Sickle Cell Disease in Primary Care

Kathryn Hassell, M.D.
Professor of Medicine, Division of Hematology
Director, Colorado Sickle Cell Treatment and Research Center
University of Colorado Denver Health Sciences Center
Objectives

- Understand the basic pathophysiological processes for acute and chronic complications of sickle cell disease
- Recognize acute complications of sickle cell disease, especially in the ambulatory setting
- Consider diagnostic and therapeutic approaches to complications of sickle cell disease, with a focus on outpatient management
Sickle Cell Diseases

One $\beta$-globin gene that has the sickle cell mutation

+ 

Another ABNORMAL $\beta$-globin gene

(S, C, E, O$_{Arab}$, D$_{Punjab}$, etc or $\beta$-thalassemia)
Objectives

• Understand the basic pathophysiological processes for acute and chronic complications of sickle cell disease
Sickle hemoglobin polymerization → deformation of RBC
RBC Sickling

Δ $O_2$, $K^+$, $H_2O$, [Hb]
# Hematologic Characteristics

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Baseline Hb</th>
<th>Retic</th>
<th>MCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sickle cell anemia (HbSS) S gene + S gene</td>
<td>6-8 Hct</td>
<td>5-30%</td>
<td>normal</td>
</tr>
<tr>
<td>Sickle-(\beta^0)thalassemia S gene + no A</td>
<td>6-8 Hct</td>
<td>5-30%</td>
<td>low*</td>
</tr>
<tr>
<td>Sickle-hemoglobin C (HbSC) S gene + C gene</td>
<td>10-14 Hct 30-38%</td>
<td>3-4%</td>
<td>normal</td>
</tr>
<tr>
<td>Sickle-(\beta^+)thalassemia S gene + some A</td>
<td>11-14 Hct 32-40%</td>
<td>3-4%</td>
<td>low*</td>
</tr>
</tbody>
</table>

*due to thalassemia – DO NOT GIVE IRON*
Implications

• The expected degree of anemia depends on the type of sickle cell disease
  – Appropriate interpretation of CBC depends on awareness of expected results
    • Hb7.5 g/dl: normal (HbSS) or severely ill (HbSC)?
  – Worsened anemia may represent:
    • Acute decompensation (e.g. aplastic crisis, chest syndrome, GI bleed, incomplete abortion)
    • Underlying co-morbid conditions (e.g. collagen vascular disease, renal failure)
Beyond Anemia: The Old Theory
Sickle RBC interaction with post-capillary venules
low flow
low oxygen tension
May also occur in arterioles, capillary beds
Pathophysiologic Mechanisms

• Abnormal cellular adhesion to endothelium (sickle RBC and WBCs)


• Constitutive elevation of WBCs noted in some patients with sickle cell disease
  – Correlated with diminished survival in Cooperative Study of Sickle Cell Disease

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>VARIABLE Estimate ±SE</th>
<th>P VALUE†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>−0.26±0.089</td>
<td>0.003</td>
</tr>
<tr>
<td>Fetal hemoglobin (%)</td>
<td>−0.11±0.04</td>
<td>0.001</td>
</tr>
<tr>
<td>White-cell count</td>
<td>0.13±0.04</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Leiken et al; *Pediatrics* 84:500, 1989; Okpala, *Blood Rev* 18:65, 2004
Pathophysiologic Mechanisms

- Direct damage to endothelium
  - Difficult to distinguish effect of RBC adhesion itself from elements that enhance RBC adhesion
    - e.g. hypoxia, cytokines
- Effects of sickle RBCs
Pathophysiologic Mechanisms

• Nitric Oxide (NO): multiple effects
  (vasoactive, antiplatelet, antioxidant, antiapoptotic)

• NO depletion in sickle cell disease
  – Hemolysis→free hemoglobin scavenges NO
  – Continuous endothelial stimulation may exhaust constitutive and inducible reserves
  – Arginine, substrate for NO production, is depleted in sickle cell patients

Pathophysiologic Mechanisms

“Hyperviscous” vs. “Hyperhemolytic”

Analysis of 177 hyper-hemolysis and 172 mild hemolysis patients from the NIH PH study and CSSCD. Studies are in progress to define additional genetic modulators of hyper-hemolysis.

