Genetic Diseases

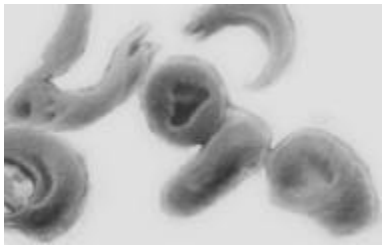
Genetic diseases are a diverse group of disorders caused by mutation and chromosome abnormalities. There are three categories:

1. **Single gene defects** – are caused by mutations which change the coding information of the gene such that it either produces protein which is defective or fails to produce any protein at all. The resulting protein deficiency is responsible for the disease symptoms. The gene mutation may be inherited or arise spontaneously in a germ cell of a parent, which after fertilisation, gives rise to a child who carries the mutation in every cell. Some examples are sickle-cell anaemia, haemophilia and glucose-6-phosphate dehydrogenase (G6PD) deficiency.

2. **Chromosomal mutations** – involve loss or gain of chromosomes or alternations in chromosome structure. Most disorders arise in the parents' germ cells, e.g. Down syndrome.

3. **Multifactorial disorders** – include many common diseases such as diabetes, cardiovascular diseases as well as most congenital abnormalities. They are influenced by genes in complex ways which are poorly understood but involve the interaction of multiple genes and interactions between genes and environmental factors.

Sickle-cell Anaemia



Sickle-cell anaemia is an inheritable genetic disorder in which there is a mutation in the gene producing normal haemoglobin. It occurs most commonly in Africans. The mutated allele is recessive. The mutation results in the wrong amino acid being incorporated into the polypeptide chains which make up the haemoglobin molecule. This in turn leads to abnormal haemoglobin being produced. The abnormal haemoglobin is less efficient at carrying oxygen and causes

red blood cells to become sickle-shaped. The abnormal shape causes the cells to clump together making their passage through blood vessels difficult, thus leading to blockage of blood vessels, depriving tissues of oxygen. As a result, the individual suffers anaemia and may even die. Treatments include blood transfusions and drug therapy, but their effectiveness are limited. Children with sickle-cell anaemia generally lead short, painful lives.

Haemophilia

Haemophilia is an inherited disease in which the blood fails to clot normally leading to slow and persistent bleeding, especially in the joints. It appears worldwide and occurs in all ethnic groups. It is a sex-linked trait in which one of the proteins needed for blood clotting (factor VIII) is missing. The mutated gene is carried on the X chromosome. Haemophilia is potentially lethal. If untreated, a slight injury on a haemophiliac can cause acute pain and severe joint damage leading to disability. Haemophilia can be treated by regular transfusions of factor VIII.

Cystic Fibrosis

Cystic fibrosis is a genetic disease that is usually caused by a recessive allele on chromosome 7. It occurs in about one in every 25,000 babies born to white Europeans, but is much less common in other ethnic groups. Cystic fibrosis causes severe respiratory and digestive problems, along with very salty sweat. The gene mutation stops the production of a protein in cells of the lung, pancreas and other organs. The absence of the protein impairs the cells' ability to transport sodium and chloride ions into and out of the cells. This results in thick, sticky mucus secretions in the lungs and organs, that clog the lungs and also obstruct the ducts of exocrine glands such as pancreas, sweat glands; and can cause irreversible damage.

The treatment depends upon the stage of the disease and which organs are involved. Means of treatment include chest physical therapy and administering antibiotics. In the 1930s the mean life expectancy of cystic

fibrosis patients was 1 year, and with the use of improved antibiotics and intensive physiotherapy, this has now been extended to 30 years. In 1989, the gene responsible for cystic fibrosis was cloned. Many research groups have now focussed their efforts on the development of gene therapy for cystic fibrosis.

Glucose-6-phosphate dehydrogenase (G6PD) Deficiency

G6PD deficiency is the most common known human enzyme disease, affecting 400 million people worldwide. It is an inherited condition caused by a defect in the gene that codes for the enzyme, glucose-6-phosphate dehydrogenase (G6PD). The G6PD gene is located on the X-chromosome and is highly polymorphic, with over 400 alleles known. G6PD deficiency leads to an abnormal rupture of the red blood cells called haemolytic anaemia (abnormally low red blood cell count).

Individuals with G6PD deficiency will have varying degrees of haemolytic anaemia. Usually, haemolytic anaemia are triggered by oxidants such as sulfonamides, anti-malarials, infection, inhaling or touching naphthalene, or by eating some herbal medicine or broad beans (fava beans), that is why it is also referred to as favism. A severe reaction or even death may result if the haemolytic condition is not properly treated. When an anaemic episode occurs, oxygen treatment and bed rest will be given to the individuals. Anaemic individuals are sometimes treated with blood transfusions or administering drugs. In order to prevent the haemolytic condition, G6PD deficient individuals are advised not to take the offending drugs and compounds.

Infants with G6PD deficiency usually develop jaundice (yellowing of the eye), with dark and often black urine. They are placed under special lights to alleviate the jaundice. The diagnosis is made by blood testing which can demonstrate the inadequate levels of the G6PD activity.

G6PD deficiency is quite common in Hong Kong. The prevalence of G6PD deficiency in local male babies is about 4.5%. A neonatal screening

programme on G6PD deficiency was introduced in 1983 by the Department of Health, which aims to prevent possible permanent disabilities caused by the condition.

Thalassaemia

Thalassaemia is a diverse group of genetic blood diseases which occurs mostly in areas surrounding the Mediterranean Sea, Africa and Southeast Asia. It is caused by a mutation in the gene that controls globin production, which leads to a decreased production of normal haemoglobin, resulting in anaemia of varying degree. The severity of thalassaemia depends on the quantity and properties of the globin chain aggregates.

There are three types of thalassaemia: thalassaemia minor (or trait), thalassaemia intermedia and thalassaemia major (disease). Thalassaemia minor is quite common in Hong Kong and accounts for about 8.5% of the population. A person with thalassaemia minor will experience no significant health problems, except a possible mild anaemic which cannot be treated with iron supplements. Thalassaemia intermedia is an intermediate form which requires regular care by a doctor. Thalassaemia major is a more serious disease which requires regular blood transfusions and extensive medical care.

Children with thalassaemia major are normal at birth but become anaemic between the ages of 3–18 months. If they are not treated, they will usually die between 1–8 years old. The only treatment for thalassaemia major is regular blood transfusions, usually every 3 or 4 weeks and lasts for life.

References:

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Websites:

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   http://www.emory.edu/PEDS/SICKLE/index.htm
3. South African Haemophilia Foundation
   http://www.haemophilia.org.za/
4. An introduction to G6PD deficiency
   http://www.rialto.com/g6pd/index.htm
5. Children's Thalassaemia Foundation
   http://www.thalassemia.org.hk/
6. National California Comprehensive Thalassaemia Center
   http://www.thalassemia.com/