

## Pathophysiology

### • Spinal cord

- alterations secondary to ectopic impulses flowing into dorsal horn

- "wind-up" – abnormal temporal summation of peripheral input

- N-methyl-D-aspartate (NMDA) antagonists may block wind-up

### • Brain

- alterations in response to abnormal input

This type of pain can originate in the spinal cord or the brain. It is thought to be mediated by n-methyl-d-aspartate. Antagonists of this agent may aid in treatment.

### 病態生理

#### ○脊髄

脊髄後根への異所性インパルスによる二次的变化  
"wind up" – 末梢性入力の異常で一過性の合計  
NMDAレセプターアンタゴニストは"wind up"を  
抑制する可能性がある。

#### ○脳

異常入力に対する反応の変化

## Etiology

- Metabolic causes – most common
  - diabetes mellitus – reported incidence varies (16% - 61%)
  - hypothyroidism
  - uremia
  - B-vitamin deficiencies (especially thiamine)
- Drug toxicity
  - chemotherapy agents: vincristine, cisplatin, taxol
  - gold, nitrofurantoin, zalcitabine

There are metabolic causes for neuropathic pain, as well as drug toxicities that cause neuropathic pain.

### 原因論

- 代謝的原因—最も一般的
  - 糖尿病—
  - 報告されている発症率 (16-61%)
  - 甲状腺機能低下症
  - 尿毒症
  - ビタミンB欠損症 (チアミン)
- 薬物毒性
  - 化学療法剤：
    - vincristine, cisplatin, taxol
    - gold, nitrofurantoin, zalcitabine

## Etiology

- Other
  - HIV
  - cancer
  - systemic vasculitis
  - rheumatoid arthritis
- Unknown etiology in ~1/3 of patients

Complications of diseases also cause neuropathic pain.  
Unfortunately, only about one-third of patients with neuropathic pain have known causes.

原因論

○その他

HIV

ガン

全身性血管炎

慢性関節リウマチ

○原因不明 (~ 1 / 3 患者)

## What would you do?

- Complete history and pain assessment performed
- Patient started on gabapentin 300mg PO TID

In this patient, the physician began treatment with gabapentin. Is this an appropriate therapy for neuropathic pain?

あなたはどうしますか？

- 完全な病歴と疼痛評価がなされた。
- Gabapentin 300mg po tidで治療開始する。

## Antidepressants

- TCAs - assumed mechanism: alterations in 5HT and NE activity in brain / nociceptive activity
- proposed mechanism: local anesthetic-type action + blockade of ectopic discharge generation
- amitriptyline, nortriptyline, desipramine

Several medications have been used to treat neuropathic pain. Most notably tricyclic antidepressants. Of the tricyclic antidepressants, amitriptyline is the most effective.

The proposed mechanism is a local anesthetic action.

抗うつ薬

○三環系抗うつ薬 (TCA)

機序：脳内セロトニンおよびノルアドレナリン  
活性/侵害活性の変化

提唱されているメカニズム：

局所麻酔薬様作用、異所性発射の抑制

amitriptyline

nortriptyline

desipramine

## Antidepressants

### • TCAs

- start at 10-25mg QHS, titrate according to guidelines
- 30-100mg usually effective, draw serum level if max doses needed

### • SSRIs

- mixed results from studies

If you were going to use tricyclic antidepressants for the patient in the case above, what doses would be used.

Usually start at 10-25 mg at bedtime only, and titrate to efficacy, usually no more than 100 mg.

抗うつ薬

○三環系抗うつ薬 (TCA)

10-25 mg 就寝前で開始、

ガイドラインに従って用量調節

通常、30-100 mgで有効

もし、最大用量が必要な時は血中濃度を測定する。

○選択的セロトニン取り込み阻害剤 (SSRI)

研究により結果が異なる。

## Antidepressants

- **Venlafaxine**

- similar effects to TCAs, without anticholinergic or cardiac effects
- limited by adverse effects (BP, gastrointestinal effects, irritability)

Other antidepressants have been used such as venlafaxine. The studies are not as numerous, but the cardiac effects of the tricyclics are not as significant a problem.

抗うつ薬

○Venlafaxine

TCAに類似した効果

抗コリン作用や心臓に対する作用がない

その他の有害作用により使用が制限される。

(血圧、胃腸に対する効果、被刺激性)

## Anticonvulsants

- Mechanism: unclear
- Phenytoin, carbamazepine
  - well studied, effective
  - side effects limit use
  - monitor levels
- Gabapentin
  - well studied, effective
  - few intolerable effects

Epilepsy agents have been used for neuropathic pain.  
Their mechanisms are not clear, however there is some positive clinical responses documented.