Implications

• Most of the pathophysiology of sickle cell disease has little to do with “sickled” red blood cells

• Future therapy will be likely directed at:
  – Inflammatory response modification
  – Reduction of RBC adhesion
  – NO supplementation/substrate repletion
  – Alteration of vascular remodeling

• Unfortunately, specific screening for underlying processes not yet available
Objectives

• Recognize complications of sickle cell disease, especially in the ambulatory setting

• Consider diagnostic and therapeutic approaches to complications of sickle cell disease, with a focus on outpatient management
Sickle Cell Disease Burden

- Autopsy Study (1929-1996)
  - Evidence of chronic organ injury in 74% of 306 cases
  - Chronic organ damage most common cause of death in >18 yrs old (after infection)

<table>
<thead>
<tr>
<th>Evidence of injury at autopsy</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic lung disease / infarcts</td>
<td>56.3%</td>
</tr>
<tr>
<td>Chronic renal failure / atrophy / infarcts</td>
<td>37.9%</td>
</tr>
<tr>
<td>Stroke</td>
<td>18.2%</td>
</tr>
<tr>
<td>Liver failure/hepatitis</td>
<td>10%</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>58.4%</td>
</tr>
<tr>
<td>CHF</td>
<td>9.9%</td>
</tr>
</tbody>
</table>


- Cohort Study of 1056 pts, 40-yr f/u: 73% with chronic organ damage

Powars, *Medicine* 83:363, 2005
## Sickle Cell Disease Burden

### Hydroxyurea Follow-Up Study

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>n (% of total population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary disease</td>
<td>21 (7%)</td>
</tr>
<tr>
<td>Accident/Homicide</td>
<td>7 (2.3%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>6 (2.0%)</td>
</tr>
<tr>
<td>Hepatic disease</td>
<td>4 (1.3%)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>4 (1.3%)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>3 (1.0%)</td>
</tr>
<tr>
<td>Death during crisis</td>
<td>9 (3.0%)</td>
</tr>
<tr>
<td>Sepsis/infection</td>
<td>5 (1.7%)</td>
</tr>
</tbody>
</table>

Steinberg, *JAMA* 289:1645, 2003
Sickle Lung Disease

• Present in up to 25-40% of sickle cell patients
  – Initial restrictive pattern
  – Subsequent progressive vascular changes in some patients
    • intimal hyperplasia, microinterstitial fibrosis, plexiform lesions may occur

– May be indicated by presence of elevated tricuspid regurgitant (TR) jet velocity on echo

Haque et al, *Human Pathol* 33:1037, 2002
Sickle Lung Disease

- Annual screening echo recommended
  - TR jet velocity of $>2.5$ mg/sec associated with 10-fold increased risk of death in adults

Gladwin, *NEJM* 350:886, 2004
Sickle Lung Disease

• Conflicting data regarding TR jet velocity
  – Cause of deaths in adults unclear; may not be due to cardiopulmonary disease
  – Children have same prevalence of elevated TR jet velocity, but not associated mortality
  – Some studies question the importance of elevated TR jet velocity in absence of “true” pulmonary hypertension
  – Recent study of sildenafil closed early, futile to show difference in 6-minute walk test
Implications

- Symptoms of dyspnea, shortness of breath, hypoxia and intermittent chest pain may indicate pulmonary hypertension
  - Full pulmonary evaluation, including echo and ultimately right heart cath may be needed
- “Heart failure” (elevated JVD, edema) is almost always due to right-sided heart failure
  - May be associated with intermittent renal failure
- Annual screening echo may reveal elevated TR jet, prompt early referral for evaluation
Sickle Cell Disease and the Heart

• Flow murmurs are common due to anemia
  – Does not usually represent valvular disease
• Ventricular hypertrophy, diastolic dysfunction may develop however
  – In general, cardiac output is high
  – Pulmonary edema is not expected

• Classic coronary artery disease does not occur
  – Risk factors (e.g. ↑ cholesterol) uncommon
  – Sickle RBCs do not appear to induce remodeling or occlude coronary arteries
Sickle Cell Anemia (HbSS) and Systemic Blood Pressure

- SBP 80-100, DBP 50-60 not uncommon
- Recent Nigerian study notes lower diastolic and mean arterial pressure, wider pulse pressure

