DREPANOCYTOSIS

OR SICKLE CELL ANAEMIA

INFORMATION AND ADVICE FOR CHILDREN AND PARENTS.

RED BLOOD CELL OUTPATIENT CLINIC

Comitato
Maria Letizia Verga
PER LO STUDIO E LA CURA DELLA LEUCEMIA DEL BAMBINO
ODV

Our thanks to Claudio Cernuschi for putting his heart and colours into the illustrations of this book.

WHAT IS DREPANOCYTOSIS OR SICKLE CELL ANAEMIA?

Drepanocytosis, also known as **sickle cell anaemia**, is a hereditary systemic disease, i.e. affecting all organs in the body, characterised by vaso-occlusive crises causing pain, inflammation and enhanced vulnerability to infection and blood vessels thrombosis.

HOW WIDESPREAD IS IT AND WHERE?

In the past, drepanocytosis was particularly widespread in **sub-Saharan Africa** and southern Europe (Albania, Italy).

Today, as a result of recent migration flows, it is **globally** widespread.

Every year thousands of children are born with drepanocytosis worldwide and cases are increasing. In 2008, the United Nations General Assembly called drepanocytosis "a global health problem" and established **World Sickle Cell Day on june 19th**.

The European Union has listed drepanocytosis among **Rare Diseases**, however its frequency (1/2300 births) is sharply increasing.

The European Commission has created special European Reference Networks (ERNs) to raise awareness of and treat Rare Diseases.

Italy has national paediatric (A.I.E.O.P. - Italian Association of Paediatric Haematology and Oncology) guidelines and adult (S.I.T.E - Italian Society for Thalassaemia and Haemoglobinopathies) guidelines for the management of acute and chronic complications of this disease, and specialised and targeted diagnostic-therapeutic pathways have been developed for these children.

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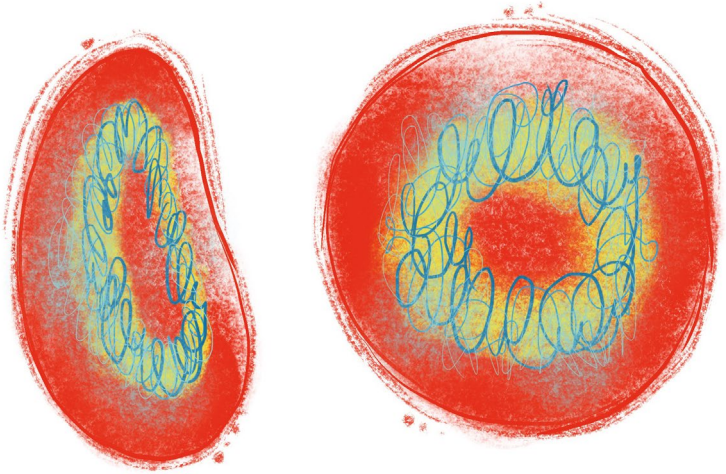
WHAT CAUSE IT?

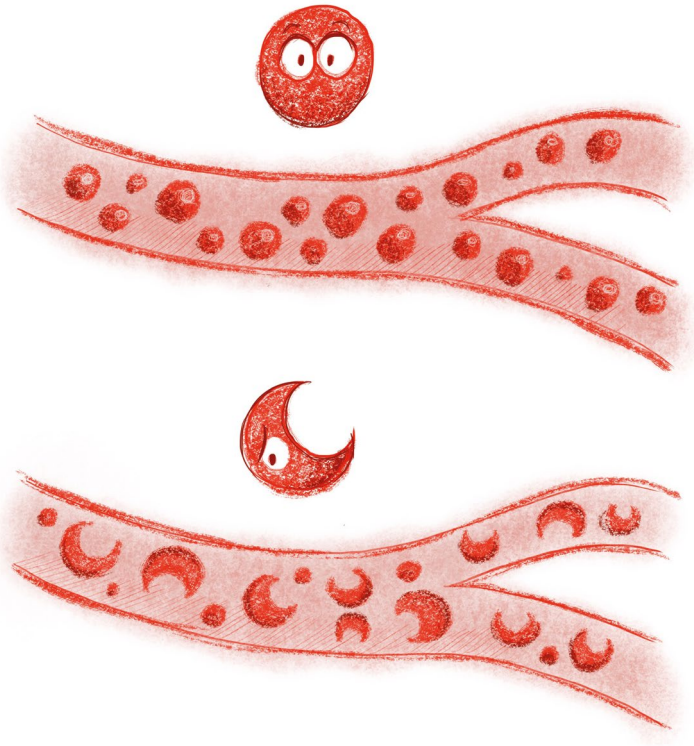
Drepanocytosis is caused by the presence of an abnormal haemoglobin, haemoglobin S, due to a DNA mutation.



