

# **Pain in Sickle Cell Disease: Syndromes and their Management**

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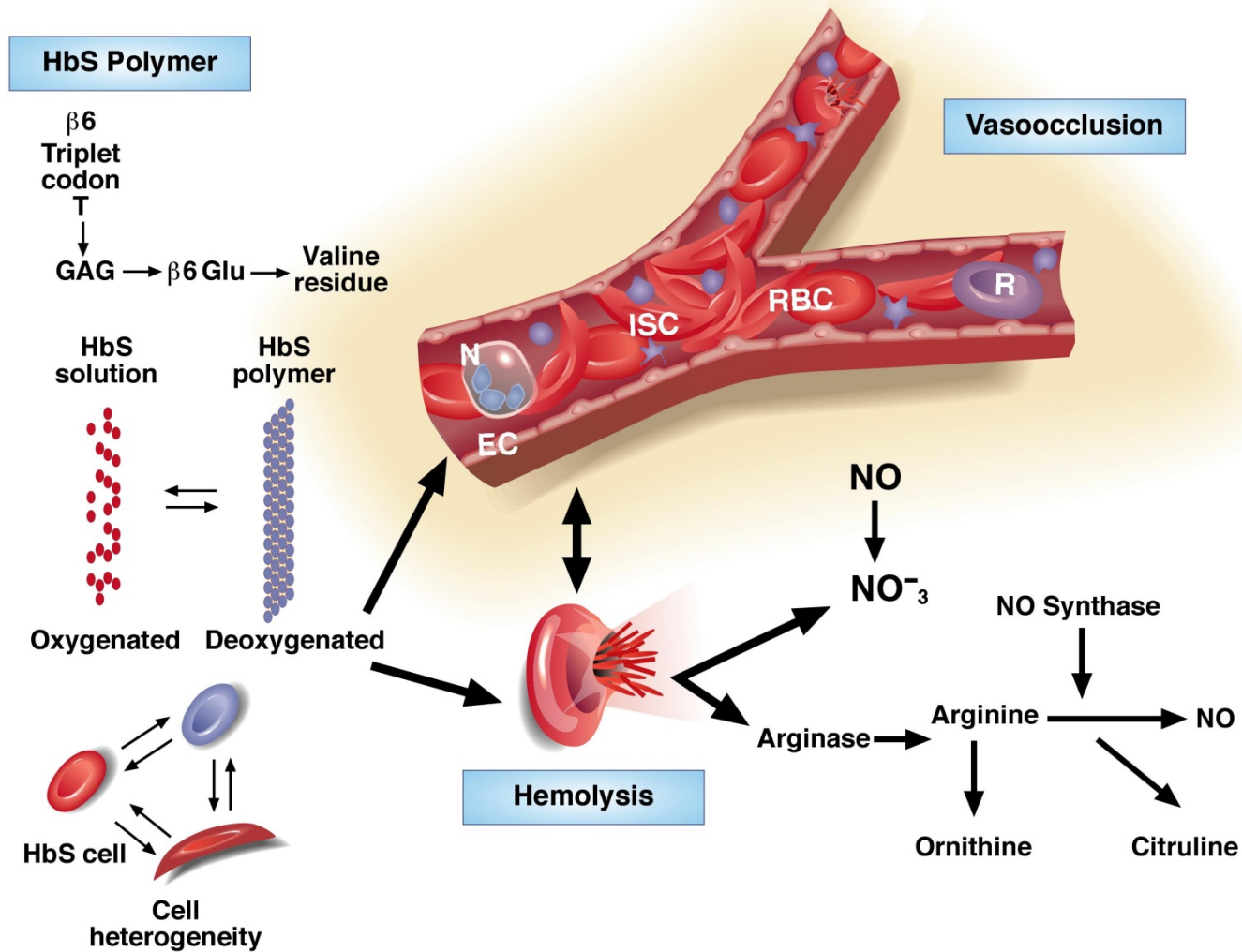
