

# Fanconi Anemia

**Fanconi anemia (FA)** is a rare, inherited chromosome instability syndrome, estimated to occur in 1 in 100,000 live births. Patients with FA have varied clinical manifestations. Most patients experience bone marrow failure at a median age of five years. Progressive pancytopenia and congenital malformations, including short stature, radial aplasia, urinary tract abnormalities, hyperpigmentation, and developmental delay are common symptoms. FA is associated with a predisposition to cancer, particularly acute myeloid leukemia and an increased risk of developing solid tumors. The symptoms of FA are highly variable; treatment depends on the symptoms experienced by the individual patient.

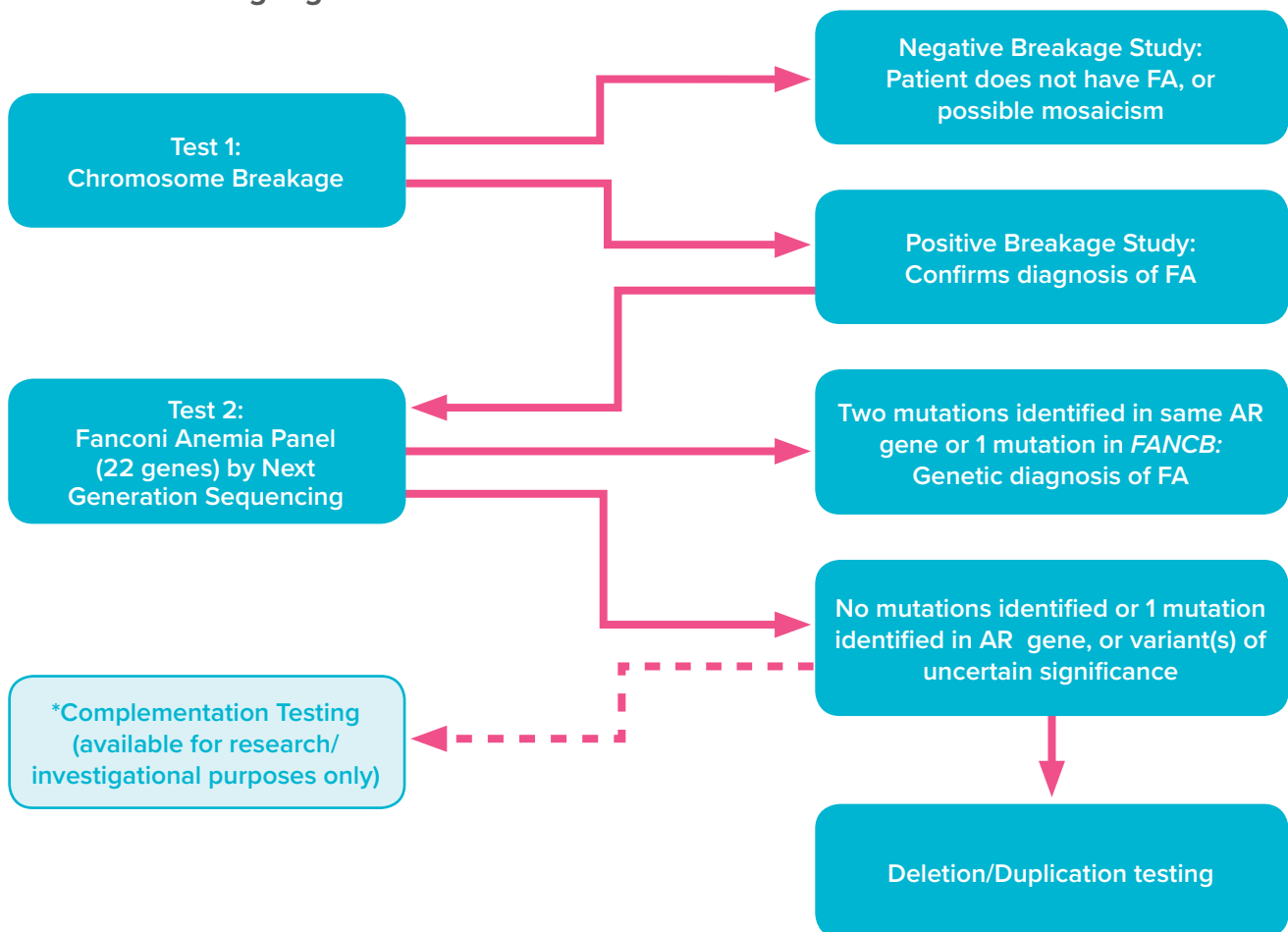
## Indications:

Testing for Fanconi anemia is indicated in young patients with aplastic anemia, arm and/or thumb, cardiac, central nervous system, genitourinary, kidney, and/or skeletal system anomalies, hyper-pigmentation, small size, and/or bleeding disorders.

