LECTURE: 12

Title: ASSESSMENT OF AUTOANTIBODIES

LEARNING OBJECTIVES:

The student should be able to:

- **Describe the indication of the presence of autoantibodies.**
- **Explain the useful value of the major autoantibodies regarding to diagnostic laboratory tests.**
- **Enumerate some major encountered autoantibodies such as:**

- **Thyroid autoantibodies**
- **Adrenocortical autoantibodies**
- **Acetylcoline receptor autoantibodies**
- **Salivary gland autoantibodies**
- **Reticulin autoantibodies**
- **Islet cell autoantibodies**
- **Gastric autoantibodies.**
- **Striated muscle autoantibodies.**
- **Smooth muscle autoantibodies.**
- **Mitochondrial autoantibodies.**
- **Myelin autoantibodies.**
- **Skin autoantibodies.**
- **Autoantibodies to nucleus (antinuclear antibodies), include anti-DNA, histone, and non-histone antibodies.**

- **Explain the action of specific autoantibodies and their use in medial diagnosis such as:**

- ***Acetylcholine receptor (AchR)***
- **Anti-adrenal antibody**
- **Anti-cenriole antibody**
- **Anti-DNA antibody**
- **Anti-glomerular basement membrane antibody**
- **Anti- LKM antibody**
- **Anti-myelin antibody**
- **Anti-neutrophil antibody**
- **Anti-platelet antibody**
- **Anti-rheumatoid arthritis nuclear antigen (Anti-RANA)**
- **Anti-nuclear ribonucleoprotein (anti-nRNP)**
- **Anti-skin(interepithelial)antibody**
- **Anti-smooth muscle antibody**
- **Anti-SS-A (SS-A precipitin; anti-Ro)**
- **Anti-striation antibody**
- **Anti-thyroglobulin and anti-thyroid microsome antibody**
- **Mi-1 antibody**
- ***Acetylcholine receptor (AcHR)***
- **Anti-cardiolipin antibody (ACA)**
- **Anti-centromere antibody**
- **Anti-intrinsic factor antibody**
- **Anti-islet cell antibody**
- **Anti-mitochondrial antibody**
- **Anti-parietal cell antibody**
- **Anti-myocardial antibody**
- **Anti-nuclear antibody (ANA)**
- **Anti-reticulin antibody**
- **Anti-ribosome antibody**
- **Anti-Sc1 or Anti-Sc1-70 antibody**
- **Anti-skin antibody (dermal-epidermal)**
- **Anti-Sm antibody**
- **Anti-sperm**
- **Anti-SS-B (SS-B precipitin, anti-La)**
- **Cardiolipin antibody**
- ***Jo-1* antibody**
- ***Ku* antibody**
- **PM-1**

LECTURE REFRENCE:

1. TEXTBOOK: MARY LOUISE TURGEON. 2ND edition. chapter 26. p 345-7
2. HANDOUT.

Human autoantibodies can be directly pathogenic

When investigating human autoimmunity directly, rather than using animal models, it is of course more difficult to carry out experiments. Nevertheless, there is much evidence to suggest that autoantibodies may be important in pathogenesis, and we will discuss the major examples here.

Thyroid autoimmune disease **–** A number of disease have been recognized in which autoantibodies to hormone receptors may actually mimic the function of the normal hormone concerned and produce disease. Graves' disease (thyrotoxicosis) was the first disorder in which such antireceptor antibodies were clearly recognized. The phenomenon of neonatal thyrotoxicosis provides us with a natural 'passive transfer' study, because the IgG antibodies from the thyrotoxic mother cross the placenta and react directly with thyroid stimulating hormone (TSH) receptor o the neonatal thyroid. Many babies born to thyrotoxic mothers and showing thyroid hyperactivity have been reported, but the problem spontaneously resolves as the antibodies derived from the mother are catabolized in the baby over several weeks.

Whereas autoantibodies to the TSH receptor may stimulate cell division and/or increase the production of thyroid hormones, others can bring about the opposite effect by inhibiting these functions, a phenomenon frequently observed in the receptor responses to ligands which act as agonists or antagonists. Different combinations of the various manifestations of thyroid autoimmune disease, chronic inflammatory cell destruction and stimulation or inhibition of growth and thyroid hormone synthesis, can give rise to a wide spectrum of clinical thyroid dysfunction (**Figure-1**).

