

# Infections In Sickle Cell Disease patients A call for action

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# Outline of the presentation

- 1. Epidemiology of SCD; The size of the problem internationally and in Bahrain
- 2. literature search:
  - A. The common Bacterial Infections in SCD
  - B. Other infections
  - C. Hospital acquired infection
- 3. Bahrain study
- 4. Conclusion

# 1. The size of the problem



# Sickle-cell disease and other haemoglobin disorders January 2011 (WHO) Key facts

- Approximately 5% of the world's population carries trait genes for haemoglobin disorders, mainly, sickle-cell disease and thalassaemia.
- Haemoglobin disorders are genetic blood diseases due to inheritance of mutant haemoglobin genes from both, generally healthy, parents.
- Over 300 000 babies with severe haemoglobin disorders are born each year.
- The health burden of haemoglobin disorders can be effectively reduced through management and prevention programmes.

# In the United States

## CDC website

- The exact number of people living with SCD in the U.S. is unknown. It is estimated that:
- SCD affects 90,000 to 100,000 Americans.
- SCD occurs among about 1 out of every 500 Black or African-American births.
- SCD occurs among about 1 out of every 36,000 Hispanic-American births.
- SCT occurs among about 1 in 12 Blacks or African Americans.

# Economic Costs

- During 2005, medical expenditures for children with SCD averaged \$11,702 for children with Medicaid coverage and \$14,772 for children with employer-sponsored insurance. About 40% of both groups had at least one hospital stay.
- SCD is a major public health concern. From 1989 through

# Mortality Among Children with Sickle Cell Disease in USA

- Among the children with Hb SS disease, 1% died as a result of SCD-related causes during the first 3 years of life.
- In California and Illinois, by the end of 1995, the cumulative mortality rate was 1.5 per 100 Black or African-American children with SCD.

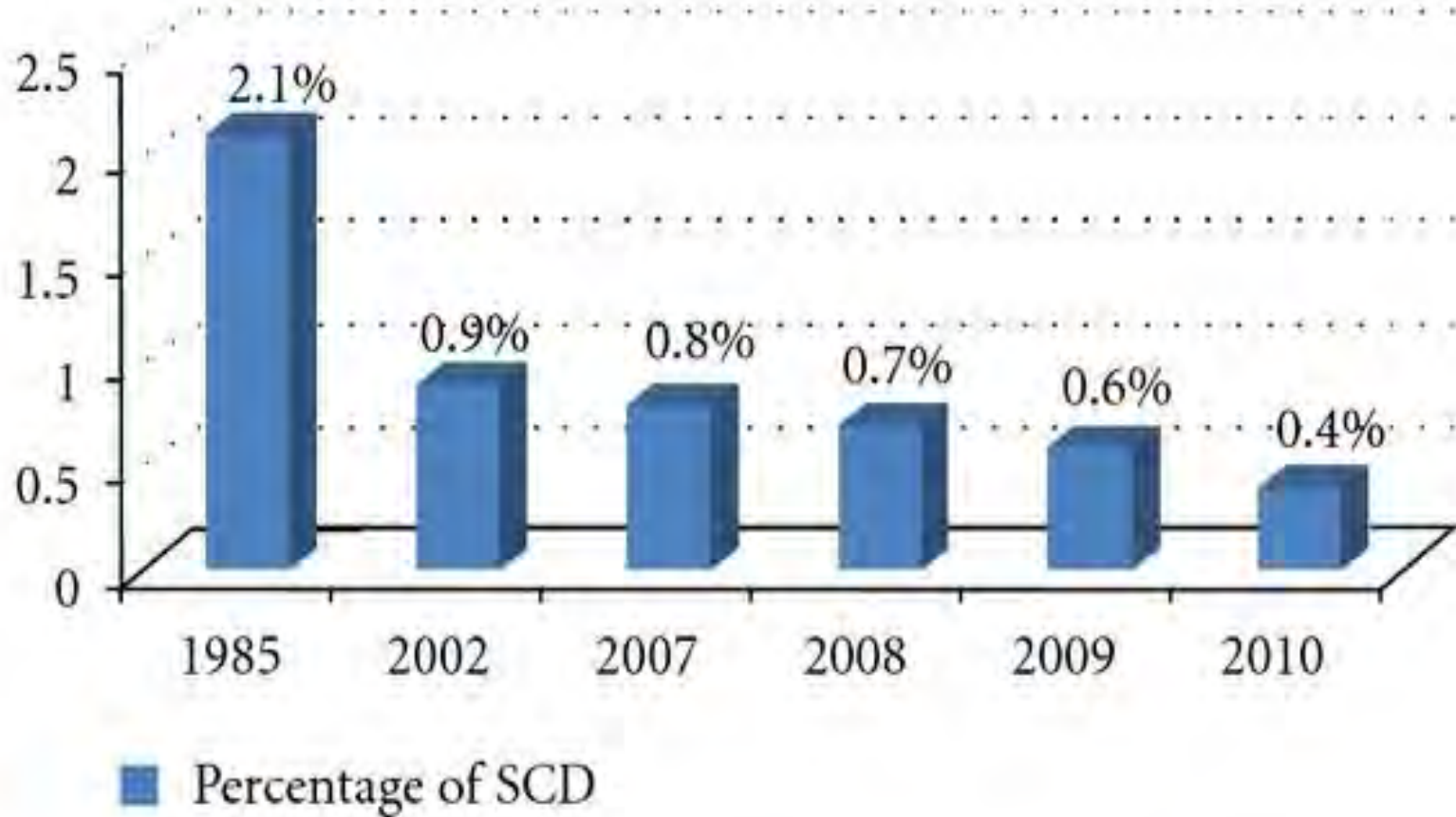
# Kingdom of Bahrain

- The prevalence of hereditary blood diseases in Bahrain is considered high.
- Previous neonatal screening in 1984-1985 showed that the birth prevalence of SCD was 2.1%, of sickle cell trait 11%,
- In 1984, the first genetics clinic was established and several several educational campaigns were started.



