pylori infection, including local IL-10 production, increases in regulatory T cells (Tregs) in the gastric mucosa and increased antigen-presenting cell (APC) phagocytosis of apoptotic cells all contribute to persistence of chronic H. pylori gastritis.

Diagnosis

Active disease can be diagnosed with endoscopic biopsy, which has high sensitivity and specificity, while simultaneously assessing peptic and malignant complications. Noninvasive testing for *H. pylori* infection includes serum antibody detection (best used in highly endemic areas to predict active infection), urea breath testing (limited by expense and possible false-positive results), and fecal antigen testing (which has potential advantages in the setting of intestinal metaplasia and after antibiotic treatment).

Lecture No. 8

Autoimmune Hepatitis

Autoimmune hepatitis(AIH) is a progressive inflammation of the liver that has been identified by a number of different names, including **autoimmune chronic active hepatitis (CAH), idiopathic chronic active hepatitis** and **lupoid hepatitis**. The reason for this inflammation is not certain, but it is associated with an abnormality of the body immune system. It is a rare condition characterized by active inflammation, liver cell necrosis and fibrosis, which may lead to hepatic failure, cirrhosis and ultimately death.The disease affects young to middle-aged women, many of whom (60%) are associated with other autoimmune diseases, such as diabetes mellitus, thyroiditis, rheumatoid arthritis, ulcerative colitis crohns disease and glomerulonephritis.

Pathophysiology

Evidence suggests that liver injury in a patient with autoimmune hepatitis is the result of a cell-mediated immunological attack. This attack is directed against genetically predisposed hepatocytes. Aberrant display of human leukocyte antigen (HLA) class II on the surface of hepatocytes (normally not expressed on liver cells), facilitates the presentation of normal liver cell membrane constituents as autoantigenic peptides to $CD4^{+}$T cells.

Causes

It is not clear why autoimmune hepatitis develops. Researchers suspect that some people inherit a genetic disposition that could make them more likely to develop it. Sometimes drugs (e.g., interferon) or viral infections (e.g., acute hepatitis A or B, Epstein-Barr virus infection) have been suggested to play a role in triggering AIH, possibly through molecular mimicry and cross-reactivity between their epitopes and liver antigens, trigger the development of the disease.

Symptoms

The clinical features of AIH can be quite variable. About 25% of individuals are asymptomatic and are diagnosed only after abnormal liver function tests are found

coincidentally when blood work is performed. Adults usually present with an unexpected onset of vague symptoms, including: fatigue, nausea, weight loss, abdominal pain, itching, and maculopapular rashes. Less often, patients have symptoms of portal hypertension such as gastrointestinal bleeding or hypersplenism. Jaundice may also be present. Rarely, the initial presentation is fulminant liver failure requiring liver transplantation.

Types of Autoimmune Hepatitis

Based on autoantibody marker, **Autoimmune hepatitis** is recognized as a heterogeneous disorder and has been subclassified into 3 types:

- Type 1 autoimmune hepatitis.
- Type 2 autoimmune hepatitis.
- Type 3 autoimmune hepatitis.

Clinical feature	Type 1	Type 2	Type 3
Diagnostic autoantibodies	ASMA, ANA, Anti-actin	Anti-LKM	Anti-SLA
Age	10 y elderly	Pediatric (2-14y) Rare in adults	Adults (30-50 y)
Women (%)	78	89	90
Concurrent immune disease (%)	41	34	58
Gamma globulin elevation	+++	+	+++
Low IgA	No	Occasional	No
HLA association	B8, DR3, DR4	B14, DR7, C4AQO	Uncertain
Steroid response	+++	++	+++
Progression to cirrhosis (%)	45	82	75

ASMA: anti-smooth muscle antibody.

ANA: antinuclear antibody, primarily in homogenous pattern.

Anti-actin: antibodies to actin a cytoskeletal protein.
Anti-LKM: anti-liver-kidney microsomal antibodyreact with epitopes on the 2D6 isoform of cytochrome P450 as autoantigen.
Anti-SLA: anti- soluble liver antigen.

	Autoimmune hepatitis	Hepatitis B or C associated
Proportion of all cases of CAH in the UK*	50–80%	20–50%
Sex	Female > male (6 : 1)	Male > female (9 : 1)
Age at onset	10–30 years 40–60 years	Elderly
Associated autoimmune disease	Common	Rare
Smooth-muscle antibodies	Positive 70% High titre	Low titre or absent
Antinuclear antibodies	Positive in 80%	Negative
Anti-DNA antibodies	May be positive	Negative
Antimitochondrial antibodies	Positive 25%	Negative
Antibodies to liver and kidney microsomes	Positive 4% (especially children)	Negative
Serum immunoglobulins	IgG ↑↑	Normal or IgG ↑
HLA type	HLA-B8, -DR3	?
Response to steroids	Good	?
Risk of hepatoma	Low	High

Lecture No. 9

Primary Biliary Cirrhosis

Primary biliary cirrhosis (PBC) is an autoimmune disease of the liver that results in chronic injury to the intrahepatic bile duct epithelium. The gradual inflammatory destruction of the bile ducts causes cholestasis with the subsequent retention of toxins, inciting further hepatic injury and resulting in fibrosis, cirrhosis, and eventual liver failure. It is most common in women over the age of 50. The ratio of affected women to men has been reported to be as high as 9:1.

Causes

The cause of the disease is unknown, but research indicates that there is immunological basis for the disease, making it an autoimmune disorder. Most of the patients (>90%)seem to have anti-mitochondria antibodies (AMAs) against pyruvate dehydrogenase complex (PDC-E2), an enzyme complex that is found in the inner mitochondria membrane. Molecular mimicry is the most widely proposed explanation as to the induction of autoimmunity in PBC. Briefly, a host is infected with a microorganism that contains antigens similar to antigens present in the host. These microbial antigens induce an immunologic response when presented to the immune system of the host. As a result, what began as a pathogen-specific response then cross-reacts with the host antigens and results in tissue injury and disease.

The predisposing role of the HLA system to the disease has not been fully clarified, although a weak but significant association with HLA-DR8 has been reported.