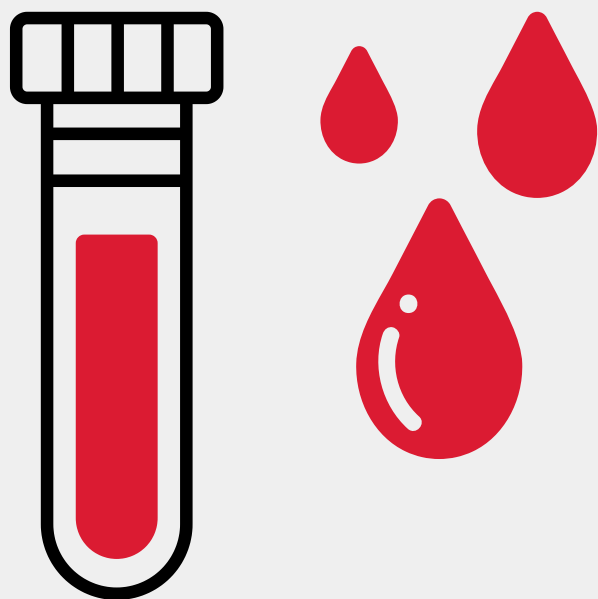


# Hematologic Issues in SDS and their Management



**SDSR**

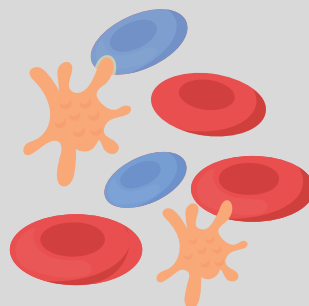
*Shwachman-Diamond Syndrome Registry*

## Blood complications

The types and timing of blood complications can vary in different patients with SDS and require different treatments.

### Blood complications can include:

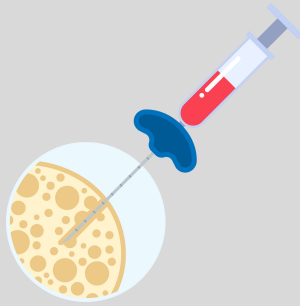
- **Low blood counts**
  - May need transfusions
    - *Low hemoglobin* - red cell transfusions
    - *Low platelets* - platelet transfusions
    - *Low neutrophils* - G-CSF
- **Bone marrow failure** (BMF, severely low blood counts)
  - May need bone marrow transplant
- **Myelodysplastic syndrome (MDS)**
- **Acute myelogenous leukemia (AML)**



## MDS/AML



- **MDS** is a pre-cancerous (leukemic) condition that is caused by abnormal blood cells
- **MDS** is characterized by the development of
  - Abnormal cells,
  - abnormal chromosomes or
  - Mutations of genes in the bone marrow often with lower or changes in blood counts
- **Leukemia** is a cancer of white blood cells - most commonly **AML** in patients with SDS
- **MDS/AML in patients with SDS is difficult to treat**
  - Standard therapies typically do not work or are too harmful



# Bone Marrow Surveillance

- You **CANNOT** wait for symptoms of MDS/AML to develop

MILD OR NORMAL

BLOOD PROBLEMS DOES

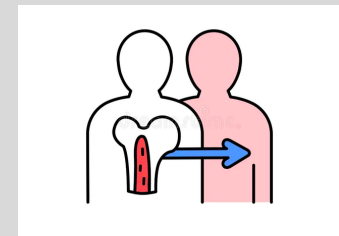
NOT EQUATE TO LOW

RISK OF MDS/LEUKEMIA

- Bone marrow surveillance is recommended as blood surveillance does not assess for abnormal changes in marrow cells, chromosomal abnormalities.
- We also do not know the sensitivity of blood surveillance in detecting abnormalities.

# Surveillance Recommendations

- Blood counts
  - Approximately every 3–4 months (quarterly)
- Bone marrow examination should include
  - **Morphology** (how cells look)
  - **Cellularity** (marrow structure)
  - **Cytogenetics** (chromosome abnormalities)
  - **FISH** (specific chromosome abnormalities)
  - **Flow cytometry** (cell maturation patterns)
  - **Loss of heterozygosity (LOH)**
  - **Microarray**
  - **Somatic mutation analysis**
- Could defer bone marrow exams until 2 years old if blood counts are not concerning
- Bone marrows are typically performed annually



