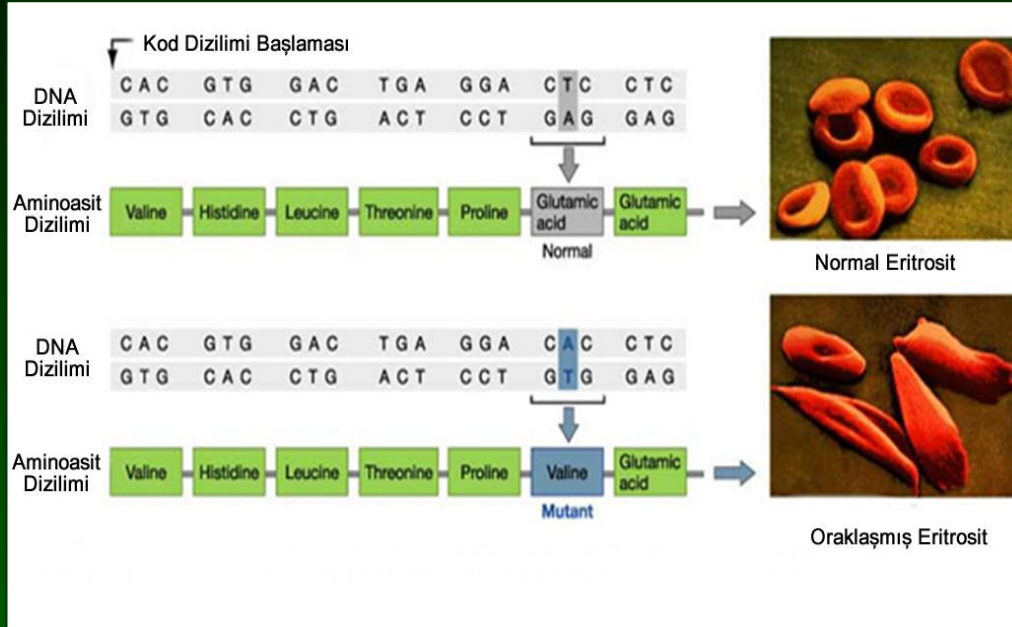


ORAK HÜCRELİ ANEMİDE ERİTROSİTAFEREZİ

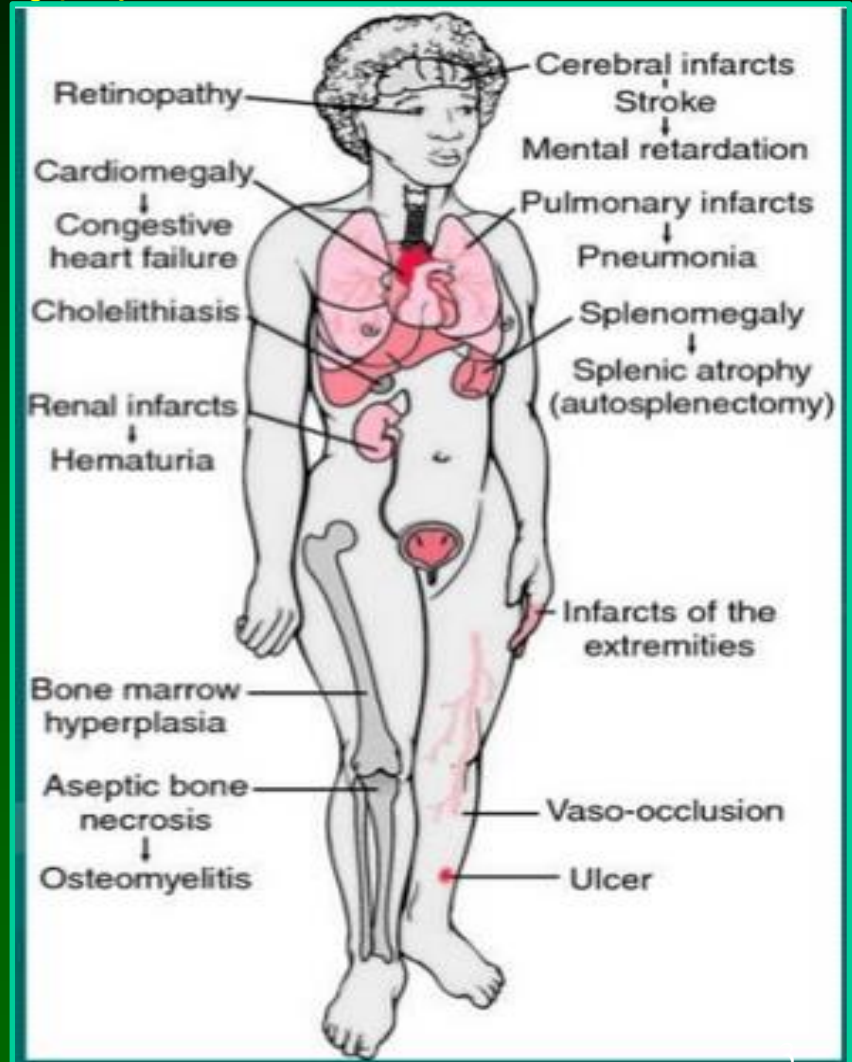
Dr. Tiraje Celkan
İstanbul Üniversitesi
Cerrahpaşa Tıp Fakültesi
Çocuk Hematoloji BD



- ★ Hemoglobinin (Hb) β -globin zincirinde bir nokta mutasyonu (*glutamik asit* \rightarrow *valin*) sonucunda HbS oluşur
- ★ *Otozomal resesif* kalıtlımlı bir hastalık

OHA

- Hemoliz
- Hayatı tehdit edebilen akut komplikasyonlar
- Çeşitli organlarda kronik hasarlar



patofizyoloji

B globin zincirinin 6. pozisyonunda glutamik asit... Valin
anormal hemoglobin Hb S oluşur

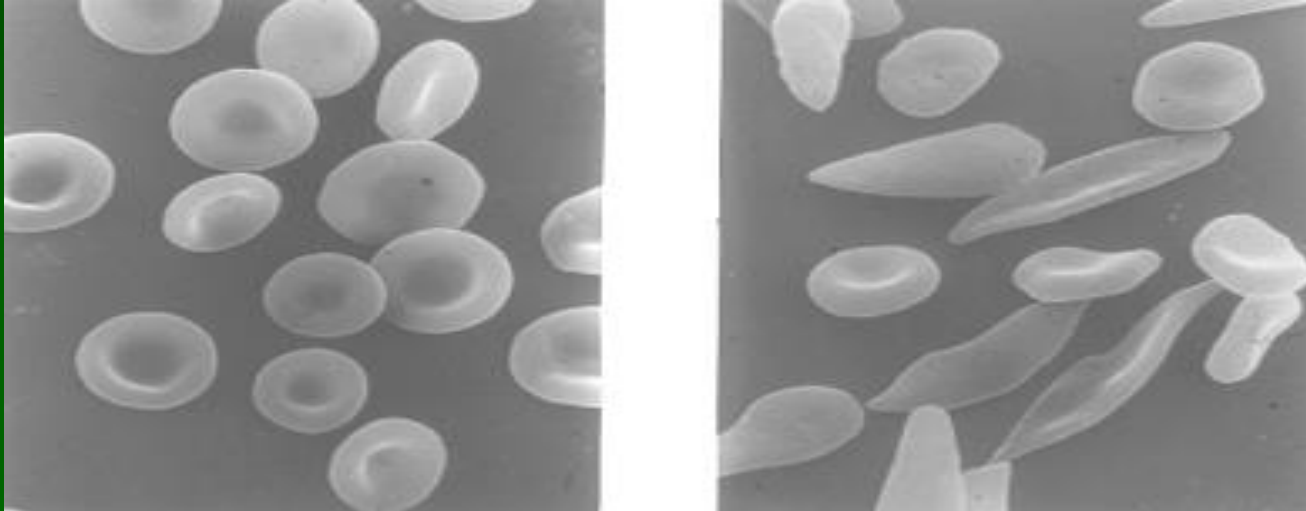
SS eritrositlerin deoksijenasyonuHb polimerizasyonuna
.....deformabilite kaybolur ...hücre morfolojisi değişir

Damar duvarına adezyon...vasokonstriksiyondamarda tıkanma, organ
iskemileri ve end-organ hasarları

