also be very effectively combined with disease-modifying treatment for HIV/AIDS and palliative care in programs that either provide integrated care or work closely with other treatment agencies.
12. Like with the use of opioids for pain management, it is important to have programmatic safeguards and controls in place to ensure the proper storage, inventory, handling, and disposal of narcotic medication, to prevent abuse and diversion of the medication for non-medical purposes. Diversion of medication is also minimized by:
  - a. Supervised once-daily dosing for patients who must attend the treatment program every day
  - b. No “take home” doses unless patients are very stable in treatment, usually after six months or more.
  - c. Exceptions may be made for patients with late-stage HIV disease who are homebound, for whom medication may be delivered by program staff or dispensed to a family member to bring to the patient.
13. The frequent contact that drug-addicted patients have with the methadone program also enhances the ability to ensure adherence with chronic medical therapy. For example, supervised anti-tuberculosis therapy (DOT) has been effectively delivered for years among patients who receive their daily anti-tuberculous therapy at the same time as they receive their daily methadone doses.
14. Initiatives have recently been started to provide once-daily anti-retroviral therapy (HAART) in a similar supervised therapy program linked to daily methadone dosing.
  - a. One sample once-daily HAART regimen is didanosine 400 mg + lamivudine 300 mg + efavirenz 600 mg.
  - b. Other potential once-daily agents include tenofovir and emtricitabine (FTC).
  - c. These options are very promising examples of the possibility that now exists to treat HIV very effectively in drug users; this has important benefits both for individual patients and for public health.
15. Detoxification
  - a. After patients have been stable on methadone maintenance for at least one year, it may be appropriate to consider gradual detoxification.
  - b. For patients with long histories of opioid addiction and relapse, it may be appropriate to continue treatment for a longer period of time, since the risk of recidivism is very high.
  - c. In general, the best long-term treatment outcomes for patients with serious addiction histories have been found to occur after treatment of two years or more, but these decisions should be individualized for each patient depending on progress in treatment.
  - d. Treatment for less than one year is generally not successful in promoting long-term abstinence.
  - e. When elective detoxification is undertaken it should be done slowly, generally by no more than 10 mg per month if possible.

D. Other Treatment Modalities for Opioid Addiction

1. Levo alpha acetylmethadole (LAAM)
  - a. A long-acting oral opioid agonist
  - b. LAAM use may be associated with cardiac conduction abnormalities and prolongation of the QT interval on electrocardiography, and there have been increasing cautions issues concerning its use.
  - c. LAAM is used much less routinely than methadone for opioid substitution therapy and should not be considered the therapy of first choice.
2. Buprenorphine
  - a. A long acting opioid mixed agonist-antagonist
  - b. Recently approved for treatment of opioid addiction.
  - c. Generally administered orally in a dose range of 8-16mg per day, or 16-32mg three times per week.
  - d. Buprenorphine has been used in Europe in recent years with success comparable to methadone
  - e. Possible effective for cocaine addiction therapy
  - f. Shorter and easier detoxification process than methadone, since it is a mixed agonist-antagonist.
3. Naltrexone
  - a. A narcotic antagonist
  - b. Available in parenteral form to treat acute opioid poisoning and overdose
  - c. Long-acting oral form used for treatment for opioid addiction.
  - d. Naltrexone has not been found to be very effective for addiction treatment, and does not prevent the drug craving and withdrawal symptoms that can be effectively managed with the other therapies described above.

IV. Drug Interactions with HIV Medications

A. Cytochrome P-450 system

1. Methadone and some other opioids are potent inducers of the cytochrome P-450 enzyme system in the liver, which is responsible for the metabolism of many drugs, including some that are used in the treatment of HIV infection.

B. Clinically important drug interactions include:

1. Non-nucleoside reverse transcriptase inhibitors
  - a. Nevirapine
  - b. Efavirenz
  - c. When patients on methadone maintenance are started on either of these two agents, their daily methadone doses often need to be increased, due to the increased metabolism of methadone which is due to these other medications. Methadone doses are typically increased in 10 mg increments every 1 to 2 days, titrated to withdrawal symptoms and sedation, often to a final dose that is 50% to 75% higher than the starting dose.
2. Protease inhibitors
  - a. Ritonavir, which although it is itself a potent inhibitor of the P-450 system, has actually been found to result in decreased serum levels of methadone.
  - b. Patients' symptoms should be monitored, and clinicians should be aware that

patients may need methadone dosage increases, but usually not as predictably as with nevirapine or efavirenz

3. Rifampin
  - a. Results in a significant decrease in serum methadone levels, often requiring an increase in methadone dose from 50% to 100% higher than the starting dose.
  - b. Lesser effect may sometimes be seen with rifabutin.
- C. Doses of HIV medications typically do not need to be adjusted to account for the effects of methadone.
- D. Failure to anticipate and manage these common drug interactions will result in methadone withdrawal symptoms and de-stabilization of drug addiction treatment, which will also then compromise HIV treatment efforts.

## V. Prevention of Drug Use -Related Transmission of HIV

### A. Prevention Strategies

1. HIV transmission dynamics among drug users in a region can be rapid and explosive. Therefore, if implemented early, prevention efforts can have an important strategic impact on the subsequent spread of HIV within the population at risk and can help to decrease secondary heterosexual transmission to the non-drug using population.
2. Drug-addiction treatment should be available and accessible for all opioid addicts, and efforts should be made to minimize any barriers to treatment.
3. Enrollment and retention in drug addiction treatment results in decreased risk of HIV acquisition and transmission, as well as the possibility for engaging in medical care and receiving other supportive services for HIV infection.
4. Harm reduction
  - a. Concept articulated in Europe in the early 1980s in response to an epidemic of drug-related hepatitis B.
  - b. Concept holds that while abstinence from drug use may be desirable, it is not always possible, even with the availability of treatment, and that therefore if drug users are going to inject illicit drugs, it is preferable to allow this to happen in ways which minimize harm to themselves and their contacts.
  - c. Includes basic education regarding the risks of HIV transmission through needle-sharing of used, contaminated injection equipment.
5. Needle and syringe exchange
  - a. Effective to varying degrees in reducing the risk of transmission of HIV and other bloodborne viruses.
  - b. Well established in certain areas of Europe, Australia, and North America,
  - c. Community-based projects utilizing outreach workers to provide HIV prevention education, in which drug users can exchange used injection equipment for new, sterile equipment.
  - d. Both stationary and mobile, based in health care agencies and street-level storefronts, depending on local needs and the specifics of the drug-using milieu.
  - e. Needle exchange programs have often been developed through joint efforts involving medical and public health agencies, community-based social service agencies, peer support organizations among addicts, and local law enforcement