- In 1993, a premarital counseling service was organized and then expanded to include all health centers.
- In 2004, the Bahrain Government passed a law requiring all couples planning to get married to undergo free premarital counseling.
- In 1998 the student screening project began, and the newborn screening program for blood diseases was launched in 2007.
- All these programs were accompanied by educational campaigns that aimed at increasing public awareness about SCD as well as other common hereditary blood disorders.

## Percentage of SCD



# In the main teaching tertiary care hospital( 1000 beds)

- 20-30 % of bed occupancy by SCD
- The A/E visits 20-30% is SCD patients
- High rate of morbidity and mortality
- Clinically: rapid deterioration, unexpected clinical pathway

## A. The common bacterial Infections

- Infections are common and an important cause of severe complications in sickle cell patients.
- Before early screening for sickle cell disease and the use of preventive antibiotics in children, 35% of infants with sickle cell died from infections.
- Fortunately, with screening tests for sickle cell now required for newborns, and with the use of preventive antibiotics and immunizations, this mortality rate has dropped significantly.

The most common organisms causing infection in children with sickle cell disease include:

- •Streptococcus pneumoniae (can cause pneumonia, blood infections, or meningitis)
- •Haemophilus influenza (also a cause of pneumonia, blood infections, and meningitis)
- Such infections pose a grave threat to infants and very young children with sickle cell disease.

# Infections in Children and Adults.

Infections are also common in older children and adults with sickle cell disease, particularly respiratory infections such as pneumonia, kidney infections, and osteomyelitis.

(The organisms causing them, however, tend to differ from those in young children.) Infection-causing organisms include:

- •Chlamydia and Mycoplasma pneumoniae. These are the important infections in acute chest syndrome.
- •Gram-negative bacteria. This group of bacteria mostly infects hospitalized patients and can cause serious pneumonias and other infections.