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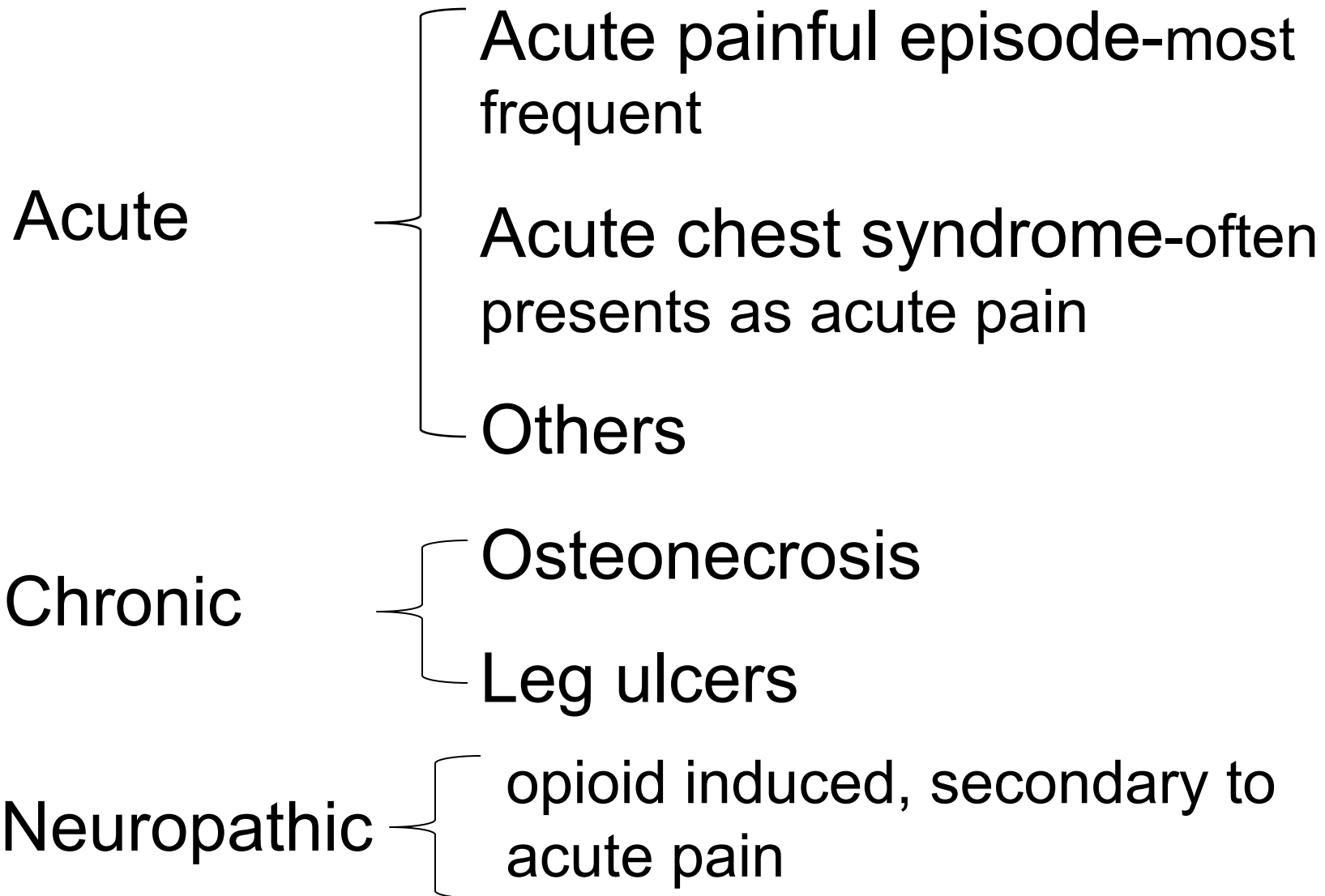
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(10/01/10)