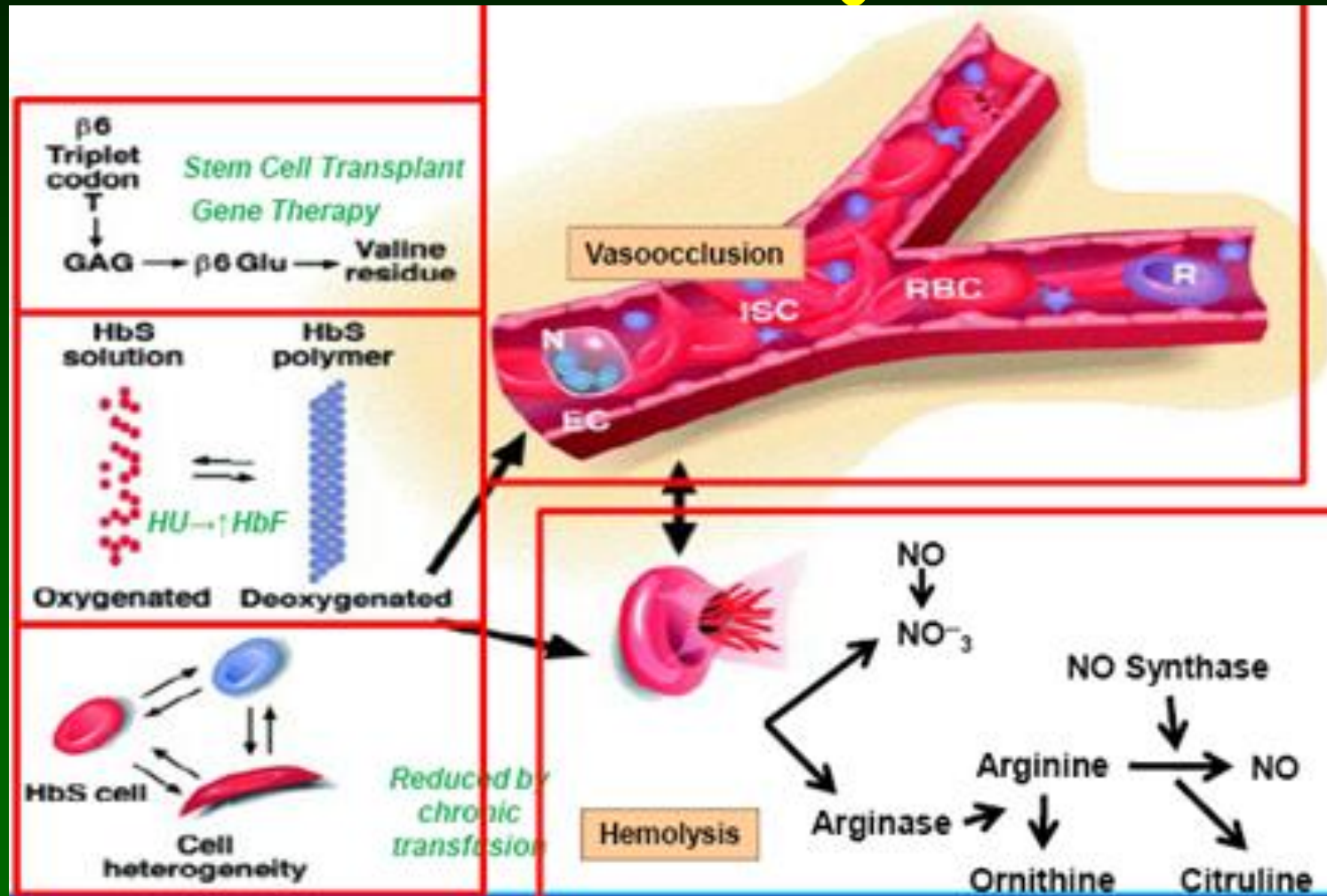
OKSİ DURUM



DEOKSİ DURUM



NO - reaktif oksigen (ROS)



Hemoglobin S;

- ★ Dünyada en sık görülen patolojik Hb varyantı
- ★ Ülkemizdeki en yaygın anormal Hb

- ♦ OHA taşıyıcılığı sıklığı;

- ♦ Türkiye'de %0,3-0,6

- ♦ Çukurova Bölgesi'nde %8,2

- ♦ bazı yörelerde %3-44

, Adana'da %6,4

Sıtma ve OHA



Dünyada önemli sorun

- ★ 2010 yılında 305,773 OHA li çocuk doğmuş
- ★ 2010-2050 yılları arasında **yeni 14,242,002** çocuk doğacak
- ★ Piel et al, Plos One, July 2013 Vol 10 (7): 1-14
- ★ Önemli sağlık sorunu
- ★ Yenidoğan tarama programlarına alınmaya başlanılmış !!!!!!!!!!!

Brezilyada OHA taramaya başlandı kistik fibrozdan önce !!!!! Türkiyede kistik fibroz girdi

Brazilian National Newborn Screening Program – Phases of Implementation

Diseases Screened

PHASE I

Congenital hypothyroidism, PKU

PHASE II

Congenital hypothyroidism, PKU
Hemoglobinopathies

PHASE III

Congenital hypothyroidism, PKU
Hemoglobinopathies, Cystic Fibrosis

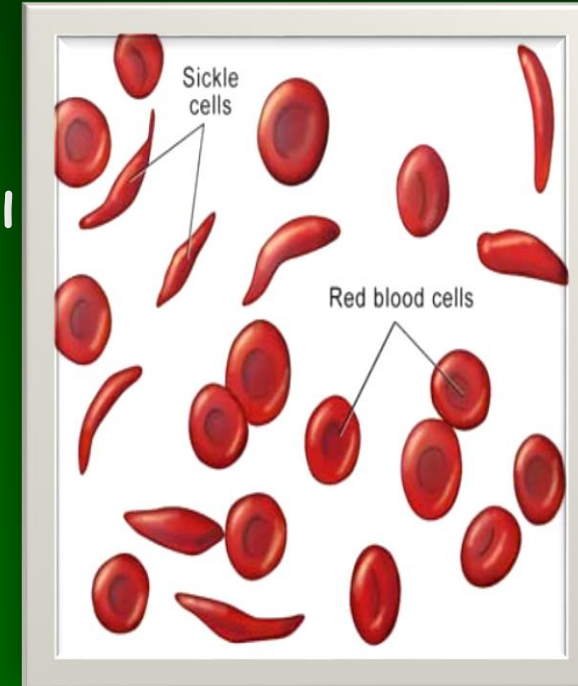
Diseases Screened

PHASE IV

Congenital hypothyroidism, PKU
Hemoglobinopathies, Cystic Fibrosis, Congenital adrenal hyperplasia, Biotinidase deficiency

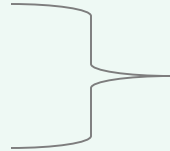
OHA Yönetiminde En Önemli Sorunlar

- Ağrılı krizler
- Enfeksiyonların yönetimi
- Akut göğüs sendromu (AGS)
- Serebrovasküler olaylar
- Kemik ve eklem komplikasyonları
- Hepatik komplikasyonlar
- Pulmoner komplikasyonlar
- Böbrek komplikasyonları
- Priapizm tedavisi