# Bone Marrow Transplant for SDS

- **Indications for BMT include:**
  - Very low blood counts (aplastic anemia/BMF)
  - Need for regular transfusions
  - Recurrent infections despite G-CSF
  - MDS/AML
  - High-risk features with expert consultation
- **BMT for Patients with SDS**
  - BMT for BMF have good outcomes with expert care
  - Patients with SDS and MDS/AML have worse outcomes compared to patients with BMF likely due to:
    - More sensitivity to standard chemotherapy
    - Relapsed disease
- **Decision to undergo BMT should be made with providers experienced with treating patients with SDS**

# Neurocognitive Considerations in SDS



**SDSR**

*Shwachman-Diamond Syndrome Registry*

[WWW.SDSREGISTRY.ORG](http://WWW.SDSREGISTRY.ORG)



## When should evaluations occur?

- **At regular intervals throughout childhood:**
  - Prior to or during kindergarten
  - At key transition points (3rd/4th grade, middle school, high school, early adulthood)
  - During periods of relative medical stability
- **Other times to seek evaluation:**
  - Bone marrow transplant
  - Neurological changes (seizures, head injury)
  - Difficulties in real life (school, home)

## How to find a neuropsychologist

- Talk to your primary care provider
- Local children's hospital
- Major children's hospital
- American Academy of Clinical Neuropsychology online directory:  
(<https://theaacn.org/directory/>)





# What can I do for academic concerns?

- **Meet with school team**

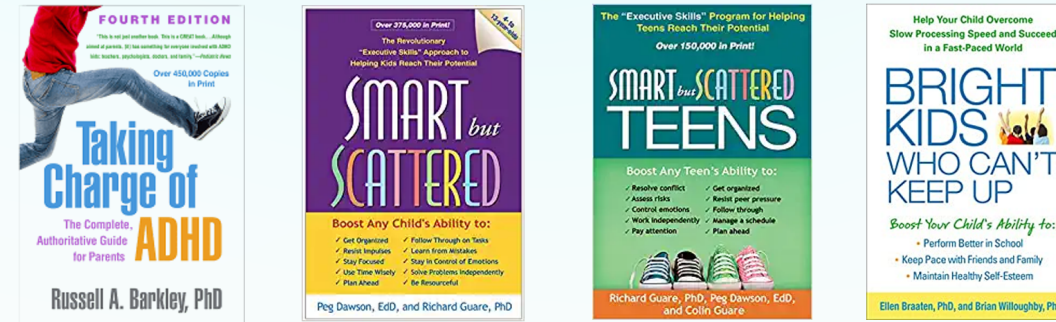
- Talk about an educational plan, such as IEP or 504 Plan
- Common accommodations include preferential seating, extended time, reduced assignments
- May need specialized instruction or support from an intervention specialist

- **Helpful resources:**

- **Wrightslaw** (<https://www.wrightslaw.com/>)
- Your state's department of special education

# What can I do for executive or attention concerns?

## Books to consider:



- **Other resources:**

- **Project Learnet** (<http://www.projectlearnet.org/>)
- **Harvard University's Center on the Developing Child** (<https://developingchild.harvard.edu/guide/a-guide-to-executive-function/>)
- **Children and Adults with Attention Deficit/Hyperactivity Disorder** (<http://www.chadd.org>)
- **National Resource Center on ADHD** ([www.help4adhd.org](http://www.help4adhd.org))

# What can I do for mood or behavioral concerns?

- **Consider therapy**

- Individual and/or family-based
- **PsychologyToday** (<https://www.psychologytoday.com/therapists>)

- **Other online resources and books**

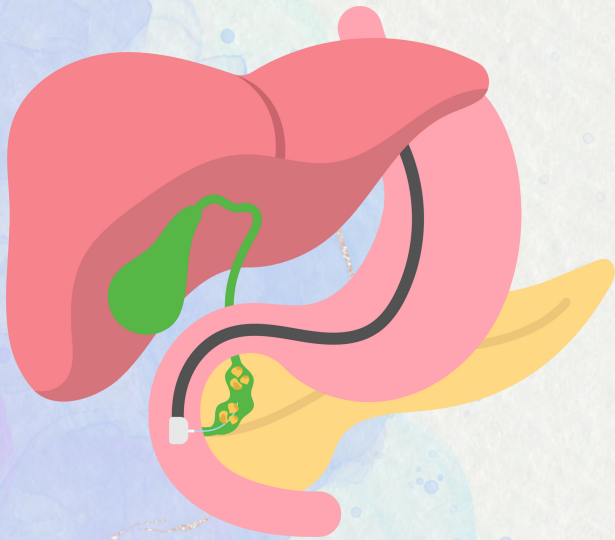
- **American Academy of Child and Adolescent Psychiatry** (<http://www.aacap.org/>)
- **National Institute of Mental Health** (<https://www.nimh.nih.gov/health/topics/child-and-adolescent-mental-health/>)
- **National Library of Medicine's Medline Plus** (<https://medlineplus.gov/childmentalhealth.html>)





