Supportive care in SCD

Enhencing the QOL and Managing complications

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13/01/2024

Introduction to SCD

- Inherited red blood cell disorders, causing the production of an abnormal version of beta-globin known as HBS.

- A mutation from glutamic acid (E) to Valine (V) at the sixth position of the beta-globin chain, denoted as E6V or Glu6Val.

- Globally in 2021 there's 8 Million of people leaving with SCD. In USA 1 out of 365 African-Americans births. In 2016 in France the highest prevalence rate was 30/100 000 inhab in some regions, becaming the first genetic disease .

Supportive care in SCD:

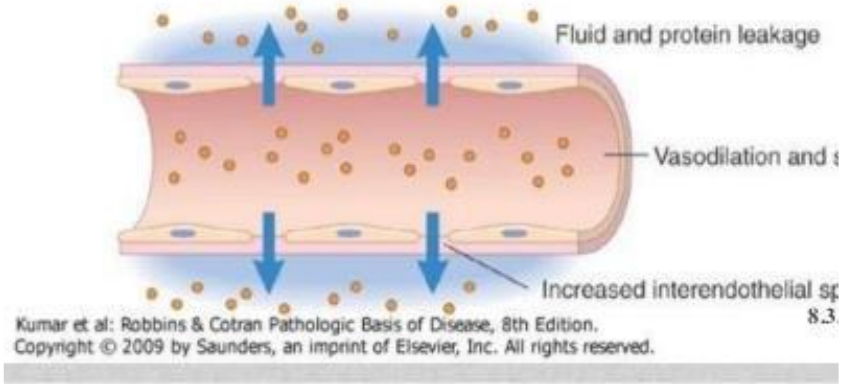
- I-To manage the symptoms
- II- To prevent complications
- III-To improve psychological/Social support

Pain Management

« parfois les moindres vibrations, le lit qu'on déplaçait par exemple, ça devenait insupportable… ». La douleur drépanocytaire ne se voit pas

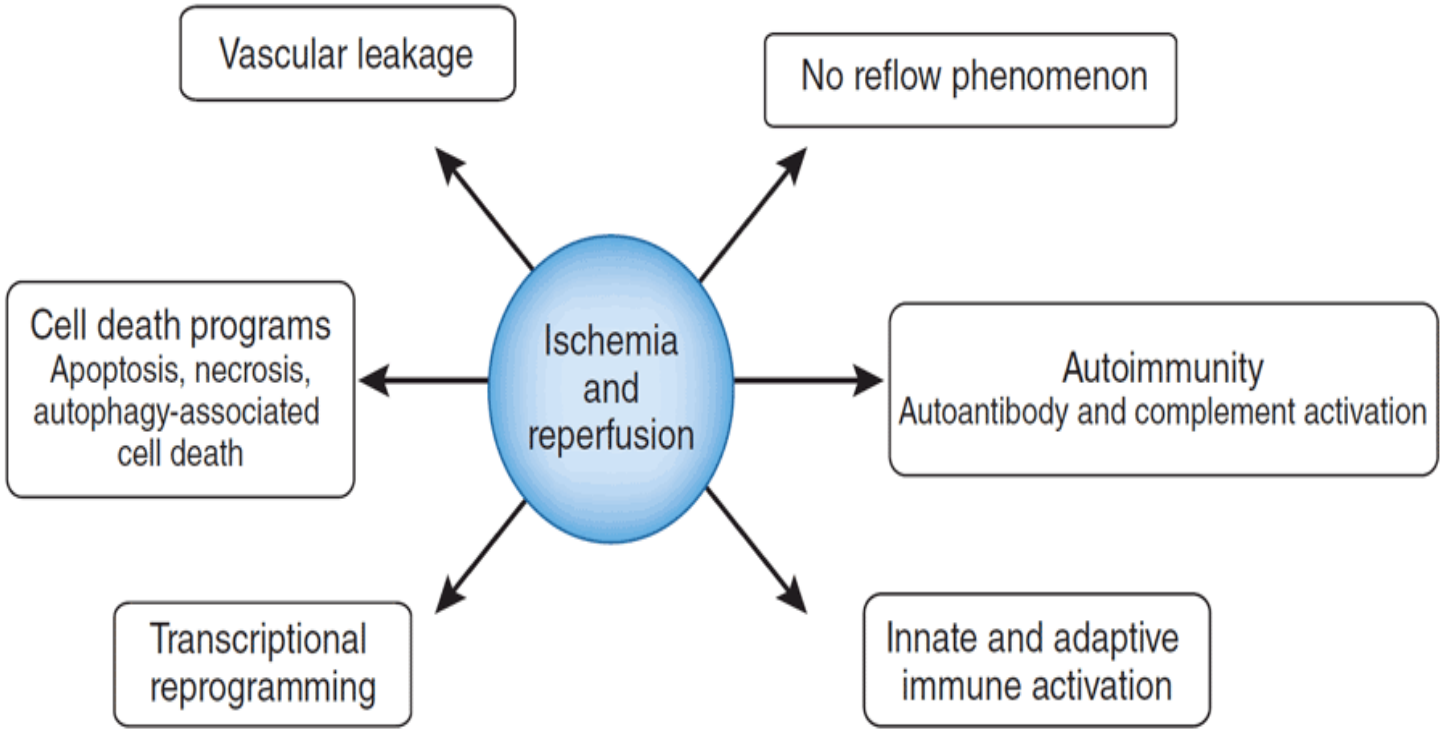
“ When I'm hospitalized, I even wish that it gets worse, that something happens to me and that I die! If they prick me in the jugular and I lose all my blood, so much the better! It will be over!... I can't do anything, I'm sad... It's not even the pain that makes me cry, it's the despair."

Mechanical stimulus



Thermal stimulus

Chemicals

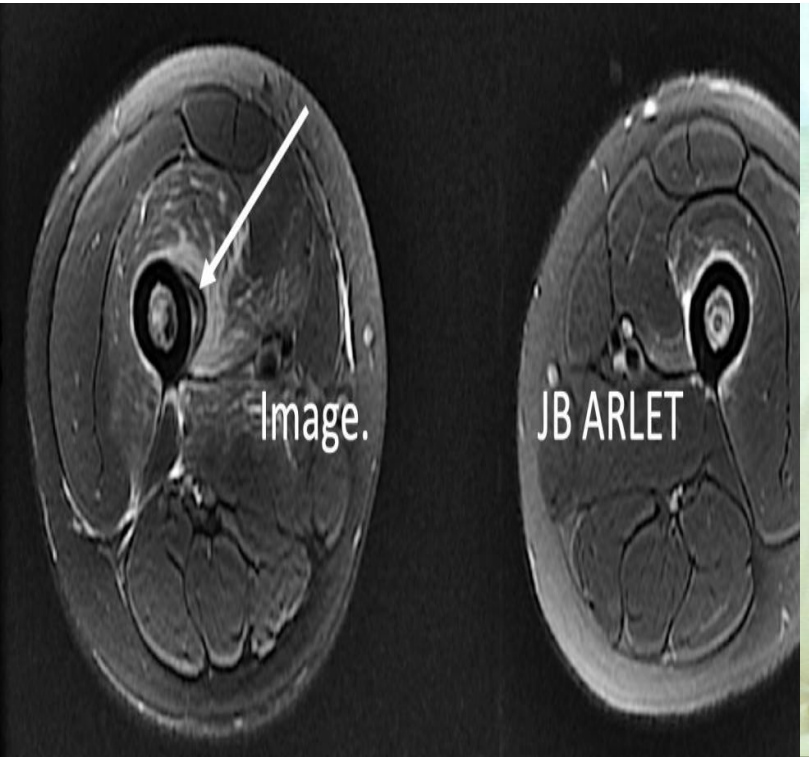


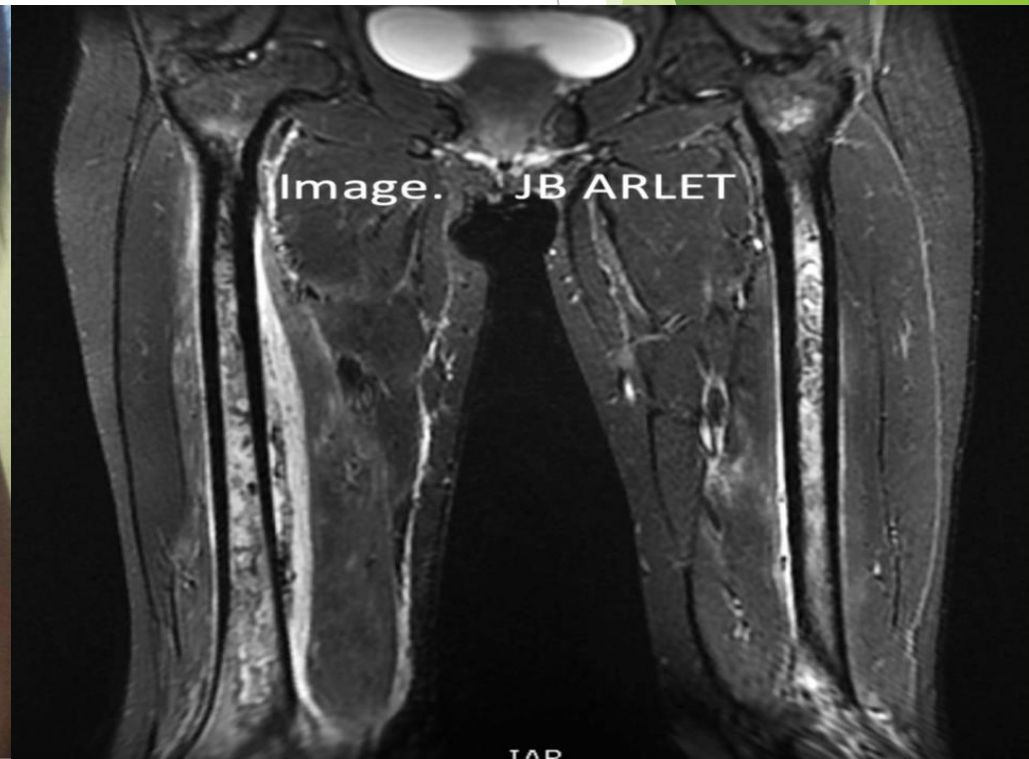
Ischemia-reperfusion phenomenon:

- **Mechanical** water leak: edema -> periosteum elevation
- Arrival of inflammatory cells: **heat** / inflammation
- Inflammation releases **chemical** substances

Clinical case: Women SS, 26 Y VOC

- Right upper leg thick and localised pain , T 40°c and CRP 200
- MRI shows muscle oedema and periostum elevation wich mimics an abscess.





Clinical case: Women SS, 26 Y VOC

- Right upper leg thick and localised pain , T 40°c and CRP 200
- MRI shows muscle oedema and periostum elevation wich mimics an abscess.
- Preparation for a surgical «Drainage» so we transfused her 2 RBC C «top up» and she was apyretic after 24h00 and no more pain after 48h00..It was a VOC localised with Periostum oedema and not an Osteomyelitis.

- She was discharged 3 D after: THAT DOES NOT MEAN TRANSFUSE EVERY VOC!

P Substance and SCD

Enfants 2-18 ans. *Michaels LA, et al. Blood. 1998*

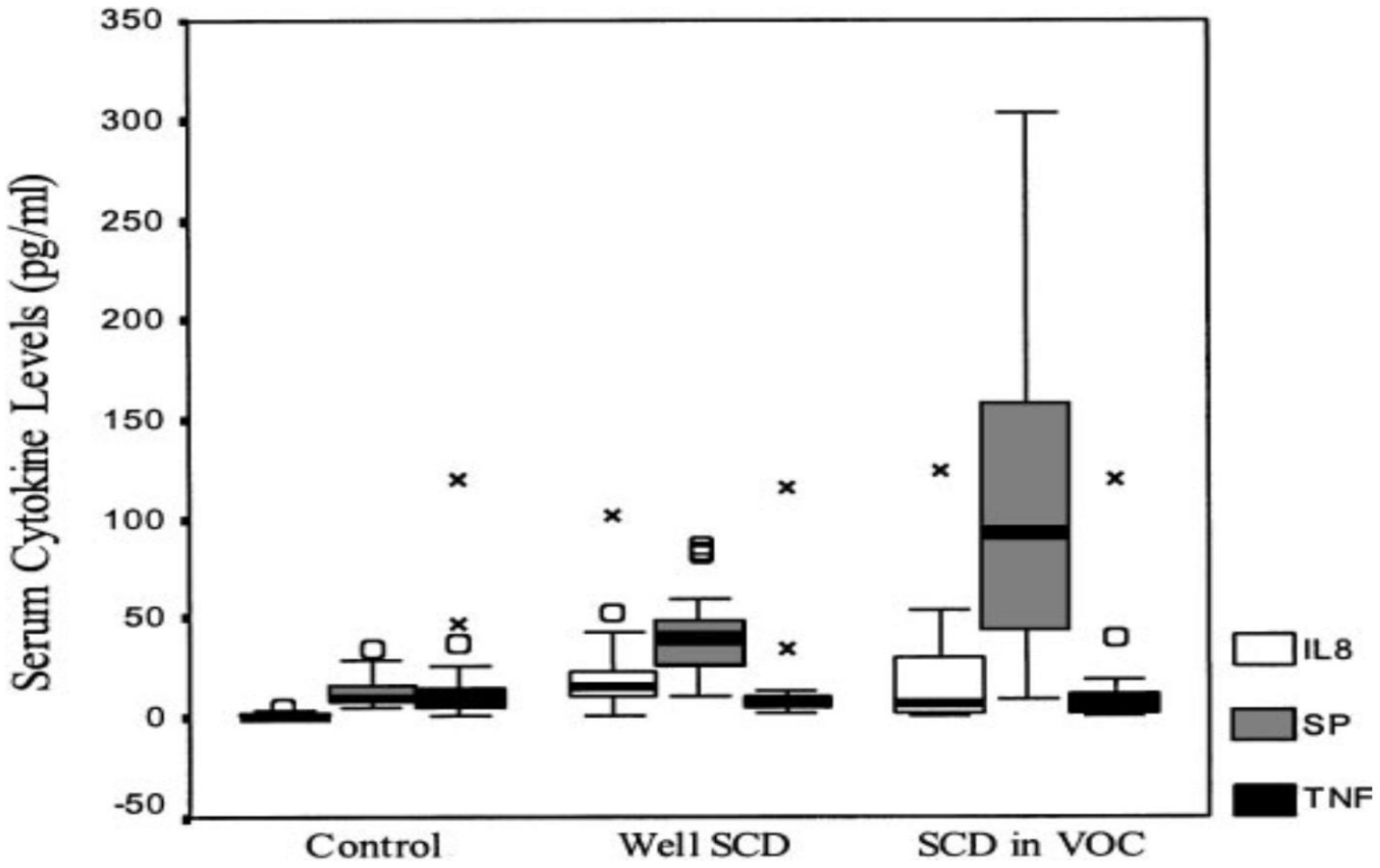
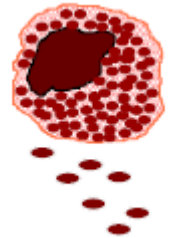
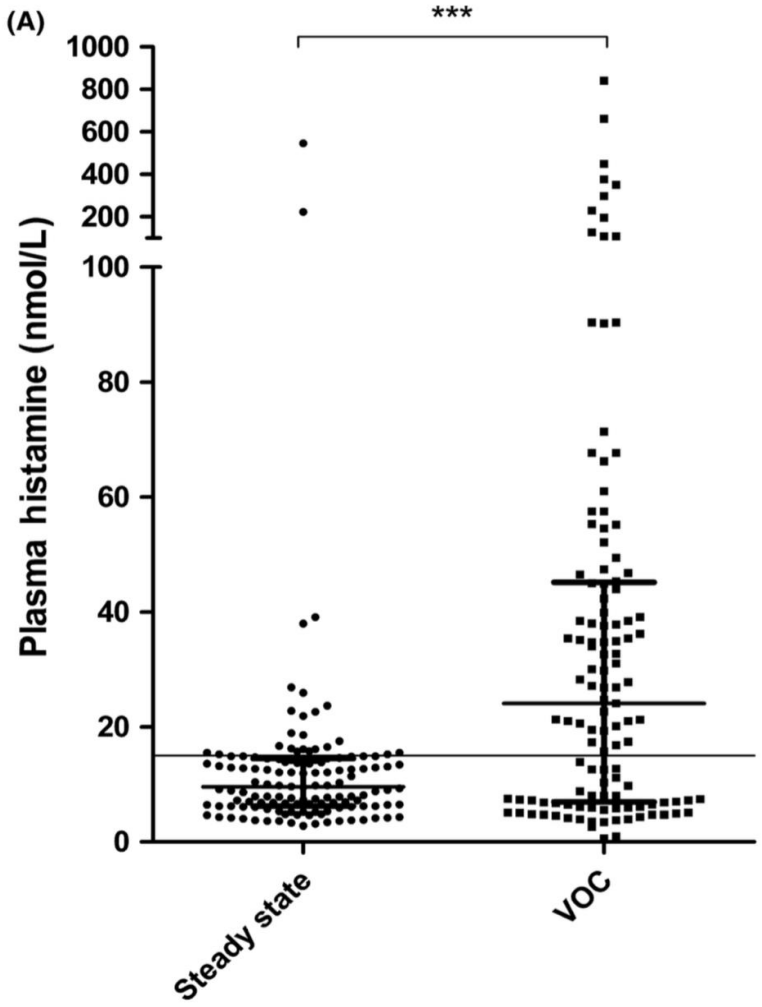