Orak Hücreli Anemide Prognoz

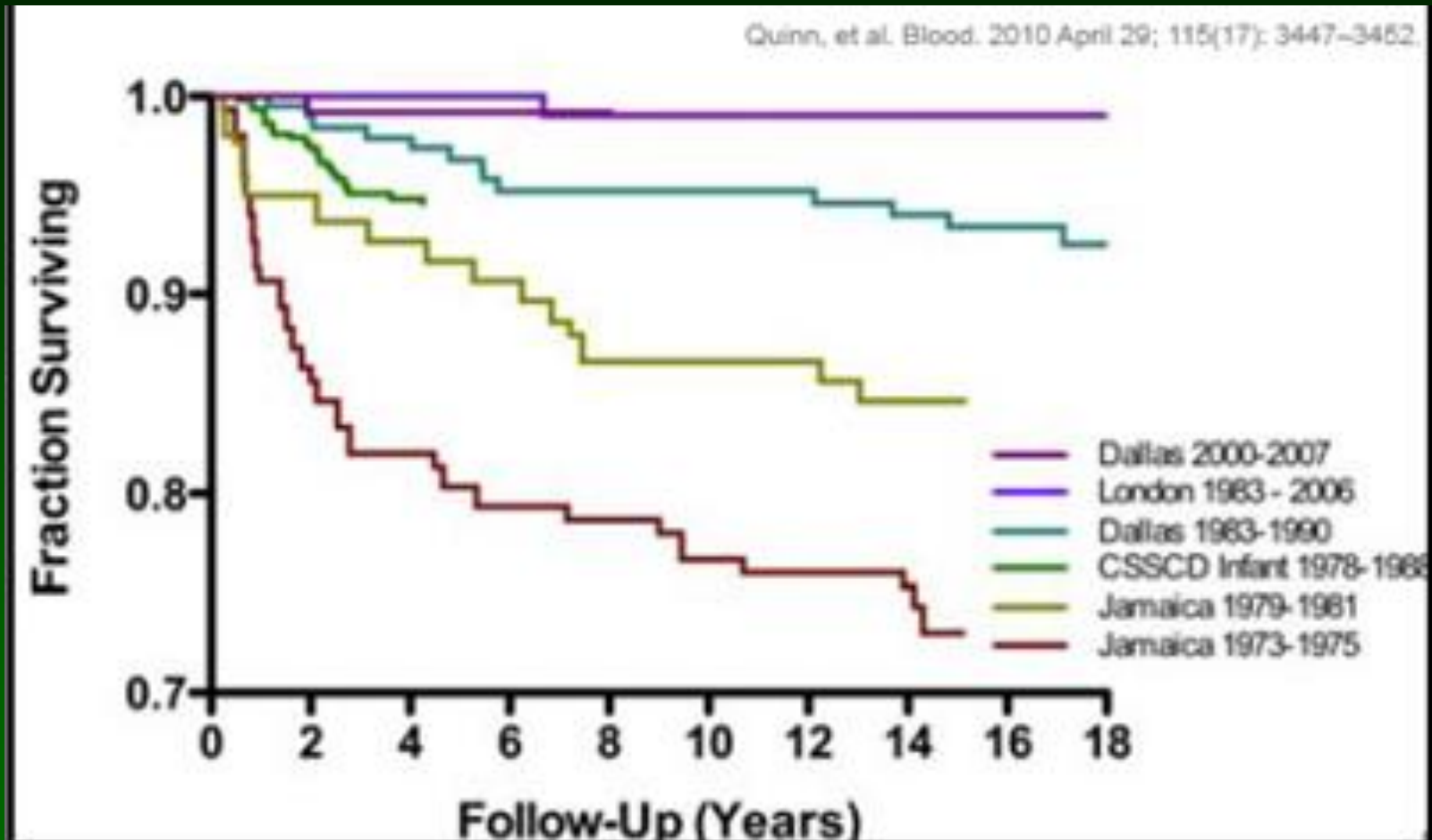
-Erken daktilit
-Hb <7 g/dL
-Lökositoz



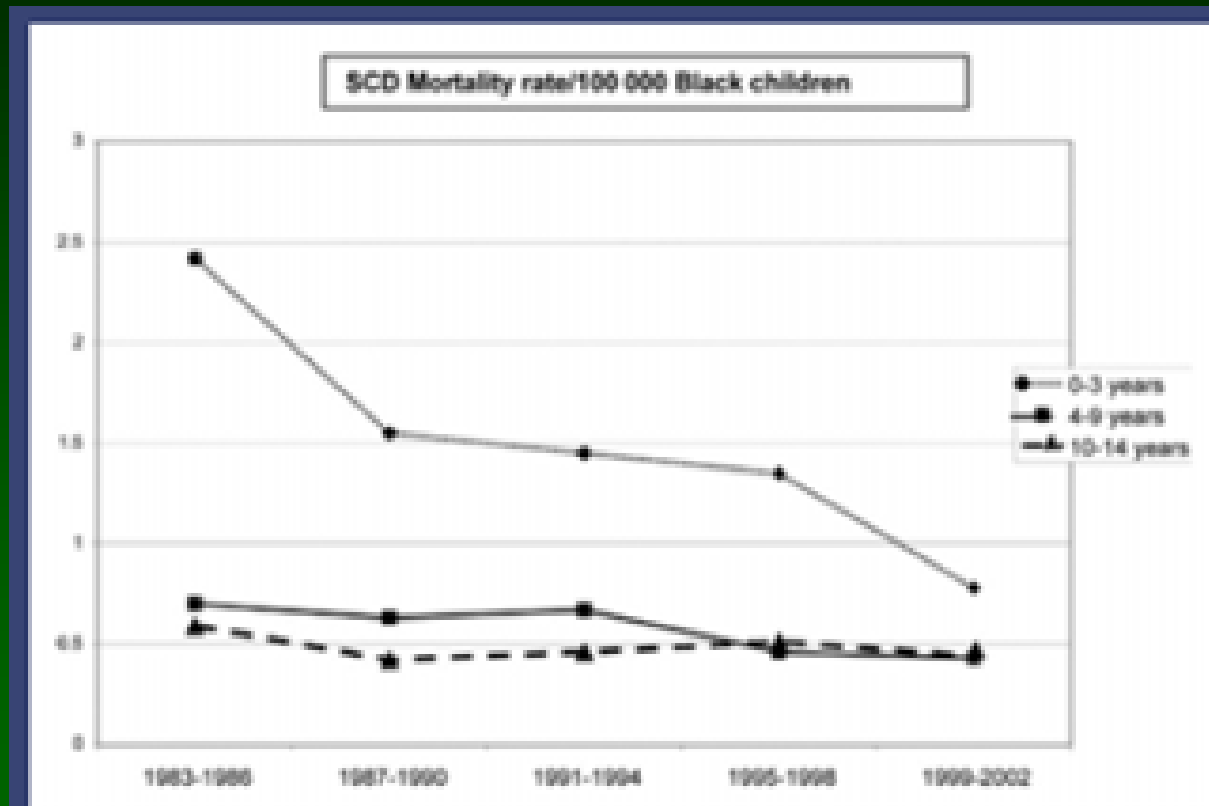
İlk 2 yaşta bu faktörler varsa
prognoz kötü !

- AGS geçirme,
- Böbrek yetmezliği,
- Konvülziyon,
- Lökosit sayısının >15,000/microL,
- Hb F düzeyinin düşük olması erken ölüm ile ilişkili risk faktörleri.

OHA de Yaşam eğrisi



<20 yılda 0-3 yaş OHA den ölüm %68 azaldı



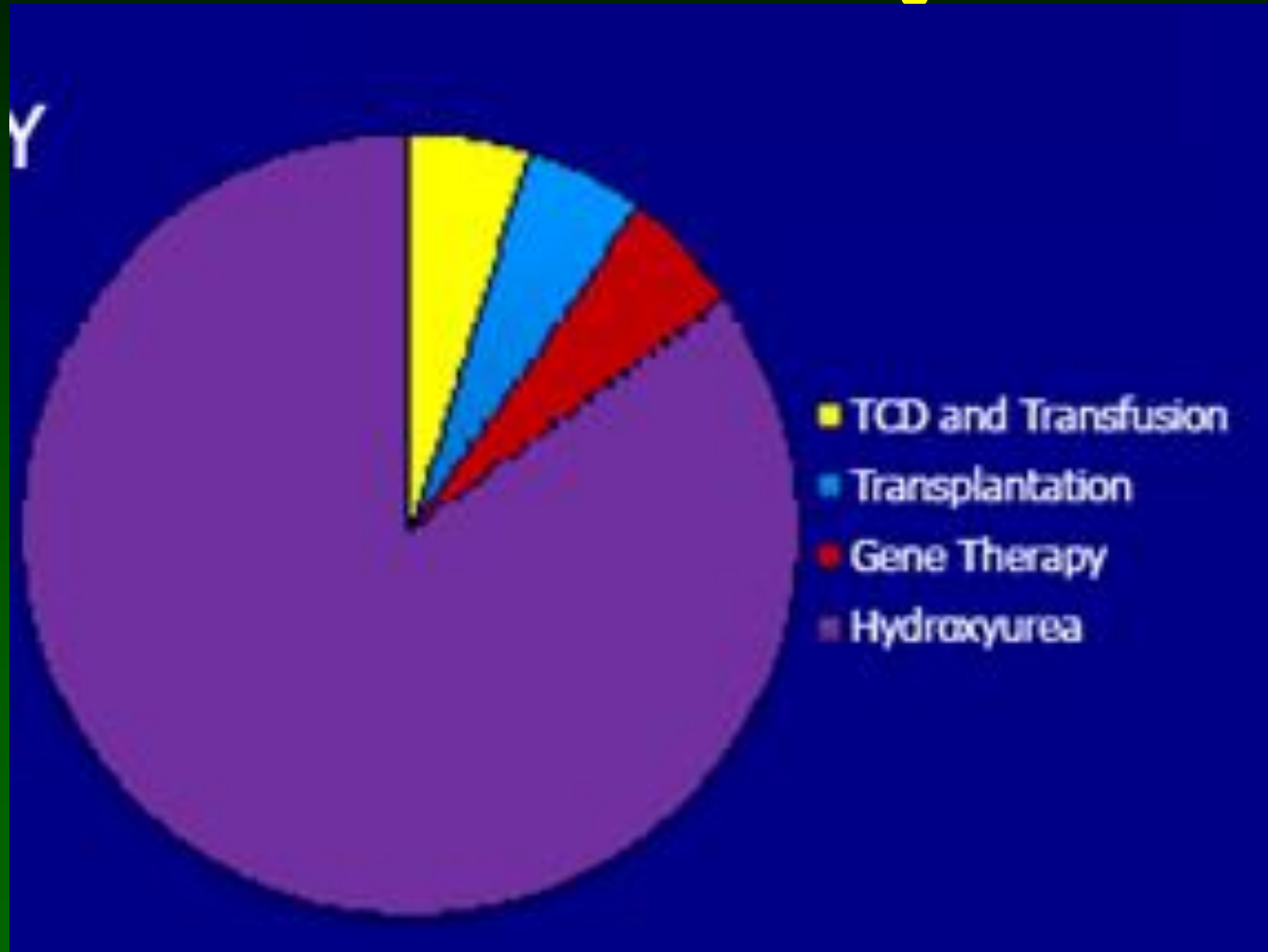
Yanni et al. J Pediatr. 2009 Apr;154(4):541-5.

