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**Primary immunodeficiency disorders are inherited conditions sometimes caused by single-gene mutations, or more often by an unknown genetic susceptibility combined with environmental factors. Although some PIDs are diagnosed during infancy or childhood, many are diagnosed later in life.  PIDs are categorised based on the part of the immune system that is disrupted**

### ****Examples of primary immunodeficiency disorders****

1. **B cell immunodeficiencies (adaptive) – B cells are one of two key cell types of the adaptive immune system. Their main role is to produce antibodies, which are proteins that attach to microbes, making it easier for other immune cells to detect and kill them. Mutations in the genes that control B cells can result in the loss of antibody production. These patients are at risk of severe recurrent bacterial infections.**
2. **T cell immunodeficiencies (adaptive) – T cells are the second of two key cell types of the adaptive immune system. One role of the T cell is to activate the B cell and pass on details of the microbe’s identity, so that the B cell can produce the correct antibodies. Some T cells are also directly involved in microbe killing. T cells also provide signals that activate other cells of the immune system. Mutations in the genes that control T cells can result in fewer T cells or ones that do not function properly. This can lead to their killing ability being disrupted, and can often cause problems with B cell function too. Therefore, T cell immunodeficiencies can often lead to combined immunodeficiencies (CIDs), where both T and B cell function is defective. Some forms of CIDs are more severe than others.**
3. S**evere combined immune deficiencies (SCID) (adaptive) – SCID disorders are very rare but extremely serious. In SCID patients there is often a complete lack of T cells and variable numbers of B cells, resulting in little-to-no immune function, so even a minor infection can be deadly. SCID patients are usually diagnosed in the first year of life with symptoms such as recurrent infections and failure to thrive.**
4. Phagocyte disorders (innate) **- phagocytes include many white blood cells of the innate immune system, and these cells patrol the body eating any pathogens they come across. Mutations typically affect the ability of certain phagocytes to eat and destroy pathogens effectively. These patients have largely functional immune systems but certain bacterial and fungal infections can cause very serious harm or death.**
5. Complement defects (innate**) – complement defects are some of the rarest of all the PIDs, and account for less than 1% of diagnosed cases. Complement is the name given to specific proteins in the blood that help immune cells clear infection. Some deficiencies in the complement system can result in the development of autoimmune conditions such as systemic lupus erythematosus and rheumatoid arthritis (please see our autoimmune briefing for more information). Patients who lack certain complement proteins are highly susceptible to meningitis.**

### ****Treatments and outcomes****

**The prognosis of patients with PIDs is extremely variable and depends on the condition. Most SCID patients will die before the age of 1 without prompt treatment, although 95% of those that receive a bone marrow transplant (BMT) before 3 months of age will survive.**

## 2) ****Secondary immunodeficiency (SID)****

**SIDs are more common than PIDs and are the result of a primary illness, such as HIV, or other external factor such as malnutrition or some drug regimens. Most SIDs can be resolved by treating the primary condition.**

### ****Examples of secondary immunodeficiency disorders****

**Malnutrition – Protein-calorie malnutrition is the biggest global cause of SIDs which can affect up to 50% of the population in some communities in the developing world.T cell numbers and function decrease in proportion to levels of protein deficiency, which leaves the patient particularly susceptible to diarrhoea and respiratory tract infections. This form of immunodeficiency will usually resolve if the malnutrition is treated.**

**Drug regimens – There are several types of medication that can result in secondary immunodeficiencies, but these drugs also perform critical roles in certain areas of healthcare. Immunosuppressant is a common side-effect of most chemotherapies used in cancer treatment. The immune system usually recovers once the chemotherapy treatment has finished. Another common use for immunosuppressive drugs is the prevention of transplant rejection, where medication is required to suppress the transplant recipient’s immune system and prevent it from targeting the transplanted tissue. These drugs can have significant side-effects and often suppress more areas of the immune system than are required, leading to susceptibility to opportunistic infections. Use of a new generation of medicines called biologics is becoming more widespread in treating transplant rejection. These drugs are derived from biological sources like cells, rather than chemical structures. Monoclonal antibodies are one such class of biologics and these drugs are made by farming antibodies from B cells that will act against a specific part of the disease process. These agents are more specific in their action than traditional drugs and have fewer side effects on non-target immune cells.**

### **Treatments and outcomes**

**For many SID disorders treatment of the primary condition will lead to resolution of the immunodeficiency. This is of limited use in chronic conditions such as organ transplantation or HIV where the emphasis is on managing the condition to minimize immunodeficiency. With advances in medical science the prognosis for these patients is now much improved. There is evidence to suggest that more patients with HIV now die from toxicity associated with the anti-retroviral therapy than the disease itself, and that managing this is the next big challenge. Comorbidities, such as secondary infections, are a major cause for concern and account for a high proportion of deaths in SID patients. As with PIDs, high community vaccine rates and herd immunity are vital to prevent transmission of common diseases to immunocompromised individuals, who cannot be vaccinated.**