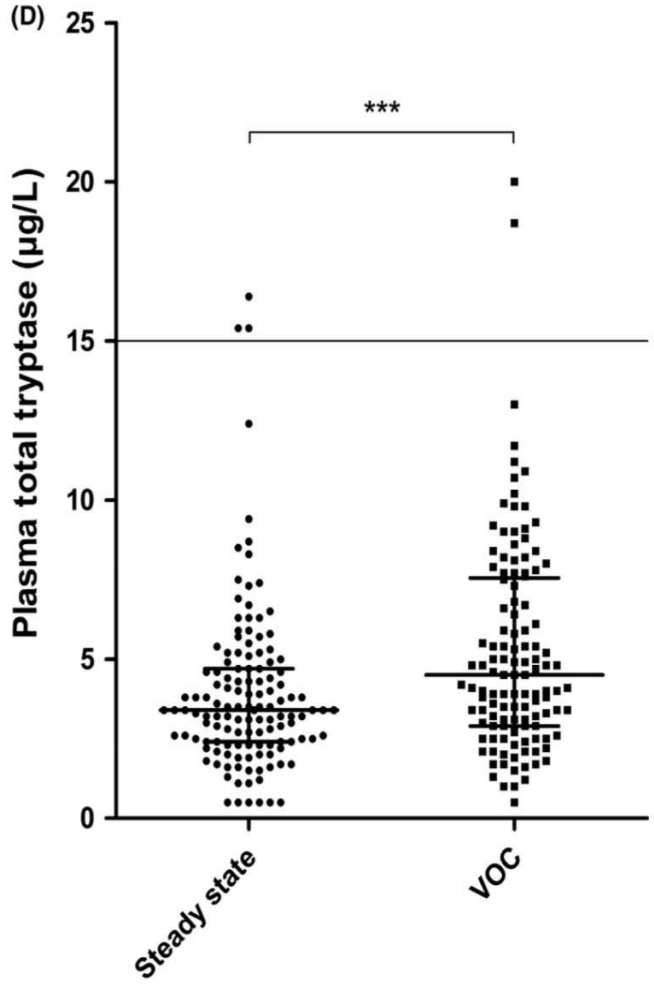
Fig 1. Serum cytokine levels of IL-8, SP, and TNF in healthy controls and patients with SCD. The measured cytokine levels box-plots are shown by SCD status. (○) Indicate outliers within each serum cytokine; X, extremes.

Mast cells activation in VOC



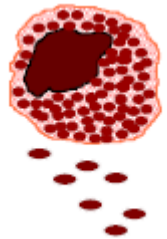
AllaliS et al. BJH 2019

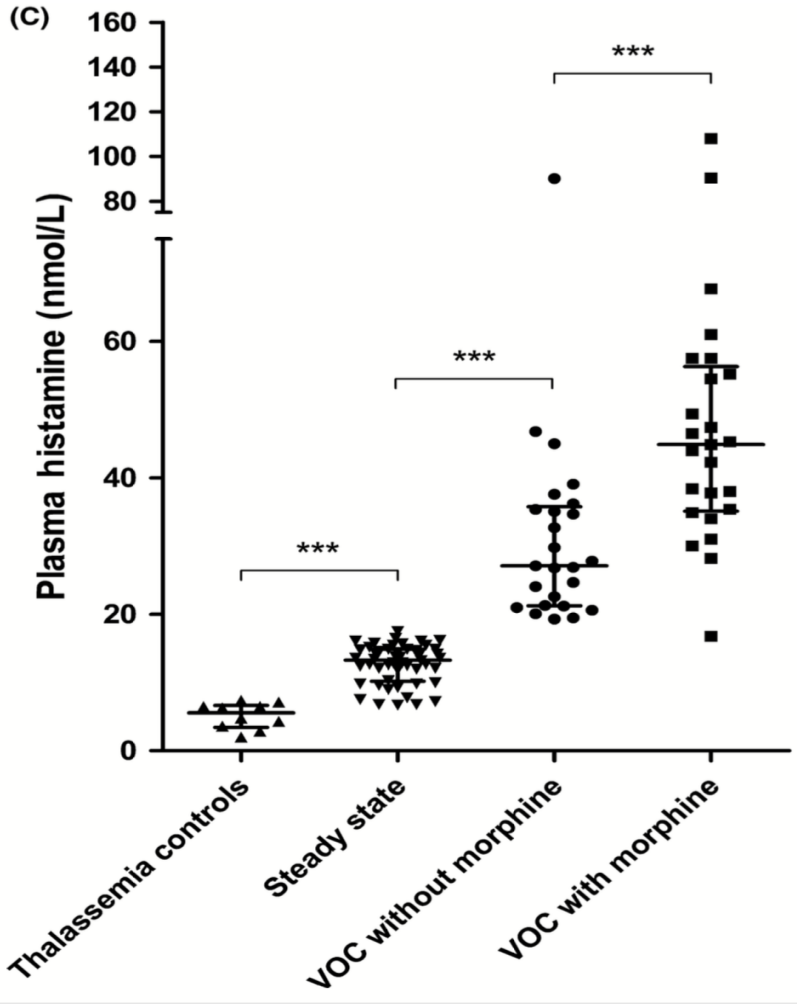




Mast cells activation in crises worsened by Morphine

AllaliS et a; BJH 2019

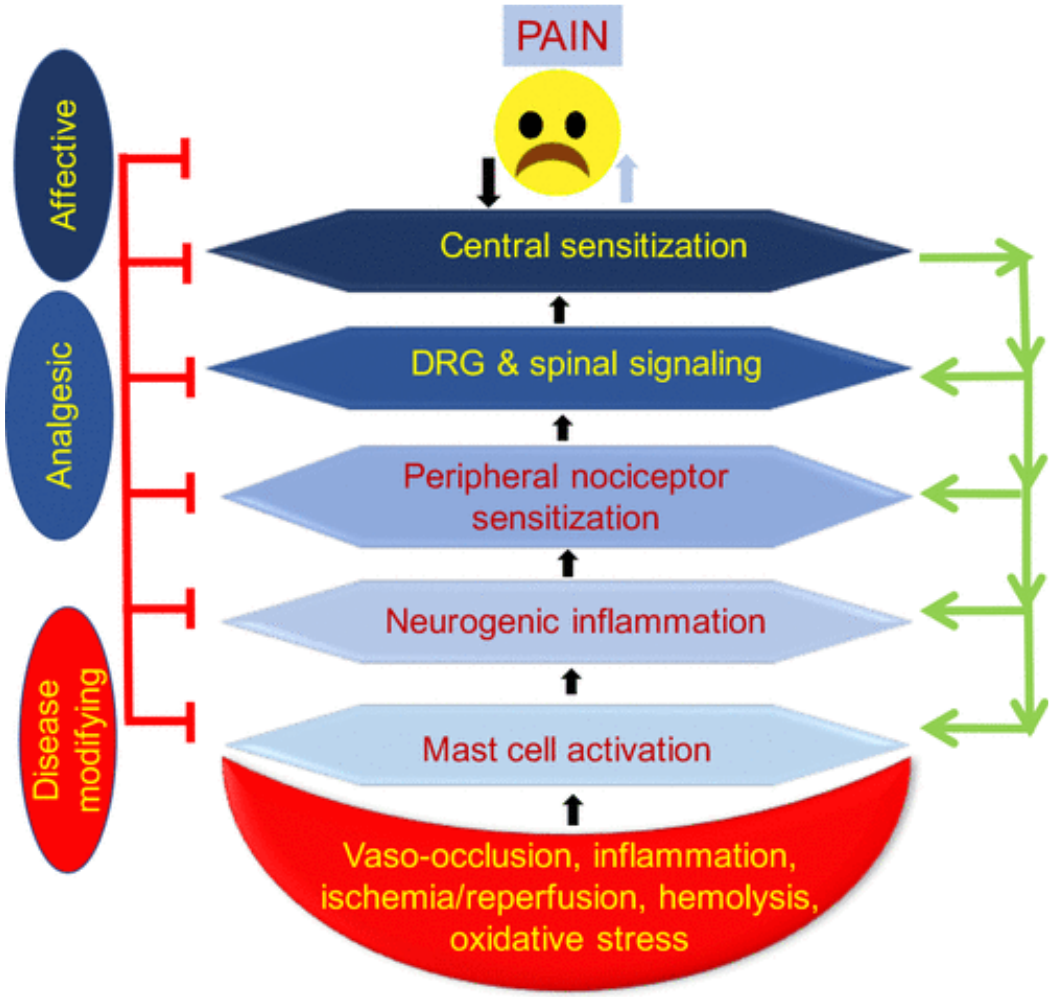




Mast cells synthesize Substance P (nerve also releases it)

- Higher levels of histamine in sickle cell patients and even higher during crisis.
- Increases even more if morphine is administered because of morphine receptor on mast cells

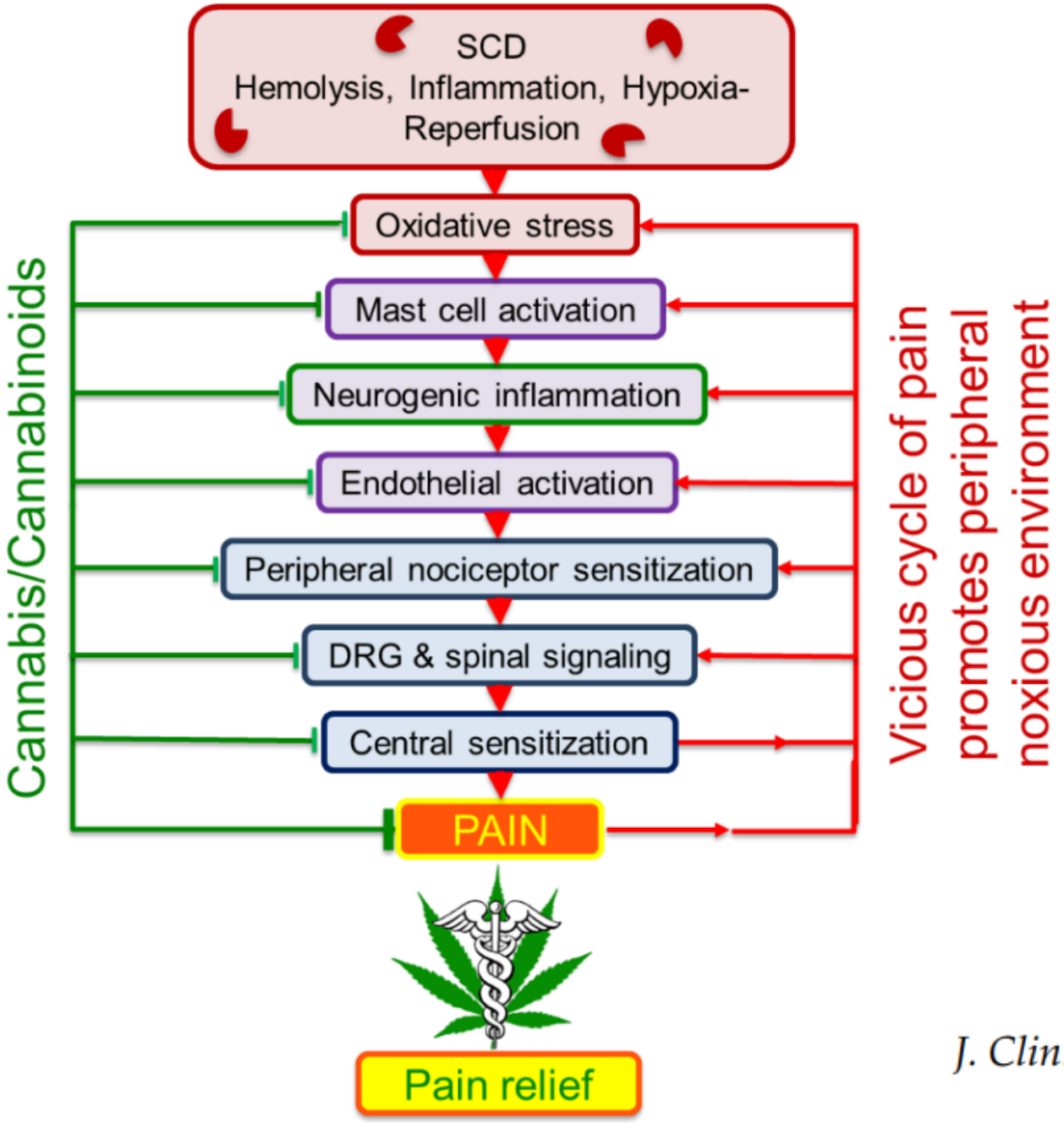
Targeting pain at its source in SCD
K Gupta 2018 AJM



If there are many crises: the volume of inhibitory gray matter is reduced compared to when there are fewer crises. The more frequent the crises, the more the brain is in a state of constant alert, leading to longer-lasting pain, sometimes even creating a loop with pain despite no current vaso-occlusive Crises (VOC).