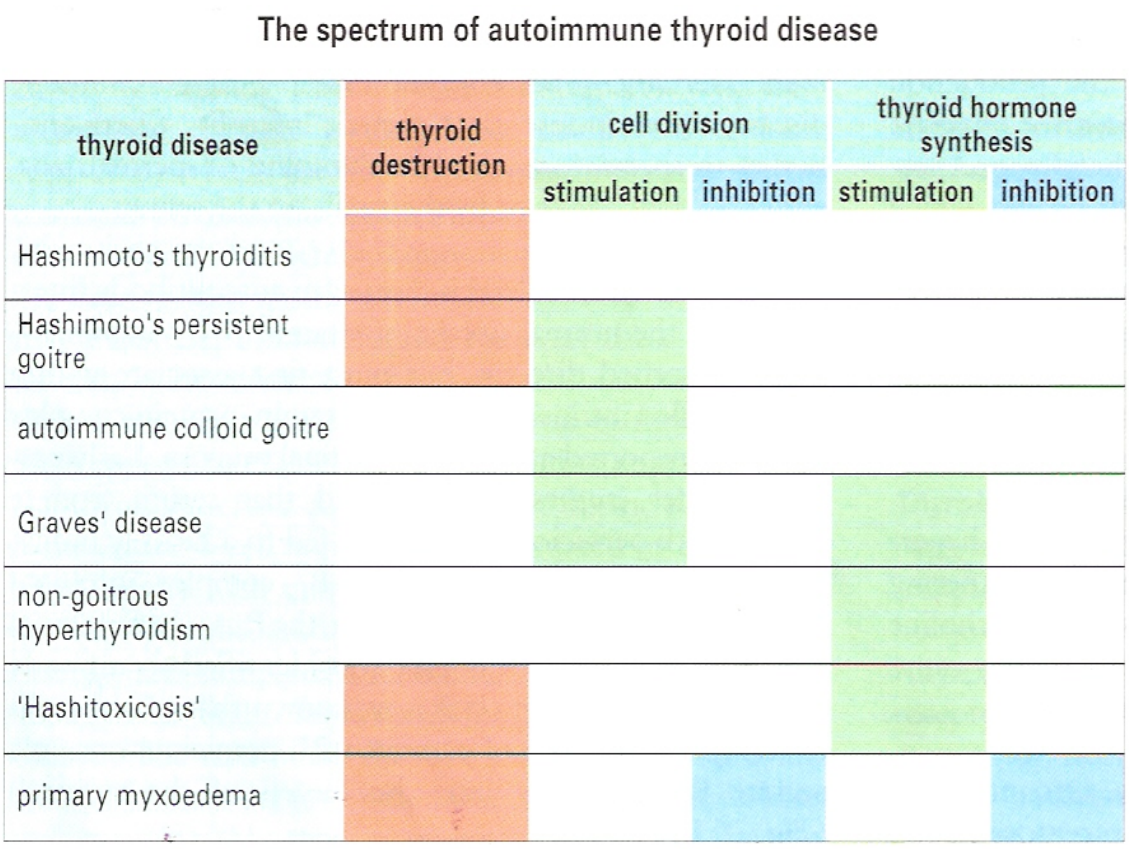

Figure1 Responses involving thyroglobulin and the thyroid peroxidase (microsomal) surface microvillous antigen lead to tissue destruction, whereas autoantibodies to TSH (and other?) receptors can stimulate or block metabolic activity or thyroid cell division. 'Hashitoxicosis' is an unconventional term which describes a gland showing Hashimoto's thyroiditis and Graves' disease simultaneously.

Myasthenia gravis – A parallel with neonatal hyperthyroidism has been observed with mothers suffering from myasthenia gravis, where antibodies to acetylcholine receptors cross the placenta into the fetus and may cause transient muscle weakness in the newborn baby.

Other receptor diseases – Somewhat rarely, autoantibodies to insulin receptors and to β-adrenergic receptors can be found, the latter associated with bronchial asthma. Neuromuscular defects can be elicited in mice injected with serum from patients with the Lambert – Eaton syndrome containing antibodies to presynaptic calcium channels, while sodium channel autoantibodies have been identified in the Guillain – Barre syndrome.

Male infertility – Yet another example of autoimmune disease is seen in rate cases of male infertility were antibodies to spermatozoa lead to clumping of spermatozoa, either by their heads or by their tails, in the semen.

Pernicious anaemia – In this disease an autoantibody interferes with the normal uptake of vitamin B_{12}.Vitamine B_{12} is not absorbed directly, but must first associated with a protein called intrinsic factor; the vitamin-protein complex is then transported across the intestinal mucosa. Early passive transfer studies demonstrated that serum from a patient with pernicious anaemia, if fed to a healthy individual together with intrinsic factor - B_{12} complex, inhibited uptake of the vitamin. Subsequently, the factor in the serum which blocked vitamin uptake was identified as antibody against intrinsic factor. It is now known that plasma cells in the gastric mucosa of patients with pernicious anaemia secrete this antibody into the lumen of the stomach (**Figure-2**).

