

Definition:

Chronic Granulomatous Disease (CGD) is a genetically determined (inherited) disease characterized by an inability of the body's phagocytic cells to kill certain micro-organisms. As a result of this defect in phagocytic cell function, patients with CGD have an increased susceptibility to infections caused only by certain bacteria and fungi.

The term "phagocytic cell" is a general term used to describe any white blood cell in the body that can "phagocytose", or ingest, micro-organisms. Although phagocytic cells from patients with CGD can move and ingest micro-organisms normally, they are unable to kill certain bacteria and fungi because of abnormal chemical reactions within the cell. Hydrogen peroxide and other oxygen-containing compounds are produced during phagocytosis in normal phagocytes. These oxygen-containing compounds are needed to kill certain bacteria and fungi. The phagocytic cells of patients with CGD are unable to process oxygen properly and create these oxygen-containing compounds. As a result, these patients lack an important mechanism to kill certain bacteria. Thus patients with CGD do not have an increased susceptibility to infection with all organisms. Patients with CGD have normal antibody production, normal T-cell function, and a normal complement system so are not particularly susceptible to viral infections.

CLINICAL PRESENTATION:

There are several genetic types of CGD meaning that about 15% of patients are girls. However the most common form affects boys being X-linked recessive. Children with CGD are usually healthy at birth. However, sometime in their first few months or years of life, they develop recurrent infections, infections that are difficult to treat, or infections that are caused by unusual organisms such as fungi (*Aspergillus* particularly). A common presentation in infancy is skin or bone infected with *Serratia marcescens*. These types of infections in children should always prompt a clinician to test for CGD. The infections may involve any organ system or tissue of the body, but the skin, lungs, lymph nodes, liver, bones and occasionally the brain are the usual sites of infection. Infected lesions may drain pus for a long time, have delayed healing and leave scars. Pneumonia is a recurrent and common problem in patients with CGD with 50% caused by fungal infection. Many of the lung infections

are chronic and in some instances, patients develop lung abscesses. Abscesses of other organs, such as the liver and spleen, can also occur. Infections of the lymph nodes are also relatively common and may affect the lymph nodes of the neck, axilla or groin. Osteomyelitis (bone infections) can also occur. It often involves the small bones of the hands and feet. Osteomyelitis often requires prolonged therapy, but complete healing and return of function usually occurs. Some infections may result in the formation of localized, swollen collections of infected tissue. In some instances, these swellings may cause obstruction of the intestine or urinary tract. They often contain microscopic collections of cells called granulomas. In fact, it is the granuloma formation that was the basis for the name of the disease. Some CGD patients develop a type of inflammatory bowel disease very similar to Crohn's Disease.

DIAGNOSIS:

The diagnosis of Chronic Granulomatous Disease (CGD) is usually first suspected because of serious infections often caused by an unusual microbial species such as *Serratia*, *Nocardia*, *Burkholderia* and *Aspergillus*. The diagnosis of CGD is made by analyzing the metabolic function and killing capacity of the patient's phagocytic cells. A number of tests can be performed to test the metabolic machinery of the cell and determine if the patient's cells can metabolize oxygen correctly and produce hydrogen peroxide and other oxygen-containing compounds. These tests can be done in most tertiary centres. A specialised lab can then confirm the genetic sub-type of CGD that the patient has.

INHERITANCE PATTERN:

Chronic Granulomatous Disease (CGD) is a genetically determined disease and therefore can be inherited or passed on in families. There are two patterns for transmission. The commonest form of the disease is inherited in a sex-linked (or X-linked) recessive manner; i.e. it is carried

on the X-chromosome. The other forms of the disease are inherited in an autosomal recessive fashion; they are carried on chromosomes other than the x-chromosome. It is important to identify the type of inheritance so families can understand the risk for any subsequent children being affected, and the possible implications for other family members.