En sık ölüm nedenleri

- Enfeksiyonlar % 48
- İnme % 10
- Tedavi ile ilişkili komplikasyonlar % 7
- Splenik sekestrasyon % 7
- Tromboemboli % 5
- Böbrek yetmezliği % 4
- Pulmoner hipertansiyon % 3

*A network model to predict the risk of death in sickle cell disease.
Sebastiani P, Nolan VG, Baldwin CT, et al. Blood. 2007;110:2727.*

OHAda tedavi seçenekleri



SCD de KIT : 8 yaş zenci kız

“This report describes the conversion of sickle-cell anemia to sickle-cell trait by marrow transplantation (done for treatment of leukemia) in a child with both sickle-cell anemia and acute myeloblastic leukemia. It raises the possibility of using marrow transplantation to treat selected patients with sickle-cell anemia.”

Johnson, et al. NEJM. 1984

OHA ve Transfüzyon

- ★ Kan transfüzyonu OHA'da temel tedavi yaklaşımlarından biri
- ★ Yaklaşık %90 erişkin olgu en az bir kere transfüzyon alıyor
- ★ Giderek daha yaygın olarak kullanılıyor
 - ◆ Endikasyonlar
 - ◆ Eritrositaferezi
 - ◆ Oral şelasyon tedavisi

Transfüzyon

- ★ Anemiyi düzeltir
 - ◆ Oksijen taşıma kapasitesini arttırır
- ★ HbS içeren eritrositlerin oranını azaltır
 - ◆ Kan reolojisi ve mikrovasküler perfüzyon düzelir
- ★ Eritropoezi (HbS sentezini) baskılar
- ★ Hemolizi azaltır
 - ◆ Organ hasarlarını engeller

Zamanına göre transfüzyon

- ♦ **Epizodik (intermitan) (on demand)**
 - ♦ Akut transfüzyonlar
 - ♦ Düzeltmek/stabilize etmek
- ♦ **Kronik transfüzyon**
 - ♦ Uzun süreli
 - ♦ Profilaktik
 - ♦ Oluşmasını/tekrarlamasını engellemek

OHAda transfüzyon tipleri

- ★ Basit transfüzyon

- ★ Exchange transfüzyon

 - ◆ Manuel exchange transfüzyon

 - ◆ Otomatize exchange transfüzyon

 - (Eritrositaferrez, terapötik eritrosit değişimi)

Eritrosit değişimi

- ★ Anormal/hastalıklı eritrositlerin bir **aferez cihazı** yardımıyla **uzaklaştırılması**, yerine sağlıklı donörlerden alınmış **eritrositlerin verilmesi**
- ★ Bir **sitaferes** (kan hücrelerini almak) işlemi
- ★ En yaygın olarak **OHA**'da kullanılıyor

OHA ve Exchange

286

Effect of Normal Cells on Viscosity of Sickle-Cell Blood

In Vitro Studies and Report of Six Years' Experience with a Prophylactic Program of "Partial Exchange Transfusion"

ROLF ANDERSON, M.D.
MONA CASSELL, B.S.
GRACE L. MULLINAX, B.S.
AND
HUGH CHAPLIN, JR., M.D.
ST. LOUIS

The protean clinical manifestations of painful sickle-cell crises have been described by many authors,^{1,2} but the factors responsible for precipitating the crises remain poorly understood. Many approaches to treatment of crises have been proposed; none has proved regularly effective. Blood transfusions are frequently disappointing in their failure to alter significantly the course of a well-established crisis, even when sufficient blood is given to raise the patient's hemoglobin concentration close to normal. However, despite the lack of immediate clinical

improvement following transfusion, the patient frequently remains free from painful crises for 2 to 3 months thereafter. This freedom from crises persists long after the transient relief of anemia by transfusion; presumably the presence of normal donor cells in the patient's circulation exerts a protective effect against precipitation of crises. The nature of this protection is not known, but a likely mechanism is the effect of the transfused cells upon the patient's blood viscosity.

Effects on blood viscosity of decreasing pH and oxygen tension have been carefully examined for blood from patients with homozygous sickle-cell disease (SS), with sickle-cell trait (SA), with sickle-cell hemoglobin C disease (SC), and with sickle-cell thalassemia disease.³⁻¹¹ Little has been written about blood viscosity in patients with homozygous sickle-cell disease following transfusion, i.e., in blood which represents a mixture of sickle cells with normal donor erythrocytes.

Received for publication June 29, 1962; accepted Sept. 21, 1962.

Fourth-year medical student during work on the investigation (Dr. Anderson), Research Assistants (Miss Cassell and Mrs. Mullinax), and Associate Professor of Medicine and Preventive Medicine (Dr. Chaplin).

From the Barnes Hospital Groups and the Departments of Medicine and Preventive Medicine, Washington University School of Medicine.

This investigation was supported by Research Grant C-2918 (Cl-5) from the National Cancer Institute.

68

Sickle Cell Disease and Exchange Transfusion

J A H Bootes MB FRCS

(Queen Charlotte's Maternity Hospital, London)

A 25-year-old Nigerian primigravida, a known case of sickle cell disease, was given an exchange transfusion at 34-weeks pregnancy for a hæmoglobin of 6 g and a PCV of 20%, when 8 pints of fresh blood were packed into 5 and given via the right ante-cubital vein in forty minutes. Outflow was via the left ante-cubital vein, a peristaltic pump being used to attempt equal inflow-outflow. Delivery at 37 weeks was by Keillands rotation and extraction under epidural analgesia.

The problems of sickle cell disease in pregnancy were discussed, and the technique and place of exchange transfusion in the adult.

İlk otomatize eritrosit değişimi 1977'de

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Transfusion. 1977 May-Jun;17(3):269-71.

Exchange transfusion in sickle cell disease using a continuous-flow blood cell separator.

Kernoff LM, Botha MC, Jacobs P.

Abstract

An exchange transfusion was performed preoperatively on a patient with sickle cell disease using a continuous-flow blood cell separator. An exchange of 2,825 ml red blood cells achieved a hemoglobin A level of 90.8 per cent. The continuous-flow blood cell separator appears to offer a safe and effective method of exchange transfusion in sickling disorders.

ASH 2006

Session Chair: Marilyn J. Telen, MD

Speakers: Paul S. Swerdlow, MD; Orah S. Platt, MD; and George F. Atweh, MD



Red Cell Exchange in Sickle Cell Disease

Paul S. Swerdlow

Red cell exchange transfusions remain an effective but possibly underutilized therapy in the acute and chronic treatment of sickle cell disease. In sickle cell disease, increased blood viscosity can cause complications when the hemoglobin exceeds 10 g/dL even if this is due to simple transfusion. Red cell exchange can provide needed oxygen carrying capacity while

reducing the overall viscosity of blood. Acute red cell exchange is useful in acute infarctive stroke, in acute chest and the multi-organ failure syndromes, the right upper quadrant syndrome, and possibly priapism. Neither simple or exchange transfusions are likely to hasten resolution of an acute pain episode.

ASH 2014

| SPIN DOCTORS: APHERESIS FOR HEMATOLOGISTS |



Red cell exchange: special focus on sickle cell disease

Haewon G. Kim¹

¹Children's Hospital of Philadelphia, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

The primary function of red blood cells (RBCs) is to deliver oxygen from the lungs to tissues. Tissue hypoxia occurs when the oxygen-carrying capacity of RBCs is compromised due primarily to 3 causes: (1) a reduction in circulating RBC mass, (2) an increase in circulating RBC mass, or (3) abnormal hemoglobin (Hb) that either does not sufficiently release oxygen to tissues (high-oxygen-affinity hemoglobin) or occludes the microvasculature due to deformed RBCs (sickled RBCs). To improve oxygenation in patients with reduced or increased RBC mass, RBC administration (simple transfusion) or RBC removal (RBC depletion) is performed, respectively. However, for patients with abnormal Hb, RBCs containing abnormal Hb are removed and replaced by healthy volunteer donor RBCs by red cell exchange (RCE). RCE can be performed by manual exchange or by automated exchange using a blood cell separator (erythrocytapheresis). In this review, indications for RCE in sickle cell disease using the evidence-based American Society for Apheresis categories¹ are presented and the rationale for RCE in each disorder are discussed. Simple transfusion versus RCE and manual RCE versus automated RCE are compared. Finally, this review briefly presents some of the challenges of performing erythrocytapheresis in small children and discusses various choices for central venous access during RCE.²

Learning Objectives

- To describe indications for RCE
- To define goals for RCE for stroke prophylaxis in sickle cell disease

RCE have rarely been documented in prospective randomized controlled trials. In this review, RCE refers to both manual and automated RCE; however, when only automated RCE is used in a study, this will be referred to as automated RCE.