**Table 2** Physiologic data in patients and controls.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>SCA Mean (SD)</th>
<th>Controls Mean (SD)</th>
<th>t-Test</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse rate (bpm)</td>
<td>87.68 (8.91)</td>
<td>72.13 (6.79)</td>
<td>11.062</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Brachial systolic BP (mm Hg)</td>
<td>119.50 (11.70)</td>
<td>121.2 (8.97)</td>
<td>0.527</td>
<td>0.599</td>
</tr>
<tr>
<td>Brachial diastolic BP (mm Hg)</td>
<td>64.867 (8.95)</td>
<td>76.88 (6.18)</td>
<td>8.629</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Brachial pulse pressure (mm Hg)</td>
<td>54.63 (12.87)</td>
<td>44.31 (10.91)</td>
<td>4.735</td>
<td>0.001*</td>
</tr>
<tr>
<td>Mean brachial arterial BP (mm Hg)</td>
<td>81.18 (12.65)</td>
<td>91.71 (5.47)</td>
<td>5.850</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>24.07 (3.10)</td>
<td>38.65 (1.97)</td>
<td>30.589</td>
<td>&lt;.001*</td>
</tr>
</tbody>
</table>

BP, blood pressure; SCA, sickle cell anemia.
* Statistically significant.

Oguanobi, *J Cardiol* 2010, epub

- “Relative” hypertension associated with pulmonary and renal disease (SBP 120-139, DBP 70-89)

Sickle Nephropathy

- CKI occurs 10-15% of sickle cell patients
- Clinical course: resembles diabetic events
  - Initial hyperfiltration and enlarged glomeruli
  - Microalbuminuria/proteinuria
  - Focal segmental glomerulosclerosis (FSGS)
Sickle Cell Disease and Proteinuria

- Common finding in adult sickle cell anemia
  - Microalbuminuria: 30-50%
  - Macroalbuminuria: 20-30%
  - Also seen in up to 30% of other types (e.g. HbSC)

- Improves/resolves with ACE-inhibitor therapy
  - Persistent for up to 18 months after discontinuation
  - Relatively well-tolerated despite normal/low BP

- Unclear if this changes the progression to renal failure
Sickle Nephropathy

- Creatinine lost through tubule → creatinine does not represent GFR
  - Creatinine does not rise until GFR falls to less than ~ 30 ml/min


- Creatinine clearance also significantly overestimates actual GFR
Implications

- Screening for proteinuria probably warranted
  - Evaluation for other causes
  - Consider therapy with ACE inhibitor or ARB
- Don’t rely on creatinine to assess renal function
  - Creatinine of >1.0 mg/dl (even >0.7-0.8) may represent significant renal insufficiency
  - Pay attention to “expected” values given weight/muscle mass (normal may be <0.5)
- Clinical suspicion for underlying renal disease
  - Relative hypertension (SBP>120?, DBP>80?)
  - Worsening anemia (epo deficiency)
Sickle Cell and Stroke

- Large-vessel ischemic stroke affects up to 10% of Hb SS patients by the age of 20

- Adults at risk for CNS hemorrhage
  - Moya-moya formation
  - Aneurysms
Sickle Cell and Stroke

• Large vessel occlusion:
  – Exuberant intimal hyperplasia
  – Proliferation of fibroblasts and smooth muscle
  – Focal splitting of internal elastic lamina
  – Medial necrosis
  – Damage to vaso vasorum?

• CNS Hemorrhage:
  – Above changes → focally weakened vessels
Sickle Cell and CNS Injury

- Silent infarction and neurocognitive dysfunction noted in children and adults without a history of overt stroke
- Up to 50% of individuals have MRI findings: infarction, ischemia or atrophy
  - Predilection to frontal lobe area in some studies
- Neurocognitive deficits in documented in otherwise neurologically intact HbSS adults

Implications

• A severe or atypical headache in an adult sickle cell patient (with or without neurologic symptoms) is a CNS bleed until proven otherwise
  – Urgent non-contrasted head CT

• Impairment of neurocognitive function may significantly impact on comprehension of disease and adherence to therapy
Sickle Retinopathy

- Occurs in 11-45% of sickle cell patients
- Arteriolar vaso-occlusion → hairpin loops and AV anatamoses → abnormal blood flow → neovascularization (sea fan formation)
- Venular occlusion →
  sea fan infraction
- Retinal detachment, hemorrhage, blindness
Implications

• Annual dilated ophthalmologic examination

• Change in vision ("floaters", loss of visual acuity or visual field) is an ophthalmologic emergency
  – Urgent ophthalmology consult
Other Affected Organs

• Hip and Shoulder Joints
  – Avascular necrosis, bone infarcts

• Skin
  – Leg ulcers

• Spleen
  – Splenic sequestration may occur in HbSC and other “milder” forms

• Gallstones
  – Assumed to be present, no intervention unless symptomatic
Spared (?) Vascular Beds

• Liver
  – Most injury due to iron deposition or infection
  – No recognized chronic “sickle hepatopathy”
  – Acute hepatic sequestration may occur
  – Remember: AST, LDH are RBC enzymes!