Haemoglobin is a protein, contained within red blood cells, that transports oxygen from the lungs to all tissues and organs in the body.

The presence of abnormal haemoglobin S changes the shape of the red blood cell, which becomes **sickle-shaped**.

NORMAL red blood cell



SICKLE-SHAPED red blood cell or **DREPANOCYTE**

HOW IS IT TRANSMITTED?

Drepanocytosis is a genetic disease **inherited from both parents**, who are carriers, but NOT sufferers, of the abnormal haemoglobin.

The sick child inherits the mutations that produce haemoglobin S from both parents.

At each pregnancy the carrier parents have a probability of:

S S

25%

that the child inherits both mutations from its parents. This child will be **SICK** with Drepanocytosis.

A S

50%

that the child inherits only the mutation from one parent, i.e. the child will be a **CARRIER**, like the parents, of haemoglobin S.

A A

25%

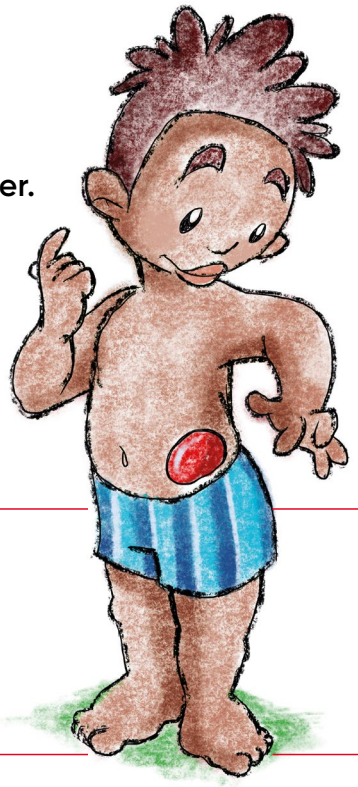
that the child does not inherit any mutation and is therefore completely **HEALTHY**.

HOW MANY TYPES OF DREPANOCYTOSIS ARE THERE?

Drepanocytosis can be:

- **S/S** where both parents are carriers of haemoglobin S.
- **S/beta** or '**thalasso/micro-drepanocytosis**' where one parent is a carrier of haemoglobin S and the other is a healthy carrier of beta-thalassaemia (or Mediterranean anaemia).
- **S/C** where one parent is a haemoglobin S carrier and the other is a haemoglobin C carrier.

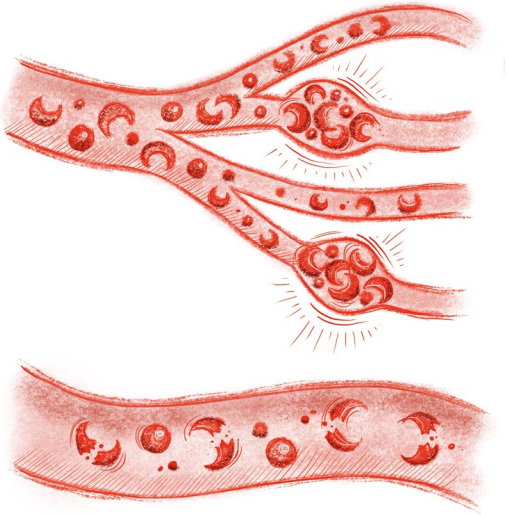
The different forms of the disease have similar clinical manifestations.



The spleen is an organ that removes old red blood cells from blood and helps defend against infection.

HOW DOES IT MANIFEST ITSELF?

Due to their **abnormal shape**, drepanocytes are more likely to become trapped in blood vessels, causing blood flow to slow down and thus hindering the delivery of oxygen to downstream tissues and organs.



Drepanocytes are more rapidly destroyed and removed from blood vessels by the spleen (chronic haemolysis).

HOW DOES IT MANIFEST ITSELF?

The main clinical manifestations are:

- **vaso-occlusive pain crises:**
  the child experiences intense pain that can affect any part of the body (chest, abdomen, limbs, etc.).

In younger children, there may be swelling of the fingers and toes (dactylitis).