- authorities.
- f. Effective bridge to treatment for addicts who have not been engaged in contact with the health care system.
  - g. The programs follow basic principles of infection control and guarantee the safe disposal of contaminated injection equipment.
  - h. Despite concerns about whether such programs might encourage drug use, needle exchange programs have generally not been found to increase the likelihood of drug injection among drug users who do not already inject drugs.
6. Needle hygiene strategies
    - a. Common household bleach, or sodium hypochlorite, can be used effectively to decontaminate needles and syringes.
    - b. Street outreach programs utilizing peer educators have dispensed small plastic bottles of bleach solution, with instructions as to its proper use to flush out injection equipment.
    - c. Drug users can also be counseled to boil injection equipment in water for five minutes in order to decontaminate the equipment before re-use.
    - d. Skin-cleaning with alcohol prior to injection may help decrease the risk of some of the injection-related bacterial infections, although through this practice would not decrease the risk of HIV or other bloodborne virus transmission.

#### V. Pain in Patients With Opioid Addiction

- A. People addicted to opioids (and stimulants) and people receiving methadone substitution therapy may have increased sensitivity to pain. This may be due to opioid-induced hyperalgesia.
- B. People addicted to opioids or receiving methadone substitution therapy are likely to have developed tolerance to opioid analgesics and are likely to require higher doses for pain relief than people not taking opioids chronically.
- C. Some patients with a history of addiction will fear taking opioid analgesics or even refuse to take them because they fear relapse. This fear should be respected.
- D. There is no reason to fear relapse or not to use opioid analgesics in addicts who are dying from advanced, terminal diseases such as cancer or AIDS. When the patient is dying and has pain (or dyspnea), risk of addiction is irrelevant.
- E. There may be misconceptions or fears about treating pain in people receiving methadone substitution therapy that lead to inadequate treatment. It is important to understand that:
  1. People receiving methadone substitution therapy do not receive pain relief from methadone because of the way methadone is dosed in substitution therapy (once per day).
  2. Methadone substitution therapy should continue uninterrupted at the usual dose while pain is treated with other drugs, opioid and/or non-opioid.
  3. There is no evidence that treating pain with an opioid in patients receiving methadone substitution therapy increases the risk of relapse to illicit drug use.
  4. The risk of serious side effects from opioid analgesics is no greater in patients receiving methadone substitution therapy than in others and probably is lower.
  5. It is unlikely that reports of pain in patients receiving methadone substitution therapy

are simply an attempt to obtain more opioids because of addiction (“drug-seeking behavior”).

F. Pain treatment in patients with opioid addiction

1. If possible, use non-opioid analgesic medications and techniques.
2. If pain is severe and/or refractory to non-opioids, opioids should be used. Because the patient may have developed tolerance to opioids, higher than normal doses may be required.
3. In patients with pain and a history of addiction who are not dying, measures can be taken to reduce the risk of diversion of opioid analgesics.
  - a. Limit amount of medication dispensed to the patient at any one time. Prescribe only a 3 – 7 day supply of opioids and require the patient to adhere to a fixed schedule for renewing the prescription.
  - b. Assess the patient frequently for any evidence of ongoing drug abuse such as evidence of fresh injection marks on the skin, suspicious changes in behavior, or changes in adherence with medical therapy.
  - c. Use long-acting opioids for chronic pain if they are available, with or without directly observed therapy (DOT). Long-acting opioids include a 12-hour oral formulation of morphine and an expensive 72-hour fentanyl transdermal patch. Patients receiving DOT with anti-tuberculosis drugs, antiretrovirals (ARV), or methadone can receive their oral long-acting opioid analgesic at the same time. A patient receiving DOT once per day can be given the second dose to be taken 12 hours later.
  - d. When available, urine tests can be used to determine whether the patient is taking an opioid. Urine tests identify which opioid the patient is taking are more expensive.
  - e. Consider making a written, signed “opioid contract” with the patient. The opioid contract can include a clear description of proper and improper medication use, plans for drug screening with urine tests, and consequences of contract violation including discontinuation of opioid therapy. Standard opioid contracts contain the following stipulations:
    - i. The patient will use opioids only as directed.
    - ii. The patient will not try to obtain opioids from any other source.
    - iii. The patient will receive opioids only at scheduled clinic appointments and will not receive an additional opioid prescription prior to the next scheduled appointment unless the patient returns to clinic and has evidence of clinically worse pain. Reports of lost or stolen medication are not acceptable unless the loss or theft is reported to the police.
    - iv. The patient is willing to submit to random drug tests.
    - v. The patient promises not to use illegal opioids or to sell or alter prescribed opioids.
    - vi. The patient accepts that opioid therapy may be decreased or terminated if the contract is broken.

VI. Summary and Conclusion

- A. Treatment for opioid addiction is effective both in reducing illicit drug use and decreasing the risk of HIV acquisition and transmission.
- B. Drug addiction treatment can be successfully integrated with HIV/AIDS treatment and palliative care to improve treatment outcomes for drug users with HIV/AIDS.
- C. Methadone maintenance is the most effective, widespread, and proven modality for treating opioid addiction.
- D. In addition to treatment, harm reduction approaches have also been developed to help decrease the risk of transmission of HIV and other bloodborne viruses for individuals who continue to inject drugs. These approaches have included needle and syringe exchange, and needle hygiene approaches such as the use of household bleach kits or instructions about boiling injection equipment before re-use.
- E. The means exist to provide effective treatment and promote behavior change for risk reduction among illicit drug users. Successful programs will require close coordination between HIV treatment, drug addiction treatment, palliative care, social service, and governmental law enforcement agencies.
- F. Pain is very common among patients with a history of opioid dependence including those receiving methadone substitution therapy.
- G. By following a few important principles, pain in patients with a history of opioid dependence can be treated effectively, usually without increasing the risk of relapse into illicit drug use.