• GI tract
  – Rare case reports of intestinal ischemia only in acutely hypotensive patients on vasopressors
Plenty of Time for Organ Damage

• Life Expectancy as of 1992 (1972)
  – Hb SS: 42-48 years
  – Hb SC: 60-69 years
  – Hb AA: 70-75 years

• Hb SS Jamaican study as of 2001 (1978)
  – Hb SS: 53-58 years
  – Hb AA: 71-76 years

• Hydrea follow-up study for Hb SS (1996)
  – 299 severely affected enrolled (mean age 32)
  – 75% still alive 9 years later

• Cohort (HbSS) born after 1975: 50-55 yrs

Acute Sickle Cell Events

- Acute pain events ("crisis")
- Acute chest syndrome
- Acute neurologic events
  - Ischemic stroke (children>adults)
  - Hemorrhage (adults)
- Priapism
- Acute hepatic sequestration
- Acute splenic sequestration (non-HbSS)
Acute Sickle Cell Events

• Acute insult to endothelium
  – hypoxia
  – cytokines (inflammation, infection)

• Consequences of acute endothelial injury
  – enhanced cellular adhesion (RBC, WBC)
  – vascular disruption and inflammation
    • oxidative/reperfusion injury
    • endothelial retraction → tissue edema
  – acute vasoconstriction
Acute Sickle Cell Events

Acute endothelial injury with RBC adhesion in post-capillary venules, vasoconstriction
Management of Acute Events

- Reverse pathophysiologic factors
  - Pain control (reduces physiologic stress)
  - Treat inflammation/infection
  - Maintain NORMAL volume: excess fluid may promote acute chest syndrome
  - Maintain NORMAL oxygen: no benefit to excess oxygen

- Transfusion for acute end-organ damage
  - Doesn’t reduce duration uncomplicated pain crisis
Disease-Modifying Therapies

• Transfusion Therapy
  – “Dilutes out” sickle RBCs
    • precludes recurrent stroke if HbS<30%
    • reduces abnormal flow in cerebral vessels in children with sickle cell disease (remodeling?)
  – Provides healthy RBCs, which may
    • restore RBC vasodilatory capacity (e.g. NO)
    • provide “sump” for toxins (e.g. FFA ?)
Disease-Modifying Therapies

• Transfusion Therapy
  – Infection
  – Alloimmunization
    • Precluded by minor-antigen matching
    • Always request minor-antigen matched blood (at least C, D, E, Kell)
  – Iron Overload
    • Precluded by exchange transfusion
    • Oral chelator available (deferasirox)
Disease-Modifying Therapies

- Bone Marrow Transplant
  - The cure: “a permanent transfusion”
  - Only 17% of eligible recipients have suitable HLA-matched sibling donor
  - Selection criteria in evolution (risk v. benefit)
  - Mini-allogeneic transplantation results in frequent rejection

Disease-Modifying Therapies

- Hydroxyurea

Induction of fetal hemoglobin
Disease-Modifying Therapies

- Hydroxyurea reduces sickle hemoglobin polymerization
  - Less hemolysis with improved anemia
  - Increased MCV (lower Hb concentration)
Disease-Modifying Therapies

• Clinical Effects of Hydroxyurea
  – 50% reduction in acute pain events and acute chest syndrome
  – Apparent improvement in mortality, correlated with HbF response; persistent even after 17 yrs of follow-up
  – No evidence of reduction in chronic organ injury (Baby-HUG study)

Disease-Modifying Therapies

• Clinical Effects of Hydroxyurea
  – Takes 2-3 months of daily therapy to see changes in fetal hemoglobin
  – Occasional patient benefits within 4-6 weeks (symptoms improve)
  – Pushed to hematologic toxicity (ANC 1-2,000)
  – Not an acute intervention; close follow-up

Coordinated, Comprehensive Health Care Needed

• Sickle cell gene does not protect against other and more common diseases
  – Asthma, COPD, collagen vascular diseases, sarcoidosis, diabetes, malignancy, peptic ulcer disease, Crohn’s, ulcerative colitis, etc.