Thalamic crises (no VOC but pain persists).

In post-transplant patients: sometimes pain similar to VOC for 6-12 months even when there's 0% of S cells. Often triggered by an event (COVID, shingles, etc.). Morphine does not work. Neuroleptics sometimes effective.



Argueta et al

J. Clin. Med. **2020**, *9*, 3902

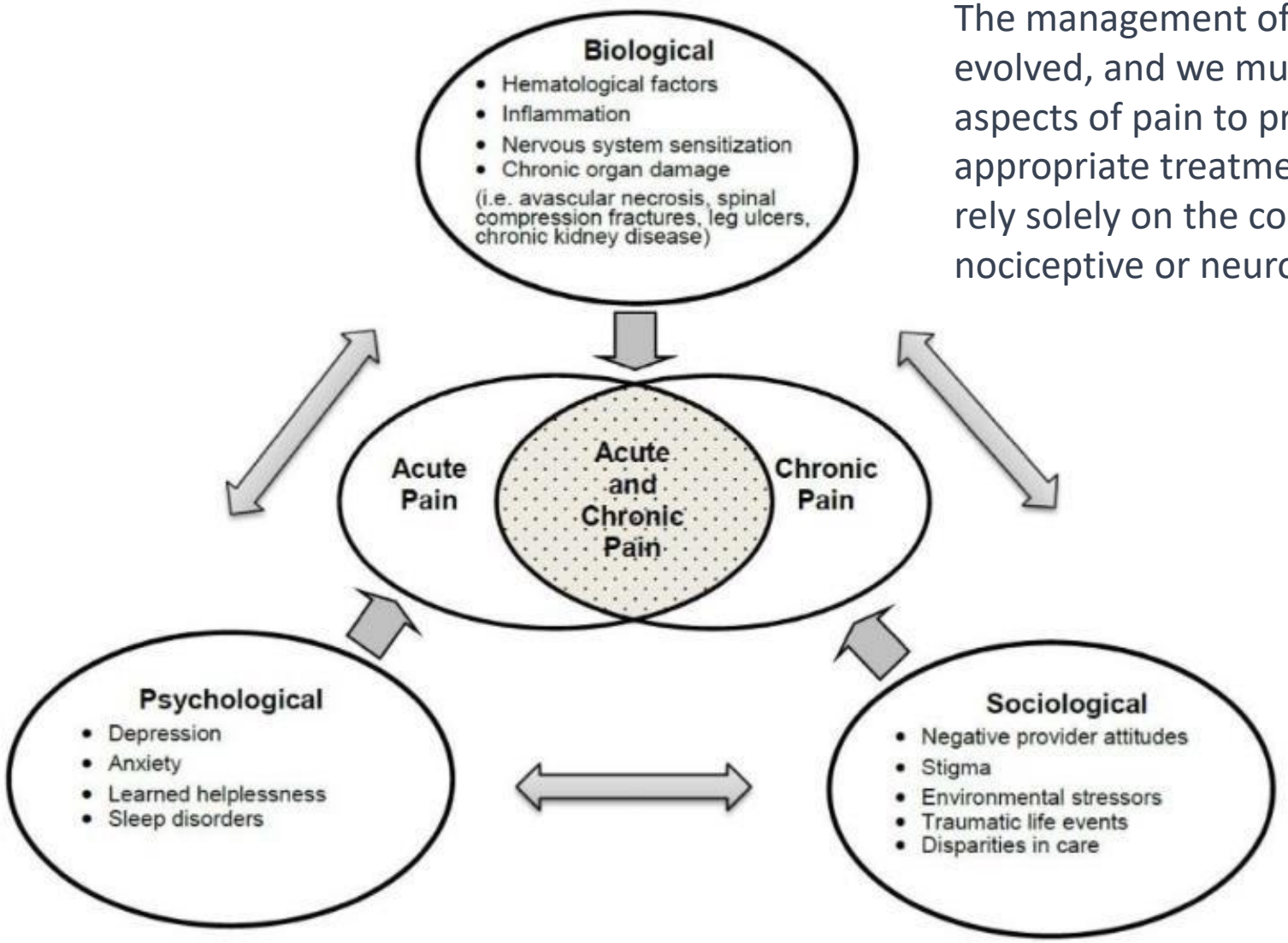


Figure 2. Biopsychosocial model of pain in individuals with sickle cell disease.
Pain management should be delivered in the context of the biopsychosocial model where interactions between biological, psychological and social influences of pain are addressed.

The management of pain has evolved, and we must analyze all aspects of pain to provide appropriate treatment. We no longer rely solely on the concept of nociceptive or neuropathic pain.

WHO analgesics classification

- Step 1 Non-opioids: Paracetamol, NSAID, Aspirine
- Step 2 Weak opioids: Codeine, Tramadol …(association adding paracetamol)
- Step 3 Strong opioids: Morphine, Fentanyl, Oxycodone, dipidolor…

Genetic polymorphisme and analgesia

Cytochrome P450 and P-glycoprotein polymorphisms are known in humans. Most painkillers are metabolized via cytochrome P450. After drug administration, either toxicity or, conversely, treatment ineffectiveness may occur. There are 35 families of this gene in humans.

- **Poor Metabolizers:** 5-10%
- **Intermediate Metabolizers**: 10 -15%
- **Extensive (Normal) Metabolizers**: 60-70%.
- **Ultra-Rapid Metabolizers**: 1-10%

- In **rapid metabolizers**, the effectiveness of codeine or morphine is limited, and they may require higher doses of morphine.
- In contrast, **slow metabolizers** can develop high plasma concentrations with usual doses, leading to increased toxicity.
- **Tramadol** is different as its metabolites (O- DM1) remain active with strong analgesic activity so preferred sometimes than morphine.
- There is some controversy, but **slow metabolizers** may be protected from opioid addiction risk due to pharmacogenetic factors.

Emergency ROOM protocol:

Morphinic titration:

- 1 mg/ 10 kg followed by 3 mg /10 kg every 15 minutes minutes until VAS<4

- handover to PCA with the following informations:

Concentration morphine: 1mg/1mL

Bolus: 2 - 3 mg

Refractory period:15 minutes

Dose max : 24-30 mg/4h

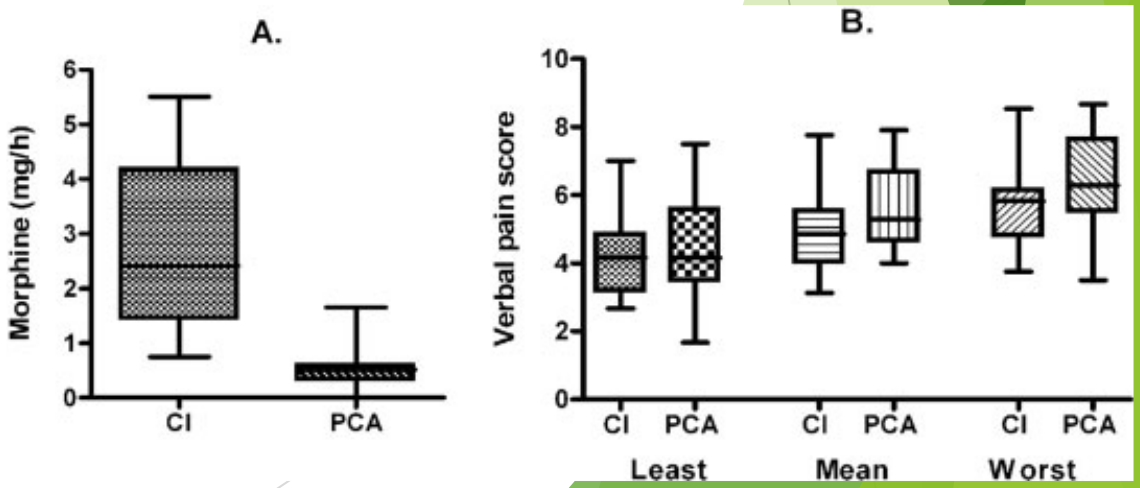
NO CONTINUOUS infusion(ml/h)

TABLE II. Outcome on Morphine Consumption, Pain Score, and Quality of Life

	Treatment group		
	CI morphine (n = 13)	PCA morphine (n = 12)	P value
Morphine consumption and pain			
Morphine dosage (mg/hr)	2.4 (1.4–4.2)	0.5 (0.3–0.6)	0.001
Total morphine dosage (mg)	260 (204–529)	33 (10–68)	0.018
Mean pain score[a]	4.9 (3.9–5.8)	5.3 (4.5–6.9)	0.09
Mean side-effect score and pain (AUC)[b]			
Nausea	18 (3–55)	11 (3–21)	0.045
Constipation	45 (36–59)	30 (10–40)	0.021
Pruritus	14 (0–28)	5 (0–25)	0.42
Sedation	12 (6–33)	18 (0–20)	0.52

Data are presented as medians with interquartile ranges.
[a]Mean verbal response pain score.
[b]Symptoms of side effects are presented as area under the curve (AUC) during treatment.

There was less morphine consumption in the PCA (patient-controlled analgesia) group, indicated by a statistically significant value (p<). The frequency of side effects was also lower in the PCA group.



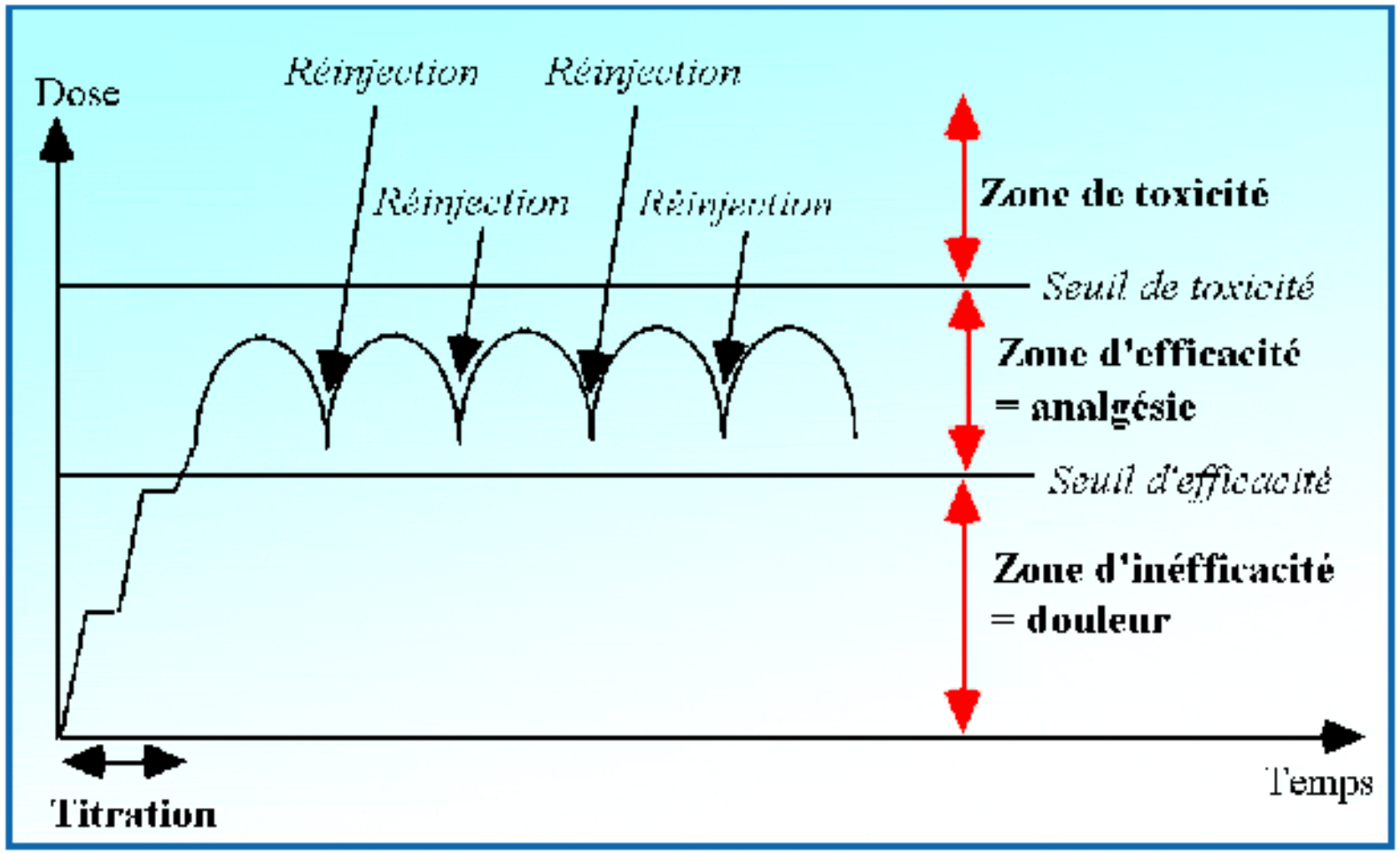


Figure 3 : Technique d'analgésie morphinique correcte associant une titration initiale et des réinjections à bonne posologie et à horaires fixes permettant de maintenir les seuils plasmatiques d'analgésique dans la zone d'efficacité. [7]

NO PCA available:

- Morphine: 5 mg IV bolus every 2 to 4 hours, based on the Visual Analogue Scale (VAS) for pain.
- A continuous infusion of 1 mg/h can be set up with monitoring of respiratory rate and sedation scale, and should be stopped as soon as possible.
- Use of an anti-reflux tubing is recommended.
- Titration should be resumed each time the patient is not relieved

STEP 3 Analgesics:

- **Not recommended** for **home use:**
- frequent occurrence of depressive syndromes.
- life's obligations.
- There's a significant risk of **dependency**, as opioids are often **taken preemptively**, leading to **addiction**.
- Furthermore, patients may arrive at hospitals in much more severe conditions...

During a vaso-occlusive crisis (VOC), opioids should not be administered orally or transcutaneously…

NSAID?

- NSAIDs (Ketoprofen) have been used for a long time.
- efficacy has not been proven.
- Caution : the risk of infection and nephrotoxicity with repeated use.
- A study involving 66 patients given 300 mg/day IV Ketoprofen for 5 days showed no effect on pain intensity, duration of the crisis, or morphine consumption.