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## Palliative Care for HIV/AIDS Patients with a History of Opioid Addiction

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## Presentation Outline

- What is Opioid Dependence?
- Common health problems in HIV infected IDU
- Role Detoxification and Relapse Prevention in Opioid Addicted
- Role Treatment/Substitution therapy in Opioid Addicted
- Pain Management in Opioid Addiction (Eric)



2



Heroin is the major opioid drug injected in Vietnam



3



## Heroin

- Smoked
- Chasing the dragon
- Injecting



4



## Smoking Heroin: Chasing the dragon



A way of smoking heroin. Involves placing powdered heroin on foil and heating it from below with a lighter. The heroin turns to a sticky liquid and wriggles around like a Chinese dragon. Fumes are given off and are inhaled sometimes through a rolled up newspaper, magazine or tube



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## ICD-10 Diagnostic Guidelines - WHO

A definite diagnosis of opioid dependence should be made only if three or more of the following have been present together at some time during the previous year:

- Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses;
- A physiological withdrawal state when substance use has ceased or have been reduced;
- A strong desire or sense of compulsion to take the substance;
- Difficulties in controlling substance-taking behaviour;
- Progressive neglect of alternative pleasures or interests because of psychoactive substance use;
- Persisting with substance use despite clear evidence of overtly harmful consequences:



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### 'Natural history' of heroin dependence

- Chronic, relapsing – remitting condition
- Dependence usually starts several years after first heroin use
- There is 2 – 5 % spontaneous remission rate per annum
- There is usually 1 – 2 % mortality rate per annum
- The 10 year outcomes (US treatment seekers) are:
  - 50% still using and / or imprisoned
  - 30% abstinent
  - 20% dead
- Most people stop heroin use by their mid 30's to 40's



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### Common health problems among HIV-positive IDUs

- Opportunistic infections characteristic of HIV
- Infection with other blood borne viruses (HBV and HCV) leading to liver disease
- Drug-related hepatitis
- Increased risk of Tuberculosis
- Other bacterial infections -soft tissue infections, pneumonia and endocarditis
- Traumatic injuries
- STIs
- Overdose
- Psychiatric co-morbidity
- **Increased susceptibility to pain**
- Poly-substance abuse



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### Profile of a drug user

- Male (but women increasing)
- Education level variable
- Often jobless or under-employed - does odd jobs to support habit
- Poor
- Criminalized, stigmatised, discriminated
- Will beg, borrow or steal to get drugs
- Homeless/ live on the streets
- This often results in:
  - Low self esteem
  - Low awareness of treatment available and of BBVs
  - Low concern for personal health
  - Low trust level

Source: Basic Principles and Practices of Drug Use Related HIV/AIDS Prevention and Care in the Mekong Region – Burnet Institute Centre for Harm Reduction



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### Caring for HIV-positive IDUs

- IDUs with HIV present with clinical and psychosocial difficulties both related to HIV and to IDU
- They need treatment for HIV and AIDS related conditions including ART, treatment of addiction and palliative care including treatment of pain and psychosocial support
- Injecting drug use is illegal and IDUs are anxious about any contact with authorities and institutions.
- Many IDU never access health care services. Special care is needed to ensure they get the best service available and keep using the services
- Most successful model of care for drug users with HIV is to combine treatment for HIV with drug addiction services



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### Opiate dependence: Treatment options

- Unassisted cessation of drug use
- Counseling
- Medicated detoxification / withdrawal
  - Outpatient
  - Home
  - Inpatient
- +/- naltrexone
- +/- residential rehabilitation
- Maintenance pharmacotherapies
  - Methadone / buprenorphine

Risk of relapse ↑



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### Medications in opioid withdrawal

- Three groups of medication used
  - Opioid substitutes controlled & weaned over a short period
    - Methadone, buprenorphine, codeine, opium, dextropropoxyphene
  - Symptomatic treatment
    - Clonidine Controversial accelerated withdrawal using opioid antagonists
    - Naltrexone, benzodiazepines, loperamide, NSAIDS
  - / naloxone / deep sedation (benzodiazepines)
- All withdrawal treatments are for symptomatic relief
  - None have been shown to have good long term outcomes
  - Some are associated with treatment mortality
  - All are associated with increased post withdrawal mortality
  - Opioid medications have highest completion rates and best symptom control:
    - Methadone ≥ buprenorphine > codeine or opium tincture
  - Need great care with outpatient benzodiazepines and opiates



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## Opioid Substitution Therapy with Methadone

Methadone is a synthetic opioid which binds to opioid receptors in the brain called the mu (morphine) receptors.

As Methadone preferentially binds to opioid receptors an individual does not feel the same physiological craving to take heroin

If an individual on methadone does take heroin it cannot bind to the mu receptors (and therefore they do not experience a 'high' from the heroin)

Methadone has a long half life (8-59 hrs) and can be administered as a single daily supervised dose



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## Abstinence/Withdrawal Symptoms and Signs

Symptoms (usually occur within 24 hrs of last dose)

- Musculoskeletal aches and pain
- Runny nose and eyes
- Chills
- Cutaneous pilo-erection
- Diarrhea
- Nausea
- Malaise

Clinical Signs

- Tachycardia
- Lacrimation
- Cutaneous pilo-erection
- Hyperactive bowel sounds



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## Objectives of substitution maintenance treatment

- To reduce heroin and other drug use
- To reduce mortality
- To reduce transmission of BBVs
- To improve the patient's general health and well being (psycho-social functioning)
- To reduce drug-related crime



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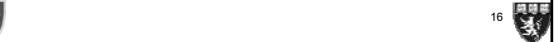
## Methadone cost effectiveness

International consensus that MMT saves the community between 7 and 10 times the program costs:

- Legal
- Law enforcement / incarceration
- Health
- Social
- Insurance
- Customs
- Deaths



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## Eligibility for opioid substitution treatment

- Opiate dependent,
- Informed consent
- Inclusion criteria (suggested):
  - More than six months dependent use
  - At least one withdrawal attempt
  - Able to travel to dispensing site
- Exclusion criteria:
  - Not wanting maintenance treatment



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## Methadone pharmacology

- Well absorbed orally. Time course of effects
  - onset 30 – 60 minutes
  - peak 2 – 4 hours after dose
- Therapeutic effects:
  - Pain relief for 4 - 6 hours (initially)
  - Relief of opioid withdrawal for 15 - 30 hrs (dose related)
- Half life = 20 to 24 hours.
- Methadone has a range of pharmacological actions: 1)analgesia for about 6-24 hours, 2) a sense of well being, 3) sedation 4) suppression of opioid withdrawal and craving for about 16-36 hours, and a mood stabilizing effect for longer periods
- Steady state equilibrium only after 5 half lives = 5 days
- Metabolised by hepatic cytochrome P450
  - impacted by drug interactions, individual variation, disease states
  - Particular interactions with ART and TB drugs