- **acute thoracic syndrome:**
  is a complication of the lungs characterised by fever and chest pain, coughing and other respiratory symptoms.

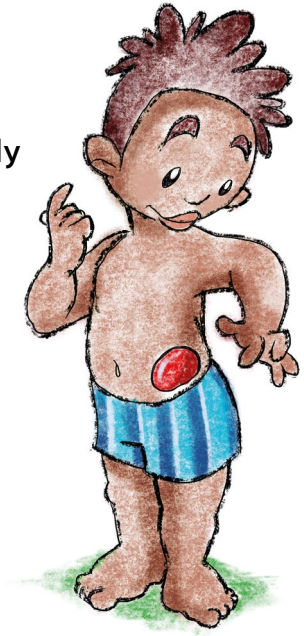
- **infections:**
  sufferers are predisposed to develop frequent and even severe infections (bone infections, muscle infections, abscesses, etc.) that may require prolonged antibiotic treatment.

  Any fever must be treated by a doctor.

- **acute and/or chronic anaemia:**
  the increased destruction of red blood cells (*haemolytic crises*) or more rarely the reduced production of young red blood cells (*aplastic crises*) can cause a drop; in haemoglobin levels.
  The child manifests tiredness, dizziness, difficulty climbing stairs and performing minor activities of daily living.

HOW DOES IT MANIFEST ITSELF?

- **splenic sequestration: ** the spleen suddenly and transiently sequesters blood cells 'like a sponge'. The spleen swells, pain appears in the abdomen sometimes associated with fever and infection.



- **priapism:** in males, drepanocytes can cause swelling and pain in the penis.

This is a medical emergency! Go to A&E immediately!

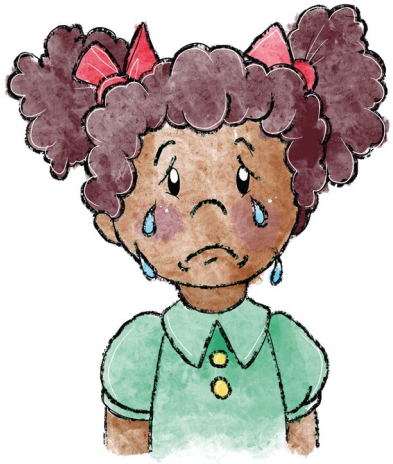
- **cerebral stroke: ** occlusion of cerebral vessels can lead to lack of oxygenation of the brain with permanent neurological damage.

This dramatic complication manifests itself in intense headaches, impaired vision, difficulty in standing, speaking, etc.

This is an emergency! Call 118 immediately.

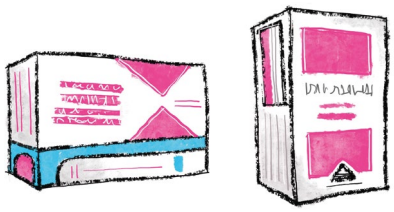
WHAT CAN I DO AT HOME WHEN IN PAIN?

It is important to take immediate action:

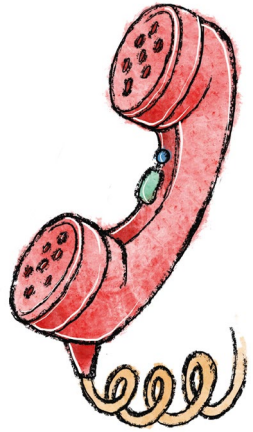


- **drink plenty of water**, reassure the child, keep him warm (except in the case of fever);

- treat the pain immediately with **paracetamol** at the age-appropriate dosage (repeat every 6 hours);



- if the pain persists **administer ibuprofen** or **oral ketoprofen** on a full stomach (repeatable every 8 hours). Notify the Centre by telephone;

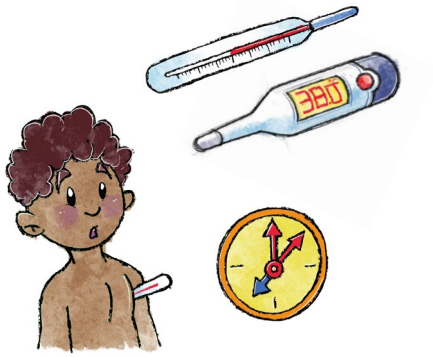


- **if the pain persists, returns or worsens,** or is associated with other symptoms (such as fever, difficulty breathing, changes in the child's general condition, lameness, etc.);

Call 118 and head to the hospital.