ASFA Guidelines For Therapeutic Apheresis

Category I

standard medical care and accepted as primary therapy or first-line therapy in conjunction with other initial therapies.

Category II

Generally accepted, but usually as adjunctive therapy to other treatment modalities.

Category III

Published data is insufficient to establish efficacy or risk/benefit. Heroic effort treatment

Category IV

Published control trials lack evidence of efficacy.

Schwartz J j clin apheresis 2013

Guidelines for Therapeutic Cytophoresis

Category I

Leukemia with
hyperleukocytosis
syndrome

Sickle cell syndrome

Thrombocytosis, symptomatic

Category II

**Cutaneous T-cell lymphoma
(cytoreduction or
photopheresis)**

Hairy cell leukemia

Hyperparasitemia (e.g.,
malaria)

Peripheral blood stem cell
collections for

Hematopoietic reconstitution
(Rheumatoid arthritis)

Endikasyonlar

Journal of Clinical Apheresis 25:83–177 (2010)

Sickle cell disease	Acute stroke	RBC exchange	I	1C
	Acute chest syndrome	RBC exchange	II	1C
	Prophylaxis for primary or secondary stroke; prevention of transfusional iron overload	RBC exchange	II	1C
	Multi-organ failure	RBC exchange	III	2C

Zbigniew M. Szczepiorkowski,^{1*†} Jeffrey L. Winters,^{2*} Nicholas Bandarenko,^{3*} Haewon C. Kim,^{4*} Michael L. Linenberger,^{5*} Marisa B. Marques,^{6*} Ravindra Sarode,^{7*} Joseph Schwartz,^{8*} Robert Weinstein,^{9*} and Beth H. Shaz^{10*}

Journal of Clinical Apheresis 28:145–284 (2013)

Sickle cell disease, acute	RBC exchange	Acute stroke	I	1C
	RBC exchange	Acute chest syndrome, severe	II	1C
	RBC exchange	Priapism	III	2C
	RBC exchange	Multi-organ failure	III	2C
	RBC exchange	Splenic sequestration; hepatic sequestration; intrahepatic cholestasis	III	2C
Sickle cell disease, non-acute	RBC exchange	Stroke prophylaxis/ iron overload prevention	II	1C
	RBC exchange	Vaso-occlusive pain crisis	III	2C
	RBC exchange	Pre-Op management	III	2A

(TED)

Avantajları

- ★ HbS içeren eritrositler hızlı/etkin uzaklaştırılır
- ★ Viskozite korunur
- ★ Demir birikimine neden olmaz
- ★ Volüm yüklenmesine neden olmaz

Dezavantajları

- ★ ↑ ES ihtiyacı
- ★ ↑ Komplikasyon riski
- ★ ↑ Alloimmünizasyon riski
- ★ Uygun damar yolu gereksinimi
- ★ Aferez cihazı ve yetişmiş eleman
- ★ ↑ Maliyet

Exchange

1. Vazookluzif kriz nedeni olan orak hücreleri azaltır
2. Hemolitik komplikasyonları azaltır
3. Oksijen taşıma kapasitesini arttırır
4. Kan vizkozitesini azaltır
 - ☑ Dolaşım yüklenmesine neden olmaz
 - ☑ Demir dengesini korur hatta azaltır

Kan transfüzyonunda bunları yapıyor !!!!!

- ★ Ama HB arttırarak kan vizkozitesini de arttırıyor
- ★ OHA de kan vizkozitesi çok önemli
- ★ Vizkozite artınca kan akımı azalır

Vizkozite !!!

- ★ OHA hastası ile aynı hb düzeyi olan hastaların kan vizkoziteleri incelenmiş
- ★ OHA ların kan vizkozitesi X10 kat fazla
- ★ Özellikle düşük akım hızı olan yerde
- ★ Vizkozite fazla.....oraklaşma fazla
- ★ Özellikle ince damar ve basınç az olan yerlerde

OHA ... hipervolemi

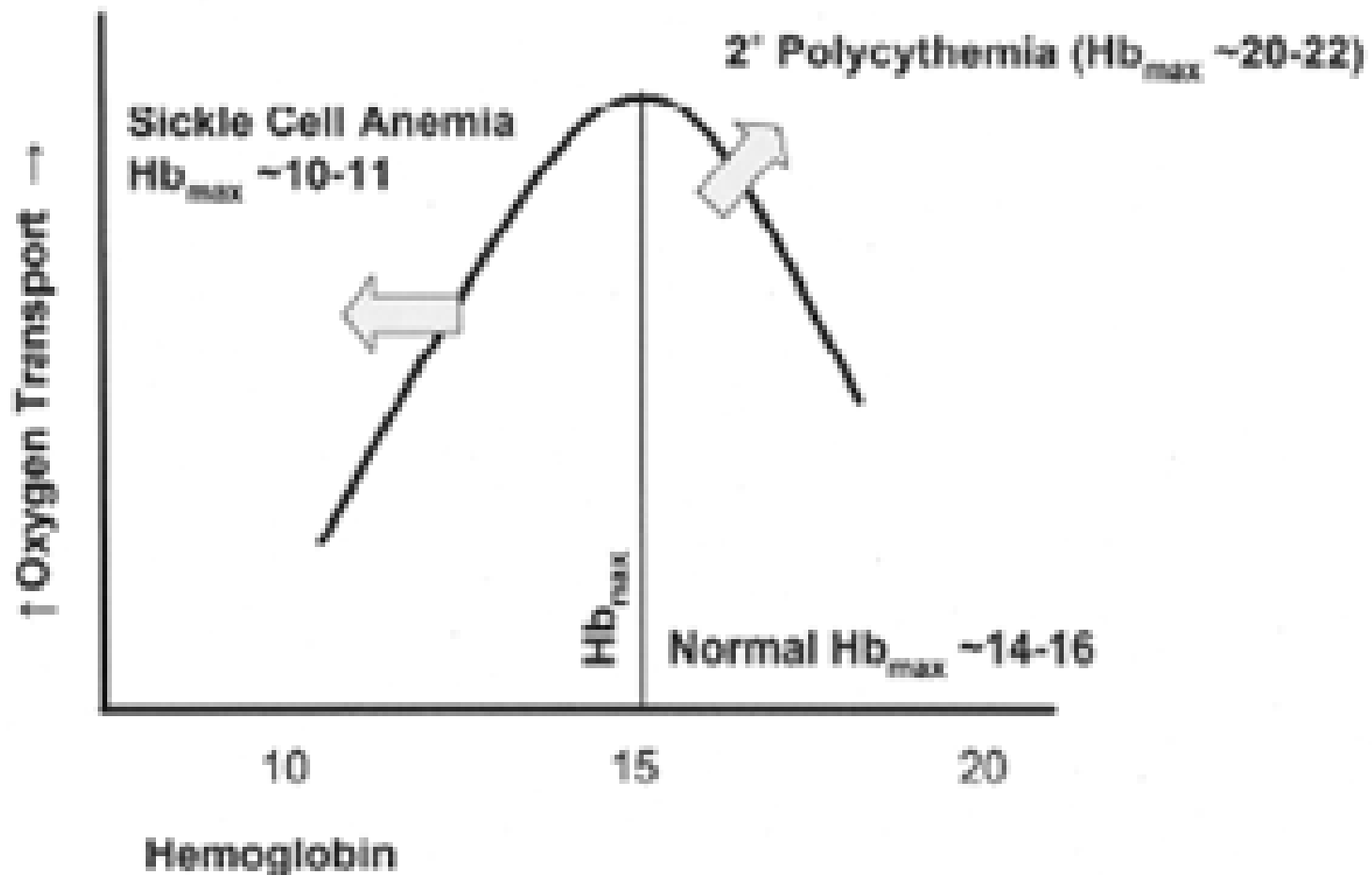
- ★ Doku Oksijen düzeyi düşük
- ★ Kardiak out put artar
- ★ Plazma volümünü arttırmaya çalışılır
- ★ Anemi daha da belirginleşir
- ★ Doku O₂ daha azalır
- ★ Oraklaşma daha artar

Hb S miktarı önemli

- ★ Oksijensiz ortamda HBs hemen oraklaşmaz
- ★ "Delay Time"
- ★ Delay time Hb S miktarı ile ilgili
- ★ HB S yüksek delay time kısa
- ★ Hb S <%30 hedefinin nedeni

OHA hb ve O2 saturasyonu....