# Pathophysiology of Sickle Cell Disease (2010)



# Pain in Sickle Cell Disease



# Management

Non-opioid analgesics

Opioid analgesics

Adjuvants

Complementary & alternative medications

Day Hospital

# Major Issues in Sickle Cell Pain

Acute vs. chronic pain

Mixed pain syndromes

Neuropathic pain

Opioid use

- Long term use
- Treatment guidelines

Tolerance

Addiction

Pseudoaddiction

Dependence/withdrawal

Hyperalgesia

“Difficult” patients

# Equianalgesic Dosing

<i>Drug</i>	<i>t/2</i>	<i>Oral</i>	<i>Parenteral</i>
Morphine	2-4	30-60	10
Hydromorphone	2-3	4-8	1.5
Oxycodone	3-5	20	na
Methadone	24	20	10
Codeine	3	200	130
Fentanyl		na	0.15-0.2
Meperidine	3.5	300	75

# Acute Painful Episodes

Most common complication

some patients always in pain; others rarely are

Most pain managed at home (Smith et al, 2008)

Etiology unclear

unrelated to "sickling" and the blood film is not helpful

Pain distribution variable

Physical findings limited

Duration variable

A bad prognostic sign

Directly related to PCV/Indirectly related to HbF

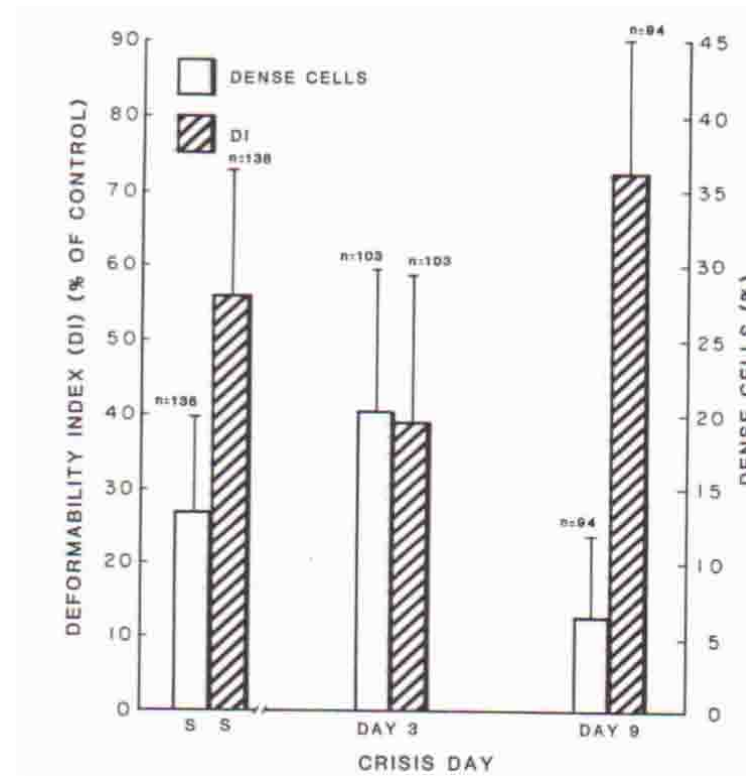
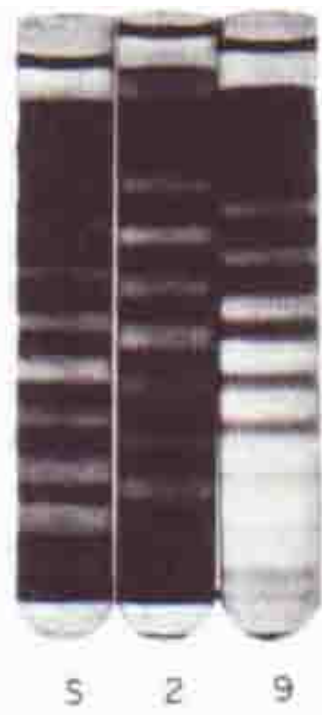
# Diagnosis of the Acute Painful Episode