TREATMENT:

A mainstay of therapy is the early diagnosis of infection and prompt, aggressive use of appropriate antibiotics. A careful search for the cause of infection is important so that sensitivity of the micro organism to antibiotics can be determined. Intravenous antibiotics are usually necessary for treating serious infections in CGD patients and clinical improvement may not be obvious for a number of days in spite of appropriate treatment. Patients with CGD can have such frequent infections, especially as young children, that continuous oral antibiotics (prophylaxis) is often recommended.

The most frequently used antibiotic for prophylaxis is a combination of trimethoprim and sulfamethoxazole (Bactrim or Septrim). A natural product of the immune system, gamma interferon, can also be used to treat patients with CGD in order to boost their immune system. Patients treated with gamma interferon may have fewer infections and when infections do occur they may be less serious. Gamma interferon is given as a subcutaneous injection three times a week.

Many physicians suggest that swimming should be confined to well chlorinated pools since fresh water lakes and salt water swimming may expose patients to organisms which are not virulent (or infectious) for normal swimmers but may be infectious for CGD patients. Patients should also avoid dusty conditions, especially spoiled or mouldy grass and hay and compost, all common sources of *Aspergillus*. Since early treatment of infections is very important, patients are urged to consult their physicians about even minor infections.

EXPECTATIONS:

The quality of life for many patients with Chronic Granulomatous Disease (CGD) has improved remarkably with knowledge of the phagocytic cell abnormality and appreciation of the need for early, aggressive antibiotic therapy when infections occur. Recurrent hospitalization may be required in CGD patients since multiple tests are often necessary to locate the exact site and cause of infections, and intravenous antibiotics are usually needed for treatment of serious infections. Disease-free intervals are increased by prophylactic antibiotics and treatment with gamma interferon. Serious infections tend to occur less frequently when patients reach their teenage years. In fact, many patients with CGD complete high school, with many adult patients holding responsible jobs, getting married and having children of their own; living relatively normal lives.

These booklets are designed to offer medical professionals, patients and their families' basic information about these rare disorders of the immune system.

For further information please contact your immunologist, paediatrician, physician or the National IDF Health Coordinator

Other booklets available:

Living with PID
What is IVIG Therapy
Recurrent infections
Common Variable Immune deficiency (CVID)
X-linked Agammaglobulinaemia (XLA)
Genetic Testing & PID
Selective IgA Deficiency

The Immune Deficiency Foundation Asia-Pacific Alliance, IDFAPA.

An alliance of not-for-profit PID Patient support groups across the Asia Pacific Region.

Contact Us:

Web: www.idfapa.org Email: info@idfapa.org

Post:

The Immune Deficiency Foundation Asia Pacific Alliance Headquarters
C/- PO Box 75-076, Manurewa, Manukau 2243, New Zealand

Members of IDFAPA include:

IDF USA*

web: www.primaryimmune.org
email: idf@primaryimmune.org

40 W. Chesapeake Avenue
Suite 308
Towson, MD 21204
USA

IDF New Zealand*

web: www.idfnz.org.nz
email: info@idfnz.org.nz

IDFNZ / KIDS Foundation
PO Box 75-076
Manurewa, Manukau 2243, NZ.
Phone: 0508 300 600 (NZ toll free)

IDF Australia

web: www.idfaustralia.org
email: info@idfaustralia.org

IDF Australia
PO Box 198, Villawood
NSW. 2163
Australia
Phone: 1800 465 849 (Aust. toll free)

IDF Pacific

web: www.idfpacific.org
email: info@idfpacific.org

IDF Pacific
PO Box 75-076
Manurewa, Manukau 2243
New Zealand.

IDF Asia

web: www.idfasia.org
email: info@idfasia.org

IDF Asia
PO Box 75-076
Manurewa, Manukau 2243
New Zealand.

* Founder Members

*Adapted from the Patient Family Handbook for Primary Immunodeficiency Diseases, 4th Ed., 2007, with the permission of the Immune Deficiency Foundation, USA.
Copyright © 2007 by Immune Deficiency Foundation, USA.*

© IFDNZ/KIDS Foundation 2008

Living with Primary Immune Deficiency Disorders

Chronic Granulomatous Disease(CGD)