Hb çok yükseltme 10 g/dL iyi



Eritrositaferezi

- ★• OHA
- ★• Talasemi
- ★• paraziter enfeksiyonlar
 - ★• Falciparum etkenli sıtma
 - ★- Babesiosis
- ★Karbon Monoksit zehirlenmesi
- ★- Methemoglobinemi
- ★- dolaşan eritrosit patolojisi ile ilişkili hastalıklar

OHA da eritrositaferezi

- ★ Hesaplanan tüm rakamlar yaklaşık rakamlardır
- ★ Hastanın fizyolojisi
- ★ Ölçüm hataları
- ★ Teknik kaynaklı olabilir
- ★ Genelde **güvenilir rakamlara işlemden 24 saat** sonra ulaşılır bu nedenle hemen işlem sonrası rakamlar yanıltıcıdır
- ★ **. 30 lar kuralı**
- ★ HbS <30
- ★ HCT <30 olmalı

Exchange

- ★ Vazookluzif kriz riskini azaltır ama oluşmuşu etkisi yok
- ★ Hemoliz hızını azaltır
- ★ Biluribin yapımını azaltır
- ★ Böbrek etkilenmesini azaltır
- ★ NO yapımını azaltır

İnmeli OHA hastasında

- ★ İnmeden hemen sonra ilk tedavi exchange olmalı
- ★ İnmekontrastsız CT
....enfark.....önce exchange
- ★ Sonra MR ve MRA (mutlaka exchange sonrası)

Göğüs tutulumlu OHA

- ★ Ağır seyirli
 - ★ Oksijen tedavisi yetersiz kalıyorsa
 - ★ Basit transfüzyonla düzelmiyorsa
 - ★ Ventilatör gerekli ise
 - ★ Multilobuler tutulum varsa
- ★ EXCHANGE DÜŞÜN

MOFS varsa

- ★ Genelde ağrılı epizodla başlar ...ağrı iyi takip et
- ★ SSS- karaciğer-böbrek tutulumu
- ★ Tedavide erken Exchange

Priapism

- ★ Genelde olgu bildirileri
- ★ Nörolojik tutulumla birlikte genelde
- ★ Çalışma pek yok
- ★ tX mi exchange mi randomize çalışma yok

İdame HB S düşük sağlandığında

- ★ İnme
- ★ Priapism
- ★ Ayak ülserleri
- ★ Kronik hipoksi
- ★ Tekrarlayan ACS
- ★ Tekrarlayan MOFS
- ★ Yaşam kalitesini bozan Kronik ağrı olma olasılığı **çok azalır**

Exchange : Kaç vumle yapılmalı

- ★ 1 vum : %37si kalır $1/3$
- ★ 1.5 vum : %22 si kalır $1/4$
- ★ 2 vum : %14 kalır $1/6$
- ★ 1xTEH değişim = hastaya ait eritrositlerin \cong %65'i uzaklaştırılır (FCR=%35),
- ★ 2xTEH değişim = orijinal eritrositlerin \sim %90'ı uzaklaştırılır (FCR = %10) (Fraction of cells remaining)

manual & otomatik

★ Transfus Apher Sci. 2013
Apr;48(2):219-22.

- ★ 5 hasta 60 eritrositaferéz
- ★ 5 hasta manuel 124 exchange
- ★ Otomatik iyi
- ★ Özellikle Hb S'in <%30 istendiğinde otomatik tercih edilmeli

Exchange aletler arası fark

- ★ Spectra optia X spectra COBE
- ★ Fark yok
- ★ Es tüketiminde ama
- ★ Optia ile bozuk erit oranı daha az

- ★ J Clin Apher. 2015 Aug 14. doi: 10.1002/jca.21422. [Epub ahead of print]
- ★ Comparative evaluation of the depletion-red cell exchange program with the Spectra Optia and the isovolemic hemodilution-red cell exchange method with the COBE Spectra in sickle cell disease patients.
- ★ Poullin P1, Sanderson F1, Bernit E2, Brun M1, Berdah Y3, Badens C4.

TED-Komplikasyonlar

- ★ Transfüzyon ilişkili yan etkiler
 - ◆ Akut transfüzyon reaksiyonları
 - ◆ Gecikmiş transfüzyon reaksiyonları
- ★ Damar yolu ilişkili problemler
- ★ Aferez işlemiyle ilişkili yan etkiler

Aferezin istenmeyen yan etkileri

- ★ sitrat toksisitesi
- ★ damar yolu problemleri(hematom, trombüs, sepsis, flebit)
- ★ Vasovagal
- ★ Hipervolemi
- ★ Allerjik reaksiyonlar
- ★ Hemoliz
- ★ Hava embolisi

Aferezin istenmeyen yan etkileri

- ★ Pıhtılaşama fak değişiklikleri
- ★ Kan protein ve Ig değişiklikleri
- ★ Solunum ve kardiyak problemler
- ★ Kanla geçen enfeksiyonlar
- ★ Lenfosit kaybı

Verilecek kan

- ★ Mümkün olduğunca taze (en fazla 5-9 günlük)
- ★ Lökositi azaltılmış
- ★ Işınlanmış (HKH nakli planlanıyor ise)
- ★ Oraklaşma (sickle cell trait) negatif
- ★ *Tercihen fenotipik olarak uygun (Rh antijenleri C, E ve Kell)*

Alloimmunizasyon

- ★ Transfusion. 2015 Feb;55(2):357-63. doi: 10.1111/trf.12875. Epub 2014 Sep 23
- ★ Transfusion. 2012 Dec;52(12):2671-6.
- ★ **Lower alloimmunization rates in pediatric sickle cell patients on chronic erythrocytapheresis compared to chronic simple transfusions.**
- ★ . Immunohematologic tolerance of chronic transfusion exchanges with erythrocytapheresis in sickle cell disease.

	Exchange (49)	Transfüzyon (139)	p
alloimmunizasyon	%33	%22	0.17
Alloim/ES	1.6	11.6	0.0001
Hasta başına alınan ES	206	19	0.0001
Hemolitik transfüzyon reaksiyonu	-	4	

Lower alloimmunization rates in pediatric sickle cell patients on chronic erythrocytapheresis compared to chronic simple transfusions

Shannon Kelly Wahl, Alicia Garcia, Ward Hagar, Ginny Gildengorin, Keith Quirolo, and Elliott Vichinsky

TRANSFUSION 2012;52:2671-2676.

WAHL ET AL.

TABLE 5. Antibody formation rates per 100 units transfused

Transfusion regimen	Patients with any new antibody, n (%)	Total units during program	Total number of new antibodies formed (new allo)	Total antibodies (auto plus allo) per 100 transfused units	Allo antibodies per 100 transfused units
ECP, n = 22	3 (13)	7447	3 (1 allo)	0.040	0.013
Simple transfusion, n = 23	4 (18)	3502	6 (5 allo)	0.171	0.143
p value				0.04	0.03

★ Aferez sırasında lökosit, trombosit ve enflamatuar sitokinlerin uzaklaştırılması immün fonksiyonları etkiliyor olabilir...

Eritrosit Alloimmünizasyonu

- ★ normal populasyonunda %0,5-1,5
- ★ OHA'da;
 - ◆ Sadece ABO/Rh uygun kan alanlarda %18-76
 - ◆ (C, E, Kell) %0,5-14,5
 - ◆ Minör RBC antijenleri uygun %7

Damar yolu

- ★ Dönüş yolu için
- ★ 17-18 G >80ml/dak
- ★ 19 G < 70 ml/dak
- ★ Diğer kol kullanılmalı
- ★ Eğer aynı kol kullanılacaksa mutlaka kan çekilen girişin üzerinde dönüş bölgesi olmalı bu sayede **resirkülasyon** engellenebilir
- ★ **Enfeksiyon ve tromboza** dikkat

Damar yolu

- ★ Erişkinde kan akım hızı ~60-150 ml/dak
- ★ küçük çocuklarda 10ml/dak kadar azalabilmeli
 - ◆ Dirsek içi bölge en uygun
 - ★ Medial, sephalik, basilik

Hickmann kullanılacaksa

- ★ Kırmızı uç : kan çekmek için
- ★ Mavi uç : kan dönüşü için kullanılmalı

Dikkat : akımda problem var!!!

- ★ Aferez seti tam doldurulmamışsa
- ★ - eritrosit filtresi tıkanmışsa
- ★ -replasman sıvısı hava almıyorsa
- ★ Dış ortam düşük ısisına bağı replasman sıvısının vizkositesi artmışsa
- ★ Klampler iyi kapatılmamışsa

Sitrat toksisitesi

- ★ Tüm aferez işlemlerinde beklenen risk
- ★ Neden sitratlı kanın tekrar tekrar verilmesidir
- ★ Sitrat infuzyon sonrası İonize kalsiyum azalması
- ★ hipokalsemik reaksiyonlara neden olabilir

Antikoagulan

- ★ Kalsiyumun %47 serbest kalsiyum
- ★ Buserbest kalsiyum sitratı bağlar
- ★ Plazmada sitratın 0.5-0.6 nmol/L artışı kalsiyumda 0.1 mmol/L azalmaya neden
- ★ Genellikle ionize kalsiyumda **%23-33** azalma olur
- ★ En hızlı azalma ilk **15 dakikada**
- ★ Genelde kalsiyum seviyesi exchangeden 4 saat sonra normale döner

Antikoagulan

- ★ Sitratın 65-95mg/kg/saat hızda verilmesi güvenli
- ★ >100mg/kg/saat dozda artan yan etki
- ★ Hipomagnesemi bulguları ağırlaştırır
- ★ Uzun süren işlem hipokalsemi iskini artırır

Hipokalsemi

- ★ Sitrat verilme hızı
- ★ Sitratın metabolize edilme hızı
- ★ İşlemin süresi
- ★ Önceden var olan hipokalsemiye
- ★ Hipotermi varlığına(düşük metabolik hız))
- ★ • Metabolik alkaloz varlığına
- ★ Düşük magnesium düzeyine

Hipokalsemi bulguları varsa

- ★ Hastaya uyuşma vb sorun
- ★ Vital bulguları kontrol edin
- ★ Giren kan hızını azaltın
- ★ O ana dek infüze edilen sitrat miktarını hesaplayın

(sitrat infüzyon hızı= ml/dak/L).