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## Initiating methadone

- Start with low methadone doses
    - According to neuroadaptation :
- (Low 15 – 20mg / Medium 20 – 25mg / High 25 – 30mg)

- Review the patient frequently
- Titrate the dose carefully to 60 – 120mg

*“Start low, go slow, aim high”*



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## Titration doses

- Increase dose after 3 to 5 days methadone (steady state)
  - More rapid dose increases can result in accumulation & toxicity
- Methadone increases of 5 – 10mg may be safe if still clearly under-medicated:
  - Dose increases of > 10 mg at a time not safe
  - Recommend maximum 30mg increase in any week
- Only increase dose after reviewing patient & where clinically indicated:
  - In withdrawal
  - Still using heroin
  - Thinking / dreaming of using heroin often
  - Unable to say no to heroin when offered



Increasing dose required

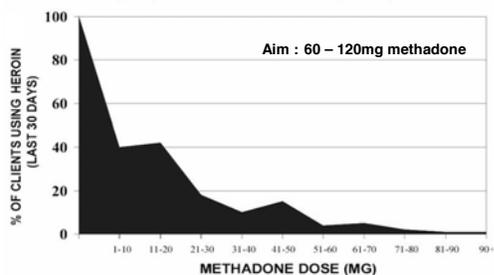


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## Reduction of heroin use

Relationship between methadone dose and heroin use  
(adapted from Ball and Ross, 1991)



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## Opioid Substitution Therapy - Side effects

- Side effects common during treatment initiation, and then tolerance develops to many
- Some early side effects can be difficult to differentiate from withdrawal symptoms
  - nausea, joint aches, sweating, poor sleep
    - (Buprenorphine – nausea, insomnia, hyperactivity)
- Some side effects are chronic problems
  - constipation; sweating; sleep disturbances
  - endocrine changes (reduced libido, menstruation)
  - dental problems



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## Overview of substitution maintenance treatment

- Provision of a long acting opioid such as methadone enables the patient to cease / reduce their heroin use and related harmful behaviors
- Long term treatment approach (number of years):
  - Provides opportunity for patients to distance themselves from drug-using lifestyle and reenter 'normal' society
  - Controls drug craving and opioid use allowing slow neurobiological recovery to occur
- Combines medication with psychosocial services
  - Repair the damage to psychology and socialisation caused by years of illicit drug use
- Can combine methadone treatment with HIV care and treatment including ART (DOTS)



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## Other treatment modalities for Opioid Addiction

- Buprenorphine
  - a long acting opioid mixed agonist-antagonist
  - administered as a sub-lingual tablet or liquid three times a week
  - Safer than methadone but more expensive and easier to divert than methadone
- Naltrexone
  - A narcotic antagonist
  - Not found to be very effective for opioid addiction as it doesn't reduce craving and withdrawal symptoms



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## Pain in Patients with Opioid Addiction

- Often increased sensitivity to pain / opioid-induced hyperalgesia
- Opioid tolerance
- Therefore higher than normal opioid doses often needed
- No reason not to use opioids for pain or dyspnea in dying patients



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## Pain in Patients Receiving Methadone Substitution Therapy (MST)

- Methadone does not provide pain relief when dosed for substitution therapy
- Methadone should continue at usual dose when treating pain
- No evidence that treating pain with opioid in patients receiving MST increases relapse
- Unlikely that reports of pain in MST patients are due to drug craving



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## Pain Treatment in Patients with History of Opioid Addiction

- If possible, use non-opioid
- If pain is severe, use opioid
  - May need higher dose than normal
- In patients who are not imminently dying and not receiving MST, steps to minimize risk of diversion:
  - Limit amount of opioid prescribed, require patient to return regularly for new prescription
  - Assess for evidence of drug abuse (injection marks, erratic behavior, non-adherence)
  - Use long-acting opioid with DOT if possible
  - Urine tests, if available
  - Consider "Opioid Contract" with the patient



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## Opioid Contract

- A clear description of proper and improper opioid use, plans to assess for opioid misuse, consequences of violating the contract.
  - Use opioid only as directed
  - Obtain opioid from no other source
  - Opioids prescribed only at scheduled appointments, no refills for lost or stolen medications (must protect the medication)
  - Patient agrees to urine tests or other tests for improper drug use
  - No use of illegal drugs or diversion of prescribed drugs
  - If contract broken, opioid therapy may be terminated



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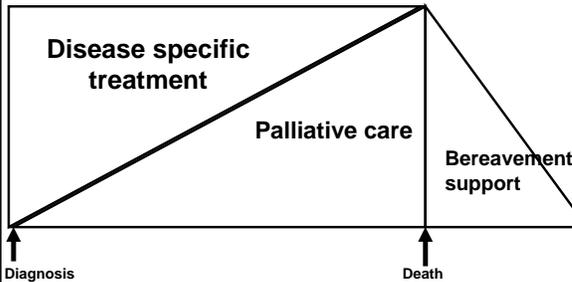


# Integrating Palliative Care into HIV/AIDS Care and Treatment

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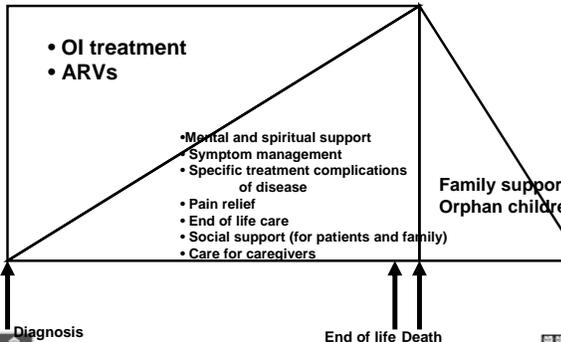

