Fanconi anemia (FA), named for the Swiss pediatrician Guido Fanconi, is an inherited DNA repair disorder that can lead to bone marrow failure (aplastic anemia), leukemia and/or solid tumors, with oral and gynecologic tumors being the most common. FA is almost exclusively a recessive disorder: if both parents carry a defect (mutation) in the same FA gene, each of their children has a 25% chance of inheriting the defective gene from both parents. When this happens, the child will have FA.

Fanconi anemia and its diagnosis

While the total number of FA patients is not documented worldwide, scientists estimate that the carrier frequency (carriers are people carrying a defect in one copy of a particular FA gene, whose other copy of that same FA gene is normal) for FA in the U.S. is 1 in 181. The incidence rate, or the likelihood of a child being born with FA, is about 1 in 131,000 in the U.S., with approximately 31 babies born with FA each year.

Scientists have now discovered 23 FA genes [FANCA, B, C, D1 (also known as BRCA2), D2, E, F, G, I, J, L, M, N, O, P, Q, RAD51, BRCA1, T, U, W and Y]. Mutations in these genes account for more than 95% of reported Fanconi anemia cases. Mutations in FANCA, FANCC and FANCG are the most common and account for approximately 85% of FA patients worldwide. FANCD1, FANCD2, FANCE, FANCF and FANCL account for 10%, while the remaining FA genes represent less than 5%. Some individuals with FA do not appear to have mutations in these 22 genes, so we anticipate that additional FA genes will be discovered in the future.

FA occurs equally in males and females, except for FANCB patients who are exclusively male. It is found in all ethnic groups. Though originally considered primarily a blood disease, it can affect all systems of the body. The majority of individuals affected by FA develop bone marrow failure, necessitating a stem cell transplant. Many patients develop Acute Myelogenous Leukemia (AML) or Myelodysplastic Syndrome (MDS). Patients who live into adulthood are extremely likely to develop head and neck, gynecologic, and/or gastrointestinal cancer which occur at a much earlier age (20s, 30s, and 40s) than the general population. Patients who have had a successful stem cell transplant and, thus, are cured of the blood problems associated with FA still must have regular examinations to watch for signs of cancer. Research has added years to the lives of people with FA. Decades ago, children rarely survived to adulthood. Now, there are adults with FA that live into their 30s and beyond.

Fanconi anemia individuals are usually smaller than average and some have developmental defects, including thumb and arm anomalies. FA usually reveals itself before children are 12 years old, but in rare cases no symptoms are present until adulthood. First signs of FA may be extreme fatigue, frequent infections, nosebleeds or easy bruising. Blood tests may reveal a low white, red cell or platelet count or other abnormalities, defined medically as anemia. Sometimes MDS or AML is the first sign of FA. On occasion, FA isn’t diagnosed until cancer (usually the type called squamous cell carcinoma) has been identified.

At least 60% of individuals affected by FA are born with at least one physical anomaly. This may include:

- Short stature
- Thumb and arm anomalies: an extra or misshapen or missing thumbs and fingers or an incompletely developed or missing radius (one of the forearm bones)
- Skeletal anomalies of the hips, spine or ribs
- Kidney problems
- Skin discoloration (café-au-lait spots); portions of the body may have a suntanned look
- Small head or eyes
- Intellectual developmental delay or learning disabilities
- Low birth weight
- Gastrointestinal difficulties
- Small reproductive organs in males
- Defects in tissues separating chambers of the heart

The definitive test for FA at the present time is a chromosome breakage test. Chromosomes are structures in the body that are made up of DNA. For the test, some of the patient’s blood cells are treated, in a test tube, with a chemical that fuses different strands of DNA together (called crosslinkers). Normal cells are able to correct most of this type of DNA damage by unfusing the DNA strands and are not severely affected. However, FA cells are unable to break apart the strands of DNA and their chromosomes snap or break. There are two chemicals commonly used for this test: DEB (diepoxybutane) and MMC (mitomycin C). These tests can be performed prenatally on cells from chorionic villi or from the amniotic fluid.

Many cases of FA are not diagnosed at all or are not diagnosed in a timely manner. FA should be suspected and tested for in anyone born with thumb/arm abnormalities.
and anyone developing aplastic anemia at any age, even if no other defects are present. Any patient who develops cancers of the head and neck, gynecologic system or gastrointestinal system (squamous cell carcinoma or adenocarcinoma) at an early age and without a history of tobacco or alcohol use, should be tested for FA. Many FA patients show no other abnormalities and therefore all siblings of FA patients (even those apparently unaffected) should be tested. It is absolutely essential to test for FA before contemplating stem cell transplantation for aplastic anemia or treatment for cancer, as standard chemotherapy and radiation protocols may prove toxic to FA patients.

Since FA is an extremely rare disease with a unique set of complications, it is recommended that whenever possible, patients consult with a comprehensive care center specific to FA (visit www.fanconi.org or email info@fanconi.org to see a current list of FA specialists and care centers). The experts at these centers may serve as consultants on a regular basis. Day-to-day care may be handled by your local hematologist and other local specialists. FARF can help you identify these specialists.

At the present time, stem cell transplantation is the only long-term cure for the blood defects in FA. Stem cells can be taken from a donor’s marrow or peripheral blood, or can be obtained through cord blood harvested at the time of a baby’s birth. To prepare for transplant, the patient’s own bone marrow is destroyed, making space for the new, healthy stem cells to engraft. Donor stem cells can be matched or partially mismatched to the patient’s tissue type. The closer the match, the less likely that the new stem cells will recognize the patient’s cells as foreign and attack them, a complication known as graft-versus-host disease.

Finding more effective treatments and a cure for FA depends on research. Please visit www.fanconi.org to learn about research opportunities and current clinical trials. Always consult your physician before taking any action based on the information presented on this page.

The Fanconi Anemia Research Fund

Lynn and Dave Frohmayer started the Fanconi Anemia Research Fund, Inc. (FARF) in 1989, to fund research into this disease and to provide support to affected families worldwide by medical referral, education, publications, and annual family meetings. More than $24 million has gone to supporting research projects and clinical trials.

The Fund convenes an annual FA Scientific Symposium at which researchers from around the world present the results of their research. This gives researchers the opportunity to connect with one another as well as with individuals with FA and their families. The Symposium also fosters mentorship so that the next generation of FA researchers is supported and strengthened. In addition, the Fund sponsors a variety of smaller, highly specialized scientific meetings, gathering researchers together to focus on specific topics like gene therapy and squamous cell carcinoma.

For families, the Fund holds an annual Family Meeting which is also a recreational camp for parents and children. Besides the networking and recreational aspects of the meeting, physicians and researchers present updates to parents during a six-day conference. This meeting is invaluable for youngsters to meet others with FA and is a fun- and activity-filled environment for parents who can relax with other FA parents and talk directly with FA medical experts. In addition, FARF holds a meeting for adults with FA every year that features both presentations from physicians and researchers and opportunities for networking.

The FA Research Fund publishes many educational materials, including Fanconi Anemia: Guidelines for Diagnosis and Management; the FA Family Newsletter; and the International Fanconi Anemia Treatment and Testing Resource Guide. FARF also encourages families to contribute research materials, such as tumor samples, for FA research. The Fund’s educational materials are sent worldwide to thousands of researchers, physicians, and families.