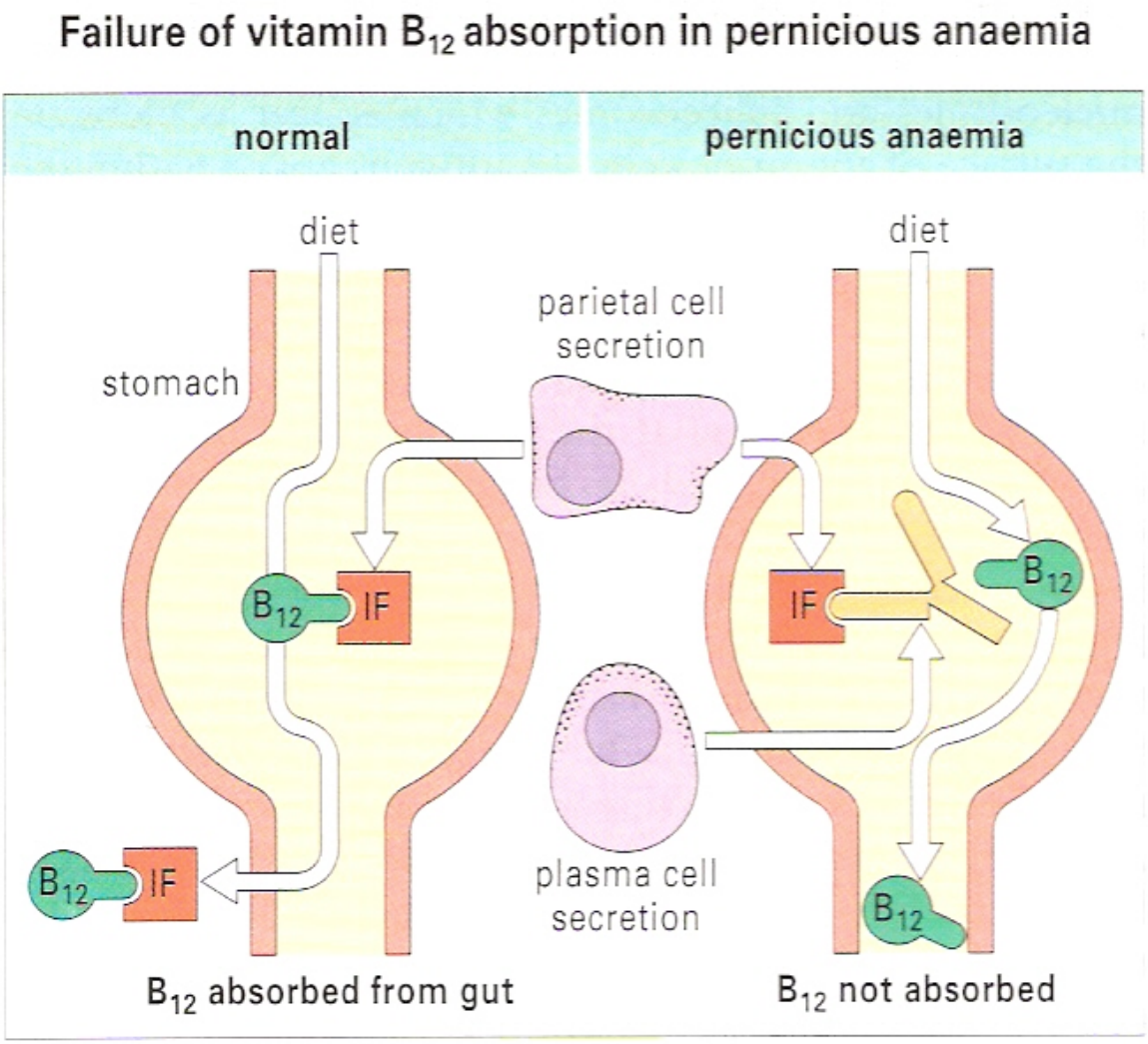

Figure-2 Normally, dietary vitamin B_{12} is absorbed by the small intestine as a complex with intrinsic factor (IF), which is synthesized by parietal cells in gastric mucosa. In pernicious anaemia, locally synthesized autoantibodies, specific for intrinsic factor, combine with intrinsic factor to inhibit its role as a carrier for vitamin B_{12}.

Goodpasture's syndrome – In goodpasture's syndrome, antibodies to the glomerular capillary basement membrane bind to the kidney *in vivo* (**Figure-3**). To demonstrate that the antibodies can have a pathological effect, a passive transfer experiment was performed. The antibodies were eluted from the kidney of a patient who had died with this disease, and injected into primates whose kidney antigens were sufficiently similar for the injected antibodies to localize on the glomerular basement membrane. The injected monkeys subsequently died with glomerulonephritis.