# Infectious complications of Sickle cell anemia

## Related to absent spleen

Pneumococcus infections

Hemophilus infections

Dramatically improved with the use of prophylactic penicillin in childhood

## Related to frequent instrumentation

Staphylococcal infections

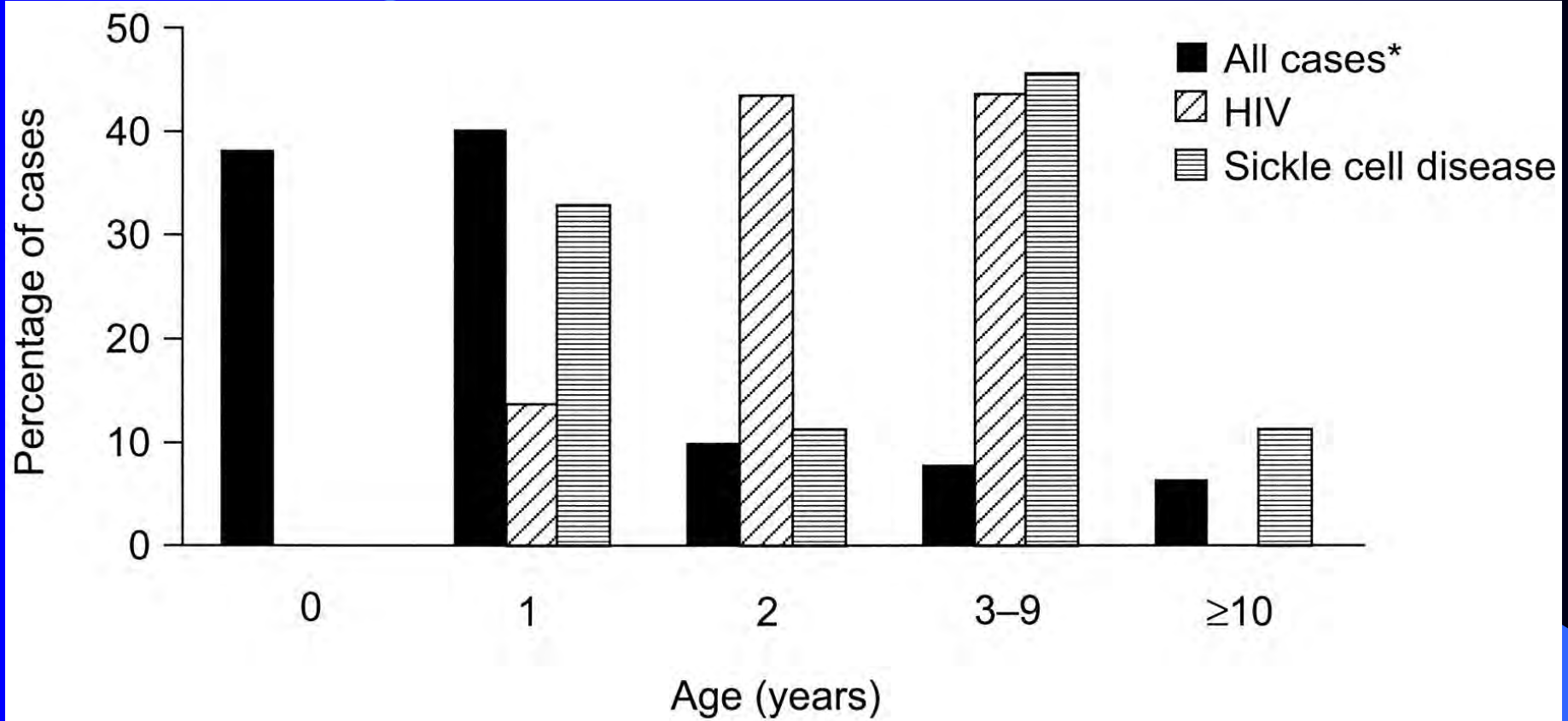
## Related to tissue infarction

Osteomyelitis

# Pneumococcal diseases in children with Sickle cell disorders :

- Children with sickle cell anaemia have an increased susceptibility to severe bacteria infection, particularly from *Streptococcus pneumoniae*. The risk of infection is greater in the first 3 years of life specially at 4 months.
- The incidence of Pneumococcal diseases for children with sickle cell disease is 18.4 cases per 100 patients/year compared with 0.02 to 0.06 patients per 100 healthy children /year
- The case fatality rate of Pneumococcal diseases in these children is 30%

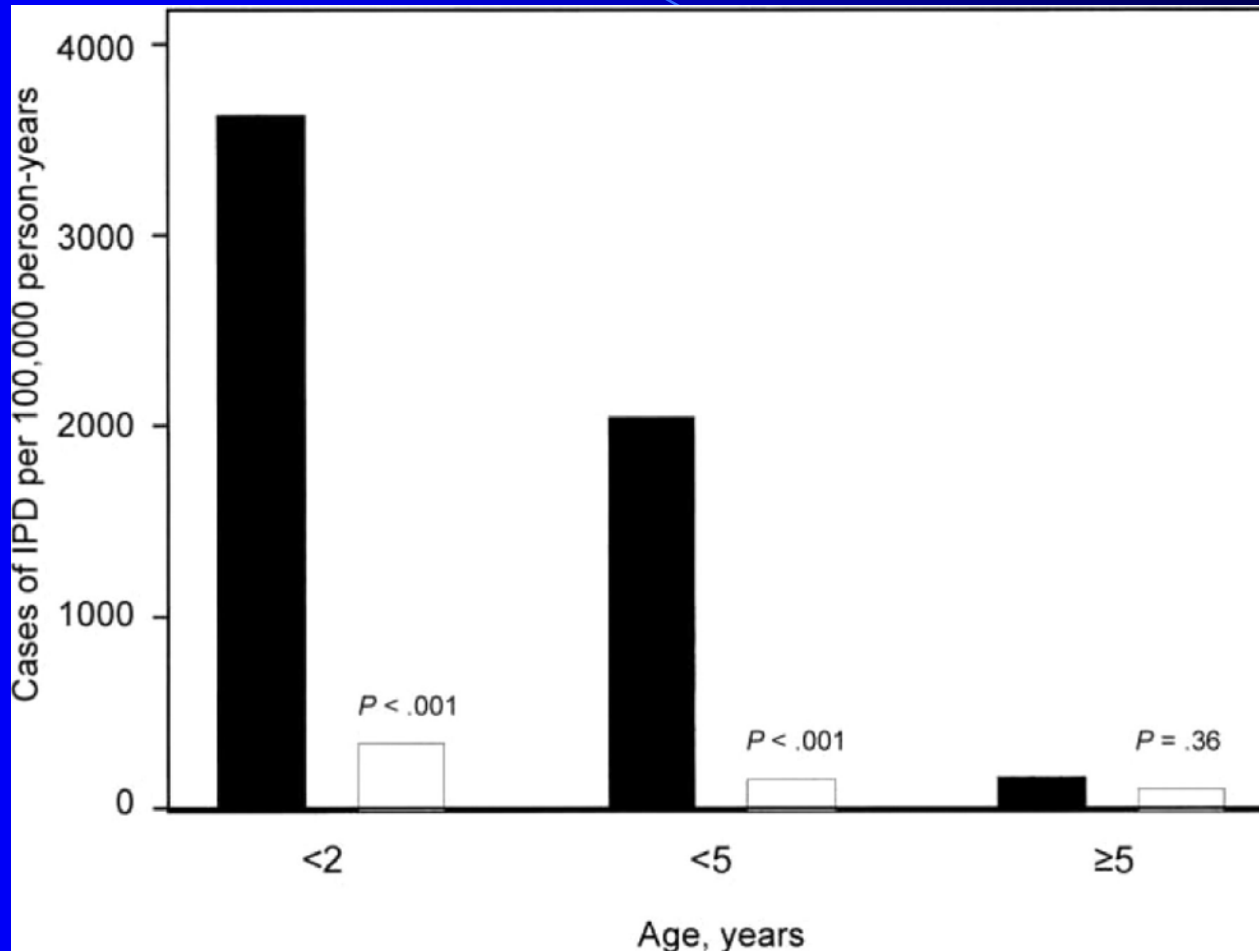




**Age distribution of pneumococcal bacteremia in children with sickle cell disease or HIV and healthy children at Boston Medical Center, 1981-1998 9.**

- The rate of IPD among children with SCD who are aged <5 years has decreased markedly since the introduction of routine administration of PCV to young children

**Rates of invasive pneumococcal disease (IPD; cases per 100,000 person-years) among individuals with sickle cell disease who were enrolled in Tennessee Medicaid and lived in selected counties in Tennessee.**



Halasa N B et al. Clin Infect Dis. 2007;44:1428-1433

# Acute Chest Syndrome

- Acute chest syndrome (ACS) occurs when the lung tissues are deprived of oxygen during a crisis. It can be very painful, dangerous, and even life threatening.
- It is a leading cause of illness among sickle cell patients and is the most common condition at the time of death. At least one whole segment of a lung is involved, and the following symptoms may be present:
  - •Fever of 101.3° F degrees (38.5° C) or above
  - •Rapid or labored breathing
  - •Wheezing or cough
  - •Acute chest pain

# Causes of Acute Chest Syndrome.

Primary causes of acute chest syndrome include:

- •Infection. Infection from viruses or small atypical organisms (Chlamydia and Mycoplasma) is the most common cause of the oxygen deprivation that leads to acute chest syndrome.
- •Blockage of blood vessels.
- •Asthma. Asthma can increase the frequency and pain of acute chest syndrome episodes in children.