- ★ İşlem öncesi ionize kalsium, magnesium, potassium düzeylerini kontrol edin
- ★ Gerekirse **parenteral kalsiyum replase** edin
- ★ -düşükse potassium ve magnesium replase edin
- ★ - işlemin devamına yada durdurmaya karar verin

Immunoglobulinde değişiklikleri

1 volum exchange sonucunda

- ★ IgG normal değerinin %34 üne
- ★ IgA %39una
- ★ IgM %31%
- ★ Düşer
- ★ 3- 5 hafta sonra normale döner
- ★ Kompleman%37 ye düşer ve 48 saatte normale döner
- ★

Pıhtılaşma faktörleri

Fibrinogen:

- ★ % 25ine düşer (1 PV),2-3 günde normale döner

Protrombin:

- ★ %30 adüşer

Faktor VII & faktor VIII:

- ★ %45-50

Faktor IX:

- ★ %60

Faktor V, X, XI:

- ★ %38

Antithrombin:

- ★ Aktivite %40, Ag % 70



Pıhtılaşma faktörleri

- ★ 24 saatte % 85-100 düzeye çıkar
- ★ Exchangeden sonra PTT, PT, TT uzar
- ★ PTT, TT 4 saat sonra
- ★ PT 24 saat sonra normale döner
- ★ Ama kanama riski pek saptanmaz

Elektrolitler

- ★ Na ve glukoz değişmez
- ★ K azalır (minimal)(0.25meq/L)
- ★ Bikarbonat azalır 6meq/L
- ★ Cl artar 4meq/L

Diğer

- ★ LDL ALP, ALT %37 azalır
- ★ AST, LDH, amilaz, CK, ferritin, transferrin %47 azalır

★ ALT, AST, amilaz	%100	48 sa
★ LDH, ALP, CK	% 60	48sa
★ LDL	%44	48sa

CBC

RBC:

- ★ %12 Hb de hemen azalma
- ★ 24 saatte %100 e çıkma(plazma volum artışına bağlı)

WBC:

- ★ Nötrofiller artar ($2 \times 10^9/L$), diğerleri değişmez

CBC

Trombositler

- ★ % 15-50 azalır
- ★ 5-10 tekrarlayan exchange sonrası trombositler % 20-25 azalabilir
- ★ Normale dönme 24 saatte %70-85%
- ★ 72-96 saatte %100
- ★ Başlangıç trombositleri <150 ise düşüş daha az olur

Komplikasyonlar

AABB American Association of Blood Banks (1999):

★ 3429 t ropatik aferez

- ◆ %1.6 transf zyon reaksiyonları
- ◆ % 1.2 sitrata baęlı kusma / bulantı /pareztezi
- ◆ %1.0 hipotansiyon
- ◆ %0.5 vasovagal olaylar
- ◆ % 0.5 terleme-solukluk
- ◆ %0.4 tařikardi
- ◆ %0.3 solunum sıkıntısı
- ◆ %0.2 tetani/havale
- ◆ %0.2 titreme- ř me
- ◆ Ciddi komp ~ %0.3

Komplikasyonlar

Ölüm:

- ★ Fransa : 1-2/10,000
- ★ İsveç: 0/14,000
- ★ Amerika : 3/10,000
 - ◆ % 60 kardiyak-solunum
 - ◆ Genelde TDP exchange de
 - ◆ Anafilaksi
 - ◆ sepsis
 - ◆ PE
 - ◆ Damar yolu ilişkili

16 Çocuk OHA fransız deneyimi 2004-2012

- ★ <20 yaş
 - ★ 10 serebrovasküler hast
 - ★ 5 tekrarlayan ağrı krizi
 - ★ 1 psikokognitif gerilik
 - ★ 4 hastada tedavi sonlandırılmış
 - ★ 2 sinde alloimmunizasyon 2 sinde damar yolu problemi nedeni ile
 - ★ her ne nedenle exc yapılsasonuç iyi
 - ★ 199 işlem 10-30 ay boyunca ,Her seans < 1.5 saat süreli
 - ★ 2-10 ayda ferritin normal sınırlara gerilemiş
- Tüm hastaların yaşam kalitesinde artma
- ★ En önemli problem damar yolu

11-25 kg çocuklarda eritrositaferezi

- ★ 3 yıllık 11-25 kg
- ★ COBE® Spectra aferez sistemi
- ★ Asit sitrat deksroz
- ★ 25 işlem 19 hastada
- ★ 17 hasta OHA
- ★ 2 lösemi ve hiperlökositoz
- ★ İşlem sırasında hiçbir hastada problem yok
- ★ 1 hastada 1 hafta sonra hemolitik reaksiyon
- ★ Tüm OHA hastalarda işlem sonrası hedeflenen hb %21-30 ve Hb A >%68 değerine ulaşılmış
- ★ Çocuklar için bir protokol önermişler
- ★ Vox Sang. 2014 Nov;107(4):375-80.

Exchange ve gebe

★ 28. hafta 10 gebe exc (manuel / alet)

	Exchange (10 gebe)	Transfüzyon (14 gebe)
Komplikasyon	%10	%37
Prematürite risk	%30	%69
Doğum haftası	38.7	34.4

2015 Sep 3. doi: 10.1111/trf.13280. [Epub ahead of print]

The effects of exchange transfusion for prevention of complications during pregnancy of sickle hemoglobin C disease patients.

Benites BD¹, Benevides TC¹, Valente IS², Marques JF Jr¹, Gilli SC¹, Saad ST¹.

ORIGINAL ARTICLE

Prophylactic red blood cell exchange may be beneficial in the management of sickle cell disease in pregnancy

Suheyli Asma,^{1,2} Ilknur Kozanoglu,^{3,4} Ebru Tarım,⁵ Cagla Sarıturk,⁶ Cigdem Gereklioglu,^{1,2} Aydan Akdeniz,⁷ Mutlu Kasar,¹ Nurhilal H. Turgut,¹ Mahmut Yeral,¹ Fatih Kandemir,² Can Boga,¹ and Hakan Ozdogu¹

BACKGROUND: Sickle cell disease (SCD) is associated with chronic hemolysis and painful episodes. Pregnancy accelerates sickle cell complications, including prepartum and postpartum vasoocclusive crisis, pulmonary complications, and preeclampsia or eclampsia. Fetal complications include preterm birth and its associated risks, intrauterine growth restriction, and a high rate of perinatal mortality. The purpose of this study was to evaluate pregnancy outcomes in patients with SCD who underwent planned preventive red blood cell exchange (RBCX).

Sickle cell diseases (SCDs) are a group of inherited single-gene autosomal recessive disorders caused by the sickle cell gene, which affects hemoglobin (Hb) structure.¹ SCD includes sickle cell anemia with the SS genotype, some heterozygous conditions of the S gene, and other clinically abnormal Hbs such as beta thalassemia, HbC, HbD, and HbE among others. The primary manifestations of SCD are chronic hemolytic anemia and episodes of severe pain crises due to vasoocclusion.¹⁻³ Repeated vasoocclusive crises can affect multiple organ systems, and individuals with SCD have increased risks of stroke, renal dysfunction, pulmo-

Kozanoglu I ve ark. 2007



Available online at www.sciencedirect.com



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TRANSFUSION
AND APHERESIS
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Automated red cell exchange procedures in patients with sickle cell disease

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Abstract

In automated red cell exchange, about 60% of the patient's red blood cells are exchanged via apheresis for those of the donor. We report the outcome of 83 patients with sickle cell anemia (48 women and 35 men; age range, 17–49 years) who underwent a total of 196 apheresis procedures between December 2003 and October 2006 at our institution. We found that automated red cell exchange involving a reduced citrate infusion rate may provide benefit in the prevention or treatment of vaso-occlusive complications in patients with sickle cell disease and may be associated with protean effects on biochemical dynamics.