## Integration with disease specific treatment



...is an important part in palliative care and comprehensive treatment




## Integration with disease specific treatment

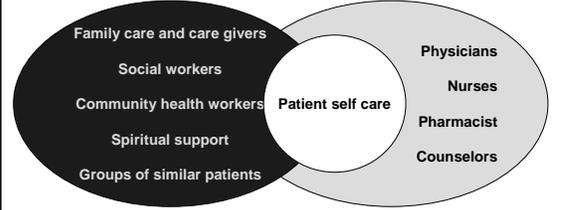


Diagnosis      End of life Death



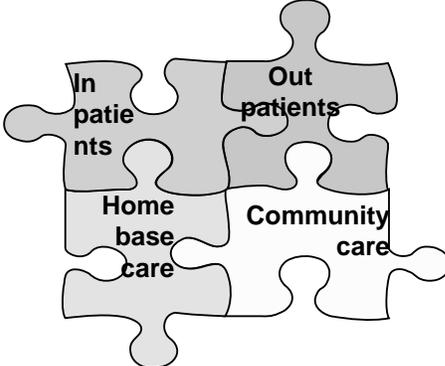

## Interdisciplinary care team:

Integrating professional care givers and non professional care givers





## Integration by locations





## Care at Home and Community (1)

- In the countries having limited human resources and infrastructure, home base care and community care are considered the main of responding to the patients' palliative care needs.
- Home and community care systems should associate with health care centers at provincial and central levels in responding to the increasing AIDS epidemic.
- Palliative care is part of comprehensive and continuous care for HIV/AIDS, cancer and other chronic illness patients
- Most patient with life threatening conditions would like to receive care at home




### Care at Home and Community (2)

- Symptom management and specific treatment of complications of disease (due to OIs and ARV treatment)
- Pain relief
- Support follow up and adherence: ARVs and OIs treatment
- Psychological and spiritual support
- End of life care
- Social support (for patients and family):
  - Nutrition support
  - Jobs, income
  - Child support: health care, reintegration into society (in accordance with age) etc
- Care for care givers



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### Care at the HIV OPC (1)

- HIV/AIDS patients need to be cared, followed up regularly and periodically at the OPC
- Patients may additionally face the following needs:
  - Psychosocial
  - Pain
  - Symptoms: nausea, vomit, weakness, fatigue, sleepless, etc.



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### Care at the HIV OPC (2)

- Health workers at OPC should collaborate with home care teams and patient's families in ensuring out patient care is comprehensive and continuous.
- Refer the patients and families to social and religious care and support facilitates if needed



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### In patient care

- When patients have OIs, complications or high level symptoms or require end of life care
- At different levels of specific hospitals or infectious diseases department of the general hospitals or other health care centers
- In addition to disease specific treatment, palliative care teams should make a comprehensive assessment of the palliative care needs of the patients admitted to hospital, including response to palliative care treatment.



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### Case discussion 1

- An HIV infected patient visits an HIV OPC and complains about severe headache and sleeplessness. The treating medical doctor did not find any cause other than severe pain and decided to give oral morphine for this patient, to be given as an out patient.
- Question:
  - What things should the treating doctor discuss with home care team?
  - What is the role of home care team in this case?



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### Case discussion 2

- A HIV infected woman comes to an HIV OPC with her child. After examination, the doctor and counselor ask more about her situation and are told that the child is at the age to go to kindergarten but, due to fear of discrimination and stigma, she did not dare to let the child go to school...
- Question:
  - What should the OPC staff do in this case?



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### Case discussion 3

- An HIV infected women currently admitted to infectious disease department of a provincial general hospital. During counseling, the patient says that her husband from HIV several months earlier, that his family was asking her to return her mother's house to live to live.
- Question:
  - What things should the staff of the infectious department do in this case?



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**Thank you**



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# Integrating Palliative Care into Cancer Care & Treatment

Prof., Dr. Nguyen Ba Duc  
Director of National Cancer Hospital




## Cancer Situation in the World

- Globally each year:
  - > 10 million people have cancer
  - > 6 million deaths due to cancer
- In developing countries: Cancer is second cause of death after cardiovascular disease.
- Cancer disease tends to increase with prolonged life span, urbanization, polluted environment, harmful life style...




## Global Cancer Situation

Incidence rate of cancer in males over all ages (excluding skin)

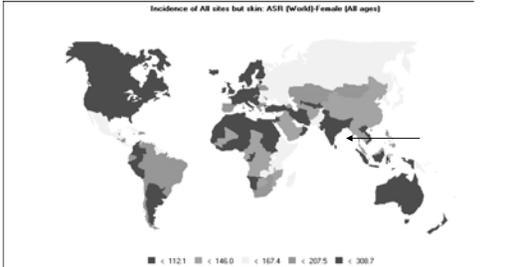


Cancer commonly seen in male: lung cancer, stomach, large intestinal and rectum, prostate, liver




## Cancer Situation in the World

Incidence rate of cancer in females over all ages (excluding skin)



Cancer commonly seen in female: Breast, large intestinal and rectum, cervix, stomach, and lung cancer




## Cancer Situation in Vietnam

- In Vietnam: with increasing development, according to mixed morbidity models, non-infectious diseases are increasing
- Estimating 150,000 new cancer cases, 75,000 death cases/year
- The most common cancer diseases in male: lung cancer, stomach, liver, large intestinal and rectum...
- The most common cancer diseases in female: breast, stomach, cervix, large intestinal and rectum...




## 10 Most Common Cancers Seen in Males, in Hanoi and Ho Chi Minh

Hanoi			Ho Chi Minh		
No	Location	Hanoi 2001-2004 (ASR)	No	Location	Hanoi 2001-2004 (ASR)
1	Bronchi - Lung	39,8	1	Bronchi - Lung	29,5
2	Stomach	30,3	2	Liver	25,4
3	Liver	19,9	3	Stomach	15,3
4	Large intestine - rectum	13,9	4	Large intestine - rectum	16,2
5	Esophagus	9,8	5	Larynx	4,8
6	Upper jaw	7,8	6	Non Hodgkin Lymphoma	4,6
7	Non Hodgkin Lymphoma	7,2	7	Upper jaw	4,2
8	Blood	4,7	8	Esophagus	4
9	Bladder	3,5	9	Skin	3
10	Lower throat	3,2	10	Prostate	2,8




10 Cancers Commonly Seen in Female, in Hanoi and Ho Chi Minh

Hanoi			Ho Chi Minh		
No	Location	Hanoi 2001-2004 (ASR)	No	Location	Hanoi 2001-2004 (ASR)
1	Breast	29,7	1	Breast	19,4
2	Stomach	15,0	2	Cervix	16,5
3	Bronchi - Lung	10,5	3	Bronchi - Lung	12,4
4	Large intestine - rectum	10,1	4	Liver	6
5	Cervix	9,5	5	Large intestine -rectum	9
6	Thyroid gland	5,6	6	Stomach	5,5
7	Ovarian	4,7	7	Ovarian	3,8
8	Liver	4,5	8	Thyroid gland	3,8
9	Non Hodgkin Lymphoma	4,0	9	Non Hodgkin Lymphoma	3,2
10	Blood	3,4	10	Skin	2,6

