IMMUNOLOGICAL ASPECTS OF LIVER DISEASE pdf

1: Some immunological aspects of liver function.

Get this from a library! Immunological Aspects of Liver Disease. [H C Thomas; Peter A Miescher; Hans J Mueller-Eberhard] -- Howard C. Thomas In normal subjects the regulatory apparatus of the immune system permits responses to foreign antigens but suppresses those directed to "self" components.

Selected References These references are in PubMed. This may not be the complete list of references from this article. Significance of increased "splenic uptake" on liver scintiscanning. Human lymphocyte migration as a parameter of hypersensitivity. Cellular immune response during rejection of a liver transplant in man. Experimental chronic active hepatitis in rabbits following immunization with human liver proteins. Cell-mediated immunity to a human liver-specific antigen in patients with active chronic hepatitis and primary biliary cirrhosis. Purification and characterization of human liver-specific membrane lipoprotein LSP. Lymphocyte cytotoxicity to isolated hepatocytes in chronic active hepatitis. Antibody-dependent cell-mediated K cell cytotoxicity against isolated hepatocytes in chronic active hepatitis. Inadequate antibody response to hBAg or suppressor T-cell defect in development of active chronic hepatitis. Detection of antibodies directed against a liver-specific membrane lipoprotein in patients with acute and chronic active hepatitis. N Engl J Med. Identification of the hepatic asialo-glycoprotein receptor hepatic lectin as a component of liver specific membrane lipoprotein LSP. Serum autoantibodies reacting with the hepatic asialoglycoprotein receptor protein hepatic lectin in acute and chronic liver disorders. T-cell-directed hepatocyte damage in autoimmune chronic active hepatitis. Cell-mediated immune response in primary biliary cirrhosis to a protein fraction from human bile. Leukocyte migration inhibition in response to biliary antigens in primary biliary cirrhosis, sclerosing cholangitis, and other chronic liver diseases. Effect of corticosteroids on suppressor-cell activity in "autoimmune" and viral chronic active hepatitis. Antigen specific suppressor cell function in autoimmune chronic active hepatitis. Cell-mediated immunity and suppressor-T-cell defects to liver-derived antigens in families of patients with autoimmune chronic active hepatitis. T-cell inducers of suppressor lymphocytes control liver-directed autoreactivity. Cellular immunity and hepatitis-associated, Australia antigen liver disease. Detection of hepatitis-B antigen by radioimmunoassay in chronic liver disease and hepatocellular carcinoma in Great Britain. Infusion of hepatitis-B antibody in antigen-positive active chronic hepatitis. Cellular and humoral immunity to hepatitis-B surface antigen in active chronic hepatitis. Autoantibodies to isolated human hepatocyte plasma membranes in chronic active hepatitis. Detection of a new antibody system reacting with Dane particles in hepatitis B virus infection. Nature and display of hepatitis B virus envelope proteins and the humoral immune response. Lymphocyte cytotoxicity to autologous hepatocytes in HBsAg-negative chronic active hepatitis. Lymphocyte cytotoxicity to autologous hepatocytes in HBsAg positive chronic liver disease. Specificity of T lymphocyte cytotoxicity to autologous hepatocytes in chronic hepatitis B virus infection: Relationship between expression of hepatitis B virus antigens in isolated hepatocytes and autologous lymphocyte cytotoxicity in patients with chronic hepatitis B virus infection. Antibodies to the surface of halothane-altered rabbit hepatocytes in patients with severe halothane-associated hepatitis. Association of autoimmune active chronic hepatitis with HL-A1,8. Histocompatibility antigens in active chronic hepatitis and primary biliary cirrhosis. Enhanced antibody responses in active chronic hepatitis: HLA A1-B8-DR3 and suppressor cell function in first-degree relatives of patients with autoimmune chronic active hepatitis. HLA determinants in chronic active liver disease: HLA associations with autoimmune-type chronic active hepatitis: Association of primary sclerosing cholangitis with HLA-B8. HLA antigens and immunoregulatory T cells in ulcerative colitis associated with hepatobiliary disease. Ulcerative colitis and persistent liver dysfunction. Controlled trial of prednisone and azathioprine in active chronic hepatitis. Relapse following treatment withdrawal in patients with autoimmune chronic active hepatitis. Clinical, biochemical, and histological remission of severe chronic active liver disease: Randomised controlled trial of azathioprine withdrawal in autoimmune chronic active hepatitis. Maintenance of remission in autoimmune chronic active hepatitis with azathioprine after corticosteroid withdrawal.

IMMUNOLOGICAL ASPECTS OF LIVER DISEASE pdf

2: Autoimmune Liver Disease - Google Books

Immunological aspects of liver disease. A L Eddleston, P T Donaldson, J E Hegarty, and B D Reed Institute of Liver Studies, King's College School of Medicine and Dentistry, London.