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Flow cytometric evaluation of circulating endothelial cells: A new protocol for identifying endothelial cells at several stages of differentiation

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Several factors may influence the analysis of endothelial cells (ECs) by flow cytometry: separation of mononuclear cell, washing and centrifugation steps, panel of monoclonal antibodies, and the lack of standardization of gating technique. Therefore, the reliable quantification of ECs remains a technical challenge. The purpose of this study is to define a new flow cytometric protocol to characterize and quantitate ECs. In previous investigations, increased numbers of circulating ECs have been found in sickle cell disease. The patients with sickle cell disease might provide useful material for the study. We performed flow cytometry on whole blood from 20 normal controls and 31 patients with sickle cell disease (20 patients with steady-state disease and 11 patients with vaso-occlusive crises) using a lyse/no-wash procedure, specific and non-specific antibody combinations (CD146, CD144, CD34, and CD117), and broad gating. This protocol pro-

TABLE I. Quantification of Circulating Endothelial Cells

Cell types	Vaso-occlusive crises mean \pm SD (cells/mL) (n = 11)	Steady state mean \pm SD (cells/mL) (n = 20)	Controls mean \pm SD (cells/mL) (n = 20)
ECs	18213.5 \pm 8451.2 ^a	6709.6 \pm 177.3 ^b	2396.5 \pm 658.3 ^c
Mature ECs	4699.2 \pm 5515.2	1257.3 \pm 917.4 ^b	596.5 \pm 563.2 ^c
Late progenitor ECs	9875.64 \pm 6592.36 ^{aaa}	3986.05 \pm 1960.78 ^{bbb}	1066.70 \pm 533.12 ^{ccc}
Early progenitor ECs	3638.18 \pm 1546.86 ^{aaa}	1465.80 \pm 635.79 ^{bbb}	733.35 \pm 463.97 ^{ccc}

ECs, endothelial cells.

^aP < 0.05; ^{aaa}P < 0.001 between Vaso-occlusive crises group and steady state group.

^bP < 0.05; ^{bbb}P < 0.001 between Steady state group and Controls.

^cP < 0.05; ^{ccc}P < 0.001 between Vaso-occlusive crises group and Controls.

Boga C ve ark. 2010

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Alterations of circulating endothelial cells after apheresis in patients with sickle cell disease: A potential clue for restoration of pathophysiology

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ARTICLE INFO

Keywords:

Sickle cell disease
Circulating endothelial cells
Apheresis
Nitric oxide

ABSTRACT

Objectives: The potential influence of automated red cell exchange (ARCE) on endothelial activation is not well established.

This study was intended to assess whether ARCE influences circulating endothelial cells (CECs) in patients with sickle cell disease.

Assessment of corrected QT interval in sickle cell disease patients who undergo erythroapheresis

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Received 23 April 2007; accepted for publication 6 September 2007

SUMMARY. Extension of the QT interval is characterized by syncope and cardiac arrest and often occurs in association with medical therapies and procedures. Whether erythroapheresis (EPH) could influence the QT interval duration in patients with sickle cell disease (SCD) is not known.

We aimed to investigate the effects of EPH on the heart rate-corrected QT (QTc) interval.

The study included 25 patients with SCD who underwent 34 EPH procedures. Two independent observers measured QTc interval duration from electrocardiograms performed continuously for 3 min at three different points during the EPH procedures (prior to EPH, after completion of 50% EPH and 15 min after EPH). Multiple regression analysis was used to determine if the ionized plasma

calcium, the level of plasma magnesium, citrate infusion rate and painful crisis significantly contributed to the QTc interval.

There was a non-significant trend ($P = 0.184$) towards increased QTc in sickle cell patients during EPH compared with pre-EPH values. QTc prolongation (>440 ms) occurred in 72% of the procedures. Fifty percent QTc values returned to baseline after the procedure. The independent variables were not significantly associated with QTc interval.

Exchange procedures can induce QTc prolongation in patients with SCD.

Key words: calcium, erythroapheresis, QT interval, red cell exchange, sickle cell disease.

[Display Settings:](#) ☒ Abstract[Send to:](#) ☐[Mikrobiyol Bul.](#) 2012 Jul;46(3):493-8.**[A severe falciparum malaria case successfully treated by exchange transfusion as an adjunct therapy].**

[Article in Turkish]

[Demiroğlu YZ¹](#), [Kozanoğlu I](#), [Turunç T](#), [Kurşun E](#), [Arslan H](#).**⊕ Author information****Abstract**

Plasmodium falciparum malaria is a type of malaria with high fatality rate despite optimal antimalarial treatment. Exchange transfusion (ET) is successfully used as a means of supportive therapy in severe P. falciparum malaria cases with hyperparasitemia. Herein, we present a case with hyperparasitemia, who received erythrocyte ET therapy due to lack of clinical response to antimalarial treatment. A 24-year-old male patient was admitted to our emergency clinic with the complaints of fever that persisted for 10 days, headache, nausea-vomiting, and impaired consciousness. Medical history revealed that he had been working in Sudan, Africa and returned back 12 days ago. On physical examination; he had fever, hypotension, tachycardia, subicterus and impaired cooperation. Laboratory examination revealed pancytopenia, elevated C-reactive protein, hyperbilirubinemia, hyponatremia, elevated creatinine level and hematuria. On thick blood smear and thin blood smear examinations, multiple (> 5%) trophozoites and gametocytes indicating P.falciparum species were observed. The case was diagnosed as P.falciparum malaria and parenteral fluid support, dopamine infusion, meropenem (IV), doxycycline (PO) and quinine sulphate (PO) were initiated in the intensive care unit. On reevaluation of the patient on the third day of hospitalization, it was observed that arterial hypotension and fever were persistent, anemia and trombocytopenia deteriorated and on thick blood smear parasitemia was not decreased. It was decided to apply automated erythrocyte ET. After ET, patient's medical status was quickly improved and patient was discharged on the 7th day of hospitalization. In conclusion, it was noted that in addition to antimalarial

Türkiyede aferez : Eritrositaferesiz : en az uygulanan

- * **National survey of hemapheresis practice in Turkey (1998).**

- * Ilhan O¹, Uskent N, Arslan O, Arat M, Ozkalemkas F, Oztürk G, Kalayoglu SB, Ozet A, Tombuloglu M, Arpaci F, Ovali E, Anak S.

- * Author information

- * **Abstract**

- * The Turkish Apheresis Group has maintained a national registry for apheresis activities since 1997. The hemapheresis practice of Turkey in 1998 is summarized in brief detail in this article. A total of 30, 136 apheresis procedures were performed at 31 different apheresis centers. At 10 centers, 145 peripheral blood stem cell (PBSC) apheresis were performed on 82 patients in allogeneic setting and at 17 centers, 981 PBSC apheresis were performed on 271 patients in autologous setting. Frequently observed adverse effects during PBSC apheresis were mild tremor and chills, paresthesia and nausea in 15% of the patients and donors. Vascular access complications, particularly observed in autologous setting due to central venous catheters were encountered in 10% of the procedures. Eight hundred and sixty-nine therapeutic plasma exchange procedures were performed at 21 centers on 172 patients, most commonly for neurological disorders and thrombotic thrombocytopenic purpura (TTP)/hemolytic uremic syndrome (HUS). Therapeutic cytapheresis procedures like leukapheresis, plateletapheresis and erythrocyte apheresis were performed especially for cytoreduction in myeloproliferative disorders. A total of 204 cytapheresis procedures (66% leukapheresis, 33% plateletapheresis and 1% erythrocytapheresis) were performed on 134 patients in 15 centers. Donor plateletapheresis was the most used apheresis procedure, reaching a total of 28.016 in 1998. Many university hospitals and a few state hospitals are performing above-mentioned apheresis procedures with great success and acceptable side effects. According to these data we are planning prospective trials and will establish National Standards of Practice.

Türkiye ve eritrositaferez: CO zehirlenmesinde

- ★ Transfus Apher Sci. 2010
- ★ Treatment of acute carbon-monoxide poisoning with therapeutic erythrocytapheresis: clinical effects and results in 17 victims.
- ★ Celikdemir A¹, Gokel Y, Guvenc B, Tekinturan F.
- ★ Abstract
- ★ Seventeen cases of acute carbon-monoxide poisoning were treated with therapeutic red cell-exchange. Glasgow Coma Scale score was used to evaluate the level of consciousness. The mean carboxyhemoglobin level decreased from 0.286 ± 0.1805 ($28.6 \pm 18.05\%$) to 0.0613 ± 0.0418 ($6.13 \pm 4.18\%$) and Glasgow Coma Scale score increased from 10 ± 3 to 13.76 ± 1.89 . While 11 patients scored 15 at the end of the treatment, four scored 15 in an hour after the treatment. **None of the patients died.** Two victims (11.7%) experienced ischemic encephalopathy. **Therapeutic red cell-exchange therapy can be an effective treatment in reducing mortality and morbidity in carbon-monoxide poisoning.**