Bartolucci et al in Blood, 2009.

Table 1. Characteristics of sickle-cell disease vaso-occlusive crises (VOCs) at inclusion, therapeutic impact, and adverse events as a function of the treatment-group assignment

Characteristic	Placebo group	Ketoprofen group
At inclusion, n	33	33
Age, y	27 ± 7*	26 ± 7
Body mass index	21 ± 3	21 ± 2
VOC duration before inclusion, hours	31 ± 13	29 ± 15
Morphine dose before inclusion, mg	44.2 ± 37	43.7 ± 32
VAS score, mm	71 ± 16	73 ± 16
Categorical pain score, points	5.7 ± 3.6	5.6 ± 2.9
Number of pain sites	2.5 ± 1.5	2.5 ± 1.3
Maximal pain score for 1 site	2.5 ± 0.6	2.6 ± 0.5
Leukocyte count, 10^9/L	14.4 ± 3.7	14.8 ± 4.2
Hemoglobin value, g/dL	9.2 ± 1.3	9.5 ± 1.1
Platelet count, 10^9/L	393.7 ± 102	373.9 ± 128
Lactate dehydrogenase, IU/L	357 ± 127	413 ± 190
C-reactive protein, g/L	63 ± 48	64 ± 69
Treatment impact, n	26†	26†
Duration of VOC, median (IQR), h	50 (36-103)	51 (35.5-87)
Morphine dose, median (IQR), mg	88 (52.5-262.5)	110 (46-195)
Total CPS, median (IQR)‡	0.4 (0.2-0.7)	0.4 (0.2-0.7)
Total VAS score, median (IQR), mm‡	9.6 (5.8-33.2)	12.6 (4.8-23.2)
Adverse events, n	33	33
Abdominal pain	1	0
Infection (urinary tract and bronchitis)	0	2
Constipation	2	0
Epigastralgia	2	1
Facial edema	1	0
Fever	5	5
Hepatic cytolysis	1	0

EMONO

Clin. Lab. Haem.
1999, **21**, 409–412

CASE REPORT

Sickle cell disease and nitrous oxide-induced neuropathy

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Gérardin *et al. BMC Psychiatry* (2015) 15:281
DOI 10.1186/s12888-015-0677-5

STUDY PROTOCOL

PHEDRE trial protocol – observational study of the prevalence of problematic use of Equimolar Mixture of Oxygen and Nitrous Oxide (EMONO) and analgesics in the French sickle-cell disease population

Marie Gérardin[1,2*], Marie-Laure Couec[3], Marie Grall-Bronnec[2,4], Fanny Feuillet[2,5], Laura Wainstein[1], Morgane Rousselet[1,2,4], Marie-Lyne Pinot[1], Fanny Perrouin[1], Olivier Bonnot[6], Marie-Hélène Drouineau[7], Pascale Jolliet[1,2] and Caroline Victorri-Vigneau[1,2]

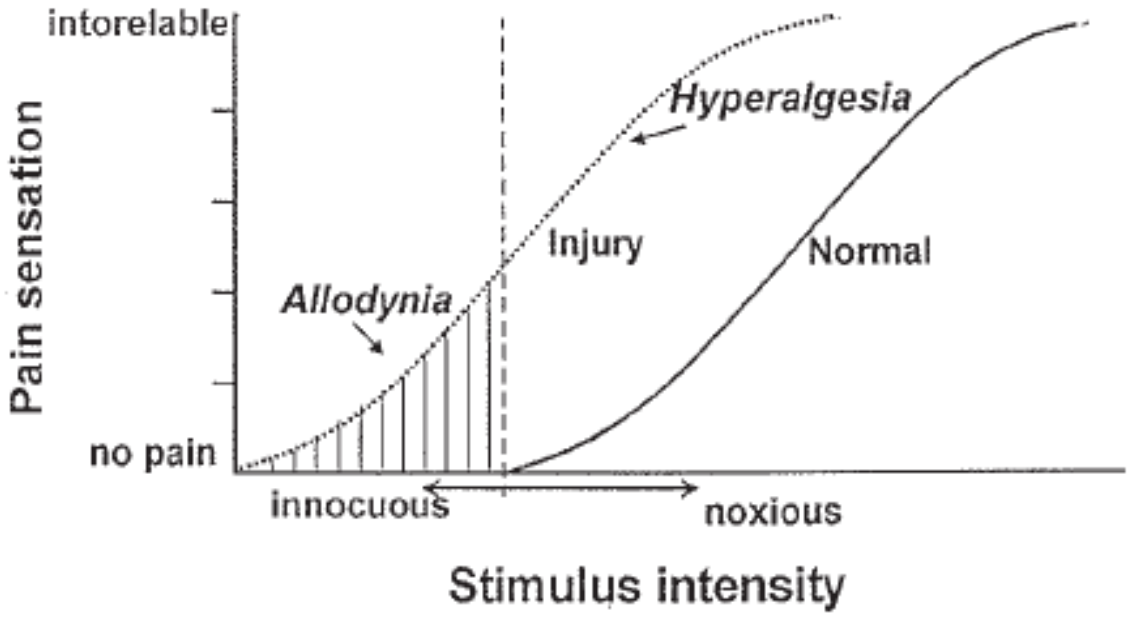
With prolonged exposure, the gas endangers the synthesis of myelin sheaths due to the inability to produce methionine.

Anxiolytics:

- **No benzodiazepines**: Caution is advised due to the risk of respiratory depression when combined with morphine.
- Major anxiety is observed during vaso-occlusive crises (VOCs).
- No studies have been conducted on the benefits of these molecules in terms of hospital stay duration or morphine consumption.
- But Hydroxyzine (Atarax) is regularly used.

NOCICEPTION/ PAIN

- A **non-nociceptive stimulus** can become pain-inducing, a condition known as **allodynia.**
- A **nociceptive stimulus** might cause an amplified response, leading to **hyperalgesia**.
- Pain can occur without **any stimulus** or nociceptors, such as in **phantom pain**.
- **Pain** is not defined by the stimulation itself but by its **consequences**.



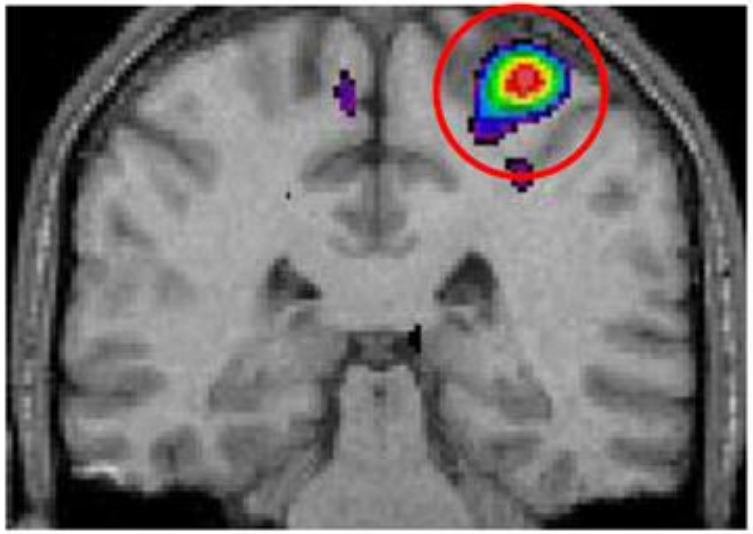
Could the use of Complementary and Alternative Medecine (hypnosis, sophrology, music therapy, or TENS (Transcutaneous Electrical Nerve Stimulation) potentially help our patients?

Frequency of the different types of CAM usage in adults with SCA.

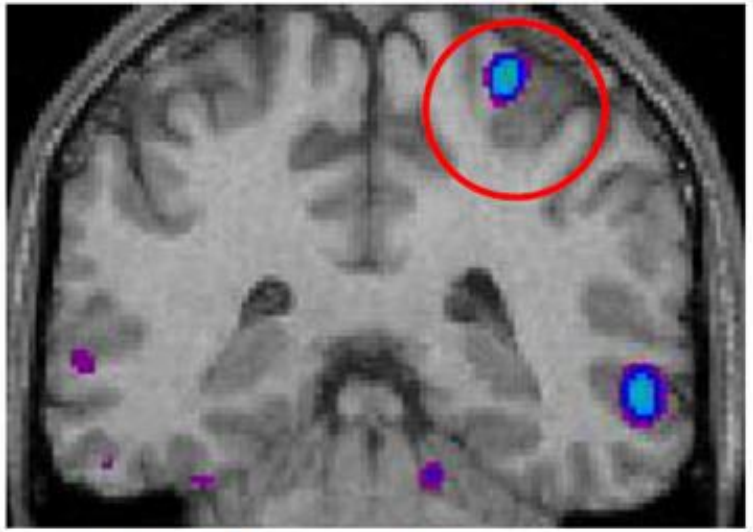
Types of CAM	Number (%)
Prayer	127 (61.1)
Relaxation technique	91 (43.8)
Massage	72 (34.6)
Exercise	58 (27.9)
Spiritual healing	26 (12.5)
Herbal medicine	19 (9.1)
Mega vitamin therapy	14 (6.7)
Folk remedy	14 (6.7)
Yoga	14 (6.7)
Homeopathy	10 (4.8)
Chiropractic	8 (3.8)
Hypnosis	6 (2.9)
Biofeedback	4 (1.9)
Acupuncture	3 (1.4)
Other	47 (22.6)

Majumdar, Complementary Therapies in Clinical Practice, 2013

Attention changes the way your somatosensory cortex processes pain

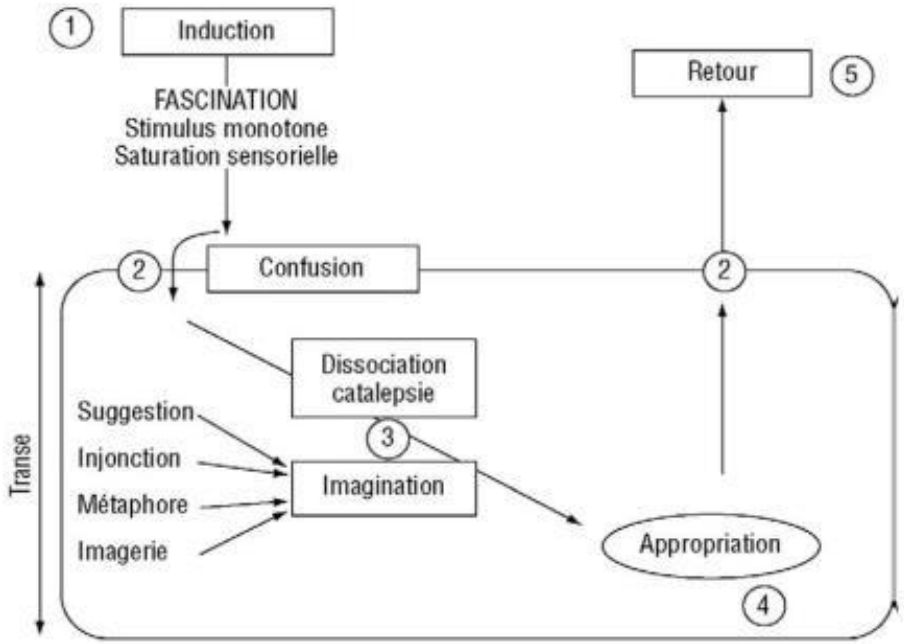


Your brain when you focus on pain



Your brain when you are distracted from pain

HYPNOSIS



The principle of hypnosis is to achieve an altered state of consciousness characterized by heightened receptivity to suggestions and easier access to emotions, ideas, and unconscious memories.

MUSIC CARE

- Music therapy is a controlled technique of music listening that utilizes its physiological, psychological, and emotional influence on a person during the treatment of a disease or trauma.
- Standardized program of music therapy guided by a digital tablet, tailored to the patient, and based on the "U-sequence" method (hypno-analgesia).
- Its effectiveness has been demonstrated in managing acute and chronic pain of various types
- sylvain.le-jeune@aphp.fr or visit http:www.music-care.com/fr/

II. Prevent complications

Acute events: Unpredictable

Chronic Events: Organs damage

ACS
VOC

- Renal
- Neurological
- Pulmonary
- Cardiac
- Hepatic
-Osteoarticular
- Ocular
- Head and Neck
- Cutaneous

HYDROXYUREA

First Meccanism

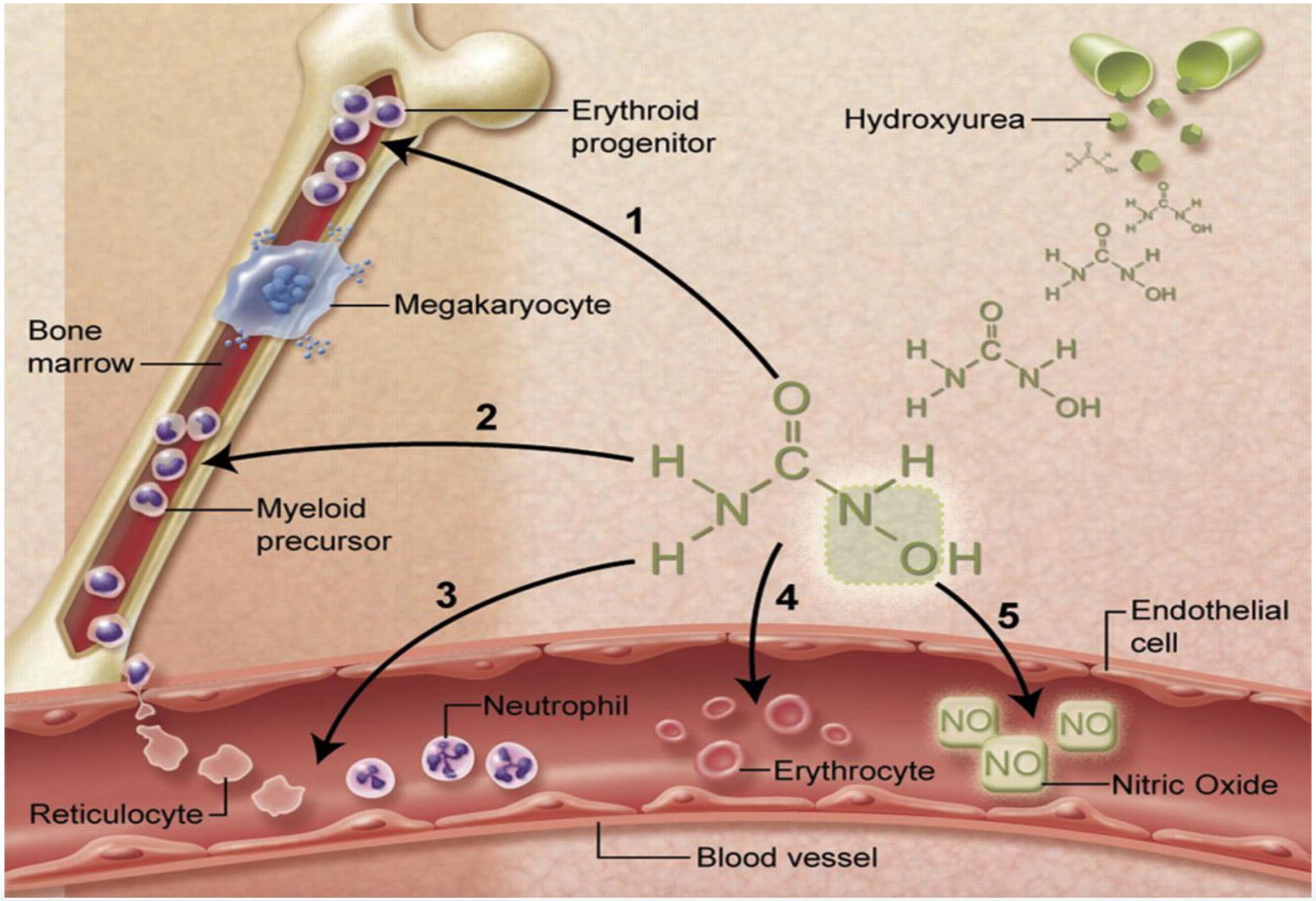
- Inhibits DNA synthesis through the inhibition of ribonucleotide reductase.
- It is supposed to increase the synthesis **of fetal hemoglobin (HbF)** by recruiting hematopoietic progenitors rich in HbF.“
- Inhibition of the polymerization of **deoxyHbS.**