WHEN SHOULD YOU GO TO A&E?

- ✓ **if the patient has a fever** (temperature higher than 38.0 C) measured with a thermometer under the armpit;



- ✓ **if there is a decline** in their general condition;

- ✓ if they **have difficulty breathing or have chest pain**;

- ✓ **if the pain does not go away** with common medications (paracetamol and/or oral ibuprofen);

- ✓ if the headache is severe or is associated with **difficulty in speaking, seeing or walking**;

- ✓ if they are very tired or sleep too much and **it is difficult to wake them up**;

- ✓ if they suddenly become **pale with a strong stomach ache**;

- ✓ **if they experience diarrhoea** (3-4 liquid discharges) and/or **vomiting** (several episodes) within a few hours and the child **is unable to hydrate**;

- ✓ if their penis **swells and hurts**.

According to national and international guidelines, a patient suffering from drepanocytosis, who is admitted to A&E due to pain, must always be given the priority 'Yellow Code' at triage!

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WHAT CAN I DO TO PREVENT THE DEVELOPMENT OF COMPLICATIONS?

To prevent the development of complications we recommend:

✓ **drinking plenty of fluids and often ** (especially in hot weather and while exercising);

✓ **eating** a varied **diet ** rich in fruit, vegetables and pulses (every day);

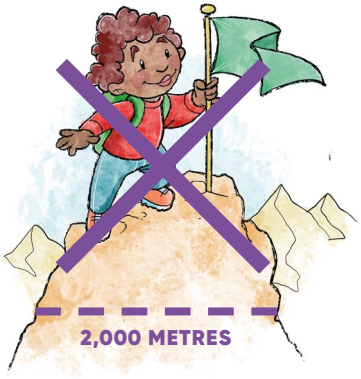
✓ avoiding exposure to **too much heat** (undress and drink a lot of fluids) or **too much cold** (cover yourself adequately);

✓ **opting for non-intensive exercise**, remembering to drink a lot of water while exercising.

The child can go anywhere (sea, mountains...) and travel by any means of transport.

They CANNOT, however:

✘ **travel by helicopter!**



✘ exceed an altitude of **2,000 metres in the mountains!**

✘ **go scuba diving** or **skin** diving!

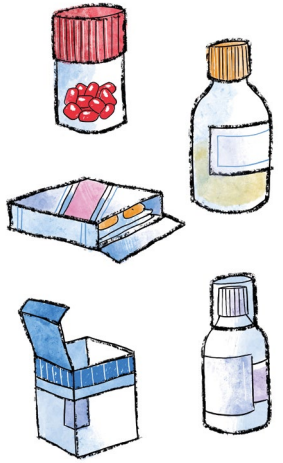
WHAT CAN I DO TO PREVENT THE DEVELOPMENT OF COMPLICATIONS?

When travelling to AFRICA, we recommend that you:

✓ **on the plane**, move around as much as possible and drink water;

✓ **drink plenty** of fluids, being careful to drink **only mineral water or water that has been boiled** and then cooled;

✓ **bring the latest medical report**, fever and **pain** relief **medication** (paracetamol, ibuprofen), antibiotics and a thermometer;



✓ take **malaria prevention medication**, if indicated;

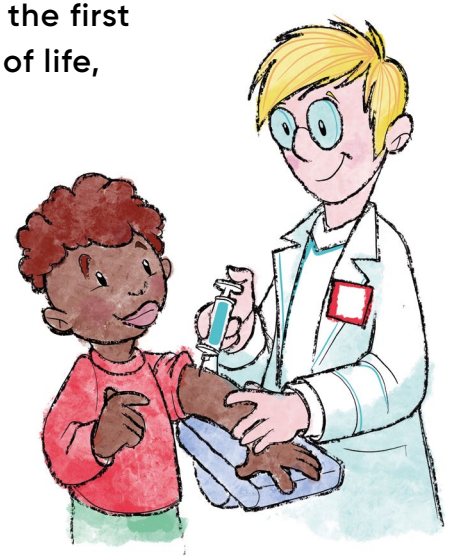
✓ **find out if there is a large hospital** where you can go to in case of an emergency.

WHAT CAN I DO TO PREVENT THE DEVELOPMENT OF COMPLICATIONS?