Health The liver is the largest solid organ and the largest gland in the human body. It carries out over essential tasks. Classed as part of the digestive system, the roles of the liver include detoxification, protein synthesis, and the production of chemicals that help digest food. This MNT Knowledge Center article will cover the main roles of the liver, how the liver regenerates, what happens when the liver does not function correctly, and how to keep the liver healthy. Fast facts on the liver The liver is classed as a gland. This vital organ carries out more than roles in the human body. It is the only organ that can regenerate. The liver is the largest solid organ in the body. Alcohol abuse is one of the major causes of liver problems in the industrialized world. Structure The liver is one of the most versatile and important organs. It is situated above and to the left of the stomach and below the lungs. The skin is the only organ heavier and larger than the liver. The liver is roughly triangular and consists of two lobes: The lobes are separated by the falciform ligament, a band of tissue that keeps it anchored to the diaphragm. This capsule is further covered by the peritoneum, a membrane that forms the lining of the abdominal cavity. This helps hold the liver in place and protects it from physical damage. Blood vessels Unlike most organs, the liver has two major sources of blood. The portal vein brings in nutrient-rich blood from the digestive system, and the hepatic artery carries oxygenated blood from the heart. The blood vessels divide into small capillaries, with each ending in a lobule. Lobules are the functional units of the liver and consist of millions of cells called hepatocytes. Blood is removed from the liver through three hepatic veins. Functions The liver is classed as a gland and associated with many functions. It is difficult to give a precise number, as the organ is still being explored, but it is thought that the liver carries out distinct roles. The major functions of the liver include: Bile helps the small intestine break down and absorb fats , cholesterol , and some vitamins. Bile consists of bile salts, cholesterol, bilirubin, electrolytes, and water. Absorbing and metabolizing bilirubin: Bilirubin is formed by the breakdown of hemoglobin. The iron released from hemoglobin is stored in the liver or bone marrow and used to make the next generation of blood cells. Vitamin K is necessary for the creation of certain coagulants that help clot the blood. Bile is essential for vitamin K absorption and is created in the liver. If the liver does not produce enough bile, clotting factors cannot be produced. Bile breaks down fats and makes them easier to digest. Carbohydrates are stored in the liver, where they are broken down into glucose and siphoned into the bloodstream to maintain normal glucose levels. They are stored as glycogen and released whenever a quick burst of energy is needed. Vitamin and mineral storage: It keeps significant amounts of these vitamins stored. The liver stores iron from hemoglobin in the form of ferritin, ready to make new red blood cells. The liver also stores and releases copper. Bile helps break down proteins for digestion. The liver filters and removes compounds from the body, including hormones, such as estrogen and aldosterone, and compounds from outside the body, including alcohol and other drugs. The liver is part of the mononuclear phagocyte system. It contains high numbers of Kupffer cells that are involved in immune activity. These cells destroy any disease-causing agents that might enter the liver through the gut. Albumin is the most common protein in blood serum. It transports fatty acids and steroid hormones to help maintain the correct pressure and prevent the leaking of blood vessels. This hormone raises blood pressure by narrowing the blood vessels when alerted by production of an enzyme called renin in the kidneys. Regeneration Because of the importance of the liver and its functions, evolution has ensured that it can regrow rapidly as long as it is kept healthy. This ability is seen in all vertebrates from fish to humans. The liver is the only visceral organ that can regenerate. It can regenerate completely, as long as a minimum of 25 percent of the tissue remains. One of the most impressive aspects of this feat is that the liver can regrow to its previous size and ability without any loss of function during the growth process. In mice, if two-thirds of the liver is removed, the remaining liver tissue can regrow to its original size within 5 to 7 days. In humans, the process takes slightly longer, but regeneration can still occur in 8 to 15 days - an incredible achievement, given the size and complexity of the organ. Over the following few weeks, the new liver tissue becomes

indistinguishable from the original tissue. This regeneration is helped by a number of compounds, including growth factors and cytokines. Some of the most important compounds in the process appear to be:

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3: Wilson Disease | NIDDK

Read "Immunological Aspects of Liver Disease" by with Rakuten Kobo. Howard C. Thomas In normal subjects the regulatory apparatus of the immune system permits responses to foreign antigens.

