DIAGNOSING & MANAGING X-LINKED CGD CARRIERS

CGD carriers are usually diagnosed when a son, brother, or other male relative is diagnosed with CGD. If there is a family history of CGD and a female patient is showing symptoms, doctors should test for this condition. The most common test today is the Dihydrorhodamine (DHR) test, which measures the percentage of the carrier’s neutrophils that are capable of oxidative burst.

The importance of determining the positive DHR percentage for X-linked CGD carriers

A recent study in the Journal of Allergy and Clinical Immunology found that carriers with CGD-type infections had a median percentage of cells that are 8 percent DHR positive, and those with only autoimmune or inflammatory manifestations had a median percentage of cells that are 39 percent DHR positive. Those with both infections and autoimmunity had positive DHR percentage in the low range of 3 percent to 14 percent.

A positive DHR percentage of less than 10 percent was strongly associated with infections. Strong association persisted when the positive DHR percentage was 20 percent or less. For this reason, it might be prudent to manage CGD carriers in much the same way as those with CGD when their DHR activity falls below 20 percent. Therefore clinical judgment will need to be exercised in deciding whom to offer prophylaxis, but it seems prudent to consider and discuss at least trimethoprim/sulfamethoxazole initiation when the positive DHR percentage is less than 20 percent. In contrast, neither autoimmune nor inflammatory manifestations were correlated with the positive DHR percentage.

The tests to determine CGD carrier status are:

- **Dihydrorhodamine (DHR) test:** can be performed on a very small sample of blood using a flow cytometer to measure the production of oxidants or oxidative function by individual blood neutrophils.
- **Nitroblue tetrazolium (NBT) test:** the principles are the same as the DHR test; the DHR test has mostly replaced the NBT test.
- **Genetic testing:** a genetic test can confirm the presence of the specific genetic mutation that results in CGD. Patients should also be referred to a genetic counselor to learn more about their exact gene mutation.
X-LINKED CGD CARRIER SYMPTOMS
Inflammatory and autoimmune manifestations of carrying the gene for CGD may include:

- Increased risk of infection
- Cutaneous or lupus-like symptoms, such as:
  - skin infections and skin rashes
  - joint pain
  - chronic fatigue
  - photosensitivity
- Acne and boils
- Aphthous ulcer / canker sores
- Gastro-intestinal symptoms
- Slower wound healing
- Chorioretinitis
- Raynaud’s syndrome
- High levels of anxiety and depression

REFERRING X-LINKED CARRIERS TO QUALIFIED SPECIALISTS/PHYSICIANS
While each X-linked CGD carrier is different due to her level of oxidative function and other unrelated health or environmental issues, it is recommended that symptomatic carriers be managed proactively by suitably qualified specialists/physicians, such as an/a:

- Immunologist: can order an NBT or DHR test to determine X-Linked CGD carrier status. Depending on a carrier’s oxidative function, it may be necessary to be treated as a patient with CGD and prescribed CGD prophylaxis as mentioned above. In addition, providers should encourage carriers to schedule regular follow-up appointments to monitor for infection and to be proactive about their health when symptoms of infection or health issues arise.
- Rheumatologist and/or Neurologist: for lupus-like symptoms, skin rashes, chronic fatigue, joint and back pain; consider testing for cutaneous lupus.
- Gastroenterologist: for symptoms of inflammatory bowel disease, e.g. pain and continuous diarrhea and bloody diarrhea.
- Dermatologist: to assess skin/cystic acne and prescribe oral antibiotics or treatment with Accutane in severe cases.
- Psychiatrist/Mental Health Therapist: to assess for anxiety and depression and prescribe appropriate treatment and therapy.
- Sleep Specialist: to assess sleeping patterns relating to symptoms listed above, such as chronic fatigue, anxiety/depression, etc., and determine if intervention is needed.
- Nutritionist: to evaluate diet and consider healthy/anti-inflammatory options to reinforce self-care.

FURTHER RESEARCH ON CGD CARRIERS & THEIR QUALITY OF LIFE
According to a recent study, "Health-Related Quality of Life and Emotional Health in X-Lined Carriers of Chronic Granulomatous Disease in the United Kingdom," published in The Journal of Clinical Immunology, more than 40 percent of those X-linked carriers surveyed experienced moderate or greater levels of anxiety. Higher anxiety scores significantly correlated with higher depression scores, lower self-esteem, presence of joint or bowel symptoms, and higher levels of fatigue. Interestingly, the study found no correlation with the age of participant or degree of oxidative function. The study underlines the importance of CGD testing to ensure carriers are treated holistically, from a medical and mental health perspective.

Increased awareness of female X-linked CGD carrier status will enable medical providers to care for the entire family affected by CGD. These efforts aim to address the serious health issues that women and girls who carry the CGD gene can experience and improve their overall quality of life.