Common diseases and disorders LYMPHATIC SYSTEM

Since the lymphatic system is responsible for draining excess fluid from tissues and organs, the most common symptom of diseases and disorders of the lymphatic system is swelling. For example, a disease known as elephantiasis, which is caused by a filarial worm infestation, involves the blockage of the lymphatics. When the lymphatics are blocked, fluid cannot be drained and swelling occurs in the affected areas. Administering ethyl-carbamazine drugs, elevating the area and wearing a compression stocking can treat elephantiasis.

Tonsillitis is another disease of the lymphatic system. Tonsillitis usually involves a bacterial or viral infection located within the tonsils. The tonsils are swollen, and the patient experiences a fever, sore throat, and difficulty swallowing. This can be treated by the use of antibiotics or through a surgical procedure called a tonsillectomy.

A condition common among individuals following surgery for breast cancer or prostate cancer is lymphedema. It is caused by blockage of lymph vessels or lymph nodes located near the surgical site and can result in swollen arms or legs. If microorganisms cause the swelling, then antibiotics are used as treatment. If microorganisms are not the cause, then compression garments and message therapy are used as treatment.

There are also cancers called lymphosarcomas and cancers of the lymph nodes that can affect the lymphatic system. The causes of these cancers are not known and there is not a consensus on what preventative measures can be taken to reduce the risk of developing these cancers. Symptoms of cancers affecting the lymphatic system include loss of appetite, energy, and weight, as well as swelling of the glands. As with many cancers, treatment includes surgical removal followed by adjuvant radiation and chemotherapy.

SOURCE: BOOKS


DISEASES OF IMMUNE SYSTEM

❖ Asthma

Asthma affects more than 5% of the population of the US, including children. It is a chronic inflammatory disorder of the airways characterized by coughing, shortness of breath, and chest tightness. A variety of "triggers" may initiate or worsen an asthma attack, including viral respiratory infections, exercise, and exposure to irritants such as tobacco smoke. The physiological symptoms of asthma are a narrowing of the airways caused by edema (fluid in the intracellular tissue space) and the influx of inflammatory cells into the walls of the airways.

Asthma is a what is known as a "complex" heritable disease. This means that there are a number of genes that contribute toward a person's susceptibility to a disease, and in the case of asthma, chromosomes 5, 6, 11, 14, and 12 have all been implicated. The relative roles of these genes in asthma predisposition are not clear, but one of the most promising sites for investigation is on chromosome 5. Although a gene for asthma from this site has not yet been specifically identified, it is known that this region is rich in genes coding for key molecules in the inflammatory response seen in asthma, including cytokines, growth factors, and growth factor receptors.

The search for specific asthma genes is ongoing. Assisting in this international human effort are model organisms such as mice, which have similar chromosomal architecture to our chromosome 5 site on their chromosomes 11, 13, and 18. Further study of the genes in these areas (and others) of the human genome will implicate specific genes involved in asthma and perhaps also suggest related biological pathways that play a role in the pathogenesis of asthma.

❖ Immunodeficiency with hyper-IgM

Immunodeficiency with hyper-IgM (HIM) is a rare primary immunodeficiency characterized by the production of normal to increased amounts of IgM antibody of questionable quality and an inability to produce sufficient quantities of IgG and IgA. Individuals with HIM are susceptible to recurrent bacterial infections and are at an increased risk of autoimmune disorders and cancer at an early age.

In a normal immune response to a new antigen, B cells first produce IgM antibody. Later, the B cells switch to produce IgG, IgA and IgE, antibodies that protect tissues and mucosal surfaces more effectively. In the most common form of HIM there is a defect in the gene \( TNFSF5 \), found on chromosome X at q26. This gene normally produces a CD40 antigen ligand (CD154), a protein on T cells which binds to the CD40 receptor on B and other immune cells. Without CD154, B cells are unable to receive signals from T cells, and thus fail to switch antibody production to IgA and IgG. The absence of CD 40 signals between other immune
cells makes individuals with HIM susceptible to infections by opportunistic organisms such as Pneumocystis and Cryptosporidium species.

- **Diabetes** is a chronic metabolic disorder that adversely affects the body's ability to manufacture and use insulin, a hormone necessary for the conversion of food into energy. The disease greatly increases the risk of blindness, heart disease, kidney failure, neurological disease, and other conditions for the approximately 16 million Americans who are affected by it. Type 1, or juvenile onset diabetes, is the more severe form of the illness.

Type 1 diabetes is what is known as a 'complex trait’, which means that mutations in several genes likely contribute to the disease. For example, it is now known that the insulin-dependent diabetes mellitus (IDDM1) locus on chromosome 6 may harbor at least one susceptibility gene for Type 1 diabetes. Exactly how a mutation at this locus adds to patient risk is not clear, although a gene maps to the region of chromosome 6 that also has genes for antigens (the molecules that normally tell the immune system not to attack itself). In Type 1 diabetes, the body's immune system mounts an immunological assault on its own insulin and the pancreatic cells that manufacture it. However, the mechanism of how this happens is not yet understood.