We recommend that you:

✓ **carry out the recommended vaccinations** according to the vaccination schedule, and in particular:

- anti-Haemophilus Influenzae (in the first year of life);
- anti-Meningococcus B, C and ACWY (the latter after 1 year of age);
- anti-Pneumococcus (in the first year and, after 2 years of life, also 23valent);
- anti-Covid 19 (recommended after 5 years of age);
- anti-influenza (every year in November/December).



✓ take prescribed medication continuously.

✓ attend **regularly** scheduled **medical check-ups** to monitor the disease and organ damage.

WHAT CAN I DO TO PREVENT THE DEVELOPMENT OF COMPLICATIONS?

We recommend that you:

✓ **once a year perform:**

- echocardiogram and electrocardiogram;
- ultrasound of the abdomen;
- Transcranial Doppler (TCD) ultrasound (between the ages of 2 and 16).

✓ **periodically perform:**

- cerebral angio-NMR;
- Lower and upper limb NMR;
- eye examination;
- ENT examination and audiometry;
- spirometry.

✓ in case of **surgery**, the doctor will evaluate whether to perform, in preparation, erythrocyte exchanges to reduce risks of complications.

Psychological support for the child and family is always recommended.

TIP:
always take pictures with your phone of the results of blood tests and examinations undergone.

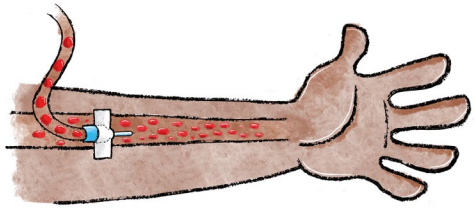
HOW IS DREPANOCYTOSIS TREATED?

There are several drugs for the treatment and control of the disease. The doctor will assess which ones are necessary:

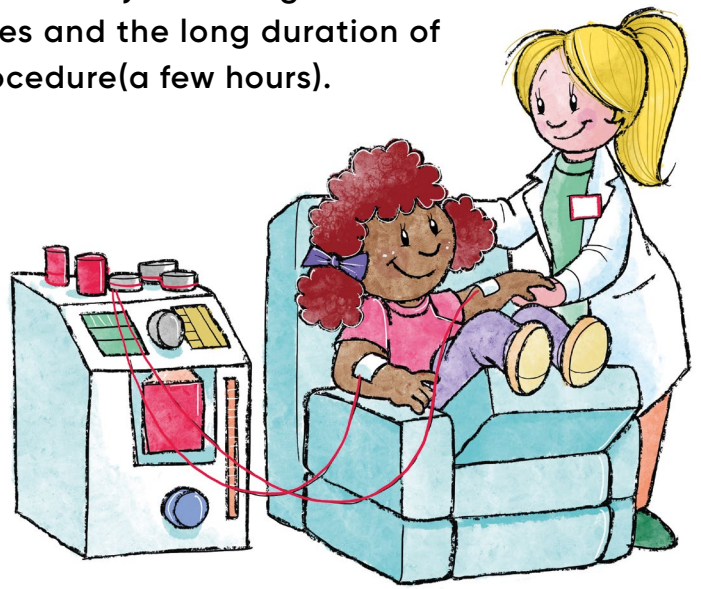
- **HYDROXYUREA**
  it is a fundamental drug that improves the deformability of drepanocytes and decreases blood viscosity. It should be taken once a day with continuity.

- **RED CELL EXCHANGES**
  drepanocytes are exchanged with healthy red blood cells to reduce haemoglobin S levels and improve tissue oxygenation.
  Exchanges can be:

1. manual exchanges: removal of the patient's blood **(bloodletting)** followed by infusion of blood from a healthy donor **(transfusion)**.
This is a simple procedure done at the patient's bedside.



2. automated exchanges or erythrocytapheresis:
performed in highly qualified centres. In children, its use may be limited due to the difficulty in finding valid venous accesses and the long duration of the procedure(a few hours).



Exchanges can take place:

- **in acute cases:** in case of disease complications.
- **in chronic cases:** in the most aggressive forms of disease every 3-4 weeks (in manual exchanges), every 8-12 weeks (in automated exchanges).

SUPPORTIVE CARE

- **ANTIBIOTIC PROPHYLAXIS**
  to be taken every day
  (e.g. oral amoxicillin)
  to prevent infections.
  Always keep
  the open antibiotic
  in the refrigerator.

- **VITAMINS**
  such as folic acid
  and vitamin D
  (according
  to doctor's
  prescription).

NEW DRUGS

Several new drugs are being tested and approved for drepanocytosis.

CAN DREPANOCYTOSIS BE CURED?

