

## Pain Modulation

- Pain mediated by multiple pathways  
Five receptors exist (mu1, mu2, delta, sigma, kappa, and epsilon)
- Endorphins have analgesic effect and act as negative feedback to pain

Once pain receptors are stimulated, central receptors are occupied. Based on the receptor or combination of receptors, we can predict a pain medication's effectiveness and many of its side effects.

Endorphins attach to some of these receptors too, providing natural pain relief.

### 痛みの調節

○痛みは多様な経路により仲介される。

5種類のレセプターの存在

(mu1, mu2, delta, sigma, kappa, epsilon)

○エンドルフィンには鎮痛作用を持ち、

痛みに対する抑制性フィードバック機構として機能する。

## Pain Assessment

### • PQRST

- Palliative and provocative factors
- Quality
- Radiation
- Severity
- Temporal

When discussing pain with a patient, one needs to know what activity or other factors cause the pain to become worse or better. What has the patient taken to treat themselves? This discussion helps us begin to assess the severity and possibly the origin of the pain.

The quality of the pain is explained by the patient which may help us understand the cause of pain, such as pressing pain in the chest being angina, or sharp piercing pain in the ear being associated with an ear infection. Radiation of pain helps us determine if the sensation of pain and origin of pain are the same, or if the pain is referred. Many abdominal and chest pains radiate.

The severity of the pain is important to know. The patient may describe it as the “worst of their life” or “like a headache”.

And, the time of the pain is important such as migraine headache occurring during times of stress.

痛みの評価

○PQRST

軽減および刺激因子

性質

放射

痛みの程度

痛みの時間

## Pain Assessment Continued

- **Psychogenic Pain**  
(anxiety, depression,  
fatigue, anger)
  - Real
  - No known cause
  - Nonlocalized
  - Ill defined
  - Not easily treated
- **Pain Threshold Factors**
  - above, plus behavioral,  
cognitive, social and  
cultural factors

Pain can be a sign of physical or emotional disorders. Underlying problems are often initially described as pain of some type. Pharmacists should suspect psychogenic pain if the pain is of unknown cause or non localized, etc.

A patient's threshold of pain is also effected by their emotional status as well as other factors.

痛みの評価 (つづき)

○心理的痛み (不安、抑うつ、疲労、怒り)

本物の痛みか

原因不明

非局所的

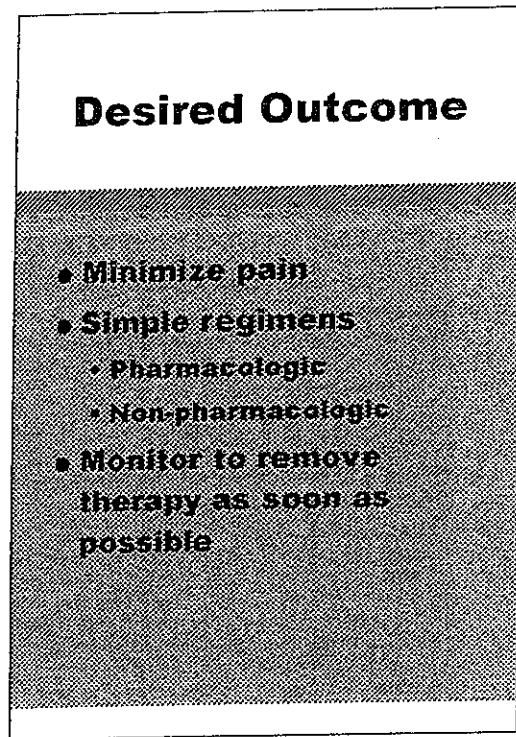
Ill defined

治療困難

○痛みの閾値に影響する因子

上記の因子および

行動的、認知的、社会的および文化的因子



Our goals in assessing and suggesting treatment if focused on:

Minimizing pain

Using simple regimens

Using non drug treatment when possible

and,

Removing therapy as soon as possible

望ましい効果

○痛みの減少

○単純な管理

薬学的および非薬学的

○できるだけ速やかに治療を中止するための監視

## Acute Pain

- Individualize dosage and dosage form to the patient
- Use scheduled dosing
- Non-narcotic agents
  - Look at all parameters
  - Use least aggressively with fewest side effects to begin

Treatment of acute pain should include calculation of a dose specific for the patient's size, age, history, and organ function.