Fallatah and Hisham O. This is an open access article distributed under the Creative Commons Attribution License , which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Abstract Autoimmune hepatitis AIH is a unique form of immune-mediated disease that attacks the liver through a variety of immune mechanisms. The outcomes of AIH are either acute liver disease, which can be fatal, or, more commonly, chronic progressive liver disease, which can lead to decompensated liver cirrhosis if left untreated. AIH has characteristic immunological, and pathological, features that are important for the establishment of the diagnosis. More importantly, most patients with AIH have a favorable response to treatment with prednisolone and azathioprine, although some patients with refractory AIH or more aggressive disease require more potent immune-suppressant agents, such as cyclosporine or Mycophenolate Mofetil. In this paper, we discuss the immunological, pathological and clinical features of AIH, as well as the standard and alternative treatments for AIH. Introduction Autoimmune hepatitis AIH is a chronic, immunologically mediated inflammatory liver disorder of unknown etiology [1 â€” 3]. It is characterized by the presence of high levels of circulating autoantibodies, hypergammaglobulinemia, and elevated levels of serum transaminases [1 â€” 3]. AIH was first recognized in by Amberg [4]. Several different names have been ascribed to this condition, including plasma cell hepatitis and lupoid hepatitis [6 , 7], but Mackay et al. In countries that are endemic to viral hepatitis, AIH is less commonly recognized than chronic viral hepatitis [9 , 16 â€” 19]. In our report on AIH, AIH type 1, which is more common than AIH type 2, mainly affects adolescent and adult females the female-to-male ratio is 4: However, AIH type 2 predominantly affects children younger than 18 years of age with a female-to-male ratio of 9: AIH has a variable onset age, which differs according to the geographic distribution and the ethnic group. For instance, Japanese AIH patients demonstrate an onset age of 50 years, whereas Caucasian patients typically demonstrate an onset age of 10â€”20 years [17 , 30 , 31]. Similarly, our report on AIH in Saudi Arabia and other reports from India have shown a younger onset age in these populations compared to other Asian countries, the US, and Europe [9 , 18 , 20 , 21 , 32 â€” 34]. Etiology and Risk Factors AIH is characterized by the loss of immune tolerance to antigens that are present on hepatocytes, as well as by impaired immune regulation [11 , 35]. No clear etiological factor has been identified for the initiation of the immune-mediated damage to the liver tissue that is observed with AIH, but many triggering risk factors have been suggested to play a role in the initiation of this immunologically mediated liver injury. Genetic predisposition is also thought to play a major role in the development of AIH. Genetic Risk Factors The major histocompatibility complex MHC , which is also known as human leukocyte antigen HLA , is located on chromosome 6 and is the most commonly reported gene associated with AIH [11 , 26 , 32 , 35 , 37 , 38]. This difference in the HLA gene association between Japanese and Western populations might explain the difference in the age of onset of AIH between the two populations [38 , 41 , 42]. Triggering Factors Antigens that are most likely triggered by autoantigen mimicry are thought to play a role in the initiation of the immune system-mediated damage that is associated with AIH [11 , 26 , 35]. Infections with hepatitis viruses A, B, and C, Epstein Barr virus, and herpes simplex virus have also been implicated as potential viral triggers [26 , 44 , 45]. Hepatitis C virus is commonly associated with immunological features that are similar to those of AIH; this results in diagnostic difficulties with some hepatitis C virus-infected patients [46 , 47]. Several medications, such as atorvastatin [48], diclofenac, isoniazid methyldopa, minocycline, nitrofurantoin, and propylthiouracil, as well as the hepatitis A vaccine [26 , 49 â€” 51], have also been reported to trigger AIH. It is important to differentiate between drug-induced AIH and immune-mediated drug-induced liver injury because short-term treatment is usually required for the former but withdrawal from the causative drug is sufficient to treat the latter [50]. Moreover, drug-induced AIH may be underrecognized because the causative drug is frequently withdrawn without any additional workup. Furthermore, the coexistence of an infectious agent and a drug, which simultaneously act as

triggering factors, was suggested in a case report by Kamiyama et al. Several environmental agents, such as herbal triggers, have also been reported to initiate AIH, including black cohosh, syo-saiko-to; and Chinese herbal tea [57 â€” 61]. Khat, which is commonly chewed by the populations of Yemen and Somalia as a common social habit, is another hepatotoxic environmental agent that has recently been recognized as a triggering agent for a severe form of AIH in young males in these countries [62 â€” 65]. In our report of 3 male patients with khat-induced AIH, all of the patients exhibited the classical biochemical and immunological features of AIH; they also all had a favorable response to steroids [62]. We recently had another patient with similar features and decompensated cirrhosis who exhibited a complete biochemical response normal ALT to treatment with prednisolone and azathioprine. Thus, even with the variety of risk factors that has been proposed, the specific underlying cause for AIH remains unknown [11]. Immunological Features of AIH 6. However, the molecular target of the T lymphocyte response has not yet been identified [66 , 67]. Furthermore, polymorphism of the gene encoding the cytotoxic T-lymphocyte antigen-4 CTLA-4 on chromosome 2q33 is more common in patients with type 1 autoimmune hepatitis and may represent a susceptibility allele for AIH [68]. CTLA4 is expressed by regulatory T cells Tregs and is an essential factor for the negative regulation of the immune response [69]. Another mechanism of immune pathogenesis is the antibody-mediated cellular cytotoxicity, which is initiated by CD8 T cells the predominant cells found in areas of hepatic inflammation. They recognize the MHC-autoantigen complex on Kupffer cells or hepatocytes [67]. A reduction in the number and proliferative activity of Tregs in response to stimulation has been reported in patients with AIH [70 , 71]. Moreover, the activity of natural killer cells, which are known to play a major role in the regulation of the immune response, might be reduced in AIH [11 , 72]. More recently, Th17 cells have been shown to play a role in human autoimmune diseases, including AIH [11]. The induction of AIH in animal models has been difficult [73], although Tu et al. Immunofluorescence IFL is the main technique that is currently used to screen for the autoantibodies that may be diagnostically relevant to liver disease [75 , 76]. Although no specific ANA nuclear antigen has been identified in AIH type 1 [75], a variety of nuclear molecular targets have been detected, including centromeres, histones, double-stranded DNA, chromatin, and ribonucleoprotein complexes [78]. ANAs are also detected in patients with drug-induced hepatitis [13 , 50 , 51 , 55] and other nonliver disorders. Since then, these have also been detected in the kidney, stomach, and liver [29 , 83]. These antibodies target arterial vessels V , the glomerular mesangium G , and the fibers surrounding the kidney tubules T , which results in the characteristic VGT pattern that is observed with AIH type 1 [84]. The VGT pattern of SMA also targets F-actin microfilaments or filamentous actin and the intermediate filaments vimentin and desmin [10 , 75]. However, the IFL SMA pattern is either absent or extremely rare in conditions other than AIH type 1 [86 , 87]; thus, this pattern provides a high level of specificity and selectivity [79]. Furthermore, although the ANA and SMA levels decrease after immune-suppressive therapy [78], neither level has been shown to correlate with the response to therapy. In addition, neither level has have been found to be associated with the clinical or histological disease severity of AIH type 1 [88]. Anti-Actin Antibodies Studies have shown that a subset of patients who are positive for SMAs also demonstrate F-actin staining [89 , 90]. These markers are of greater prognostic value and have been associated with a poor response to treatment with corticosteroids [91 â€” 93]. Similarly, the same report described that 10 out of the 11 studied patients who had liver transplantation were anti-actin positive and seropositive for SMA antibodies [91]. These antibodies were also shown by Berg et al. These antibodies are highly disease specific for severe forms of AIH type1 and are typically associated with a fatal outcome [96]. LKM-1 staining is localized to the cytoplasm of liver cells and the P3 portion of renal tubules. However, these antibodies do not stain gastric parietal cells [ ]. The LKM-1 staining pattern can sometimes be confused with the anti-mitochondrial antibody AMA IFL pattern [25 ,]; however, the LKM-1 staining pattern is localized to the P3 portion of the proximal renal tubules, whereas the AMA pattern is found in the distal renal tubules [ ]. LKM-3 and Other LKM Antibody Subtypes The presence of LKM-2 antibodies has been described in patients with drug-induced hepatitis that is caused by tienilic acid which was subsequently withdrawn from the market [ ]. The main molecular target of LKM-3 antibodies is uridine diphosphate glucuronyl transferase [,]. In addition, CYP1A2 may also play a role in drug-induced liver disease [ ]. In addition, LC-1 antibodies also