# COMMON GI AND PANCREAS ISSUES IN SDS AND TREATMENT STRATEGIES

AMIT GROVER, MD



SDSR

Shwachman-Diamond Syndrome Registry

## ISSUES WITH THE INTESTINE IN SDS



- More than half of patients with SDS have abnormalities by endoscopy

## GROWTH ISSUES

**Growth can be impacted in patients with SDS due to:**

- Feeding difficulties
- Impaired digestion
- Poor absorption in the intestines
- Lack of essential fats/vitamins/minerals
- Impaired liver function
- Endocrine abnormalities
- Behavioral feeding issues

## LIVER ISSUES IN PATIENTS WITH SDS

**Abnormalities in infants and young children may include:**

- Liver enlargement
- Abnormal liver function tests

**Other abnormalities include:**

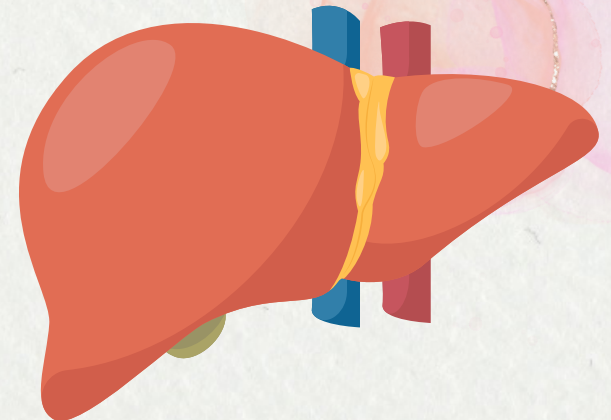
- Chronic liver disease
- Scarring (cirrhosis) of the liver

**Long-term outcomes related to the liver are not known.**

**Many patients with liver issues may be asymptomatic.**

**Current guidelines recommend:**

- Follow liver function tests annually or more often as indicated





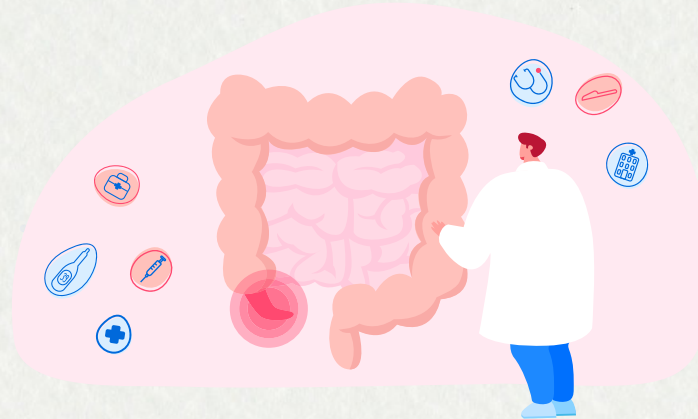
# CURRENT APPROACH CONSIDERATIONS

- **Try to identify GI providers with experience in seeing more than one with SDS or expertise in pancreatic disease**
- **Multi-disciplinary management is important and may include providers from these disciplines:**
  - GI
  - Hematology
  - Nutrition
  - Feeding specialist
  - Endocrinology
  - Psychology
  - Social Work
  - Genetics



# GI SPECIFIC ASSESSMENTS

- Age-relevant pancreatic testing
  - Isoamylase >3 years old
  - Trypsinogen <3 years old
- Liver function testing
- Fat soluble vitamins (ADEK)
- Nutrition consultation should be considered early on



## Also remember, patients with SDS can also get common GI issues including:

- Constipation
- Abdominal pain
- Irritable Bowel Syndrome
- Acid reflux
- Lactose intolerance



# GI SPECIFIC THERAPIES

- **Pancreatic enzyme supplementation**
  - Coated or uncoated formulations
  - Oral, NG-tube feeds, G-tube feeds
  - Dosing is based on age
  - Ensure enzymes are being administered correctly
- **Vitamin supplementation**
  - ADEK
- **Feeding issues**
  - Consider seeing feeding specialist
- **Behavioral issues/oral aversion**
  - Consider seeing behavioral specialist or feeding therapist