For more information call 513-636-4474 or visit [www.cincinnatichildrens.org/FanconiTesting](http://www.cincinnatichildrens.org/FanconiTesting)

We also offer testing for other chromosome breakage disorders including Sister Chromatid Exchange (SCE) analysis for Bloom syndrome. Please see our website for additional information.

## Recommended Testing Algorithm



This is the suggested testing algorithm. Please note that any test can be requested in any order.

\*Contact 513-636-5998 for details regarding complementation testing on a research/investigational basis.

# Fanconi Anemia Testing Details

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## Test 1: Chromosome Breakage

When exposed to DNA cross-linkage agents (MMC and DEB), the chromosomes of FA patients will show increased rates of breakage and form abnormal patterns including radials.

### Methodology

Lymphocytes are stimulated and cultured from peripheral blood. Baseline breakage, without a DNA damaging agent, is recorded. Then DNA damaging agents Mitomycin C (MMC) and Diepoxybutane (DEB) are added and breakage is recorded. Twenty-five baseline metaphase cells and 50 cells each from MMC and DEB culture conditions are evaluated concurrently against a control.

### Sensitivity/Specificity

Chromosome breakage in the presence of DEB is the most specific tool when testing for FA and is considered diagnostic. The additional analysis using MCC increases detection rate, especially in the presence of mosaicism.

### Turn-Around Time

14 days (additional time may be needed for fibroblast culture). Please contact the lab if STAT results are needed.

### Specimen

5-10mL peripheral blood in sodium-heparin (green-top) **OR** 5-10mL bone marrow in sodium-heparin (green-top) **OR** skin biopsy **OR** (2) T25 flasks of primary fibroblast cell line.

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## Test 2: Genetic Testing

For patients with a positive chromosome breakage study, the Fanconi Anemia Panel is used to identify the causative mutation(s). This 22 gene panel uses next generation sequencing (NGS) to analyze *BRCA1*, *BRCA2*, *BRIP1*, *ERCC4*, *FANCA*, *FANCB*, *FANCC*, *FANCD2*, *FANCE*, *FANCF*, *FANCG*, *FANCI*, *FANCL*, *FANCM*, *MAD2L2*, *PALB2*, *RAD51*, *RAD51C*, *RFWD3*, *SLX4*, *UBE2T*, and *XRCC2*. Single gene sequencing of each gene on the panel is also available, as is mutation specific analysis for the *FANCC* common IVS4+4 A>T mutation in patients of Ashkenazi Jewish descent.

### Methodology

This test is performed by enrichment of the coding exons, flanking intronic and untranslated regions (5' and 3'), as well as known pathogenic variants (HGMD 2018.4) in the promoter and deep intronic regions of the genes specified above using oligonucleotide probe hybridization followed by next-generation sequencing with >50X coverage at every target base. All pathogenic and likely pathogenic variants, as well as variants of unknown (indeterminate) significance, as determined bioinformatically, are confirmed by Sanger sequencing. Regions with <50X will be filled in by Sanger sequencing. A detailed non-coding variant list is available upon request.

### Sensitivity/Specificity

Greater than 85% of patients with a clinical diagnosis of Fanconi anemia will have mutations in the genes included in the Fanconi Anemia Panel. Large deletions have been reported in most of the FA genes and are not detected by this panel. Targeted deletion and duplication analysis of each gene on this panel is clinically available at an additional charge.

### Turn-Around Time

Up to 6 weeks for NGS of the entire Fanconi Anemia Panel, up to 28 days for analysis of any gene by Sanger sequencing.

### Specimen

At least 3 mLs whole blood in a lavender top (EDTA) tube. Label tube with patient's name, birth date, and date of collection. Please call 513-636-4474 for other specimen types.

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**Complementation Testing** is available on a research basis only. Please call 513-636-5998 for additional details and to arrange testing.