- **BONE MARROW TRANSPLANT FROM ANOTHER DONOR**

  The transplant heals the disease.
  It is not surgery but a complex procedure that takes several months, very demanding on the child and his family.
  It involves risks.

  It requires:

  1. the placement of a **central venous catheter** for access to blood vessels;

  2. hospitalisation in a sterile room for several weeks, or months;

  3. infusion of chemotherapy drugs;

  4. bone marrow infusion;

  5. checks in day hospital, when discharged, several days a week;

  6. limitation of contacts in community for months (you can not attend school, crowded places or indoors).

- **GENE THERAPY**

  In gene therapy, the patient is both donor and recipient of the cells of his or her own blood, which is modified and corrected in the laboratory.
  It is a curative and effective therapy but still at an experimental stage. **It involves risks**.

WHAT AM I ENTITLED TO?

The subject with drepanocytosis is entitled
to a **ticket exemption** (code RDG010) for visits,
tests and drugs.

The child may be entitled to **financial compensation**
by the INPS
(recognition of civil disability)
and parents can get extraordinary permits
from work (Law 104.92).

For information contact the cultural **mediator**
and **social worker** of the Centre
or your GP.

THE CARRIER OF HAEMOGLOBIN S OR DREPANOCYTIC TRAIT

Carriers of abnormal haemoglobin S are generally asymptomatic with normal life expectancy.

The **diagnosis** of the carrier status is made by **haemochrome and haemoglobin electrophoresis**, performed on a blood draw.

Very rarely and predominantly in extreme situations (as in severe dehydration), are reported possible manifestations of the disease. Appropriate measures to prevent dehydration and excessive physical fatigue, prevent the development of complications.

In the first few years of life, regular haematochemical tests are recommended.

In the reproductive age it is recommended to **study the partner** with blood tests (blood count, haemoglobin electrophoresis).

GENETIC COUNSELLING AND ANTENATAL DIAGNOSIS

In couples at **reproductive risk**, in which both parents are carriers of haemoglobin S or Mediterranean anaemia or other haemoglobin variant (e.g. haemoglobin C or haemoglobin E, etc.), genetic counselling should be performed.

The visit with the geneticist provides information and start, if necessary, the **prenatal diagnosis**.

With the known mutations of the parents, it is possible to carry out chorionic villus sampling and amniocentesis **chorionic villus sampling** and **amniocentesis** in the first weeks of pregnancy to find out whether the unborn child will be healthy, a carrier of haemoglobin S or a patient with drepanocytosis.

The couple, with the appropriate information, will make the appropriate decisions.

RED BLOOD CELL OUTPATIENT CLINIC

Manager: Dr. P. Corti
Referring doctors: Dr. G. M. Ferrari

EMAIL:
emopatie.dhe@fondazionembbm.it

WARNING!
MOBILE PHONES AND E-MAILS ARE NOT VALID TOOLS IN CASE OF MEDICAL EMERGENCIES

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

PAEDIATRIC CLINIC
DIRECTOR
PROF. ANDREA BIONDI

CONTACT DETAILS

DAY HOSPITAL PAEDIATRIC HAEMATOLOGY
Opening hours: weekdays 8.00 am - 6.00 pm
Manager: Dr A. Colombini
Head Nurse: A. Proserpio
SECRETARY/ADMISSION
Tel. 039.233.3529 Fax 039.233.2470
acceptance.dhe@fondazionembbm.it

For **urgent** calls during public holidays/night hours:
DEPARTMENT OF PAEDIATRIC HAEMATOLOGY 039.233.3530

CULTURAL MEDIATOR
Dr Eudoxie Magne Fotsing
Cell. 3402151182
emagnefotsing@fondazionembbm.it

Social worker
Dr S. Malorni
Tel. 039.233.3573
smalorni@fondazionembbm.it

PSYCHOLOGIST
Dr. F. Nichelli, Dr. E. Schivalocchi
Tel. 039.233.2462
fnichelli@fondazionembbm.it
eschivalocchi@fondazionembbm.it

SCHOOL IN HOSPITAL
Tel. 039.233.3292
sio@iccdacquistomonza.edu.it

SPORT THERAPY
Dr F.Lanfranconi
Tel. 039.233.6868
sport-therapy@unimib.it

Centro
Maria Letizia Verga

Sistema Socio Sanitario

Fondazione IRCCS
San Gerardo dei Tintori

Regione
Lombardia