But not only…

- Benefit is not significantly correlated with the level of HbF in all studies
- Sometimes the benefit is there before the increas of HbF blood level

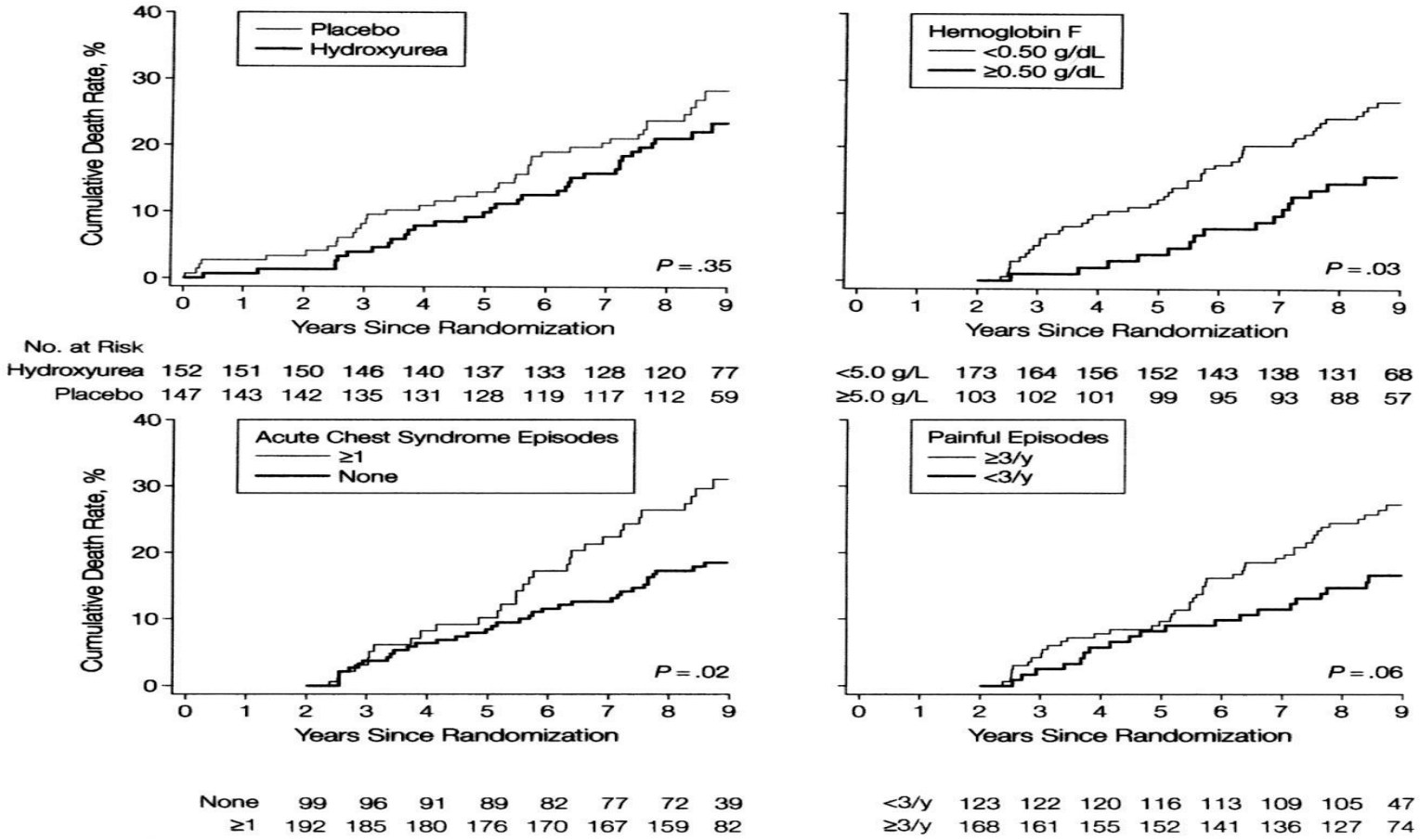
WHY?

Hydroxyurea Therapy



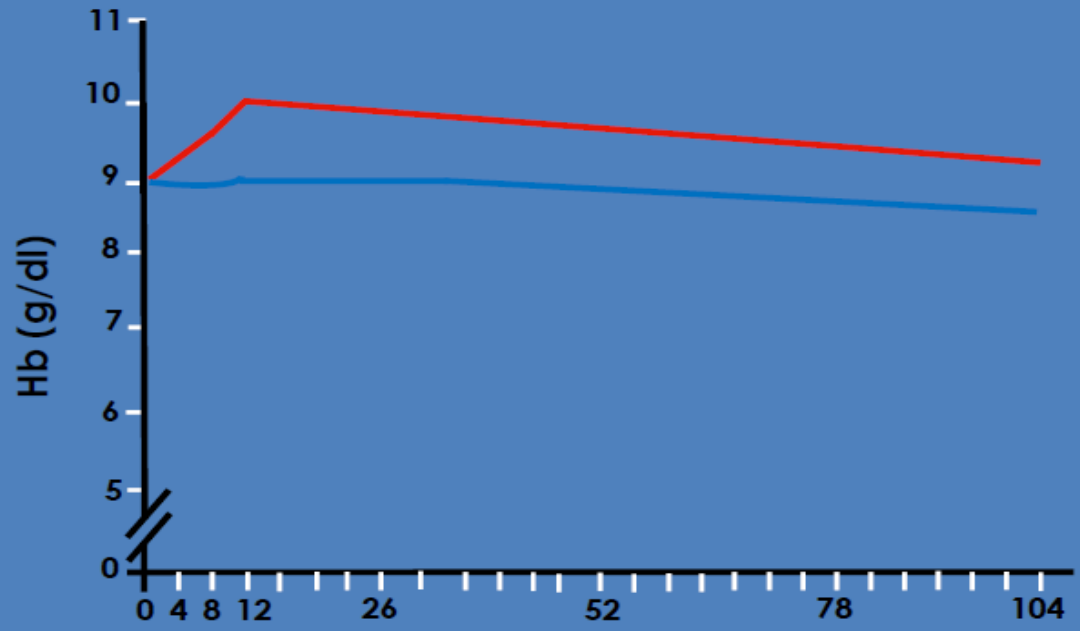
Ware RE, Blood 2010

Effects of HU on the frequency of painful crises in SCA MSH study



Charache S et al, NEJM 1995

HU increases Hb level in infants



N of patients	Weeks from onset of the study drug				
Hydroxycarbamide	96	91	91	90	84
Placebo	97	92	90	86	96

Placebo – HU
(Wang et al, (BABY HUG), Lancet 2011)

"The effect on survival is very likely but not demonstrated by controlled studies."

Off-labels indications for hydroxyurea:

- Severe anemia (baseline Hb level < 7g/dL)
- Past history of allo-immunization
- Kidney impairment
- Brain protection
- Pulmonary hypertension?

Recommendation for prescription of hydroxyurea

- Initiation by a physician experienced in the management of SCA
- Starting dose: 15-20 mg/kg/d
- Usual dose: 15-30 mg/kg/d
- Blood count, HbF, renal and hepatic function checked
before starting HU
- Blood count checked/ 2 wks in the first 2 months,
then every 1 or 2 months
- Decrease or stopping of treatment in case of hematological toxicity

Treatment follow up:

- Blood sample/2-3 mths
- Toxic values tresholdes:
  - Neutrophils < 1500/ mm^3
  - Platelets <80 000/mm^3
  - Hemoglobin <4,5 g/dL
  - Reticulocytes < 80 000/mm^3 if Hb si <9 g/dL

Long term safety data:

Concerns, because HU is a S-phase specific agent that arrests the cell cycle at the G1 and S phases

- **But encouraging data, notably from the Hydroxyurea Study of Long-Term Effects (HUSTLE study) : no increas in the number of malignancies and significantly reductions in death in patients exposed long therm of HU.**

- Growth (Rana S, et al. Pediatrics 2014)
- Genotoxicity (Hanft VN et al. Blood 2000; Mc Gann PT et al, Pediatr Blood Cancer
- 2012)
- Teratogenicity (Liebelt EL et al. Birth Defects Res B Dev Reprod Toxicol 2007)
- Malignancy (Castro O et al. Br J Haematol 2014;)
- Immune function (Lederman HM et al. Pediatrics 2014)

HYDROXYUREA and Fertility

- No special concern about fertility in women
- • SCA by itself impairs sperm count and spermatozoa motility
- • HU decreases significantly sperm count (Berthaut, I, Haematologica 2008)
- • Whether hypofertility resolves afterHU discontinuation is likely but not demonstrated in SCD pts
- • Impact on boys treated early and fora long period ?

Blood Transfusion

- **Acute Transfusion Indications:**

1. **Stroke or (TIA**
2. **ACS**
3. **Priapism**
4. **Acute Hepatic Sequestration**
5. **Preoperative Cases**: For surgeries lasting more than 1 hour and requiring general anesthesia.
6. **Pregnancy**: Especially in cases with severe or frequent SCD-related complications or high-risk pregnancies and since HU is stopped.
7. **Rarely Symptomatic Anemia**: aplastic crisis (Parvo B 19) and acute splenic/hepatique sequestration

Blood Transfusions

- **Chronic transfusions indications**:

1. **Primary/ Secondary Stroke Prevention**: Both simple and exchange transfusions can be used.
2. **Vital organ damage: Cardiomyopathy, dialysis…**
3. **Recurrent Vaso-Occlusive Crises (VOC)**: mostly noncompliance of HU….

Different Goals:

- **Goal HbS < 30%**

1. **Primary/ secondary Prevention of Strokes.**
2. **Confirmed Pulmonary Arterial Hypertension.**
3. **Preparation for Allo-transplantation**

- **Goal HBS < 40-60%**

1. **Recurrence of Severe or Recurrent Acute Chest Syndrome**
2. **Frequent Painful Crises.**
3. **Severe Chronic Kidney Disease.**
4. **Symptomatic Chronic Heart Failure.**
5. **Refractory Leg Ulcers.**
6. **Pregnancy**: Although not systematic, reducing HbS levels may be considered during pregnancy, particularly in cases with complications or high-risk factors.

Inappropriate indications of blood transfusions

1. **Stable Chronic Anemia**.
2. **Uncomplicated Painful Crises.**
3. **Non-Severe Infections.**
4. **Minor Surgery Not Requiring Prolonged General Anesthesia.**
5. **Aseptic Osteonecrosis of the Hip or Shoulder**.

Transfusion decision making:

Increasing PTH Risk:

1. **History of Delayed Hemolytic Transfusion Reaction (DHTR) or Transfusion Inefficiency**.

2. **Patients Infrequently or Never Transfused**

3. **Presence of Alloimmunization**: Patients with alloantibodies due to prior exposure to foreign antigens in transfused blood are more susceptible to PTH.

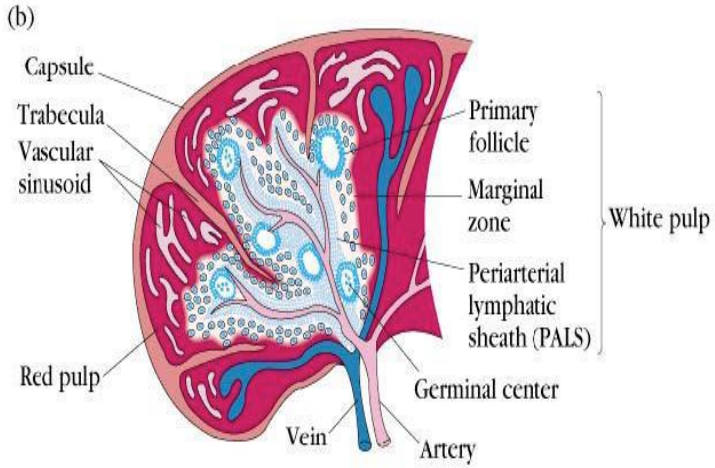
Lower Risk of PTH:

1. **Patients Previously Transfused More Than 12 Times Without Issues**

Venous access in SCD:

1. **Often Difficult**: Venous access in SCD patients can be challenging due to various factors, such as frequent use of veins for blood draws and transfusions, leading to scarring or collapse of veins.
2. **For Occasional Exchange Transfusions**: Insertion of a Central Venous Catheter (CVC) either in the femoral vein or the jugular vein is suggested
3. **For Long-term Exchange Transfusions**:
    1. **AVF: AJH** February 2017 publication by M. Delville.
    2. **Vortex/Double-Lumen Implantable Port**: The experience Necker and H Mondor hospital, Hopital de la Citadelle Liege.

Infections/vaccination: About the spleen…..



ASPLENIA in SCD:

1. **Functional Asplenia**: between 6 months and 3 years of age.
2. **Absence of T-Independent B IgM+ Response**
3. **Serious Infections in Asplenic Individuals**: higher risk 30 to 600 times greater than the general population) for invasive pneumococcal infections
4. **Mortality Rate**: There's a 30% mortality rate associated with pneumococcal septicemia/meningitis in asplenic individuals. There's less data available for meningococcal infections.