Therapy should be prescribed on a schedule, and non narcotic agents should be preferred.

急性疼痛

○患者ごとの用量設定

○計画的投与

○非麻薬性鎮痛薬の使用

総てのパラメータを観察する。

最も緩和で副作用の少ない薬物から開始する。

## Acute Pain

- **Non-narcotic agents**

- They ALL reduce prostaglandins, except acetaminophen, reducing pain impulses

- Caution using aspirin products with NSAIDs - GI side effects

- Avoid aspirin products in children with viral syndrome (Reye's syndrome)

When we teach students in class or in clinic, we begin the discussion of therapies with case scenarios. Let us try one!

Suppose you have a 32 year old male coming to you with a sprained ankle, due to a soccer accident at practice. The patient is very healthy otherwise. What would you recommend as far as medication is concerned?

Virtually all non narcotic analgesics reduce the levels of prostaglandins, except acetaminophen. Consequently acetaminophen is of less benefit when we are treating an inflammatory response such as a sprained ankle. A better choice would be a non-steroidal anti-inflammatory agent.

急性疼痛

○非麻薬性鎮痛薬

アセトアミノフェンを除き全ての薬物が  
プロスタグランジンの合成を抑制し、痛みの衝撃を減少する。

消化管に対する副作用を有するアスピリン系薬剤の  
使用には注意を要する。

ウイルス感染症候（ライ症候群）を呈している小児には  
アスピリン系薬剤の使用を避ける。

## Acute Pain

### • Non-narcotic agents

- NSAIDs and ASA should be given cautiously in renal patients to prevent further damage.
- Salicylate salts - few GI effects and do not inhibit platelet aggregation.
- NSAIDs do both while plasma levels are therapeutic. NSAIDs cause fewer GI effects than ASA.

Suppose the next patient you encountered was a 78 year old with severe renal disease and has a broken wrist. The patient fell on the ice. Other drug therapy the patient has is warfarin for a heart valve replacement. What drug therapy would you recommend?

Any elderly patient or other patients known to have significant renal disease should be given an adjusted dose of pain medication.

Salicylate salts may be given cautiously to patients on anticoagulants.

Most patients would receive an initial dose of narcotic for the acute pain, but non-steroidal anti-inflammatory agents are still the agents of choice when treating pain of this type for several days.

急性疼痛

○非麻薬性鎮痛薬

腎機能の低下した患者には、悪化を防止するために NSAIDs および ASA は注意して投与する。

サリチル酸塩 - 消化管に対する副作用は少なく 血小板凝集を抑制しない。

NSAIDs は血中濃度が治療域でも両作用を示す。

ASA に比較して NSAIDs は消化管に対する副作用が少ない。

## Acute Pain

### • Narcotic agents

- These are the second step for pain management
- Work by occupying opiate receptor sites (partial or full block)

The next patient we will consider has been in a motor vehicle accident. The patient has a broken arm, torn ligaments in the ankle. The patient's jaw is severely bruised.

Narcotic agents should only be used when non-steroidal anti-inflammatory agents are not likely to work, or have failed.

Narcotic agents are very effective in preventing patients from perceiving pain.

急性疼痛

○麻薬性鎮痛薬

同等の鎮痛作用を示す用量は基準に過ぎない。

交差感受性の可能性は少ない。

副作用は一般的であり、治療が必要である。

吐き気、便秘、呼吸抑制



## Acute Pain

### • Narcotic agents

- Equianalgesic doses are only a guide
- Cross sensitivity is NOT likely
- Adversities are common and need to be "treated"
- Nausea
- Constipation
- Respiratory depression

The next patient situation is a patient on morphine 4 mg every 2 hours intravenously who needs to change to an oral agent. How is this done?

Remember, changing from one dosage form to another is an estimation, and deserves conservative adjustment. It is important to change without causing side effects, or allowing for breakthrough pain.