History

Hematological changes are not diagnostic

Other laboratory not useful

Changes in RBC deformability and density



(Ballas and Smith, Blood, 1992)

# **Complications of the Acute Painful Episode**

Days 1-5

- Acute chest syndrome
- Acute multiorgan failure
- Sudden death

Relapse/hospital readmission

# **Acute Sickle Cell Pain**

## Principles of management

### Short-acting Parenteral Opioids

Morphine

Hydromorphone (Dilaudid)

Fentanyl

Avoid Meperidine (Demerol)

# **Acute Sickle Cell Pain**

## Principles of management

Assessment

Analgesic choice

type, dose, route, PCA vs. bolus dosing

Titration

Adjuvants-antidepressants, NSAIDs, antihistamines

Maintenance

Manage side-effects

# **Acute Sickle Cell Pain**

## Principles of management

Adjustment for tolerance/rotation

Tapering

Switch to orals

# Opioid Rotation

Ineffectiveness

Adverse effects

Incomplete cross tolerance receptor SNPs

# Benefits of Hydroxyurea in Adult Sickle Cell Disease

*Pain* and ACS reduced 40%-50%

Mortality likely to be reduced 40%

Improved anemia; fewer Tx, less hemolysis

Fewer hospitalizations

Reduced medical costs

Improved physical capacity

Increased well-being

(Charache et al, NEJM, 1995; Steinberg et al, JAMA, 2003, Am J Hematol, 2010; Ballas et al, Health Qual Life Outcomes, 2006; Hackney, Clin Sci, 1997)

# Chronic Pain Management

Non-pharmacologic

Pharmacologic

Behavioral

Psychosocial issues

Referrals

- Physical therapy
- Psychiatry
- Addiction medicine

Quality of life

- Physical activity
- Nutrition, hobbies, etc

# Long-acting Opioids

Pharmacologically long-acting

Methadone

Levorphanol

Pharmaceutically Long Acting

Oxymorphone extended release

MS Contin

Sustained-release oxycodone (Oxycontin)

Tramadol extended release (Ultram ER)

Transdermal fentanyl (Duragesic)

# Opioid Risks

Sedation

Confusion

Nausea

Dizziness

Constipation

Gonadal suppression

Respiratory depression

Sleep apnea

Dental complications

Abuse, Misuse, Diversion

Physical Dependence

Withdrawal

Tolerance

Hyperalgesia

Pseudoaddiction: seeking  
more Rx because of  
inadequate Rx

Addiction

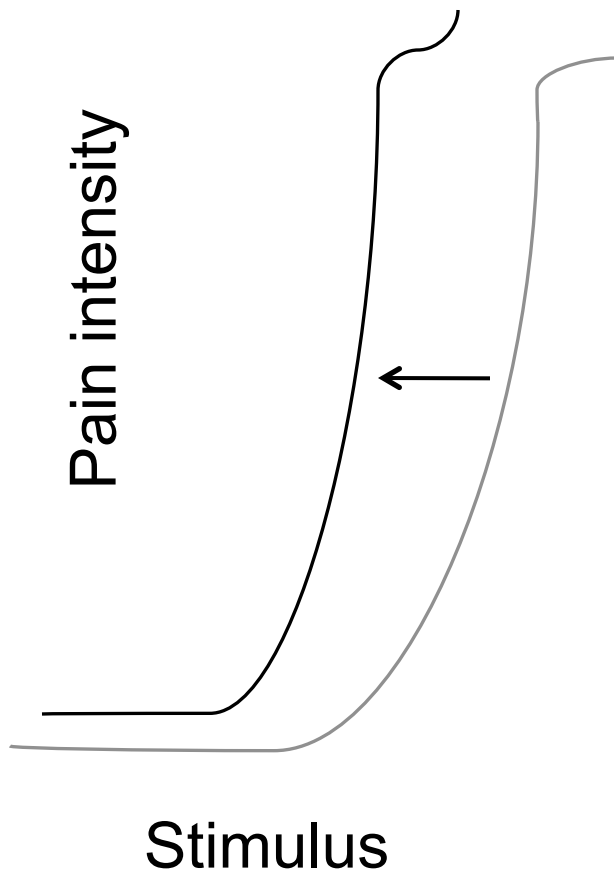
# **Opioid-Induced Hyperalgesia and Tolerance**