• Having sickle cell disease does not eliminate the need for routine health care maintenance
  – Specialists are notoriously poor at primary care
  – Each specialist focuses on their own area
Primary Care: What to Look For?

- Everything as for anyone else
- Additional annual screening:
  - Retinal exam
  - Urinalysis for protein, serum creatinine
  - Echo
- If on transfusions:
  - Ferritin for iron overload
  - Hepatitis/HIV if indicated
- If on hydrea: CBC, neutrophil count
Pain in Sickle Cell Disease

- Acute, intermittent, unpredictable, severe episodes called “crisis”
  - Typical duration said to be 7-10 days
  - Associated by some patients with death
  - Onset may occur in early infancy
- Chronic pain may develop in adolescence and adulthood
  - Not necessarily acute vaso-occlusion
- Other pain still occurs (e.g. injury, menses, SLE)
  - To be distinguished from acute vaso-occlusion
### Pain in Sickle Cell Disease

<table>
<thead>
<tr>
<th>PAIN TYPE</th>
<th>ORIGINS &amp; SYNDROMES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nocioceptive</td>
<td></td>
</tr>
<tr>
<td>Deep somatic</td>
<td>Vaso-occlusion, bone infarction, priapism-</td>
</tr>
<tr>
<td>Superficial somatic</td>
<td>Leg ulcers</td>
</tr>
<tr>
<td>Visceral</td>
<td>Splenic/hepatic sequestration, splenic infarction, cholelithiasis</td>
</tr>
<tr>
<td>Neuropathic</td>
<td></td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>Vaso-occlusion, neuropathies</td>
</tr>
<tr>
<td>Central neuropathic</td>
<td>CNS damage, central sensitization (?)</td>
</tr>
<tr>
<td>Mixed</td>
<td>Vaso-occlusion</td>
</tr>
<tr>
<td>Breakthrough</td>
<td></td>
</tr>
<tr>
<td>Incident (movement)</td>
<td>Vaso-occlusion, skeletal damage</td>
</tr>
<tr>
<td>Nonincident</td>
<td>Transient flares of pain during analgesia</td>
</tr>
</tbody>
</table>

Adapted from Niscola, *Pain Medicine* 10:470, 2009
Utilization of Healthcare for Pain: The Exception, Not the Rule

Adapted from Platt et al, *NEJM* 325:11, 1991
Pain in Sickle Cell Disease

- Old cohort study data
  - Acute crisis rate (utilization):
    - Hb SS: 0.8 events/year
    - Hb Sβ^0+thalassemia: 1.0 events/year
    - Hb Sβ^+thalassemia: 0.4 events/year

- For HbSS:
  - 5.2% of patients sought care for 3-10 crisis/year
  - These patients accounted for 32.9% of all episodes

Survival by Pain Rates

Projected Median Survival for CSSCD Subjects ≥ 20

Adult Sickle Cell Pain – PiSCES

- **Pain in Sickle Cell Epidemiology Study (PiSCES)**
- 232 patients, aged 16-64, completed up to 180 daily pain diaries
  - Mean number of diaries: 158
  - Included if at least 30 diaries
  - 31,017 diaries available
  - **Subjects:**
    - Mean age 32.6 years
    - 87% HS graduates
    - 76% single, 61% female
    - 66% Hb SS

Adult SCD Pain Common But Managed At Home

PiSCES data from 31,017 daily pain diaries from 232 patients

- Crisis – Utilization: 3.5%
- Crisis – No utilization: 12.7%
- Pain – Not Crisis: 38.3%
- No Pain: 45.5%

Adult Sickle Cell Pain - PiSCES

- Frequency of pain
  - More than half of patients had pain more than half the time
  - 29% had pain nearly every day
  - 15% rarely had pain

- Intensity of pain correlates with characterization of pain:
  
  - Crisis - utilization: 5.9 ± 0.1
  - Crisis - no utilization: 5.0 ± 0.1
  - Pain – not crisis: 3.9 ± 0.1
  - No pain: 0.0 ± 0.0