# Prevention

- Babies and children with SCD should have all of the regular childhood vaccines, plus a few extra. The extra ones are:
  - Flu vaccine (influenza vaccine) every year after 6 months of age.
  - A pneumococcal vaccine
  - H.Influenza vaccine
  - Meningococcal vaccine, if recommended by a doctor.
- In addition, children with SCD should receive a daily dose of penicillin, an antibiotic medicine, to help prevent infections. This can begin at 2 months of age and continue until the child is at least 5 years of age.

Adults with SCD should have the flu vaccine every year, as well as the pneumococcal vaccine and any others recommended by a doctor

# Adult Immunization Schedules

- ❑ Published at least annually since 2002
  
- ❑ Adult Schedule approved by :
  - American College of Physicians (ACP)
  - American Academy of Family Physicians (AAFP)
  - American Congress of Obstetricians and Gynecologists
  - American College of Nurse-Midwives
  - Advisory Committee on Immunization Practices (ACIP) and CDC
  
- ❑ 2012 schedule published February 2, 2012
  - ❑ (see <http://www.cdc.gov/vaccines/recs/schedules/adult-schedule.htm>)



# 2012 ACIP Adult Immunization Schedule, Medical, Occupational and Behavior-Based Recommendations

FIGURE 2. Vaccines that might be indicated for adults, based on medical and other indications<sup>1</sup> — United States, 2012

INDICATION▶	Pregnancy	Immunocompromising conditions (excluding human immunodeficiency virus [HIV]) <sup>4,6,7,14</sup>	HIV infection <sup>4,7,13,14</sup> CD4 <sup>+</sup> T lymphocyte count		Men who have sex with men (MSM)	Heart disease, chronic lung disease, chronic alcoholism	Asplenia <sup>13</sup> (including elective splenectomy and persistent complement component deficiencies)	Chronic liver disease	Diabetes, kidney failure, end-stage renal disease, receipt of hemodialysis	Health-care personnel
			<200 cells/ $\mu$ L	$\geq$ 200 cells/ $\mu$ L						
Influenza <sup>2,*</sup>		1 dose TIV annually		1 dose TIV or LAIV annually		1 dose TIV annually			1 dose TIV or LAIV annually	
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>3,*</sup>		Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 years								
Varicella <sup>4,*</sup>		Contraindicated				2 doses				
Human papillomavirus (HPV) <sup>5,*</sup> Female		3 doses through age 26 years				3 doses through age 26 years				
Human papillomavirus (HPV) <sup>5,*</sup> Male		3 doses through age 26 years				3 doses through age 21 years				
Zoster <sup>6</sup>		Contraindicated				1 dose				
Measles, mumps, rubella <sup>7,*</sup>		Contraindicated				1 or 2 doses				
Pneumococcal (polysaccharide) <sup>8,9</sup>		1 or 2 doses								
Meningococcal <sup>10,*</sup>		1 or more doses								
Hepatitis A <sup>11,*</sup>		2 doses								
Hepatitis B <sup>12,*</sup>		3 doses								

\* Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

Contraindicated

No recommendation



# B.The other infections

# ***The impacts of genetic disorders on infectious diseases***

## **(Malaria & Sickle cell disorders)**

- Many studies showed reduced morbidity and mortality from malaria ( *Falciparum*) patients with ***thalassemia major and minor (the carriers)*** (up to 50%), and decreased numbers of circulating parasites (by 80%) The mechanism of resistance may consist of **decreased parasite replication** within the erythrocyte or **enhanced splenic clearance of parasitized erythrocytes.**
- A person who carries the sickle cell gene has a survival advantage against malaria

# The impact of the 2009 H1N1 influenza pandemic on pediatric patients with sickle cell disease.

George A, , Ohio, pediatric blood cancer Oct; 2011

- Respiratory infections are associated with clinically significant illness in patients with (SCD).
- The 2009 H1N1 pandemic was perceived as a significant threat to this population
- Approximately half of the patients with confirmed H1N1 infection were managed successfully on an outpatient basis with oseltamivir therapy.
- Among the patients admitted, the most common diagnosis was acute chest syndrome (ACS).

- Most admitted patients had uncomplicated clinical courses, with a median length of admission of 3 days and no mortality or requirement for mechanical ventilation
- A past history of ACS or reactive airway disease correlated with a higher rate of admission and of ACS incidence
- Chronic transfusion therapy or hydroxyurea therapy with high hemoglobin F levels had a strong inverse correlation with incidence of ACS.

# Emergency department visits made by patients with sickle cell disease: a descriptive study, 1999-2007.

Yusuf HR, et al Atlanta

American Journal of preventive medicine 2010

- This study assessed characteristics of emergency department visits made nationally by patients with SCD.
- The data 1999-2007 were analyzed.
- On average, approximately 197,333 emergency department visits were estimated to have occurred each year between 1999 and 2007 with SCD
- Approximately 29% of visits resulted in hospital admission;
- Patient-cited reasons for the emergency department visit included **chest pain (11%); other pain or unspecified pain (67%); fever/infection (6%); and shortness of breath/breathing problem/cough (5%)**, among other reasons.