serve as a marker of liver inflammation and the rapid progression of liver disease in AIH patients [ ]. However, the applicability of ASGPR antibody detection for the diagnosis of AIH has been limited by the lack of disease specificity and the difficulty in the development of a reliable molecular-based assay [75 ,]. A typical form of p-ANCAs has been identified in patients with AIH type 1, primary biliary cirrhosis, and primary sclerosing cholangitis [,]. These antibodies target a peripheral nuclear perinuclear antigen p-ANCA [,] and are associated with more severe forms of AIH type 1 [,]. In the report published by Roozendaal et al. The presence of these antibodies has been associated with high immunoglobulin G IgG levels and a poor immediate response to corticosteroid treatment compared to anti-dsDNA-negative patients [ ]. These antibodies are associated with high levels of IgG and active disease [ ]. In our previous report comparing serum IgG levels between AIH patients and patients with other chronic liver diseases, we found that the mean serum IgG level was AIH Type 1 AIH type 1 is the predominant form of AIH and affects all age groups, although it is more commonly diagnosed in individuals between 20 and 40 years of age [17 , 18 , 21 , 24]. Both markers are non-disease specific and can be used to determine patient prognosis [25 , 26 , 75 ,]. SLAs, which represent the most specific autoantibody for AIH type 1, are also detected in one-third of cases [,]. Occasionally, patients with AIH type 1 are negative for both ANAs and SMAs, although these antibodies may be detected at a later point during the course of the disease [ ]. AIH type 2 is a severe form of acute hepatitis that occurs mainly in children [ ]. These patients typically have a favorable response to immune-suppressive therapy [,]. In our experience, we have diagnosed all of the adult patients in our center to have AIH type 1 based on biochemical, immunological, and histological features [18 , 62]. Unpublished data from the Pediatric Gastroenterology Department in the same center showed that most of our pediatric AIH cases are of type 1 and only a few of the patients exhibit AIH type 2. The clinical presentation of AIH can be in the form of asymptomatic liver disease with abnormal liver test results [13 , 15 , 18 , 21 , 26 , 29 ,] and nonspecific symptoms, such as arthralgia and fatigue [26]. The AIH type 2 patients have a higher rate of acute hepatitis compared to type 1 patients [ ]. AIH and advanced cirrhosis patients exhibit all the features of portal hypertension and hepatocellular dysfunction, including ascites, hepatic encephalopathy, and variceal bleeding [18 , 24 , 33 ,]. Fulminant liver failure is rare in the presentation of AIH [10]. Tables 1 and 2 Table 1: Revised scoring system for the diagnosis of autoimmune hepatitis. Simplified diagnostic criteria for autoimmune hepatitis. There is no single diagnostic marker for AIH. Therefore, the diagnosis is based on a combination of clinical, biochemical, immunological, and histological findings [11]. This scoring system was revised in by the same group, as shown in Table 1 [36]. More recently, a simplified set of diagnostic criteria was proposed by the IAIHG in , as shown in Table 2 [ ]. This simplified set of criteria, which was validated by Yeoman et al. However, the simplified criteria perform less efficiently for the diagnosis of acute forms of AIH [ ]. Similarly, both the original and the simplified scoring systems do not perform well in patients with AIH who also have fulminant liver failure or cholestatic disease [,]. Another limitation of both the revised and the original scoring systems is that these have not been carefully evaluated in children [25]. The treatment response is graded positive in both the original and the revised AIHG scoring systems, and a posttreatment reassessment may upgrade the diagnostic score from probable to definite [10 ,]. However, the two criteria exhibited a similar performance in the diagnosis of definite AIH [ ]. Initial clinical data should be collected from the patient to evaluate the history of alcohol use and the use of any hepatotoxic medication [10 ,].