When narcotic analgesics are given, both early and late or cumulative side effects need to be considered.

急性疼痛

○麻薬性鎮痛薬

この使用は疼痛管理の第2段階である。

オピオイド受容体に結合することにより作用する。

(部分的あるいは完全アゴニスト)

## Acute Pain

### • Narcotic agents

#### • Mixed narcotic agonist-antagonists

- For moderate to severe pain
- Ceiling effect on respiratory depression
- Low abuse potential
- Decreased constipation
- BUT, may cause pain on withdrawal

When narcotic agents are combined, there is a lowered potential for abuse, and a decrease in side effects.

However, these agents are usually not as effective or as useful as non-steroidal anti-inflammatory agents or narcotics.

急性疼痛

○麻薬性鎮痛薬

アゴニスト/アンタゴニスト性麻薬性鎮痛薬

中程度から激痛

呼吸抑制に対する天井効果

依存性が低い

便秘誘発が少ない

使用中により疼痛を誘発する可能性がある。

## Acute Pain

### • Narcotic agents

#### • Mixed narcotic agonist-antagonists

- Nalbuphine - reduced O<sub>2</sub> demand on the heart compared to similar medications
- Buprenorphine may have a longer duration of effect with less respiratory depression.
- Binds tightly to opioid receptors
- Butorphanol and nalbuphine are not controlled

Our next patient unfortunately got up at night and ran into the door of his bedroom. He broke his nose. It has been set, and he is going home from the clinic. What pain medication would work in this situation?

Several things would work.

One type of agent we see used for localized trauma pain is the narcotic agonist-antagonist. Examples are nalbuphine and buprenorphine. These are becoming more popular in America because buprenorphine is available in a nasal spray.

急性疼痛

○麻薬性鎮痛薬

アゴニスト/アンタゴニスト性麻薬性鎮痛薬

Nalbuphine：類似薬に比較して心臓の酸素消費量が少ない。

Buprenorphine：呼吸抑制が少なく、作用持続が長い。

オピオイド受容体に対して強く結合する。

NalbuphineとBuprenorphineは規制されていない。

## Chronic Pain

- **Non-cancer chronic pain**
  - Treat as described above
  - Strongly consider psychologic and other techniques also
    - biofeedback
    - stress relief
    - counseling
    - exercise
    - less rest

The next patient we see has chronic low back pain. This patient is a truck driver. His pain is diffuse. He states he takes ibuprofen and it does not work. When on ibuprofen he took 300 mg four times a day, every day.

Chronic pain can be treated using many different methods, which include non-pharmacological techniques. In fact, accupressure, accupuncture, and magnet therapy can be added to this list.

For other patients who will not accept these methods, we can use other agents. Let us list some.

慢性疼痛

○非ガン性疼痛

急性疼痛と同様の治療

心理的、その他の治療法を考慮する。

生物学的フィードバック

ストレスの除去

カウンセリング

運動

過剰な静養を控える

## Chronic Pain

### • Non analgesic medications

#### • Antidepressants

#### • Local anesthetics

• Bupivacaine (Marcaine)

• Direct injection or epidural injection

#### • Hydroxyzine / dextroamphetamine

• Potentiate analgesic efficacy of parenteral narcotics

• Phenothiazines ???

Chronic pain can effectively be treated with non-traditional medications.

Amitriptyline has been shown clinically to work, using small to moderate doses, particularly for neurogenic and phantom limb pain.

Local anesthetics such as bupivacaine are being used very often by direct injection. These give long term pain relief (two weeks to three months), after trauma or corrective surgery or chronic low back pain.

慢性疼痛

○鎮痛薬以外の治療薬

抗うつ薬

局所麻酔薬

Bupivacaine (Marcaine)

直接または硬膜外注射

Hydroxyzine/dextroamphetamine

非経口的に投与された麻薬鎮痛薬の作用を増強する。

Phenothiazines ???

## Cancer Pain

- Patients with frequent or constant pain
- Fixed schedule
- Base interval on the half-life of medication

Our next patient is a 62 year old female with esophageal cancer. She has experienced moderate to severe pain for several days. You are asked to recommend treatment and a dosing schedule.