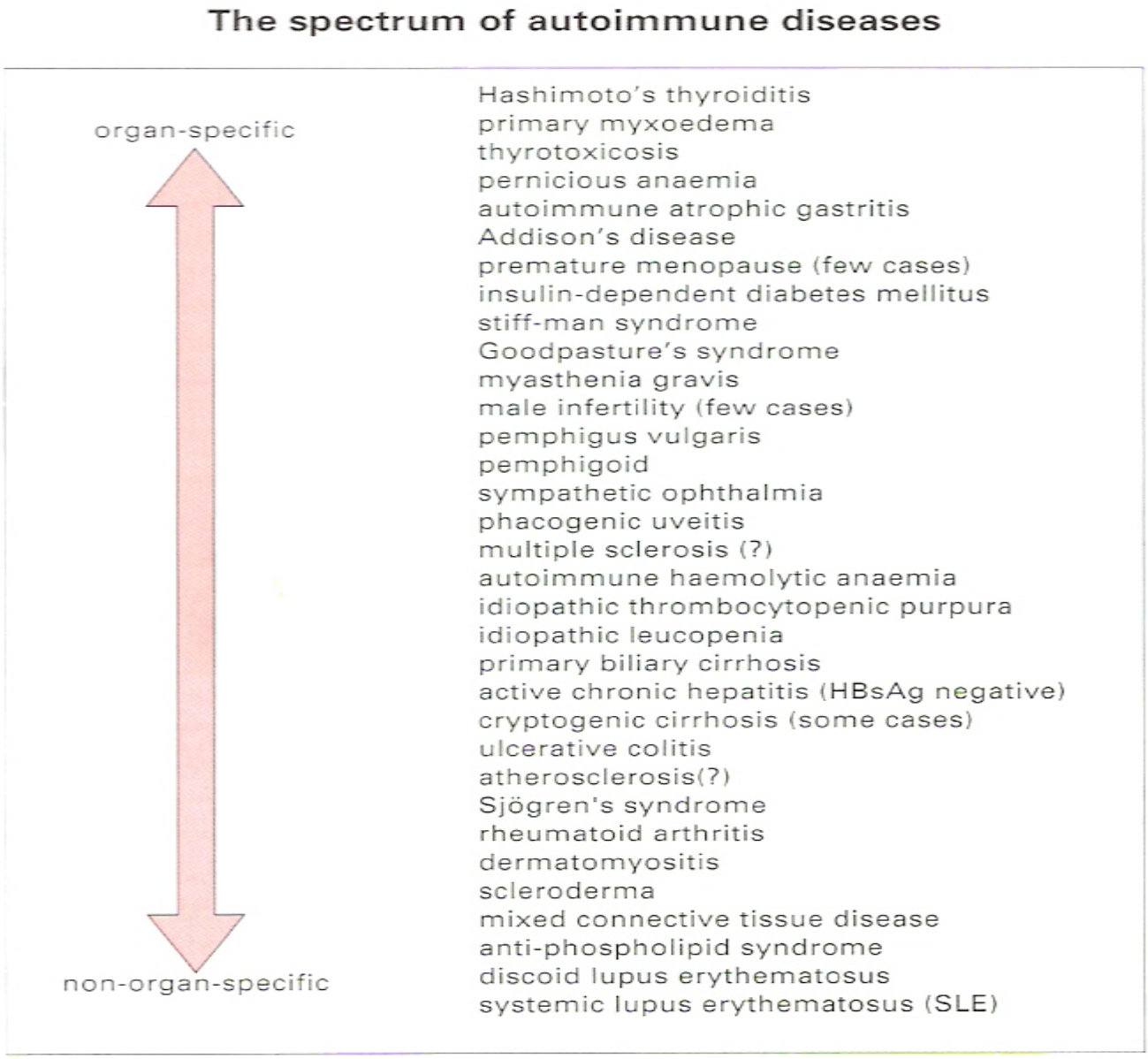

Figure-3 Autoimmune diseases may be classified as organ-specific or non-organ-specific depending on whether the response is primarily against antigens localized to particular organs, or against widespread antigens.

Blood and vascular disorders – Autoimmune haemolytic anaemia and idiopathic thrombocytopenic purpura result from the synthesis of autoantibodies to red cells and platelets, respectively. The primary antiphospholipid syndrome characterized by recurrent thromboembolic phenomena and feta loss is triggered by the reaction of autoantibodies with a complex of β_2-glycoprotein turns up again as an abundant component of atherosclerotic plaques and there is increasing attention to the idea that autoimmunity may initiate or exacerbate the process of lipid deposition and plaque formation in this disease, the two lead candidate antigens being heat-shock protein 60 and the low-density lipoprotein, apoprotein B. The necrotizing granulomatous vasculitis which characterizes Wegener's granulomatosis is associated with anibodies to neutrophil cytoplasmic proteinase III (cANCA) but their role in pathogenesis of the vaculitis is ill defined.

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