## National Cancer Prevention Program

- Disease prevention
- Improve quality of disease diagnosis and treatment
- Improve quality of life of cancer patient

## Needs of Cancer Patients

- > 80% patients are late stage
- Pain occurs in more than 75% of cancer patients, and is moderate or severe in 53%

↓

**Huge need for palliative care**

## Palliative Care

- General principals

Palliative care should be performed from the disease diagnosis and continued for whole course of disease

## Palliative Care

- General principals:
  - Integrating with disease specific treatment
  - Promoting treatment adherence and reducing side effects
  - Actively supporting patients to end of life
  - Psycho-social support is very important

## Palliative Care

- General principals:
  - Support families while patients are sick or die
  - Develop a palliative care model of a multidisciplinary care team with the patient at the center
  - Implement this model at health facilities, and at the home and community

## Palliative Care

- Pain management:
  - Evaluating pain levels so as to improve patients' quality of life at all levels
    - *Pain Severity Scales*
    - *Wong-Baker Faces Pain Rating Scale*
  - Pain management assisted by combining drug and non drug therapy
  - Always paying attention to psychological support and psychological factors



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## Palliative Care

- Symptom management:
  - Nausea, vomiting
  - Diarrhea, constipation,
  - Mouth pain and pain on swallowing
  - Cough, dyspnea
  - Weakness, fatigue, agitation
  - Delirium
  - Fever
  - insomnia, pruritis
  - Bed sores...



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## Palliative Care

- Psychosocial care for patient and caregiver
  - Should satisfy the emotional, psychological and social needs of the patient and family
  - Should be continued when patients pass away (bereavement support)
- Means:
  - Active listening, understanding and sharing grief, ensuring confidentiality and psychological needs assessment



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## Palliative Care

- Patients on radiation therapy:
  - Local: care for mouth and teeth, irradiated skin, and other supportive measures.
  - Whole body care
  - Psychological care.
  - Encourage co-orporation between patient and family



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## Palliative Care

- Patient on chemotherapy:
  - Locally: manage leaking chemicals
  - Entire body care:
    - Management of chemical shock
    - Reduce white blood cells
    - Management of vomiting, care to ulcers of digestive membrane, anemia treating
    - Proper nutrition
    - Psychological care



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## Palliative Care

- Care for patient with surgery:
  - Pre surgical care: explain, careful clinical assessment, improve health status, pre surgical hygienic preparation
  - Post surgical care:
    - Locally: care for the wound and drainage tubes.
    - Entire body care: Supplementary water and electrolytes, antibiotics
    - Psychology support
- Pediatric palliative care
  - Based on children development at different stages to understand their needs



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## Palliative Care

- End of life care
  - Emotional and spiritual support
  - Pain relief
  - Nursing care



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**Thank you very much!**



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## **The Palliative Care Team**

Cynthia R Goh, MBBS, PhD  
National Cancer Centre Singapore

### **I. Introduction**

Palliative Care is active total care of patients with life-threatening illness. Patients with advanced disease may not only have distressing symptoms, but they also may suffer from social, financial, emotional, or spiritual problems that significantly diminish quality of life. In order to address such a wide spectrum of need, an interdisciplinary team is often needed.

### **II. The Unit of Care**

Care is needed not only for the patient, but also for the family. In certain clinical situations, such as end-stage AIDS of a child or advanced dementia, it is well recognized that some or even most of the suffering occurs in the family. This is true to a certain extent with all life-threatening illness. The family includes not only blood relatives, but all who are providing the day-to-day, sometimes hour-to-hour, care for the patient, and all who are emotionally attached to the patient.

### **III. The Core Palliative Care Team**

The core team looking after the patient usually is comprised of the patient's primary doctors, nurses and medical social workers. In places where trained medical social workers are unavailable, their place may be taken by workers who are familiar with the welfare system in the community and those who are skilled at counseling.

The following are possible roles taken by members of the palliative care team, all of which have some overlap:

- A. The doctor assesses the medical condition of the patient and treats pain and other symptoms. He/she is also responsible for communicating with the patient or family about the illness, the goals of care, and the treatment including its potential benefits, burdens, and cost. He assesses the patient's mood and response to the illness, and updates the family on the patient's condition.
- B. The nurse deals with nursing care, including oral hygiene, bowel habit, skin care, advising on diet, ensuring medications are taken correctly, and teaching family members to provide care. The last task might include instruction on HIV prevention.
- C. The medical social worker or equivalent assesses the financial and social needs of the patient, facilitates access to help from the community, assesses the patient's coping and the coping of other family members, and intervenes with emotional support or counseling when needed.

All members of the team are responsible for giving moral and emotional support to the patient, family and to each other, as well as to members of the wider care team, to ensure that members are not overly distressed by the situation of the patient.

Though local practices may differ, palliative care teams generally have little hierarchy. The leader of the team may be a doctor, a senior nurse or a senior social worker.

An important aspect to ensure effective team functioning is mutual respect, and an understanding of the roles of the different members of the team. Members should learn to value their diversity of background, skills and training as the strength of the interdisciplinary team.

#### **IV. The Wider Care Team**

Other health professionals may have input to the patient. These include:

- A. Allied health professionals
  - 1) Physiotherapists help prevent de-conditioning, give chest physiotherapy, and help with rehabilitation. Specialized care includes treatment of lymphoedema.
  - 2) Occupational therapists help patients with activities of daily living and provides aids for mobility.
  - 3) Speech therapists assess swallowing and protection of the airway.
  - 4) Dieticians advise on nutrition and diets.
  - 5) Pharmacists help with ordering, stocking and dispensing of medications, advise on dosing and routes of administration and preparation of specialized drug preparations, such as for intrathecal analgesia.
  - 6) Stomatherapists help with management of stomas, fistulae and wounds.
  - 7) Laboratory staff give support for haematology, biochemistry, microbiology and immunology investigations.
  - 8) Psychologists help with psychological assessment and counseling.
  
