DEFINITIONS

1. **Pernicious Anaemia** is a disease in which there is **atrophy of the fundus and body of the stomach,** leading to severely reduced or absent secretion of intrinsic factor. The consequence of this is severe malabsorption of vitamin B12, thus leading to B12 deficiency. Although primarily a disease of the stomach, it is best considered with the blood diseases since it usually presents with anaemia.

2. **Intrinsic factor** is a glycoprotein secreted in the stomach. The secretion of intrinsic factor is necessary for the absorption of vitamin B12.

3. Pernicious anaemia is a **megaloblastic anaemia** in type. This is characterised by abnormally large red blood corpuscles (macrocytes) and distinctive morphological abnormalities of the developing haemopoietic cells in the bone marrow. In severe cases, the anaemia may be associated with a reduction in the number of white blood cells and platelets.

CLINICAL FEATURES

4. The anaemia usually develops gradually, perhaps over several years, and symptoms may not appear until the condition is severe.

5. The most common complaints are those due to the anaemia (eg. weakness, tiredness, dyspnoea on exertion). There is loss of mental and physical drive. The tongue is sore and may be red, smooth and shiny in appearance.

6. Mild jaundice, loss of appetite and weight, indigestion and episodic diarrhoea are frequent. An intercurrent infection may precipitate severe anaemia. Older patients may present with congestive cardiac failure, and in a few patients there may be marked bruising.

7. Paraesthesiae in the feet or hands, numbness, or difficulty in walking may occur; the vitamin deficiency causes a severe neuropathy, in particular degeneration of the lateral and posterior columns of the spinal cord. This is known as **subacute combined degeneration of the spinal cord,** and leads to a symmetrical neuropathy affecting the lower limbs more than the upper. It may occur before anaemia develops.

AETIOLOGY

8. **Chronic gastritis** is a necessary precursor of pernicious anaemia; the sequence is that superficial chronic gastritis leads to atrophic gastritis, which in turn progresses to gastric atrophy. There are two types of chronic gastritis, named type A and type B. Gastric mucosal biopsy is the most reliable investigation for distinguishing between the different types of chronic gastritis.

9. Type A gastritis is less common, affects the fundus and body of the stomach, and produces antibodies to parietal cells and to intrinsic factor. Type A chronic gastritis is the type which is associated with pernicious anaemia.

10. Type B gastritis is much more common. It affects the gastric antrum initially but eventually comes to involve the whole stomach. It becomes increasingly common with age and is thought to be present in nearly everybody aged 70 or over. It is now accepted that this type of gastritis is caused by the bacterium Helicobacter pylori.

11. **Pernicious anaemia is an autoimmune disease** and in about 50% of cases antibodies to intrinsic factor can be demonstrated. It may be associated with other autoimmune diseases such as primary hypothyroidism, thyrotoxicosis, Hashimoto's disease, Addison's disease, vitiligo and type 1 diabetes mellitus.

12. The body's immune system provides an essential barrier to a large range of pathogenic organisms. **Autoimmune disease** occurs if the immune network response becomes directed at the body itself rather than at foreign antigens, and thereby causes damage to the body's tissues.

13. Most work on autoimmune disease and its mechanisms has been done in animals. Despite recent advances in the molecular biology of the immune response, the precise aetiology of autoimmune disease remains unknown. In humans genetic factors are thought to play a part. This is supported by studies of familial aggregation of the conditions, and high concordance in monozygotic twins. However concordance is not complete and therefore genetic factors alone are insufficient for disease to develop.

14. Environmental factors which have been postulated as producing disease in predisposed individuals include infection (viral and bacterial), drugs and toxins. However positive identification of specific factors in the individual conditions and cases is very rare.

15. As noted above, individuals with one autoimmune disease appear to be at increased risk of other autoimmune conditions. These further conditions do not arise as a consequence of the first, rather the common factor is the genetic predisposition.

16. In Western countries pernicious anaemia is the most frequent cause of megaloblastic anaemia. It is a disease of older people, less than 10% of cases being aged under 40 years, most occurring between the ages of 45-65 years. There is a higher incidence in females and in people of blood group A. Within the United Kingdom there are regional differences in incidence, the disease being more common in Scotland and less common in Southeast England. It occurs in all races but is most frequent in Northern Europeans and persons with early greying and blue eyes. There is a higher incidence in close relatives of either sex.

17. No specific environmental factors have been identified in the causation of pernicious anaemia.

CONCLUSION

18. **Pernicious anaemia** is a sequel of type A chronic gastritis; it is a disorder in which atrophy of the fundus and body of the stomach leads to malabsorption of vitamin B12, which in turn gives rise to a megalobastic anaemia. Pernicious anaemia is recognised as an **autoimmune disease**. No specific external factors have been identified in its causation.

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