

In continuation with the Gastrointestinal Pathology series for undergraduates, let's learn another interesting topic in GI Pathology that is Celiac disease. We talked about the epidemiological aspect and understood in simpler terms about the pathogenesis. The celiac is from the latin word called celiacus which basically an ancient greek word called you know uh coleacus which means belly whereas sprue is an adaptation this is an english word an adaptation from the dutch sprou which was originally used to refer to persistent Diarrhea disease in Holland, you know, probably because of celiac disease itself So that's how it was referred to as celiac sprue But then now because we know the etiology very well it is referred to as gluten sensitive enteropathy Now coming to the epidemiology The worldwide incidence of celiac disease is around 0.6 to 1 percent where the prevalence varies very widely among countries and regions Now straight away we will move into understanding the pathogenesis of Celiac disease. These are the two major autoantibodies and there are some variants of tissue transglutaminase antibodies which can bind to transglutaminase isotypes outside of the intestine and that's why these patients also manifest skin manifestations like dermatitis, epideformis and fertility and other neurological compounds. It's also known as gluten sensitive enteropathy, which is basically a chronic immune mediated disorder, which is triggered by the ingestion of gluten containing foods, such as you know the wheat, the rye and the barley. When I talk about nutritional deficiency, because of malabsorption there can be iron deficiency with anemia, there can be deficiencies of vitamin D, vitamin B12, folic acid and even zinc and if steatorrhea is predominant they can manifest with vitamin A, E, R, K deficiency. Now we know the major antibodies produced by this interaction is autoantibodies to tissue, transglutaminase II and autoantibodies to deamidated gliadin peptides. So this is the aggressive proliferation or neoplastic transformation of this proliferation is basically enteropathy associated T cell lymphoma and second important type of malignancy is small intestinal adenocarcinoma. Now we will look into the definition, the epidemiology, the pathogenesis, the morphology, the clinical features, diagnosis and a bit about treatment including prognosis of Celiac disease. So whenever the cell is stressed due to any of those trigger factors which I told earlier, what happens is that these stressed cell, they express this particular antigen that is MICA which basically stands for MHC class 1 chain related protein A. This is a normal intestinal epithelium with microvilli. There will be a resolution of symptoms, there will be reduced antibody titers, there will be restoration of normal or near normal mucosal histology and there can be reduction of the risk of long term complications. See this gliadin is alcohol soluble and this is the one which gives plasticity and elasticity to the gluten whereas glutinin is water soluble and that's the one which gives strength and structure to the gluten protein. So there is damage of epithelial cells by intra epithelial T lymphocytes and also by the CD4 positive T lymphocytes which are activated by the antigen presenting cells with the help of deamidated gliadin, right. So there is epithelial damage because of interaction between the telomphocytes, intra epithelial telomphocytes which are activated and then they attack the cell which carry MICA molecule, right. Now this deamidated gliadin interacts with the antigen presenting cells in the lamina And this antigen presenting cell has the receptor for the deamidated gliadin. And as I told you the skin manifestations can be. There can be itchy blistering skin lesions or dermatitis herpity formus. They present with irritability, abdominal distension, anorexia, chronic diarrhea, failure to thrive, weight loss or even muscle wasting. So it is the gliadin component of the gluten which is the culprit in

celiac disease pathogenesis. There are some non-HLA genes also which basically deal with regulation of T cell differentiation, survival, migration and cytotoxicity by these T cells. So gluten basically you know it is digested in the lumen of the intestines by various enzymes. And this gliadin you know when they interact with the intestinal epithelial cell, it stimulates the epithelial cell to produce interleukin-15. The passage of other gliadin molecules or other gliadin peptides into the lamina propria. Now in the lamina propria this gliadin is deamidated by tissue transglutaminase. So stimulation of CD4 positive T lymphocytes results in the production of interferon gamma, okay and many other cytokines. So the interferon gamma damages the epithelial cells and the T cell also stimulates the other B cells to produce antibodies. That's because interleukin-15 as we saw it triggers activation and proliferation of intraepithelial lymphocytes, right? Other than that, this interleukin-15 also renders T cells resistant to inhibition by regulatory T cells which basically means there is loss of tolerance. Celiac disease average age of diagnosis is around fifth decade of life and you know they present with diverse clinical manifestations and that's a challenge by itself to make a diagnosis of celiac disease. They can be present with delayed gastric emptying time, heartburn, steatorrhea and weight loss in severe cases. Whereas in children, it affects both males and females equally and classically the symptoms begin. And these villi are lined by colonic epithelium interspersed with goblet cells. So shortening of villi and increased number of intraepithelial villi is very characteristic of celiac disease. IgA antibodies are IgG antibodies against deamidated gliadin peptides. Once if there is any cytological test which comes out positive, then you have to subject the patient for endoscopy and duodenal biopsy for confirmation because in the background of these antibodies, presence of antibodies. Now, if the symptoms persist even after adherence to strict gluten free diet, then you consider this could be a refractory sprue. That's what we are looking at. The sequel of celiac disease is that there is increased risk of malignancy and the most common type of malignancy is enteropathy associated. T cell lymphoma and this malignancy is basically an aggressive lymphoma of intra epithelial T lymphocytes. We looked into morphology and clinical features and the diagnosis and treatment aspect of celiac disease. And remember in genetically predisposed individuals, that's very important to note that this disease does not occur in every individual. In all the individuals basically it occurs in genetically predisposed individuals. It's basically a major storage protein which is they are deposited in starch endosperm cells of the developing grain. So for us. To understand the celiac disease we need to remember that gliadin is the one which contains most of the disease producing components. Now we know that celiac disease occurs in a genetically predisposed or a genetically susceptible host, right? That means the ones who are susceptible are the individuals who carry the genes for HLA-DQ2 and HLA-DQ8. They are also implicated but the most important ones are the individuals who carry these genes HLA-DQ2 and HLA-DQ8. These MICA cells, the cells with MICA .marker, they are attacked by this NKG2D expressing lymphocytes