- B. Other medical and dental professionals
  - 1) Medical oncologists provide chemotherapy, hormonal and targeted therapies.
  - 2) Radiation oncologists treat bone pain and shrink tumors causing symptoms or bleeding.
  - 3) Orthopedic surgeons fix fractures and do spinal decompression.
  - 4) General surgeons remove tumors causing obstruction, perforation or distressing symptoms
  - 5) Dental surgeons help with tooth and mouth problems.
  - 6) Rehabilitation physicians help assess rehabilitation potential and plan care.
  - 7) Infectious disease specialists help deal with complicated infections.
  - 8) Psychiatrists help assess and treat delirium, dementia, anxiety and depression.

#### **V. Miscellaneous**

- A. Volunteers – Many palliative care services worldwide involve volunteers who take a variety of roles, ranging from being trustees of a charitable service organization, to care provision by professionals, fund-raising, public education, help and support of patients and their families.
- B. Art therapists and music therapists work with patients through art and music, allowing patient or family members to deal with emotions and grief through creativity.
- C. Massage therapists help with their touch to aid relaxation or relieve pain and stiffness and provide comfort.
- D. Acupuncturists, traditional medicine practitioners, herbalists use alternative methods of therapy to treat diseases or restore balance to the body's systems.

- E. Faith healers also have a role for those who believe in traditional folk healing.
- F. The patient and the family, though they are the beneficiaries of care, should also be considered as part of the care team. Empowerment of the family to provide care and emotional support for the patient is emphasized. The patient is also empowered to take as much responsibility for his or her own care as possible, while respecting his ability and preference.
- G. Practitioners of complementary therapies are often an important support for the patient or family. A judgmental attitude towards such non-evidence-based practice on the part of western trained medical practitioners is not helpful. It is important to keep the patient's welfare at the forefront. At a stage when western medicine has no disease-modifying treatment to offer, it should allow harmless practices desired by the patient and advise only against interventions likely to be harmful.

## The Palliative Care Team

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National Cancer Centre of Singapore  
Faculty and Fellows of Vietnam Fellowship in Palliative Medicine



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1



## Of Whom Does the Palliative Care Team Consist?

- Depends on who are the receivers of care:
  - Patient
  - Family, other caregivers, anyone emotionally attached to the patient
    - In some situations, family & friends suffer most
      - Advanced dementia
      - Dying child
    - Relationship between physician and family / caregivers is uncertain
      - Counseling and emotional support
      - Medical treatment?
      - Referral?



2



## Of Whom Does the Palliative Care Team Consist?

- Depends on the type of suffering (palliative care is a **response** to suffering)
  - Physical
  - Psychological
  - Social
  - Spiritual
- Palliative care is best provided by a **multidisciplinary team** because:
  - Multiple receivers of care
  - Multiple types of problems
  - The work can be emotionally difficult (although also extremely satisfying)



3



## Of Whom Does the Multidisciplinary Palliative Care Team Consist?

- In rich countries:
  - Primary physician (often oncologist or infectious disease specialist)
  - Consulting physicians
    - Medical sub-specialties
    - Oncology specialties (medical, radiation)
    - Surgeon
    - Psychiatrist
    - Palliative care specialist
    - Traditional medicine
  - Nurses
  - Pharmacists
  - Social worker
  - Physical, occupational, and speech & swallowing therapists
  - Other therapists: massage, music, art
  - Chaplain
  - Volunteers
  - Family



4



## Roles of Team Members

- Physician
  - Assessment & treatment of symptoms
  - Communication with patient and/or family
    - Diagnosis
    - Prognosis
    - Goals of care
    - Treatments, including potential burdens & benefits
    - Changes in patient's condition



5



## Roles of Team Members

- Nurse
  - Give medication or assure medication taken properly
  - Hygiene
  - Skin care
  - Bowel habit
  - Instruction for family in providing care, including HIV prevention



6



### Roles of Team Members

- Pharmacist
  - Ordering, safely stocking, dispensing drugs
  - Advise on taking medications, drug interactions
  - Special medication preparations
- Social worker or peer support group
  - Assess social and financial needs
  - Arrange for social supports
  - Assess coping of patient and family
  - Provide emotional support and counseling (also done by all other members of team)




7

### Roles of Team Members

- Volunteers
  - Manage support groups
  - Emotional support
  - Education and stigma reduction
  - Other roles
- Chaplains
  - Emotional (spiritual) support
  - Assist in search for meaning




8

### Roles of Team Members

- Family
  - Part of the team
  - Can be empowered to provide care and emotional support
- Patient
  - Also can be empowered to take responsibility for some of her/his own care
- Important to learn the skills and potential contributions of each member of team to optimize care
  - Effective team functioning requires mutual respect




9

### The Core Palliative Care Team

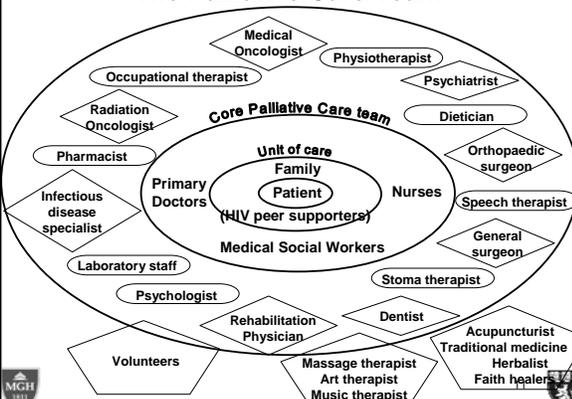


There may be some overlap in role in members of the core team




10

### The Palliative Care Team





11

### The Strength of the Palliative Care Team

Lies in its **diversity**  
of skills, language ability, personalities

Lies in its **unity**  
unity of purpose & goals

Lies in its ability to **support** each member




12

### Of Whom Does the Multidisciplinary Palliative Care Team Consist?

- In Viet Nam
  - Inpatient
    - Treating doctor
    - Consultant specialists
      - Psychiatrist, Rehabilitation, Surgeon, others
    - Nurses
    - Housekeeping staff
    - Pharmacist
    - Volunteers / peer supporters / “social workers” (HIV/AIDS)
    - Medical students (as volunteers)
    - Dietician / Kitchen staff
    - Family (of patient and of other patients)
    - Other patients