Adult Sickle Cell Pain - PiSCCES

- Few differences between men and women

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days with pain (%)</td>
<td>58.6%</td>
<td>56.5%</td>
</tr>
<tr>
<td>Number of pain episodes over 6 mos</td>
<td>7.7</td>
<td>9.6</td>
</tr>
<tr>
<td>Mean pain scores in crisis/not in crisis</td>
<td>5.5/2.5</td>
<td>5.6/2.2</td>
</tr>
<tr>
<td>Hb SS - Days in crisis (%)</td>
<td>18.5%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Hb SS - Days of utilization (%)</td>
<td>5.1%</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

- No difference in distress or interference scores overall or during crisis
- Women reported higher bodily pain score (SF-36)

McClish, J of Women’s Health 15:146, 2006
Sickle Cell Pain: Health-Related Quality of Life

- PiSCCES Study using SF-36
  - Patients with SCD:
    - Worse than the general population in all categories except mental health
    - Comparable or worse than asthma, cystic fibrosis, hemodialysis patients
  - Strong correlation with pain
    - Less physical functioning, physical and emotional role, bodily pain, general health, vitality, social function with increased pain, especially crisis
    - No change in mental health domain

McClish, Health and Qual Life Outcomes 3:50, 2005
Adult Sickle Cell Pain - PiSCES

- **Role of depression and anxiety**
  - 27% (64/168) depressed by PHQ questionnaire
  - Higher than general African-American population
  - Comparable to other chronic conditions (e.g. DM)
  - Impact on pain and utilization

<table>
<thead>
<tr>
<th></th>
<th>Not depressed</th>
<th>Depressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days in pain (%)</td>
<td>49.6%</td>
<td>71.1%</td>
</tr>
<tr>
<td>Days in crisis (%)</td>
<td>14.7%</td>
<td>16.7%</td>
</tr>
<tr>
<td>Days using opioid at home (%)</td>
<td>40.5%</td>
<td>58.3%</td>
</tr>
<tr>
<td>Hospitalization (median % days)</td>
<td>2.8</td>
<td>2.77</td>
</tr>
<tr>
<td>ED visits (median % days)</td>
<td>1.35</td>
<td>1.34</td>
</tr>
<tr>
<td>Unscheduled clinic visits (% days)</td>
<td>1.26</td>
<td>1.63</td>
</tr>
<tr>
<td>Scheduled clinic visits (% days)</td>
<td>1.89</td>
<td>2.82</td>
</tr>
</tbody>
</table>
Substance Abuse in the Community

• General population figures (college kids):
  – Use in the last year

<table>
<thead>
<tr>
<th>Substance</th>
<th>Caucasians</th>
<th>Hispanic</th>
<th>African Americans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>38-41%</td>
<td>40-45%</td>
<td>18-33%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>3-5%</td>
<td>4.4-6.5%</td>
<td>0.7-1.8%</td>
</tr>
<tr>
<td>Pain meds</td>
<td>8.2-8.9%</td>
<td>8.7-9.8%</td>
<td>4.9-6.4%</td>
</tr>
</tbody>
</table>


• Estimated addiction and substance abuse in the community at-large: 6.4-8.8%


• Substance abuse in health care providers: 10-15%

Sickle Cell and Substance Abuse

• Addiction and substance abuse estimates for adult sickle cell cohorts ≤ general population
  – Cincinnati, 1988 14/160 (9%)
  – Philadelphia, 1992 0/501 (0%)
  – London, 2002 4/800 (0.5%)
  – New Haven, 2007 8/96 (8.3%)

• Alcohol abuse in sickle cell – PiSCES
  – 31% of cohort met criteria for abuse
  – No difference in pain between abusers and nonabusers, equal/less utilization by abusers
    • Better physical quality of life reported by abusers
Sickle Cell and Pain Behaviors

- Pseudoaddiction: behaviors to obtain pain medication because of poorly controlled pain
  - Distinguished when behaviors resolve with effective pain management

- Pain Coping Strategies in SCD: pseudoaddiction (vs. addiction) associated with:
  - Disputes and arguments over pain medication
  - Active coping behaviors, e.g. distraction
    - “I do anything to get my mind off the pain”
  - Use of over-the-counter medication

Coordinated Care for Sickle Cell Disease

- Sickle cell disease is about more than pain and requires comprehensive care.
- Fewer than 50% of all adults with sickle cell disease receive care from specialists.
- The number of adults will grow with improvements in life expectancy.
- All providers need to understand the basic tenets of sickle cell disease management and incorporate new therapies as they develop.
Colorado Sickle Cell Care Network