IMMUNOLOGICAL ASPECTS OF LIVER DISEASE pdf

4: Cannabis for Cirrhosis and Liver Disease

Howard C. Thomas In normal subjects the regulatory apparatus of the immune system permits responses to foreign antigens but suppresses those directed to "self' components. Autoimmune disease occurs as a failure ofthis system either as a result of a primary defect in the regulatory apparatus (primary.

This section does not cite any sources. Please help improve this section by adding citations to reliable sources. Unsourced material may be challenged and removed. February Learn how and when to remove this template message Classical immunology ties in with the fields of epidemiology and medicine. It studies the relationship between the body systems, pathogens , and immunity. The earliest written mention of immunity can be traced back to the plague of Athens in BCE. Thucydides noted that people who had recovered from a previous bout of the disease could nurse the sick without contracting the illness a second time. The study of the molecular and cellular components that comprise the immune system, including their function and interaction, is the central science of immunology. The immune system has been divided into a more primitive innate immune system and, in vertebrates , an acquired or adaptive immune system. The latter is further divided into humoral or antibody and cell-mediated components. The immune system has the capability of self and non-self-recognition. An antigen is a substance that ignites the immune response. The cells involved in recognizing the antigen are Lymphocytes. Once they recognize, they secrete antibodies. Antibodies are proteins that neutralize the disease-causing microorganisms. The humoral antibody response is defined as the interaction between antibodies and antigens. Immunology rests on an understanding of the properties of these two biological entities and the cellular response to both. Besides, there are direct implications of the immune system in the infectious diseases tuberculosis, malaria, hepatitis, pneumonia, dysentery, and helminth infestations as well. Hence, research in the field of immunology is of prime importance for the advancements in the fields of n the modern medicine, biomedical research, and biotechnology. February Learn how and when to remove this template message Clinical immunology is the study of diseases caused by disorders of the immune system failure, aberrant action, and malignant growth of the cellular elements of the system. It also involves diseases of other systems, where immune reactions play a part in the pathology and clinical features. The diseases caused by disorders of the immune system fall into two broad categories: Other immune system disorders include various hypersensitivities such as in asthma and other allergies that respond inappropriately to otherwise harmless compounds. In fact, many of the infections acquired by neonates are caused by low virulence organisms like Staphylococcus and Pseudomonas. In neonates, opsonic activity and the ability to activate the complement cascade is very limited. Phagocytic activity is also greatly impaired in newborns. This is due to lower opsonic activity, as well as diminished up-regulation of integrin and selectin receptors, which limit the ability of neutrophils to interact with adhesion molecules in the endothelium. Although, the number of total lymphocytes is significantly higher than in adults, the cellular and humoral immunity is also impaired. At birth, most of the immunoglobulin present is maternal IgG. Some IgA is provided by breast milk. These passively-acquired antibodies can protect the newborn for up to 18 months, but their response is usually short-lived and of low affinity. If a child is exposed to the antibody for a particular antigen before being exposed to the antigen itself then the child will produce a dampened response. Passively acquired maternal antibodies can suppress the antibody response to active immunization. Similarly the response of T-cells to vaccination differs in children compared to adults, and vaccines that induce Th1 responses in adults do not readily elicit these same responses in neonates. This can be the reason for distinct time frames found in vaccination schedules. Oestradiol usually begins to act around the age of 10 and testosterone some months later. Other androgens, however, such as DHEA , increase immune response. Physical changes during puberty such as thymic involution also affect immunological response. Ecoimmunology and Behavioral immune system Ecoimmunology, or ecological immunology, explores the relationship between the immune system of an organism and its social, biotic and abiotic environment. More recent ecoimmunological research has focused on host pathogen defences traditionally considered "non-immunological", such as pathogen avoidance, self-medication, symbiont -mediated defenses, and fecundity trade-offs. For example, the Monarch

butterfly often lays its eggs on certain toxic milkweed species when infected with parasites. These toxins reduce parasite growth in the offspring of the infected Monarch. However, when uninfected Monarch butterflies are forced to feed only on these toxic plants, they suffer a fitness cost as reduced lifespan relative to other uninfected Monarch butterflies. Aphids , for example, rely on several different symbionts for defense from key parasites, and can vertically transmit their symbionts from parent to offspring. Immunotherapy The use of immune system components to treat a disease or disorder is known as immunotherapy. Immunotherapy is most commonly used in the context of the treatment of cancers together with chemotherapy drugs and radiotherapy radiation. However, immunotherapy is also often used in the immunosuppressed such as HIV patients and people suffering from other immune deficiencies or autoimmune diseases. Immunodiagnostics The specificity of the bond between antibody and antigen has made the antibody an excellent tool for the detection of substances by a variety of diagnostic techniques. Antibodies specific for a desired antigen can be conjugated with an isotopic radio or fluorescent label or with a color-forming enzyme in order to detect it. Cancer immunology The study of the interaction of the immune system with cancer cells can lead to diagnostic tests and therapies with which to find and fight cancer. Reproductive immunology This area of the immunology is devoted to the study of immunological aspects of the reproductive process including fetus acceptance. The term has also been used by fertility clinics to address fertility problems, recurrent miscarriages, premature deliveries and dangerous complications such as pre-eclampsia. Theoretical immunology[edit] Immunology is strongly experimental in everyday practice but is also characterized by an ongoing theoretical attitude. Many theories have been suggested in immunology from the end of the nineteenth century up to the present time. The end of the 19th century and the beginning of the 20th century saw a battle between "cellular" and "humoral" theories of immunity.