Adults SCD vaccinations schedul:

1. **Pneumococcal Vaccines**:
    1. One dose of PCV20 (Pneumococcal Conjugate Vaccine), followed by PPSV23 (Pneumococcal Polysaccharide Vaccine) at least 2 months later.
    2. Additional doses of PPSV23 are recommended at age 5.
2. **Influenza Vaccine**:
    1. An annual flu shot is recommended.
3. **Hepatitis B Vaccine**:
    1. A three-dose series at months 0, 1, and 6, with booster doses if Hepatitis B surface antibody (HBsAc) levels are below 10.
4. **Meningococcal Vaccines**:
    1. Two doses of a conjugate ACWY135 vaccine, spaced 6 months apart.
    2. For Meningococcal B, a two-dose series of a monovalent conjugate vaccine, one month apart, with booster doses as determined.
5. **Haemophilus influenzae type b (Hib) Vaccine**:
    1. One dose of the conjugate vaccine if not received in childhood.
6. **Hydrea and Live Attenuated Vaccines**: no CI but well balance Risks /benefits….

1.Diphtheria, Tetanus, Poliomyelitis (DTP):

One dose every 10 years is recommended.

2.Pertussis (Whooping Cough):

A booster vaccination around the ages of 26-28 years is advised if there has been no vaccination in the previous 10 years. (dTcaPolio).

3.Measles (Plus Mumps and Rubella):

2 doses are recommended if not previously vaccinated. For those born after 1980 and women of childbearing age who are seronegative a single dose of the trivalent vaccine (covering measles, mumps, and rubella) is recommended.

4.Varicella (Chickenpox) for Unimmunized Adults:

1. If serology is, particularly in cases of planned pregnancy, healthcare professionals, or those in close contact with vulnerable individuals, two doses spaced 4-8 weeks apart are recommended.

5.Human Papillomavirus (HPV):

1. A three-dose schedule at months 0, 2, and 6 is recommended.

Management of fever in SCD Adults:

1. **Looking for Signs of Severe Sepsis/Septic Shock/ BUT ALSO ACS (Predictif score PRESEV)**
2. **Identifying the Source of Infection**:

   Common sources include catheters, urinary tract infections, and osteomyelitis.
3. **Diagnostic Tests**:

   Blood Cultures, Urinalysis and Urine Culture (BU/ECBU), **Pneumococcal and Legionella Antigenuria Tests**

   Multiplex PCR on Nasopharyngeal Samples: To detect a wide range of respiratory pathogens.

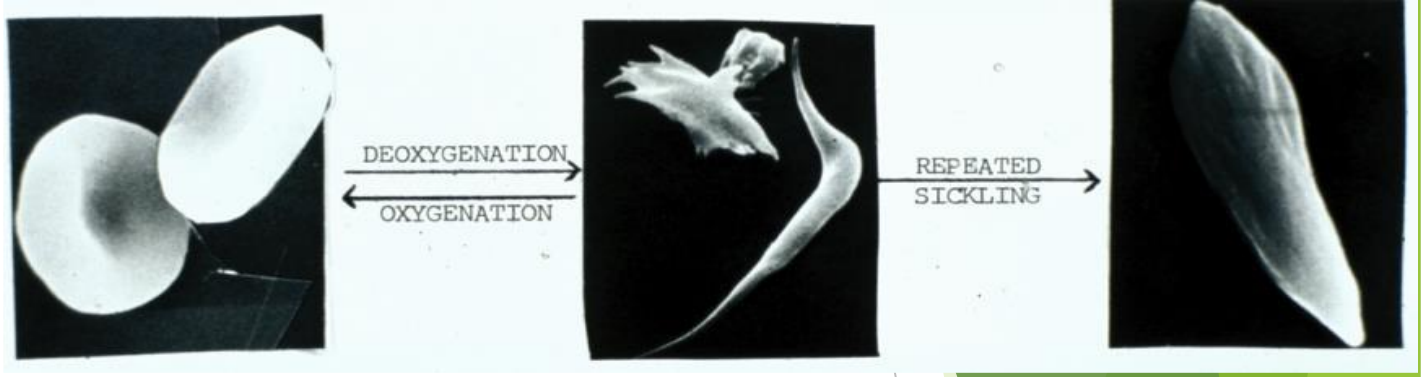
   Sputum Culture and Analysis (ECBC).
4. **Imaging**:

   Chest X-Ray or Thoracic CT Angiography (useful in diagnosing EP, ACS, HTAP)

Variables aux Urgences	Points
Douleur rachis et/ou bassin (cf échelle)	
0 ou 1	0
2	4
3	6
Réticulocytes (10^9/L)	
≤ 216	0
> 216	6
Leucocytes (10^9/L)	
≤ 11	0
> 11	3
Hémoglobine (g/dL)	
> 9	0
≤ 9	1

Risque de STA	Score prédictif
Elevé	≥ 11
Intermédiaire	6 - 10
Faible	≤ 5

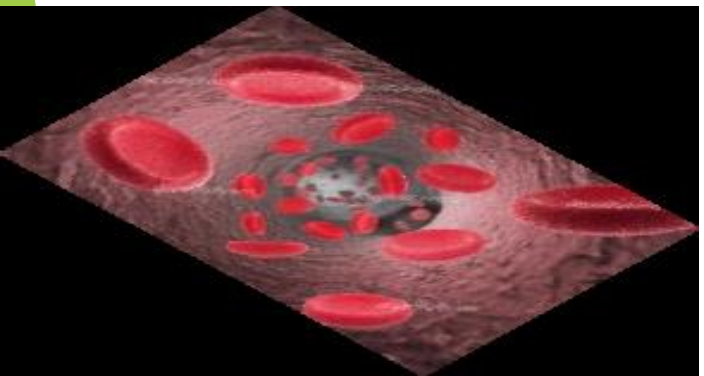
Kassasseyaet al., 2020, Blood

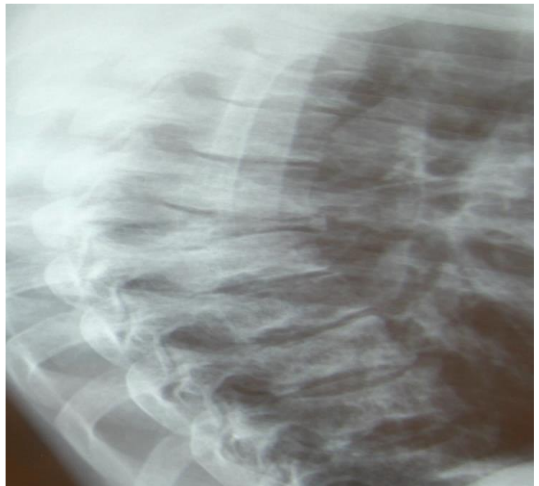


Hydration
Zinc, magnésium
Vitamine E
L-Glu

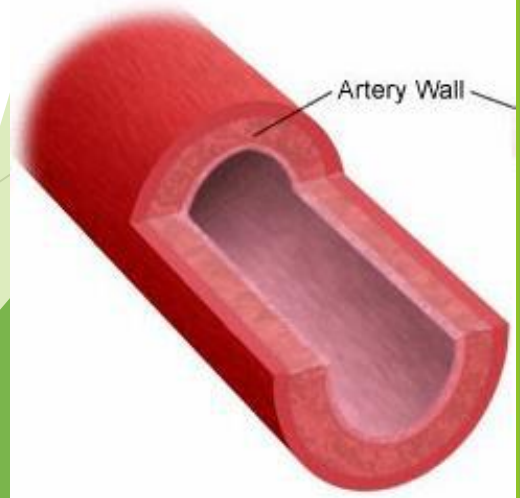
Nutrition and SCD

Vitamine B12
Folates
25 (OH) D, Ca++

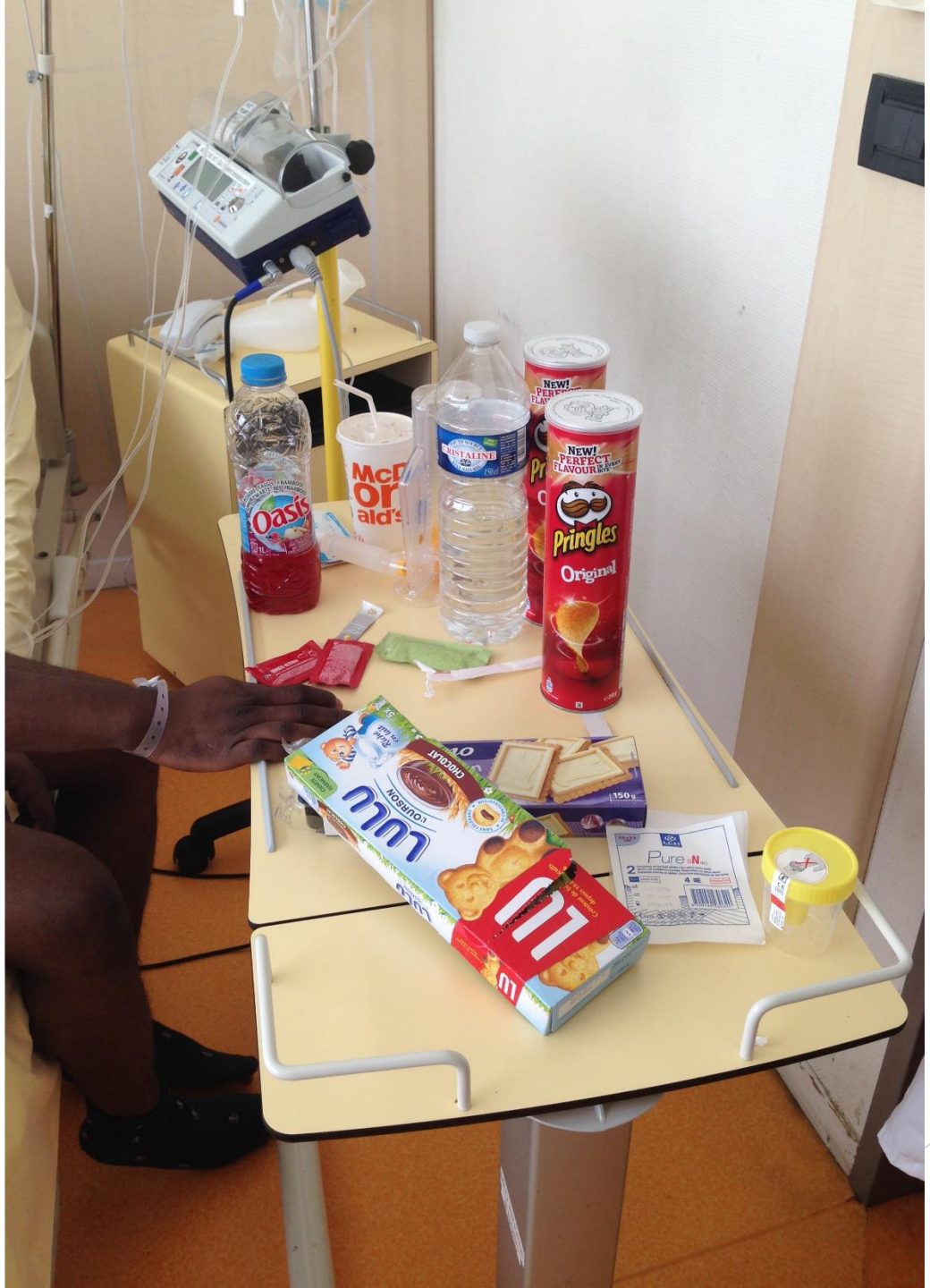




Anti-oxydants
L-Arginine
Statine?



Nutrition and
SCD



1. **Abundant Fluid Intake**: 2L/D
    - Hepar, Contrex, Vittel, and Taillefine.

2. **Zinc and Antioxidant Intake**:
    - **Eggs**: Zinc, Vitamin E, Vitamin A, and L-Glutamine.
    - **Dried Fruits (Hazelnuts, Walnuts, Peanuts)**:
      Vitamin E, Zinc, Calcium, Selenium, Arginine, Glutamine, and Magnesium.
    - **Dairy Products**: Calcium, Vitamin A, Zinc, Arginine, and L-Glutamine.
    - **Whole Grain Bread and Cereals**: Zinc, Magnesium, and L-Glutamine.
    - **Meats (Red, Poultry), Seafoods**: Zinc.
    - **Chocolate**: Zinc, Vitamin E, and Magnesium.
    - **Fruits (such as Avocados)**: Vitamins C, A, E, and Magnesium;
    - Vegetable Oils for Vitamin E.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Phase 3 Trial of L-Glutamine in Sickle Cell Disease

Yutaka Niihara, M.D., M.P.H., Scott T. Miller, M.D., Julie Kanter, M.D.,

Table 2. End-Point and Additional Analyses.

Through Week 48	L-Glutamine (N = 152)	Placebo (N = 78)	P Value
Primary end point			
No. of pain crises			0.005*
Mean	3.2±2.24	3.9±2.54	
Median (range)	3 (0–15)	4 (0–15)	

III. Psychological/social Support

Long-Term Goals for the SCD patients:

1. **Autonomy.**
2. **Project: Family and Social Integration.**
3. **Professional Project.**

What can the Doctor provide:

1. **Importance of a Welcoming Atmosphere and Trust-Building**
2. **Post-Hospitalization Follow-Up Care 15 days after discharge.**
3. **Plan for Regular Follow-Up with a Reference Doctor**

But Real life SCD is more challenging:

1. **Anemic Syndrome**: variable fatigue from one individual to another and shortness of breath during physical exertion.
2. **Intolerance to Physical Effort**: Difficulty in carrying loads, the need to avoid long journeys, and discomfort in standing for prolonged periods.
3. **Pain**:

   Acute Pain: VOC, ACS and priapism.

   Chronic Pain: AON of the femoral and humeral heads, and leg ulcers.

1. **Functional Disability**:

   motor deficits, visual impairments, and hearing difficulties.

2. **Moral Suffering**:
   1. Feelings of incapacity and a sense of impending short-term mortality.
   2. Post-traumatic stress disorders.
   3. Difficulties in constructing or pursuing life projects.

Invisible Disability

Multidisciplinarity:

- Reference Hospital and ER
- Therapeutic education
- Physiotherapist/ Sport
- Nutritionist
- Speech therapist
- Psychiatrist/ Psychologist

Regular Médical check-ups

- Importance of ongoing monitoring /3 Mths

- Early detection of complications:

Transthoracic Echocardiography and BNP Testing, **Pulmonary Function Tests (EFR) with a 6-Minute Walk Test**, **Abdominal Ultrasound**, **Hepatic MRI**, fundoscopy, An audiogram and Auditory Brainstem Response (ABR), dentist ….