13



### Of Whom Does the Multidisciplinary Palliative Care Team Consist?

- Outpatient clinic
  - Treating doctor
  - Consultant specialists
    - Psychiatrist
    - Adherence & harm reduction counsellor (HIV)
    - Others
  - Nurses
  - Pharmacist
  - Volunteers / peer supporters / “social workers” (HIV/AIDS)
  - Family



14



### Of Whom Does the Multidisciplinary Palliative Care Team Consist?

- Community-based & Home care
  - Local health staff
    - Nurses
    - Communal or family doctor
    - Community healthcare worker
  - Pharmacist
  - Volunteers / peer supporters / “social workers” (HIV/AIDS)
    - Women’s Union
    - Youth Union
    - Trade Unions
    - Red Cross
  - Spiritual supporter
    - Monk, Priest, Nun
  - Family



15



**Comments and evaluation form for VCHAP training**

Thank you very much for your time in completing this evaluation. Your sincere comments will help us prepare improvements for further trainings. We would like to know what things you did or did not like about the training and what things did or did not benefit you. Please suggest any kind of changes, we will take your suggestions seriously. The evaluation form is confidential; you do not need to write your name on the form.

*Please rate each part of day training as following levels: 1-Not useful 2-Somewhat useful 3-Useful 4-Very useful 5-Extremely useful*

**Not useful**       $\longrightarrow$       **Extremely useful**

---

*Part 1: Life-threatening Illness in Vietnam*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

*Part 2: What is Palliative Care: Definition and Principle*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

*Part 3: Palliative Care in Vietnam*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

*Part 4: Medical ethics, the patient-doctor relationship, and team-work in pall care*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

*Part 5: The pall care team*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....

.....

*Part 6: Palliative care assessment and approach to the patient*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....

.....

*Part 7: Small group role play: Breaking bad news*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....

.....

*Part 8: Small group role play: Psychosocial assessment*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....

.....

*Part 9: Bedside rounds in small groups*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....

.....

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**3-Useful    4-Very useful    5- Extremely useful**

**Not useful**                      **Extremely useful**

---

*Part 1: Principles of pain management*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

*Part 2: Adverse effects of analgesics and adjuvant analgesics*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

*Part 3: Barriers to pain relief- Opioid Policy in Vietnam*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

*Part 4: Adult learning theory and Training of Trainers (TOT) techniques*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

*Part 5: Small group cases (Pain management)*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

*Part 6: Bedside rounds in small groups*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments .....

.....

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**Not useful**       $\longrightarrow$       **Extremely useful**

---

*Part 1: Dyspnea*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comment.....  
 .....

*Part 2: Nausea/vomiting*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comment.....  
 .....

*Part 3: Constipation / diarrhea*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comment.....  
 .....

*Part 4: Constitutional symptoms*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comment.....  
 .....

*Part 5: Skin problems*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comment.....

.....

*Part 6: Small group case discussions*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comment.....

.....

*Part 7: Bedside rounds in small groups*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comment.....

.....

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**3-Useful    4-Very useful    5- Extremely useful**

**Not useful**                      **Extremely useful**

---

**Part 1: Psychological / Psychiatric problems: Depression, Anxiety and Insomnia**

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....  
 .....

**Part 2: Psychological / Psychiatric problems: Dementia and Delirium**

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....  
 .....

**Part 3: Panel discussion: Social suffering**

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....  
 .....

**Part 4: Panel discussion: Spiritual suffering and care:**

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....  
 .....

*Part 5: Panel discussion: Loss, grief, bereavement:*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....

.....

*Part 6: Health Care Worker self-care and Memorial Service*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments

.....

.....

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**Not useful**       $\longrightarrow$       **Extremely useful**

---

*Part 1: Psycho-social-spiritual suffering: small group role plays*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....  
 .....

*Part 2: Integrating Palliative Care with HIV/AIDS care and treatment\**

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....  
 .....

*Part 3: Palliative care for Injection Drug Users: Addiction management*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....  
 .....

*Part 4: Palliative care for Injection Drug Users: Treatment of pain*

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....

.....  
**Part 5: Integrating pall care into cancer care and treatment**

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....  
 .....

**Part 6: Plans for development of Palliative Care in Vietnam**

Contents	1	2	3	4	5
Presentation	1	2	3	4	5

Comments.....  
 .....

1. The training materials provided satisfy your expectation??

Yes \_\_\_\_\_ (go to question 2)

No \_\_\_\_\_

*If no*, what things did not meet your expectations?

2. What part of training materials do you like??

3. What part of training course do you not like?

4. What part of training course is most useful for you?

5. What part of training course is not useful for you?

6. What topic/content you would like to learn, but we did not mention to?

7. You learn better through the presentation or through small groups discussion? Please explain.

8. How these training courses change your opinions/attitude on treatment and care for HIV/AIDS patient?

9. What things should be changed for further training?

---

Thank you!





Palliative Care Module I “Master Trainers” Train-the-Trainers Course, faculty and trainees. National Cancer Hospital, Hanoi, Vietnam, March 2007.



Palliative Care Module I Train-the-Trainers Course, faculty and trainees. National Institute for Infectious and Tropical Diseases, Hanoi, Vietnam, March 2007.



Palliative Care & HIV/AIDS Basic Training Course, Part 1, faculty and trainees. Nhan Ai Humanitarian Hospital, Binh Phuoc Province, Vietnam, April 2007.



Palliative Care & HIV/AIDS Basic Training Course, Part 2, faculty and trainees. Nhan Ai Humanitarian Hospital, Binh Phuoc Province, Vietnam, October 2007.



Palliative Care Module I Basic Training Course, faculty and trainees. Hospital for Tropical Disease, Ho Chi Minh City, Vietnam, October 2007.



Palliative Care Module I Basic Training Course, faculty and trainees. Haiphong Viet Tiep Provincial Hospital, Haiphong, Vietnam, October 2007.



Palliative Care Module I Basic Training Course, faculty and trainees. Nhan Ai Humanitarian Hospital, Binh Phuoc Province, Vietnam, October 2008.



Palliative Care Module I Basic Training Course, faculty and trainees. Danang, Vietnam, October 2008.



Palliative Care Module 1 Basic Training Course, faculty and trainees. Bach Mai National Hospital, Hanoi, Vietnam, March 2009.



Palliative Care Module 1 Basic Training Course, faculty and trainees. Ho Chi Minh City Cancer Hospital, Ho Chi Minh City, Vietnam, March 2009.



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