IMMUNOLOGICAL ASPECTS OF LIVER DISEASE pdf

5: Immunological Aspects of Liver Disease | Angus & Robertson

*Immunological Aspects of Liver Disease [H.C. Thomas, P.A. Miescher, H.J. Mueller-Eberhard] on www.enganchecubano.com *FREE* shipping on qualifying offers. Howard C. Thomas In normal subjects the regulatory apparatus of the immune system permits responses to foreign antigens but suppresses those directed to self' components.*

According to the Centers for Disease Control and Prevention, hepatitis C alone chronically infects more than 1. It would not be unusual for these two diseases to occur by chance in the same person, which explains in part the apparent association between liver disease and diabetes mellitus. The liver plays a central and crucial role in the regulation of carbohydrate metabolism. Its normal functioning is essential for the maintenance of blood glucose levels and of a continued supply to organs that require a glucose energy source. This central role for the liver in glucose homeostasis offers a clue to the pathogenesis of glucose intolerance in liver diseases but little insight into the mechanisms of liver disease in diabetes mellitus. This review will draw on sources in the literature that address both pathogenetic directions. The Role of the Liver in Glucose Homeostasis An appreciation of the role of the liver in the regulation of carbohydrate homeostasis is essential to understanding the many physical and biochemical alterations that occur in the liver in the presence of diabetes and to understanding how liver disease may affect glucose metabolism. The liver uses glucose as a fuel and also has the ability to store it as glycogen and synthesize it from noncarbohydrate precursors gluconeogenesis. Mann and Magath demonstrated that a total hepatectomy in a dog results in death within a few hours from hypoglycemic shock,1,2 underscoring the important role the liver plays in maintaining normoglycemia. Glucose absorbed from the intestinal tract is transported via the portal vein to the liver. Although the absolute fate of this glucose is still controversial, some authors suggest that most of the absorbed glucose is retained by the liver so that the rise in peripheral glucose concentration reflects only a minor component of postprandial absorbed glucose. Therefore, it is possible that the liver plays a more significant role than does peripheral tissue in the regulation of systemic blood glucose levels following a meal. Many cells in the body, including fat, liver, and muscle cells, have specific cell membrane insulin receptors, and insulin facilitates the uptake and utilization of glucose by these cells. Glucose rapidly equilibrates between the liver cytosol and the extracellular fluid. Transport into certain cells, such as resting muscle, is tightly regulated by insulin, whereas uptake into the nervous system is not insulin-dependent. Glucose can be used as a fuel or stored in a macromolecular form as polymers: Glycogen storage is promoted by insulin, but the capacity within tissues is physically limited because it is a bulky molecule. Insulin is formed from a precursor molecule, preproinsulin, which is then cleaved to proinsulin. Further maturation results in the conversion of proinsulin into insulin and a smaller peptide called C-peptide. A small amount of proinsulin enters the circulation. Insulin is metabolized by insulinase in the liver, kidney, and placenta. Insulin promotes glycogen synthesis glycogenesis in the liver and inhibits its breakdown glycogenolysis. It promotes protein, cholesterol, and triglyceride synthesis and stimulates formation of very-low-density lipoprotein cholesterol. It also inhibits hepatic gluconeogenesis, stimulates glycolysis, and inhibits ketogenesis. The liver is the primary target organ for glucagon action, where it promotes glycogenolysis, gluconeogenesis, and ketogenesis. It is oxidized to pyruvate in the cytosol, and electrons generated from this process are transferred to the mitochondria. Pyruvate generated by this Emden-Meyerhof pathway is oxidized to acetyl CoA in the mitochondria, which in turn undergoes further oxidation by the Krebs tricarboxylic acid cycle. Nearly 36 moles of high energy phosphate are generated from each molecule of glucose by aerobic glycolysis. Should oxygen not be available, pyruvate is converted to lactate by the action of lactate dehydrogenase. Lactate is a potential fuel, or it may be converted back to glucose. The formation of glucose from lactate and various noncarbohydrate precursors is known as gluconeogenesis and occurs mainly in the liver and kidneys. The liver, kidney, intestine, and platelets contain the enzyme glucosephosphatase, which produces glucose from glucosephosphate and is the final step in the production of glucose via gluconeogenesis. This enzyme is absent in other tissues. Glucose that is metabolized peripherally may therefore be converted back to glucose or to hepatic glycogen via gluconeogenesis with