Disease- Modifying Therapies

- **New Treatments (Voxelotor, Crizanlizumab, L-Glutamine)**:
- **Voxelotor**: A medication that works by increasing hemoglobin's affinity for oxygen, thus preventing hemoglobin polymerization and red blood cell sickling.
- **Crizanlizumab**: A drug that prevents the cells from sticking to the walls of blood vessels and helps reduce vaso-occlusive crises.
- **L-Glutamine**: An amino acid that is thought to help reduce the incidence of pain crises.
- **Mitapivat**:binding to and activating pyruvate kinase, improving adenosine triphosphate (ATP) production and reducing levels (2,3-DPG) increasing hemoglobin levels and hemoglobin-oxygen affinity.
- Genetherapy:the CRISPR/Cas9 gene-editing technology to modify patients' bone marrow cells. The modified cells are designed to induce the production of fetal hemoglobin.
- Potential Allotransplant also for AYA (Drepa RIC…)

Conclusion

1. **Essential Part of Supportive Care** is Treating THE PAIN. **Rapid Pain Management is Vital**, with step 3 analgesics but also with complementary and alternative medicine.

2. **Preventing the complications** is our role as care giver, using all the tools that we have: Disease modifying treatments, antibiotics/vaccination but also Bio/nutri-therapy.

3. For a complex disease a **multidisciplinary approach** is needed to improve **overall WELL-BEING**: Hematologist, Pain specialists, nurses, psychologist and social workers.

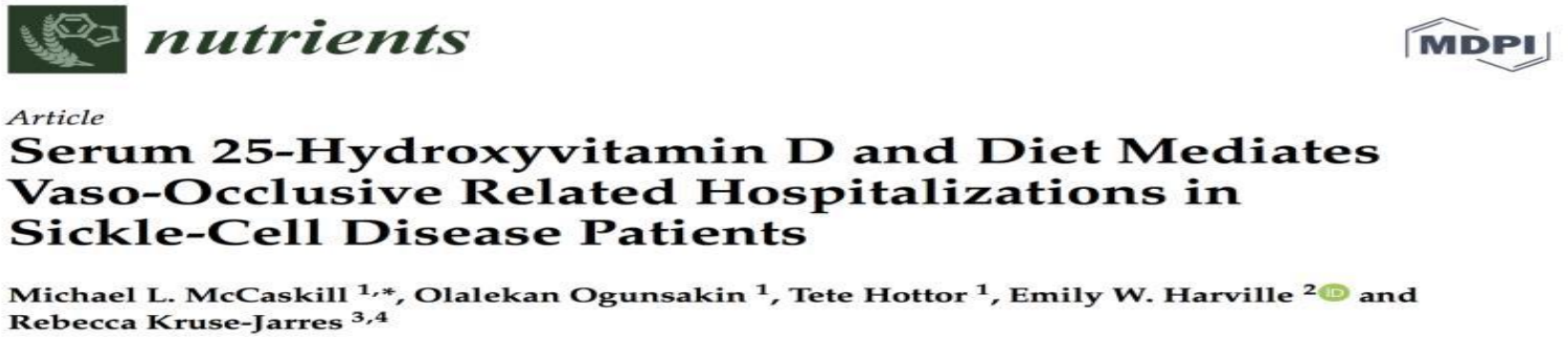
THANK YOU FOR YOUR ATTENTION

References

- **Souffrance et plainte chez le patient adulte drépanocytaire en crise douloureuse**

Jacqueline Faure, Patricia Hanquet

Dans Recherche en soins infirmiers 2009/2 (N° 97), pages 104 à 115

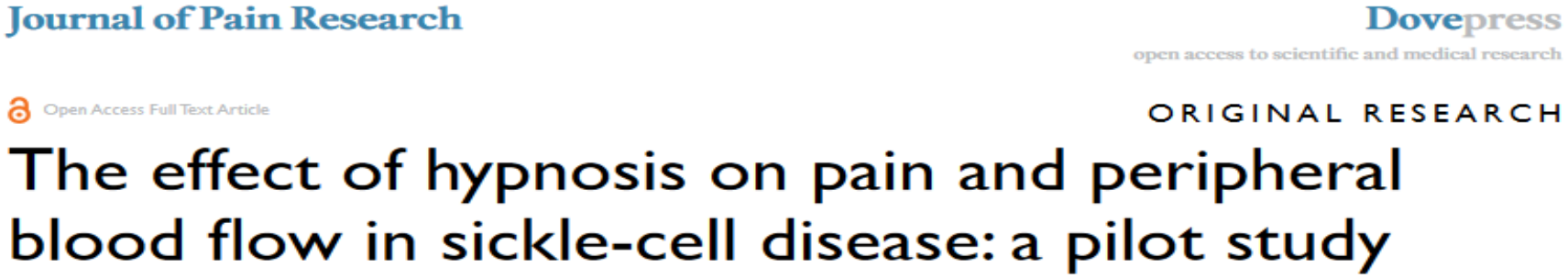

nutrients

MDPI

Article

Serum 25-Hydroxyvitamin D and Diet Mediates Vaso-Occlusive Related Hospitalizations in Sickle-Cell Disease Patients

Michael L. McCaskill [1,*], Olalekan Ogunsakin [1], Tete Hottor [1], Emily W. Harville [2] and Rebecca Kruse-Jarres [3,4]


Journal of Pain Research

Dovepress

open access to scientific and medical research

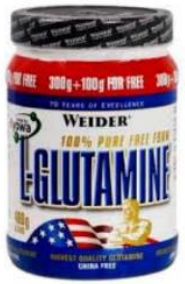
Open Access Full Text Article

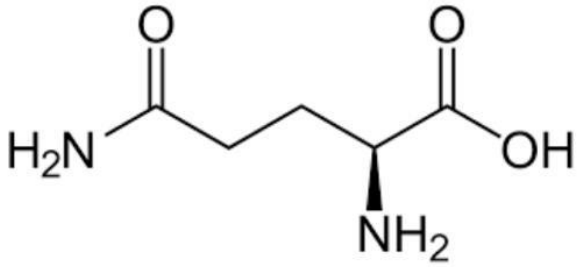
ORIGINAL RESEARCH

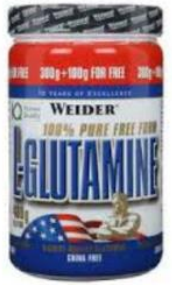
The effect of hypnosis on pain and peripheral blood flow in sickle-cell disease: a pilot study

For more information about nutrition here below…

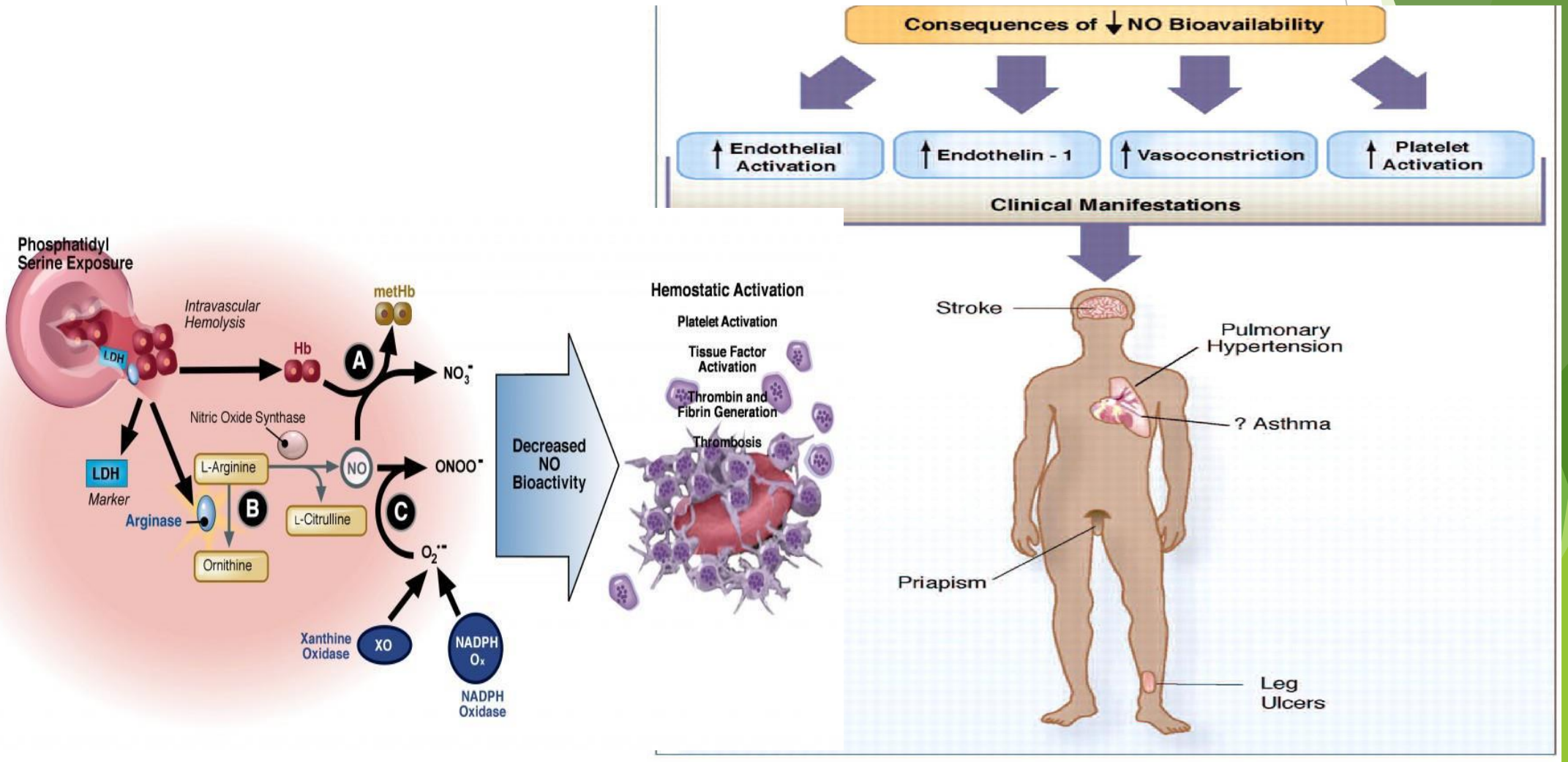
ANTIOXIDANT: L-GLUTAMINE







NO, L-Arginine and Oxidative stress



Intérêt des compléments alimentaires hypercaloriques et hyperprotidiques?

→Fractionner les repas, notamment dans les moments d'accalmie de la crise

→Evaluer l'état nutritionnel en consultation (poids, taille, IMC)

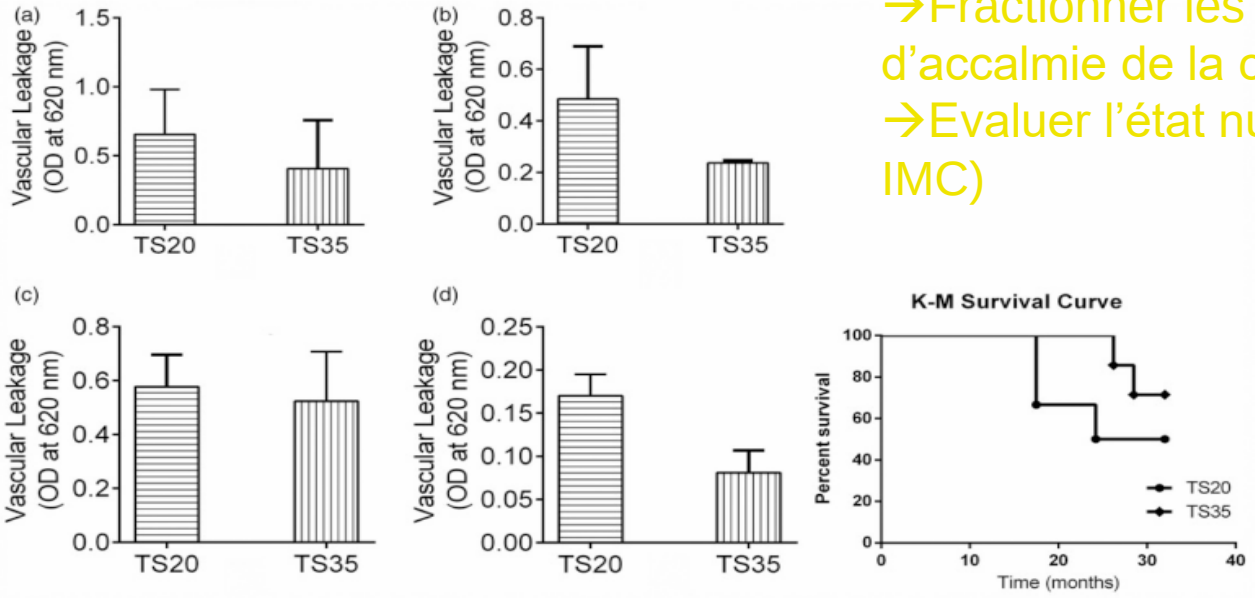


Figure 4.
High protein diet reduced vascular leakage and mortality in transgenic sickle mice. Analysis of vascular leakage in TS20 (Townes mice given a standard diet) and TS35 (Townes mice given high protein) showed that higher protein diet was associated with reduced vascular leakage in the lungs (a), heart (b), kidneys (c) and brain (d), and improved survival

Hydration of RBC strategies

ZINC
Magnesium
Selenium

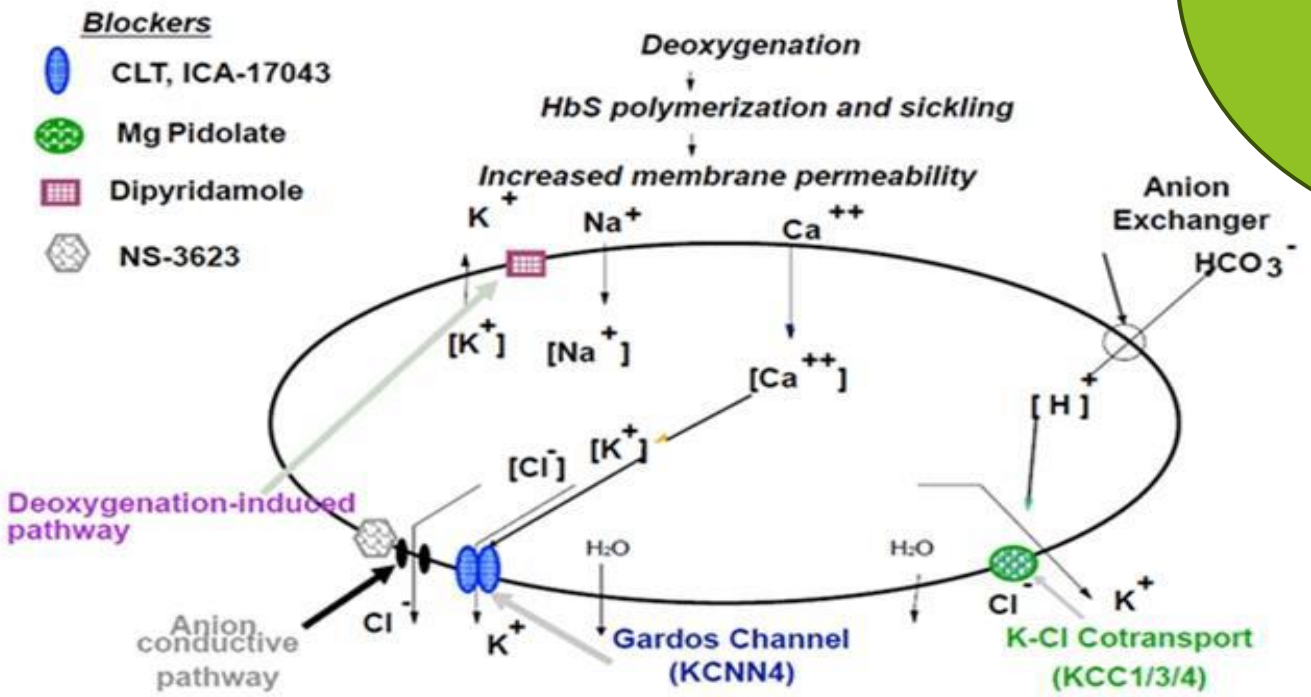


Figure 1: Schematic diagram of the ion transport pathways involved in sickle cell dehydration and action sites of potential therapeutic blockers: *Ca2+activated K+ channel (Gardos channel, KCNN4):* Clotrimazole (CLT) and ICA-17043; *K-Cl cotransport (KCC1/3/4):* Magnesium (Mg) Pidolate; *Deoxygenation-induced pathway:* Dipyridamole; *Anion conductive pathway:* NS3623. Deoxygenation induces Hb S polymerization and sickling, with associated increased membrane permeability and abnormal function of different ion transport pathways, resulting in K+, Cl- and water loss and red cell dehydration (modified from De Franceschi L et al. Haematologica 89: 348, 2004).