## **Tuberculosis in adult patients with sickle cell disease**

**J Infect. 2007 Nov;55(5):439-44. Epub 2007 Aug 22.**

**France**

- Although infection, in particular pulmonary infection, is a common complication of sickle cell disease (SCD) and although SCD is frequent in populations where the prevalence of tuberculosis is high, the relationship between the two diseases has never been studied.
- Review of the cases of tuberculosis reported within the cohort of 457 SCD patients from January 1998 to April 2006 in the adult sickle cell center of Hôpital Tenon, Paris, France.

- Identified 12 cases of tuberculosis, 8 men and 4 women.
- There were 7 lymph node lesions, 3 pulmonary lesions and 2 vertebral lesions.
- The incidence of pulmonary and extrapulmonary tuberculosis was respectively of 82 and 246 cases per 100,000, to compare with an expected incidence of 184 cases, and 65 cases per 100,000.
- In SCD patients, lymph node tuberculosis appears to have a higher incidence
- Pulmonary tuberculosis seems to be less frequent than expected.

# C. Hospital acquired infection



## **Bacterial blood cultures in children with sickle cell disease.**

Rogovik AL, et al.

Am J Emerg Med. 2010 May;28(4):511-4. BC Children's Hospital,  
Vancouver, BC, Canada.

- To determine the incidence of bacteremia in children with SCD presenting with or without fever to a pediatric ED.
- A retrospective chart review of 692 pediatric ED visits of children with SCD during a 2-year period was conducted.
- Seven blood cultures had bacterial growth (1.3%; 95% confidence interval, 0.5-2.1), 3 of which were among febrile children (1.7%; 95% confidence interval, 0-3.6). All identified microorganisms are part of the normal skin or oral flora and could represent contamination. None of the patients had growth of the *Streptococcus pneumoniae* species.
- A very low rate of bacterial growth

**Infectious complications of implantable venous access devices in patients with sickle cell disease.**

J Vasc Interv Radiol. 2004 Apr;15(4):375-8.

Wagner SC, et al.

Thomas Jefferson Hospital, PA

- a retrospective ; from January 1, 1996 to December 31, 2001 to identify hospital admissions with SCD
- 2703 admissions in 293 patients.
- The radiology system identified 23 patients had placement of an implantable venous access device.
- 30 implantable venous access devices (25 venous ports, five tunneled catheters)

- In 21 patients with 30 devices, 18 device infections (60%) occurred in 12 patients (57%) involving 15 venous ports and three tunneled catheters.
- There were a total of 12389 days of catheter use and a rate of 1.5 infections per 1000 catheter days.
- Infections occurred from 16 to 1542 days (mean, 349 days) after device placement.
- This study shows a high incidence of infection associated with placement of implantable venous access devices in patients with sickle cell disease.
- It recommended to avoid placing these devices in this patient population.

## Nosocomial infection in adult patients with sickle cell anemia.

Crowe HM,

Infect Control Hosp Epidemiol. 1988 Sep;9(9):405-8.

Boston University School of Medicine, Massachusetts.

- Describe eight serious, nosocomially transmitted infections in four adult patients hospitalized for complications of sickle cell disease, which led to death in one patient and prolonged hospital stays in three others.
- **Risk can be reduced if health care workers are especially vigilant in adhering to handwashing and other infection control measures when caring for these patients.**
- Additionally, it was recommended that a patient with sickle cell disease not share a room with a patient known to have or suspected of having a nosocomial or community-acquired infectious disease.

# **Bloodstream infections in hospitalized adults with sickle cell disease: a retrospective analysis.**

Chulamokha L, American journal of hematology 2006  
Jefferson Medical College, Pennsylvania, USA

- **There is a surprising paucity of medical literature that is focused on evaluating SCD adults with BSI.**
- The charts of adults with SCD and BSI who were admitted between April 1999 and August 2003 were reviewed. During this period a total of **1,692** hospital admissions for **193** adults with SCD were identified and **28%** of these patients had at least 1 episode of positive blood cultures, with 69 episodes (17%) considered true BSI.
- Nosocomial BSI occurred in 34 episodes (**49%**). Streptococcus pneumoniae was rarely encountered. **A high incidence of staphylococcal BSI in adults with SCD was noted.**

**Bloodstream infection in adults with sickle cell disease: association with venous catheters, Staphylococcus aureus, and bone-joint infections. Medicine 2006 Jan**  
**Zarrouk V, France.**

- Through a 5-year retrospective analysis of a cohort of **900 patients followed at the institution, identified 56 episodes of BSI in 47 patients.**
- The incidence rate of BSI was 1.2 episodes per 100 patient-years.
- As compared to the patients followed in the cohort, those with BSI were more likely to be younger ( $p = 0.001$ ), to have Hb-S disease ( $p = 0.008$ ), severe disease ( $p = 0.001$ ), or additional immunosuppression ( $p = 0.05$ ).
- **BSI was hospital-acquired in 46% of cases and mainly associated with venous catheters (41%) and Staphylococcus aureus (34%).** Pneumococci were rarely identified (10.7%).

- Despite an adequate duration of antibiotic therapy, the course of BSI was marked by a high frequency of associated bone-joint infection.
- Factors associated with the occurrence of bone-joint infection were previous osteonecrosis (relative risk, 2.5; 95% confidence interval, 1.2-5.3) and *S. aureus* infection (relative risk, 3.8; 95% confidence interval, 1.8-8.4).
- BSI is a rare event in adults with SCD compared to children.