lactate as the primary substrate. In type 2 diabetes, excessive hepatic glucose output contributes to the fasting hyperglycemia. Increased gluconeogenesis is the predominant mechanism responsible for this increased glucose output, while glycogenolysis has not been shown to be increased in patients with type 2 diabetes. However, studies attesting to this were usually performed on animals with recently induced diabetes. In patients with chronic diabetes, glycogen accumulation is seen, and it is postulated that long-standing insulin deficiency may actually facilitate synthase activity. This and enhanced gluconeogenesis may account for the net accumulation of glycogen in diabetes. No correlation between hepatic glycogen content and fasting blood glucose levels has been demonstrated. There is also no demonstrable association between the type of diabetes or the fat content of the hepatocytes and the presence of glycogen. The mechanism for nuclear glycogen deposition is also unclear, with the stored glycogen resembling muscle glycogen more than hepatocyte cytoplasmic glycogen. The finding of glycogen nuclei in a patient with fatty liver is useful confirmatory evidence that the fatty liver is secondary to diabetes even if the glucose tolerance test is normal. However, Creutzfeldt and associates have reported the combination also in obese patients. All these abnormalities may improve with sustained glucose control. Unfortunately, associated obesity is a frequently occurring confounding variable. Fat is stored in the form of triglyceride and may be a manifestation of increased fat transport to the liver, enhanced hepatic fat synthesis, and decreased oxidation or removal of fat from the liver. The steatosis may be microvesicular or macrovesicular and may progress to fibrosis and cirrhosis. The degree of glycemic control does not correlate with the presence or absence of fat. CT scan and ultrasound are claimed to be sensitive tests for detecting hepatic fat accumulation. A negative ultrasound, however, does not exclude the presence of microscopic fatty infiltration. It is unclear at this time whether a biopsy is always necessary in patients with suspected steatohepatitis. Biopsy probably should be performed when the diagnosis is unclear, although some authors suggest that it is necessary in all cases to confirm the diagnosis and assess the degree of fibrosis. A number of drugs, such as amiodarone, perhexilene, glucocorticoids, estrogens, and tamoxifen, may cause macrovesicular steatosis. The amount of fat frequently diminishes with improvement of the underlying condition. Nonalcoholic steatohepatitis NASH is a variant of fatty liver in which fat in the hepatocytes is accompanied by lobular inflammation and steatonecrosis. The diagnosis can only be made in the absence of alcohol abuse or other causes of liver disease, particularly hepatitis C. In patients with diabetes and steatohepatitis, Mallory bodies such as those seen in alcoholic liver disease may be seen. Nonalcoholic steatohepatitis has been associated most commonly with obese women with diabetes, but the disease is certainly not limited to patients with this clinical profile. Patients with nonalcoholic steatohepatitis can develop progressive liver disease and complications to the point that they may need liver transplantation. However, the histopathological changes in diabetes tend to be periportal situated in zone I , while those in alcoholic hepatitis are predominantly pericentral in zone III. It is not clear whether the diabetes is causally related to the steatohepatitis. Diabetes increases the risk of steatohepatitis, which can progress to cirrhosis. Obesity is a significant confounding variable in determining the prevalence of cirrhosis in diabetes. Even with normal glucose tolerance, obesity can cause steatohepatitis and cirrhosis. Likewise, the lack of a clear definition of diabetes in the past somewhat confounds these statistics. Biliary Disease, Cholelithiasis, Cholecystitis There is a reported increased incidence of cholelithiasis in diabetes mellitus, but obesity and hyperlipidemia may again be confounding variables. Several articles have reported a two- to threefold increased incidence of gallstones in diabetic patients, whereas others have failed to demonstrate a significant association. There is no indication in the literature that the natural history of gallstones is different in diabetic and nondiabetic individuals. The relative risk of mortality following acute cholecystitis is not significantly greater in diabetic patients than in the general population, and neither is the risk for serious complications. For that reason, prophylactic cholecystectomy cannot routinely be recommended for asymptomatic gallstones in patients with diabetes. Patients with diabetes have comparable survival outcomes from laparoscopic or open cholecystectomy. Adhering to good infection-control practices should significantly reduce this risk. The biguanide metformin Glucophage does not undergo hepatic metabolism and, like chlorpropamide Diabinese , is excreted unchanged in the urine. The sulfonylurea glipizide Glucotrol, Glucotrol XL is metabolized mainly by the liver, and, in theory, hepatic disease may result in increased blood levels. There is a rare association

between the use of oral hypoglycemics and hepatic injury, but sulfonylureas can cause chronic hepatitis with necroinflammatory changes. They are described as having a well-circumscribed cellular infiltrate comprised of acidophilic histiocytes and eosinophils surrounding necrotic hepatocytes. The mechanism of liver injury is not known. Chlorpropamide appears to be the most hepatotoxic of these drugs, with cholestatic hepatitis occurring in 0. Hepatic disease is very rare with tolbutamide Orinase and generics , and tolazamide Tolinase and generics. Although very uncommon, acetohexamide and glyburide can cause acute hepatocellular necrosis, and fatalities have been reported. At least two cases of granulomatous hepatitis thought secondary to glyburide have been reported in the literature. Lactic acidosis can be associated with the use of metformin to treat diabetes, but it is reported to occur occasionally and usually in patients with major contraindications to the drug. It is therefore listed as a contraindication. Its package insert carries a warning that severe idiosyncratic hepatocellular injury, usually reversible but possibly leading to death or liver transplantation, has been reported in patients using the medication, usually during the early months of therapy. Serum transaminases should be checked at the start of therapy, monthly for the first 6 months of therapy, every 2 months for the remainder of the first year, and periodically thereafter. In addition, any symptoms suggesting hepatic dysfunction necessitate having liver tests performed. Diabetes and Abnormalities of Glucose Homeostasis Occurring as a Complication of Liver Disease Viral Hepatitis There is no evidence in the literature that viral hepatitis has a worse prognosis in patients with diabetes. There is an increased prevalence of viral hepatitis in diabetes possibly due to an increased exposure to needles for the injection of insulin or for blood testing. Possible contamination of the platform in spring-loaded lancet devices may increase the risk of acquiring hepatitis B or C from these instruments. In , hepatitis B outbreaks were noted in an Ohio nursing home and a New York hospital. Transmission was thought to be related to the use of spring-loaded devices for fingerstick glucose testing. In a study by Grimbert and associates, patients with hepatitis C and the same number with either hepatitis B or alcohol-induced liver disease were compared over the same period. The authors suggested a causative role of hepatitis C in the pathogenesis of diabetes. The association has been described also by others and was thought to be statistically significant. Most of their diabetic patients with hepatitis C had abnormal liver tests. This increased incidence appears to be significant, and the presence of the virus appears to be an independent risk factor. However, only 10 patients developed de novo diabetes mellitus. This suggested that children should perhaps be vaccinated with four injections instead of three.