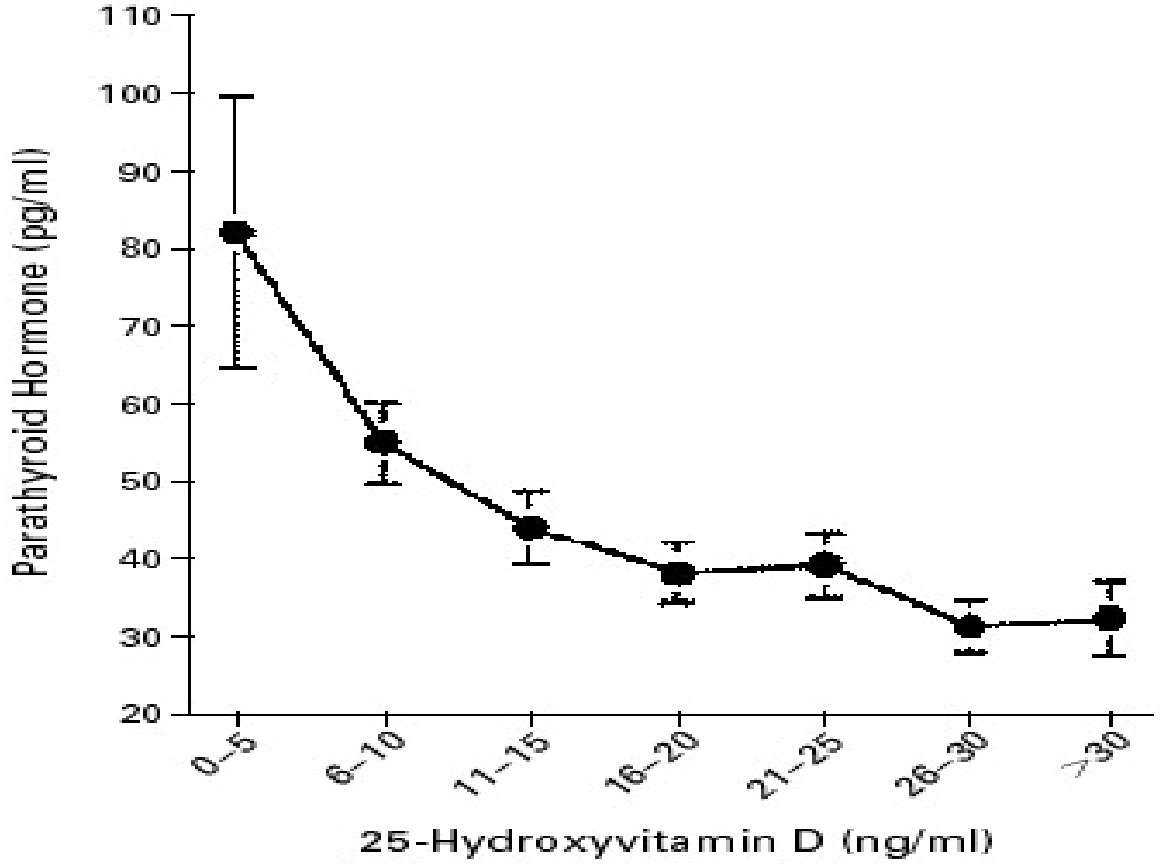
ZINC 2° Metal after Iron:

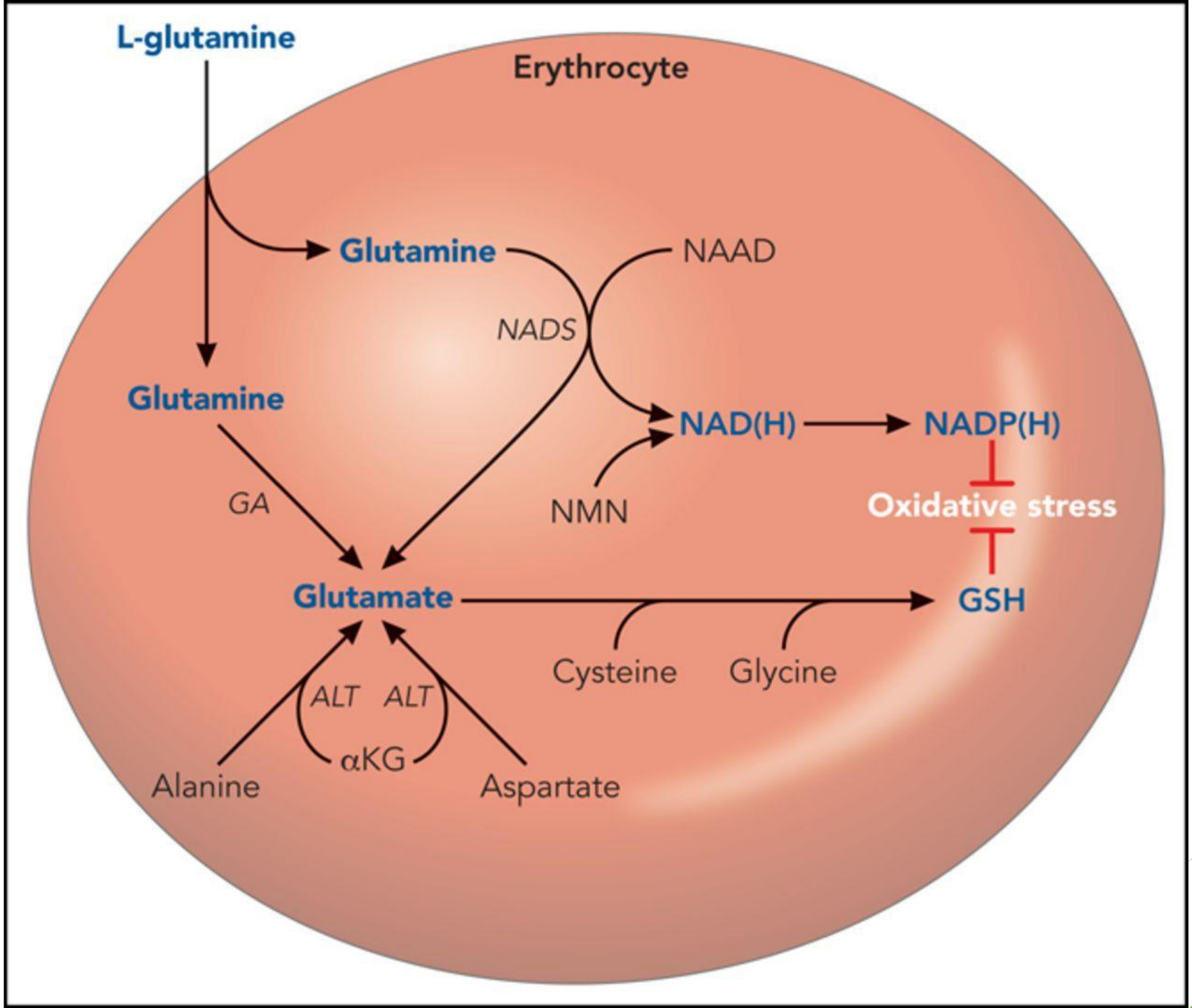
1.Antioxidant

2.Anti-inflammatory: Lowering TNF, IL-1β involved in the body's inflammatory response.

3.Endocrine Effects: Hypogonadism, Growth Defects

4.**Effect on Bone Formation**: influencing the density and strength of bones.


Parathyroid Hormone (pg/ml)
110
100
90
80
70
60
50
40
30
20
0–5
6–10
11–15
16–20
21–25
26–30
>30
25-Hydroxyvitamin D (ng/ml)



Quinn CT Blood 2018

Exp Biol Med (Maywood). 2014 August ; 239(8): 966–974. doi:10.1177/1535370214531863.

High protein diet attenuates histopathologic organ damage and vascular leakage in transgenic murine model of sickle cell anemia

Elizabeth Ann Manci[1,#], **Hyacinth I Hyacinth**[2,3,*,#], **Patrice L Capers**[3], **David R Archer**[4], **Sydney Pitts**[5], **Samit Ghosh**[4], **John Patrickson**[5], **Michael E Titford**[1], **Solomon F Ofori-Acquah**[4], and **Jacqueline M Hibbert**[3,*]

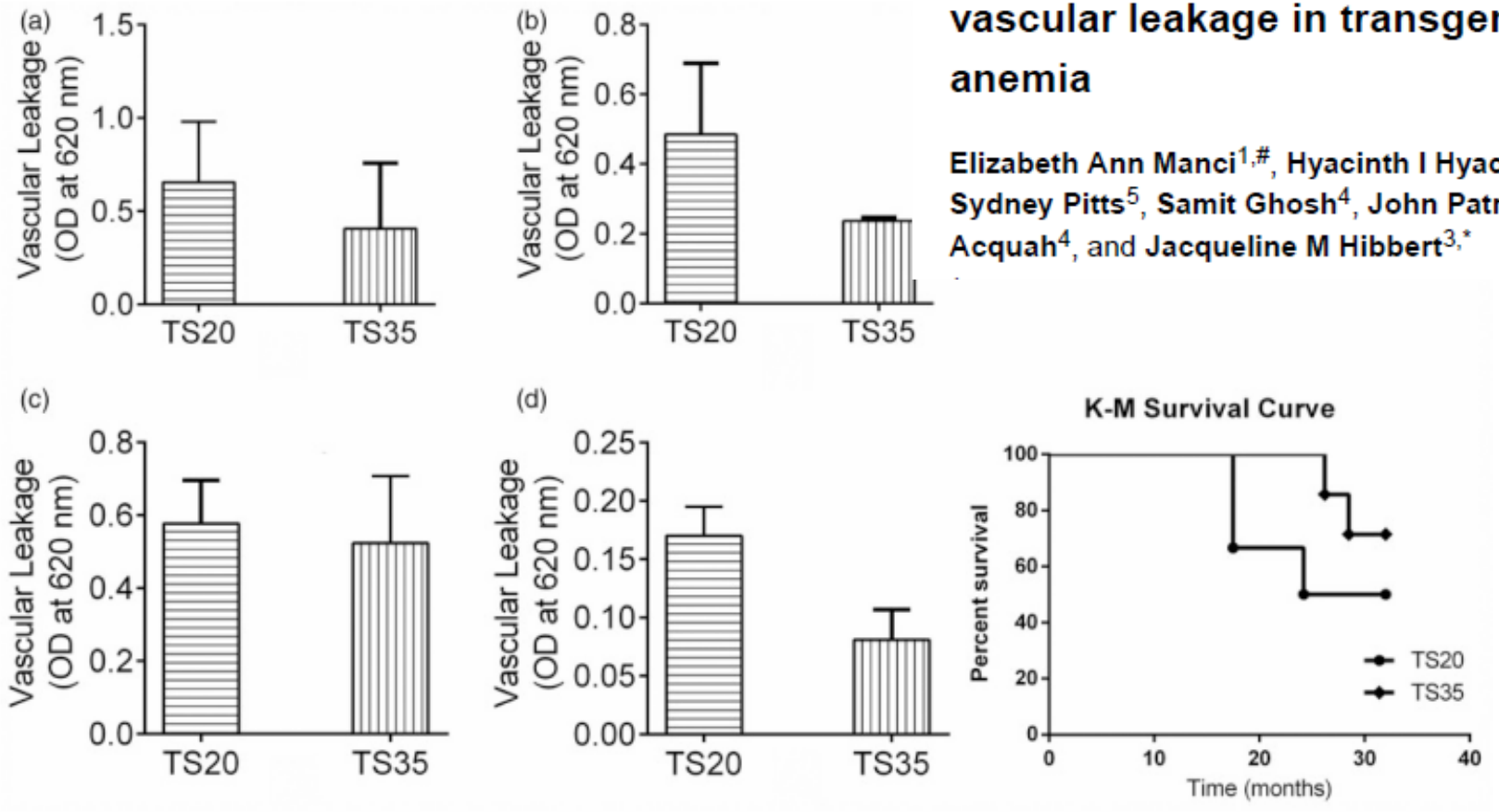


Figure 4.

High protein diet reduced vascular leakage and mortality in transgenic sickle mice. Analysis of vascular leakage in TS20 (Townes mice given a standard diet) and TS35 (Townes mice given high protein) showed that higher protein diet was associated with reduced vascular leakage in the lungs (a), heart (b), kidneys (c) and brain (d), and improved survival

MAISON DEPARTEMENTALE DES PERSONNES HANDICAPEES:MDPH

- Evaluation des besoins
- Accés aux droits et prestations pour handicapés
- Falicilité la vie du patient et sa famille en fournissant des informations, conseilset prenant des décisions sur les droits à la compenation du handicap
- Equipe:GP, Psychologist, social workersand reinsertion specialists
- After a VOC an reeavaluation if a complication is added in themedical history of the patient and discussion with the reference doctor.

Pregnancy and SCD:

- Avoid spontaneous pregnancy
- Genetic counseling before any plan
- Very strict follow up in collaboration with obstetrician
- Transfusion programme or at the end of the prgnancy
- Providing oxygenne for the last months
- Prevention of HELP syndrome
- Rarecases under HU .. Discusion case by case…
- POST PARTUM HR period for complications
- Choosing natural or cesarean section because of retinopathie… etc…