Asymptomatic bacteriuria in sickle cell disease: a cross-sectional study.

Cumming V, et al. BMC Infect Dis. 2006 Mar 15;6:46  
Sickle Cell Unit, Mona Campus, Kingston 7, Jamaica.

- To determine the prevalence of ASB, in a cohort of patients with SCD.
- Of the 266 urines collected, 234 were sterile and 29 had significant bacteriuria yielding a prevalence of probable ASB of 10.9% (29/266).
- **Fourteen patients had confirmed ASB (prevalence 5.3%) of which 13 had pyuria.**



- Females were 14.7 times more likely to have confirmed ASB compared to males (95% CI 1.8 to 121.0).
- The number of recorded visits for symptomatic UTI was increased by a factor of 2.5 (95% CI 1.4 to 4.5,  $p < 0.005$ ).
- There was no association with history of gram negative sepsis.
- ASB is a significant problem in individuals with SCD

## **Urinary tract infection in febrile children with sickle cell anaemia. West Afr J Med. 2011 Jul-Aug;30(4):268-72.**

- Sickle cell anaemia (SCA) is very common in Maiduguri, North-Eastern Nigeria. .
- **Bacteriuria was found in 65 (26%) of children with SCA and controls 514 (20.4%) of controls,  $p>0.05$ .**
- Escherichia coli [16 (27.7%)] and Klebsiella species [16(24.6%)] were the predominant isolates in SCA group
- Significant bacteriuria occurred in patients with other clinical conditions such as pneumonia and septicaemia.
- Urinary tract infection is common in children with SCA.
- **Routine screening is therefore recommended during febrile illnesses.**

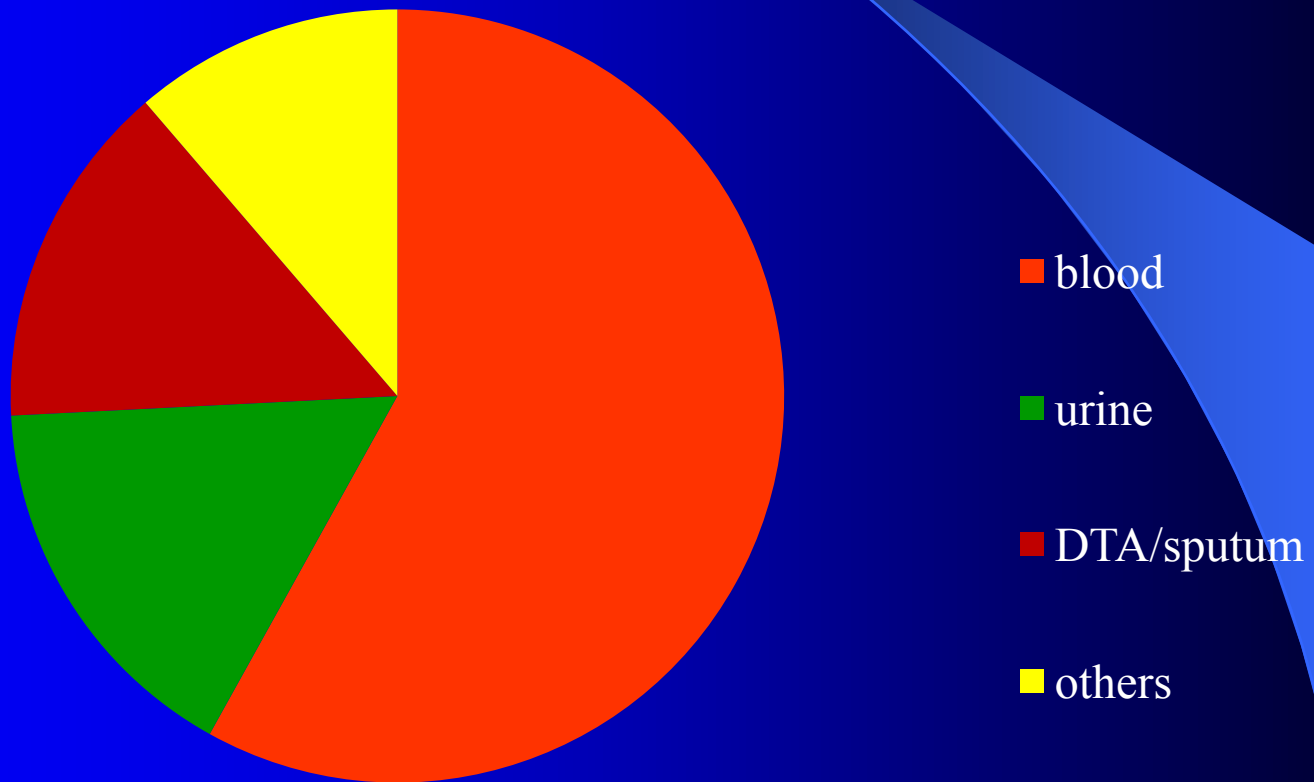
# Infections in SCD patients in Kingdom of Bahrain

- Objective : to look at the prevalence of different bacterial infection/ hospital acquired infection in SCD patients .
- Population: all patients that were admitted to the **medical department** over a 6 months period to SMC
- Method : a retrospective study
- Period from 1/7/2012 -1/1/2013
- All the admissions with SCD diagnosis