抗けいれん薬

○機序：不明

○Phenytoin, Carbamazepine

よく研究され、効果的

副作用により使用が制限される

血中濃度のモニター

○Gabapentin

よく研究され、効果的

不耐性の効果がほとんどない



## Anticonvulsants

- **Gabapentin**

- titrate by 300mg every 3-7 days

- 2100-3600mg usually effective, max dose 6000mg/day

When gabapentin is used, start and titrate as is indicated on the slide. Other epilepsy agents have been used, but not successfully, such as clonazepam, lamotrigine and valproic acid.

抗けいれん薬

○Gabapentin

300 mg、3 - 7 日毎に用量調節

通常、2100-3600 mgで効果的

最大用量は6000 mg/日

## Local anesthetics

- Mechanism: reduction of abnormal spontaneous and evoked discharges in damaged peripheral nerves responsible for neuropathy
- Intravenous lidocaine
  - 1-5 mg/kg infused over 30 min-1 hr
  - concentration monitoring not useful for predicting effect

Local anesthetics are being used for neuropathic pain as well, including lidocaine infusions. It works by reducing abnormal spontaneous discharges in the damaged peripheral nerves. When used, it is dosed in the low range, at 1-5 mg per kg given over 30 minutes to one hour.

### 局所麻酔薬

- 機序：障害のある末梢神経において異常な自発および誘発発射を減少する。
- リドカインの静脈内投与
  - 1-5 mg/kgの用量で30分から1時間かけて注入
  - 血中濃度の測定は効果の予想に有用ではない。

## Local anesthetics

### • IV lidocaine

- monitor ECG, BP, and signs of toxicity (tinnitus, dizziness, seizures, etc) during infusion
- duration of relief: hours to weeks; ideally, repeat dosing Q 3-4 weeks

Patients given lidocaine infusions for neuropathic pain should be monitored during the infusion for toxicity. Relief lasts for hours to weeks. Most patients need repeat infusions every three or four weeks.

### 局所麻酔薬

#### ○リドカイン静注

静注の間は心電図、血圧および毒性徴候

(耳鳴、めまい、てんかん発作など)を監視する。

改善の期間：数時間から数週間

3-4週間毎に繰り返す。

## Local anesthetics

### • Oral mexilitene

- should be taken with food
- monitor ECG in patients with cardiac history
- 150 mg per day, titrate Q 5-7 days

Oral mexilitene is used as well with some positive effects.

局所麻酔薬

○経口mexilitene

食べ物と一緒に飲む

心臓病の経歴のある患者ではECGをモニターする。

150 mg/day、5-7日毎に用量調節

## Other agents

- Clonidine
- Dextromethorphan
- Opioids oral
- Tramadol oral
- Capsaicin topical
- Lidocaine topical

Additional agents have been used with some positive effects. Results are mixed.

その他の薬剤

Clonidine

Dextromethorphan

麻薬性鎮痛薬 経口

Tramadol 経口

Capsaicin 局所性

Lidocaine 局所性

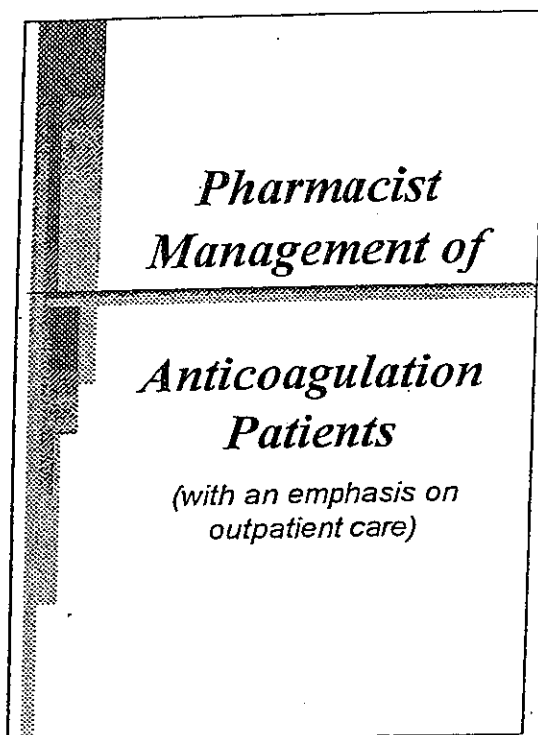
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# Anticoagulation therapy management by pharmacists

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Thank you for this wonderful opportunity to visit your country, to work with you, and share ideas. It is indeed, a great honor to be with you. I also want to thank my hosts who have made this opportunity possible.

Our purpose in the next hour, is to discuss the role of pharmacists who manage patients on anticoagulation patients. Our emphasis will be on patients who are prescribed warfarin or enoxapirin for treatment or prophylaxis. We will also discuss roles of the pharmacist beyond patient care issues; including policies and functions in the clinic area that should be considered.