About 10 loci in the human genome have now been found that seem to confer susceptibility to Type 1 diabetes. Among these are 1) a gene at the locus IDDM2 on chromosome 11 and 2) the gene for glucokinase (GCK), an enzyme that is key to glucose metabolism which helps modulate insulin secretion, on chromosome 7.

Conscientious patient care and daily insulin dosages can keep patients comparatively healthy. But in order to prevent the immunoresponses that often cause diabetes, we will need to experiment further with mouse models of the disease and advance our understanding of how genes on other chromosomes might add to a patient’s risk of diabetes.

- **DiGeorge syndrome** is a rare congenital (i.e. present at birth) disease whose symptoms vary greatly between individuals but commonly include a history of recurrent infection, heart defects, and characteristic facial features.

DiGeorge syndrome is caused by a large deletion from chromosome 22, produced by an error in recombination at meiosis (the process that creates germ cells and ensures genetic variation in the offspring). This deletion means that several genes from this region are not present in DiGeorge syndrome patients. It appears that the variation in the symptoms of the disease is related to the amount of genetic material lost in the chromosomal deletion.

Although researchers now know that the DGS gene is required for the normal development of the thymus and related glands, counteracting the loss of DGS is difficult. Some effects, for example the cardiac problems and some of the speech
impairments, can be treated either surgically or therapeutically, but the loss of immune system T-cells (produced by the thymus) is more challenging and requires further research on recombination and immune function.

- **Burkitt lymphoma** is a rare form of cancer predominantly affecting young children in Central Africa, but the disease has also been reported in other areas. The form seen in Africa seems to be associated with infection by the Epstein-Barr virus, although the pathogenic mechanism is unclear. Burkitt lymphoma results from chromosome translocations that involve the *Myc* gene. A chromosome translocation means that a chromosome is broken, which allows it to associate with parts of other chromosomes. The classic chromosome translocation in Burkitt lymphoma involves chromosome 8, the site of the *Myc* gene. This changes the pattern of *Myc*’s expression, thereby disrupting its usual function in controlling cell growth and proliferation.

We are still not sure what causes chromosome translocation. However, research in model organisms such as mice is leading us toward a better understanding of how translocations occur and, hopefully, how this process contributes to Burkitt lymphoma and other cancers such as leukemia.

- **Severe combined immunodeficiency (SCID)** represents a group of rare, sometimes fatal, congenital disorders characterized by little or no immune response. The defining feature of SCID, commonly known as "bubble boy" disease, is a defect in the specialized white blood cells (B- and T-lymphocytes) that defend us from infection by viruses, bacteria and fungi. Without a functional immune system, SCID patients are susceptible to recurrent infections such as pneumonia, meningitis and chicken pox, and can die before the first year of life. Though invasive, new treatments such as bone marrow and stem-cell transplantation save as many as 80% of SCID patients.

All forms of SCID are inherited, with as many as half of SCID cases linked to the X chromosome, passed on by the mother. X-linked SCID results from a mutation in the interleukin 2 receptor gamma (IL2RG) gene which produces the common gamma chain subunit, a component of several IL receptors. IL2RG activates an important signalling molecule, JAK3. A mutation in JAK3, located on chromosome 19, can also result in SCID. Defective IL receptors and IL receptor pathways prevent the proper development of T-lymphocytes that play a key role in identifying invading agents as well as activating and regulating other cells of the immune system.

In another form of SCID, there is a lack of the enzyme adenosine deaminase (ADA), coded for by a gene on chromosome 20. This means that the substrates for this enzyme accumulate in cells. Immature lymphoid cells of the immune system are particularly sensitive to the toxic effects of these unused substrates, so fail to reach maturity. As a result, the immune system of the afflicted individual is severely compromised or completely lacking.
Some of the most promising developments in the search for new therapies for SCID center on 'SCID mice', which can be bred deficient in various genes including ADA, JAK3, and IL2RG. It is now possible to reconstitute the impaired mouse immune system by using human components, so these animals provide a very useful model for studying both normal and pathological immune systems in biomedical research.

- **Familial Mediterranean fever (FMF)** occurs most commonly in people of non-Ashkenazi Jewish, Armenian, Arab, and Turkish background. As many as 1 in 200 people in these populations have the disease, with as many as 1 in 5 acting as a disease carrier. FMF is an inherited disorder usually characterized by recurrent episodes of fever and peritonitis (inflammation of the abdominal membrane).

In 1997, researchers identified the gene for FMF and found several different gene mutations that cause this inherited rheumatic disease. The gene, found on chromosome 16, codes for a protein that is found almost exclusively in granulocytes—white blood cells important in the immune response. The protein is likely to normally assist in keeping inflammation under control by deactivating the immune response—without this "brake," an inappropriate full-blown inflammatory reaction occurs: an attack of FMF.

Discovery of the gene mutations will allow the development of a simple diagnostic blood test for FMF. With identification of the mutant protein, it may be easier to recognize environmental triggers that lead to attacks and may lead to new treatments for not only FMF but also other inflammatory diseases.