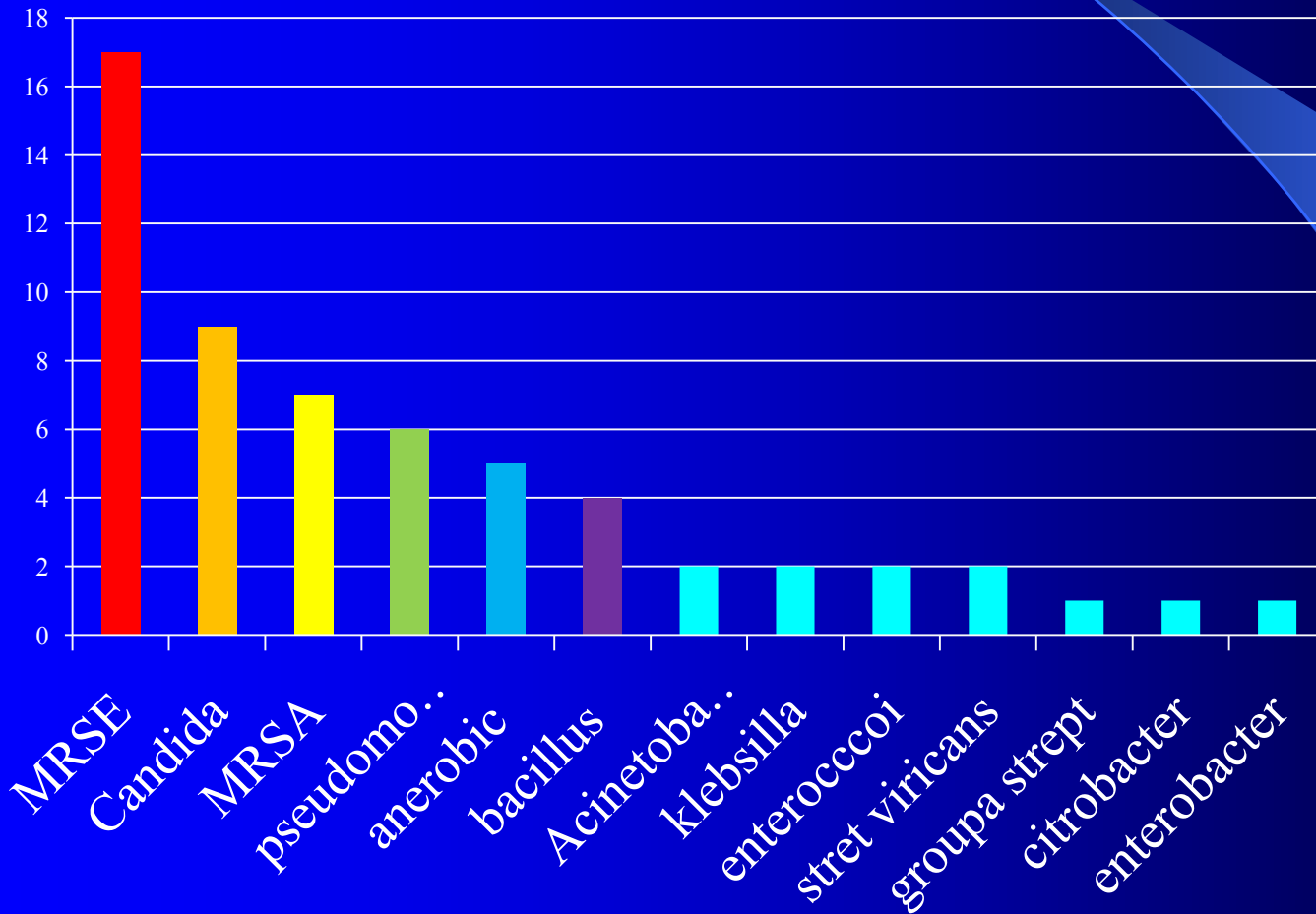
# Results

- Out of 565 SCD patients admissions
- Most of the cases have repeated admissions (**77 patients**)
- **No. admissions ranged form 2-24 (average 7.3)**
- We found 59 total positive cultures in 26 patients (**34%**)

