

UCLA ORPHAN DISEASE TESTING CENTER

David Geffen School of Medicine at UCLA, Department of Pathology and Laboratory Medicine
Phone: (310) 206-3694, Fax: (310) 825-0285
ODTC@mednet.ucla.edu

<http://www.odtc.ucla.edu>

Nijmegen Breakage Syndrome (NBS) Test Information and Diagnostic Criteria:

Sample Requirement:

One 10 ml green-topped tube (sodium heparin) of whole blood.

FOR A SUSPECTED DIAGNOSIS OF NBS

1. If the parents are clearly of eastern European origins, an NBS patient would most likely carry the 657del5 mutation. Thus, the DNA single mutation NBS sequencing test would be very specific (~98%) for the diagnosis. Downside: In the US, ethnic origins are often unclear beyond the first generation and if the patient does not have 657del5, the diagnosis of NBS has not been effectively ruled out. Thus, for most US patients, it may be more cost-effective to start with Step 2 and not Step 1.
2. For all other patients suspected of NBS, the most cost-effective approach is to send a 10 ml green-topped tube (sodium heparin) of whole blood. This is automatically processed for 1) DNA isolation, and 2) the cells are transformed with EBV within 4-8 weeks. The DNA is initially tested only for the 657del5 mutation. If it is homozygous for 657del5, the clinical diagnosis is confirmed; no further testing is required and no further charges are made. Turnaround time: 2 weeks. List price: **\$350**.
3. If one or both NBS mutations are still unknown, the transformed cells are tested by a combined western blot and radiosensitivity (colony survival) laboratory procedure with a turnaround time of 3 months (list price: **\$1400**). The sensitivity and specificity for NBS exceed 99% since virtually all NBS patients reported to date lack the NBS protein (nibrin) and this is obvious on a western blot. The radiosensitivity assay also confirms the diagnosis since all NBS patients are radiosensitive using this assay. In addition, if nibrin protein is found but the cells are nonetheless radiosensitive, the physician is alerted that the phenotype may be caused by another double strand break DNA repair disorder, for which followup testing can be discussed with Dr. Gatti.
4. If a diagnosis of NBS is confirmed by our Western blotting and colony survival assay, the entire coding region of the gene should be sequenced to identify the specific mutations since 1) recent data in our lab suggest that certain mutations are associated with milder phenotypes (unpublished) and 2) certain types of mutations may soon be amenable to chemicals that partially correct the expression of a functional protein. Furthermore, gene sequencing is recommended for genetic counseling, prenatal diagnosis and carrier detection. Turnaround time: 1 month. List price: **\$1400**.

For questions, please contact: Richard A. Gatti, M.D.
UCLA School of Medicine
Department of Pathology & Laboratory Medicine
310-825-7618 (tel/fax), rgatti@mednet.ucla.edu