**Tolerance:** a biological process where opioid dosing causes receptor downregulation or decreased activation that result in the need for higher doses for similar levels of analgesia

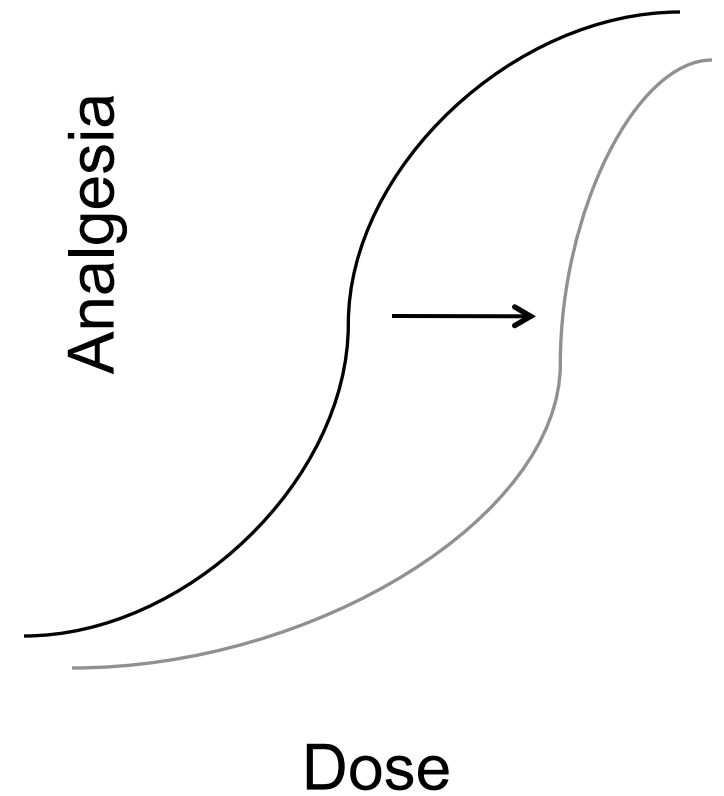
**Hyperalgesia:** ? Excitatory pathway induced by M6G. Pain more neuropathic

# Opioid-Induced Hyperalgesia and Tolerance

Hyperalgesia



Tolerance



# Neuropathic Pain

Damage or dysfunction of the nervous system  
Associated with dysesthesia and allodynia  
Continuous and/or episodic

- Burning
- Tingling
- Shooting
- Lancinating
- Numb
- Paroxysmal
- Emotional Distress
- Behavioral Dysfunction

Rx: antidepressants, anticonvulsants, opioids, others

# **Causes of Persistent Severe Pain**

Progressive tissue damage

Inadequate treatment

Tolerance

Hyperalgesia

Changes at receptors

Maladaptive behavior

# **"Difficult" Patients**

Acute upon chronic pain

Often alienate the entire health care team

No single cause

- severe sickle cell disease

- severe psychosocial disease

- poor treatment

- excessive or ineffective opioid use

Our approach

# Minimizing Risk

Detailed history & exam

Screening & risk stratification

Consent form

Treatment plan

Opioids at 1 month intervals

Psychosocial support

Clear refill policy

Pill & patch counts

Random urine testing

Document everything

Diagnose do not judge

“Do Not Expel”

# **Prerequisites of Effective Pain Management**

Know & believe the patient

Know the disease

Know the pharmacology of analgesics

Consider alternative/complementary RX

Consider non-pharmacological RX

Education