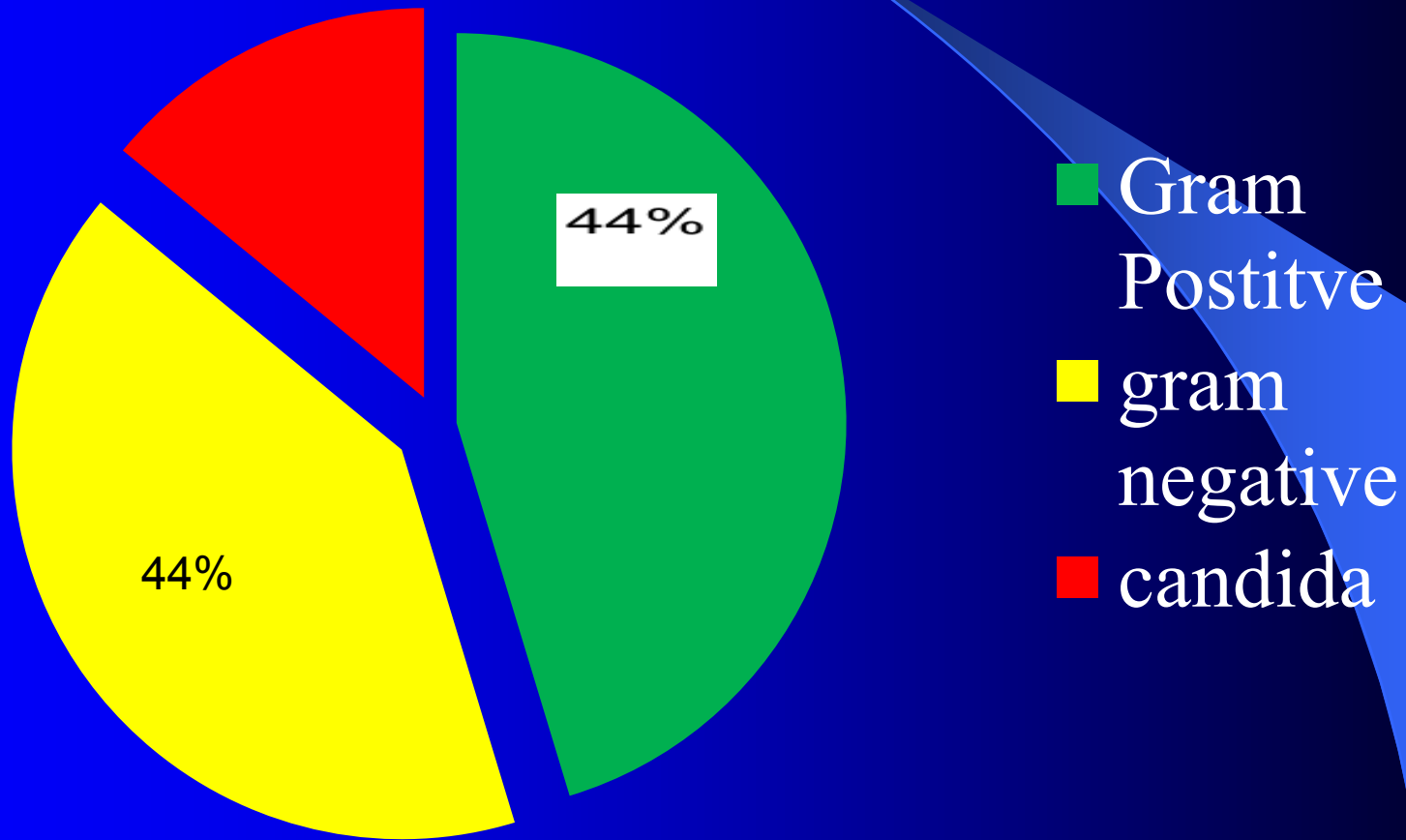
# The positive cultures



# The number of different Bacterial organisms



# The ratios of the different Bacteria



# The results

- The 59 positive cultures , were for 26 patients
- We found the medical records for only 17 patients (41 positive culture)
- The length of stay ranges from 5-37 days with an average of 12.6 day **longer than the average length of stay than all the other admission diagnosis**)



- Antibiotics on admission : **(53%) of the patients.**  
Rociphene : 8 and Tazocin and erythromycin 1
- **(antibiotic study in A/E department)**
- **The initial diagnosis was :**
  - VOC in 13
  - Fever in 2
  - PE in 1
  - And abdominal pain 1

# During the admission

- **The majority received antibiotics (94%)**
- Only one did not receive anything
- How many antibiotics each received?
- 1 antibiotic in 6 patients
- 2 or more antibiotics in 9 ( 2 is 2 , 2 is 3, 4 is 4 , 1 is 5)
- All of the patients received different combination of antibiotics. ( **antibiotic stewardship program** )

# Fever

- On admission: only one patient has fever
- In the hospital : the majority 13/17 (**76.5%**) patients developed fever after 72 hours of admission.
- The fever duration ranged 1-24 days with an average of 7.23

# Clinically On admission

- One has fever
- All has pain
- 1 chest pain ( same to other studies)
- 10 has nothing
- 2 hypoxia
- 2 distended abdomen
- WBC was high in 12 patients ranging form 3.2 to 22.1

# Imaging for the fever

- CXR: in all; Normal: 10 (**59%**)
- Us : done in 7 (**41%**)
- Echo: 2 (**11.2%**)
- CT: 3 (**17.6%**)
- Bone scan :1

# Hospital acquired infection

- BSI : 2/17 (**11.7%**)
- ( Klebsiella esbl, Candida)
- HAP/VAP: 4/17 (**23.5%**)
- UTI: 1/17
- Asymptomatic bacteruria: 3/17 (**17.6%**)
- **the rest of the cultures were contamination or colonization (31 cultures).**

# Documentation

- **The final diagnosis;**
  - VOC : 9
  - ACS :2
  - CAP: 3
  - UTI: 3

# Consultations

- There were 18 consultations for 8 patients including all .
- Outcomes; all discharged and two developed ACS



# In conclusion

- A high rate of hospital acquired infection among SCD patients.
- A special attention to the infection control measures in SCD patients.
- A high rate of contamination or colonization
- None has any of the preventable common infections because of high vaccination coverage
- High rate of inappropriate use of antibiotics
- Most of the cases of fever has non infectiuos etiology.

# Recommendations:

- Based on the results of this study:
- 1. antibiotic study in the A/E department
- 2. strengthen the infection control measures for SCD patients.
- 3. a special protocol for antibiotic utilization in SCD patients
- 4. SCD patients to be included in the current antibiotic management team activities.
- 5. further analysis of the current data
- 6. more studies in the same fields

# In Summary

- 1. SCD patients are at high risk of different bacterial infections
- 2. the common organisms are : streptococcus Pneumonia, H . Influenza , these are preventable by a good vaccination program
- 4. A high risk of **Hospital acquired infections** which is very costly
- 5. further studies has to emphasize the importance of HAI in SCD and their impact in morbidity and mortality
- 6. infection control measures have to be strneghten in SCD patients.

**KNOWLEDGE  
IS POWER**





**Thank you for  
listening**