薬剤師による抗凝血薬服用患者の管理  
特に外来患者について

## *Issues*

- *Patients on anticoagulants are at risk*
- *Patients on anticoagulation are at risk because of their underlying disease*
- *Pharmacists are seeking patient types that they can safely monitor*
- *Health care funding will force physicians to seek other health professionals to see these patients*

There are four issues we should be aware of that influence how pharmacists work with anticoagulant patients.

First, we know that patients on anticoagulant medications are at greater risk than many other patients on medications. The incidence of fatal and major bleeds in patients taking warfarin is approximately 0.6% and 3% respectively. These patients need careful instruction, and continuous monitoring to assure safe use.

Second, patients on anticoagulant medications are at risk as a result of their underlying disease. Many of these patients have multiple diagnoses and multiple medications. This too, causes the health care professional to care for these patients more intently.

Third, pharmacists, along with other ancillary health professionals in America, are interested in maintaining these patients, and to be recognized for it. Pharmacists desire to expand their role.

And fourth, in America, physicians are seeking assistance from others to maintain patients who need more extensive education, careful monitoring, and good outcomes. Many times the physician does not have the time or resources to follow a number of these patients.

### 論点

- 抗凝薬服用患者は高リスクである。
- 抗凝薬服用患者は、基礎疾患のために高リスクである。
- 薬剤師は監視できる患者タイプを求めている。
- ヘルスケア基金の関係で、医師はこれらの患者を監視する専門家を求めている。



## *Anticoagulant Patients are a Good Choice!*

- *Pharmaceutical care is practiced*
  - *Prevention/Healing disease*
  - *Solving problems*
  - *Diagnosing problems*
- *The risk are primarily drug oriented*
- *Pharmacists are very good at dealing with detail*

Anticoagulant patients' needs match many of the goals of providing pharmaceutical care. These include prevention and elimination of disease; solving healthcare problems; and diagnosing problems.

Anticoagulation management success and failures are strongly associated with the pharmacology of the active agent, and many other agents which interact with warfarin or enoxaparin. The pharmacist is a particularly good choice as an assistant to the physician for monitoring these patients.

And, in my experience, pharmacists have been quite successful in this role because they are able and willing to work with the detailed record keeping and communication necessary in such a practice.

抗凝血薬服用患者はよいチャンスである！

○ファーマシューチカルケアの実施  
予防／病気の治療

問題の解決

診断上の問題

○リスクは主としてに適応された薬である。

○薬剤師はこれらの点に関して得意である。

## *Anticoagulant Patients are a Good Choice!*

- *These are usually a high cost and low revenue office visit for a physician*
- *Managed care companies are requesting them to avoid risks*
- *Pharmacists find the work satisfying*
- *Quick results are likely*

There are other reasons the management of anticoagulant patients by a pharmacist is successful.

We have learned that physicians are interested in someone else managing these patients because they use many clinic resources including people and time.

Managed care companies or insurance companies request support the utilization of other professionals.

Pharmacists find the work very satisfying and motivating.

and,

The results of your work with an individual patient, or a group of patients are apparent early in the project. It is easy to tell you are doing a good job!

抗凝薬服用患者はよいチャンスである！

○医師にとってこれは経費が高くなり、  
収入は低いものである。

○管理看護の会社はリスクを避けることを要求する。

○薬剤師は満足な仕事を見つける。

○迅速に結果を得ることが期待できる。

### *What Patients are Candidates?*

- *Patients who have abnormal blood flow*
- *Patients with abnormalities of surfaces in contact with blood*
- *Patients with clotting component abnormalities*

Who are the patients the pharmacists would work with? Who are candidates for anticoagulation therapy?

Here you see the general types of patients. Basically, we are working with patients who have flow, contact and clotting problems.

どんな患者が候補者となるか？

- 血流に異常がある患者
- 血液と接触する表面に異常がある患者
- 凝固因子に異常がある患者

***Abnormal Blood Flow***

- *Atrial fibrillation*
- *Dysfunction of the left ventricle*
  - *congestive heart failure*
  - *myocardial infarction*
  - *cardiomyopathy*
- *Immobilization*
  - *in bed*
  - *paralysis*
- *Venous obstruction*
  - *tumor*
  - *obesity*
  - *pregnancy*

Some of the patients we work with have abnormal blood flow. These patients come from several disciplines, and have different needs. Based on their medical history, our approach with them can be quite different. Therapy can be directed toward prophylaxis or treatment.

Patients with these disorders are referred potentially from internal medicine, cardiology, geriatrics, oncology or gynecology.

- 血流異常
- 心房細動
  - 左心室の機能不全
    - うっ血性心不全
    - 心筋梗塞
    - 心筋症
  - 非可動
    - ベッドにて
    - 麻痺
  - 静脈閉塞
    - 腫瘍
    - 肥満症
    - 妊娠