Cancer pain should be treated until the pain is relieved, but with fixed doses and with a regular schedule.

ガン性疼痛

○患者には、しばしばあるいは常時痛みがある。

安定した投与計画

半減期に基づいた投与間隔

## Cancer Pain Starting Doses

- Mild pain -  
acetaminophen or  
NSAID
  - NSAID for bone pain
- Moderate pain
  - Opioid or mix, or  
oxycodone
- Moderate to Severe
  - MSIR 30 mg po q4h ATC  
or equivalent

Moderate or severe pain is very adequately treated in most cases with immediate release morphine. It is given in doses of 30 mg every 4 hours by mouth around the clock. Doses are then adjusted to patient tolerance.

ガン性疼痛

初期投与量

○軽度の疼痛

acetaminophenまたはNSAID（背中の痛み）

○中程度の疼痛

オピオイド、アゴニスト／アンタゴニスト型または

oxycodone

○中程度から激痛

MSIR 30 mg 経口4時間毎継続、または同等量

## Cancer Pain Starting Doses

- Moderate to Severe but, Opioid naive/frail/elderly
- MISR 15 mg po q4h ATC or equivalent
- Morphine has a longer T<sub>1/2</sub> in the elderly and may need q6-12 hours

Our next patient is an 82 year old frail patient with bone cancer. Are the doses of morphine the same for this patient?

No.

Doses should be halved and titrated to the patient's needs. In a frail individual, always start with a smaller dose and titrate more slowly. The goal is still pain resolution with minimal side effects.

ガン性疼痛

初期投与量

○中程度から激痛

虚弱な高齢者におけるオピオイド初期投与量

MISR 15 mg 経口4時間毎継続、または同等量

高齢者ではモルヒネの半減期は延長し、

6-12時間毎の投与が必要かも知れない。



## **Cancer Pain - Unstable Pain**

- **Immediate release formulations and titrate every 12 to 24 hours to relief**
- **Change to sustained release with resolution of pain**

Once the cancer pain responds to prescribed therapy and side effects are minimal, then sustained release products can be used. Again, treat to effectiveness. Some patients can very safely be maintained on 600 to 900 mg of morphine sulfate sustained release without serious side effects.

ガン性疼痛

安定していない疼痛

○速効性の処方および改善するまで12-24毎に力価測定を行う。

○痛みがとれたら持続性製剤への処方変更

## Cancer Pain - Stable Pain

- Definition - 4 or fewer rescues per 24 hours
- Titration method by percent
  - Mild to moderate pain - increase 24 hour narcotic total by 25%
  - Severe pain - increase 24 hour narcotic total by 50%
  - Total narcotic dose is fixed dose plus rescue dose

Our next patient scenario is a woman on 160 mg of morphine sulfate per day taken orally. She is having pain she rates as a "seven" on a scale of "ten", and describes it as some of the worst chronic pain she has experienced in her life. How much of an increase in her dose would you make today to attempt to control her pain?

Increase the dose 25% to 50% of her total daily dose.

ガン性疼痛

安定した疼痛

○定義—24時間で4回以下の追加投与

○パーセントによる力価測定法

軽度から中程度の疼痛—

1日量を25%増量する。

激痛—

1日量を50%増量する。

1日量は固定し、追加投与する。

## **Cancer Pain - Stable Pain**

- Titration method by documentation of rescue dosing
- Patient documents number of rescue doses per 24 hours
- Increase 24 hour fixed dose by number of mg of rescue medication needed to control pain
- Increase rescue dose as needed

Continue to titrate morphine sulfate or narcotic as needed until the patient is stable.

ガン性疼痛

安定した疼痛

○追加投与量による力価測定法

○1日当たりの追加投与の回数を測定する。

○疼痛コントロールに必要であった1日当たりの追加投与量分を1日量に追加する。

○必要に応じて追加投与量をあげる。

## **Cancer Pain - Stable Pain**

• **Sustained release  
medications are to be  
used only in stable pain**

**Do not use sustained release medication for unstable cancer pain!**

ガン性疼痛

安定した疼痛

○安定した疼痛にのみ持続性製剤を使用する。