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6: Immunological aspects of liver disease. - Europe PMC Article - Europe PMC

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Medical and Family History A health care provider may take a medical and family history to help diagnose Wilson disease. Physical Exam A physical exam may help diagnose Wilson disease. A health care provider may perform liver enzyme or function testsâ€”blood tests that may indicate liver abnormalities. Since the copper is deposited into the organs and is not circulating in the blood, most people with Wilson disease have a lower-than-normal level of copper in the blood. In cases of acute liver failure caused by Wilson disease, the level of blood copper is often higher than normal. Most people with Wilson disease have a lower-than-normal ceruloplasmin level. A health care provider may recommend genetic testing in cases of a known family history of Wilson disease. Urine Tests hour urine collection. A health care provider sends the sample to a lab for analysis. A hour urine collection will show increased copper in the urine in most patients who have symptoms due to Wilson disease. Liver Biopsy A liver biopsy is a procedure that involves taking a small piece of liver tissue for examination with a microscope for signs of damage or disease. The health care provider may ask the patient to stop taking certain medications temporarily before the liver biopsy. He or she may also ask the patient to fastâ€”eat or drink nothingâ€”for 8 hours before the procedure. During the procedure, the patient lies on a table, right hand resting above the head. The health care provider applies a local anesthetic to the area where he or she will insert the biopsy needle. If needed, a health care provider will also give sedatives and pain medication. The health care provider uses the needle to take a small piece of liver tissue. He or she may use ultrasound, computerized tomography scans, or other imaging techniques to guide the needle. After the biopsy, the patient must lie on the right side for up to 2 hours and is monitored an additional 2 to 4 hours before being sent home. A pathologistâ€”a doctor who specializes in diagnosing diseasesâ€”examines the liver tissue in a lab. The test can show cirrhosis of the liver. Sometimes the liver biopsy will show copper buildup in the liver cells; however, the results can vary because the copper does not always deposit evenly into the liver. Therefore, health care providers often find it more useful to analyze a piece of liver tissue for copper content. Most patients with Wilson disease have high levels of copper in the liver tissue when compared with carriers or with people who do not have Wilson disease. Imaging Tests A health care provider may order imaging tests to evaluate brain abnormalities in patients who have nervous system symptoms often seen with Wilson disease, or in patients diagnosed with Wilson disease. Health care providers do not use brain imaging tests to diagnose Wilson disease, though certain findings may suggest the patient has the disease. Magnetic resonance imaging MRI. A specially trained technician performs the procedure in an outpatient center or a hospital, and a radiologistâ€”a doctor who specializes in medical imagingâ€”interprets the images. The patient does not need anesthesia, though people with a fear of confined spaces may receive light sedation, taken by mouth. An MRI may include the injection of a special dye, called contrast medium. With most MRI machines, the patient will lie on a table that slides into a tunnel-shaped device that may be open ended or closed at one end. Some machines allow the patient to lie in a more open space. The technician will take a sequence of images from different angles to create a detailed picture of the brain. During sequencing, the patient will hear loud mechanical knocking and humming noises. Computerized tomography CT scan. A CT scan uses a combination of x-rays and computer technology to create images. For a CT scan, a health care provider may give the patient a solution to drink and an injection of contrast medium. CT scans require the patient to lie on a table that slides into a tunnel-shaped device where a technician takes the x-rays. An x-ray technician performs the procedure in an outpatient center or a hospital. A radiologist interprets the images. The patient does not need anesthesia. How is Wilson disease treated? A health care provider will treat Wilson disease with a lifelong effort to reduce and control the amount of copper in the body. Treatment may include medications a liver transplant Medications A health care provider will prescribe medications to treat Wilson disease. The medications have different actions that health care providers use during different phases of the treatment. Chelating agents are medications that remove extra copper from the body by releasing it from organs into the

bloodstream. Once the copper is in the bloodstream, the kidneys then filter the copper and pass it into the urine. A health care provider usually recommends chelating agents at the beginning of treatment. A potential side effect of chelating agents is that nervous system symptoms may become worse during treatment. The two medications available for this type of treatment include trientine Syprine â€”the risk for side effects and worsening nervous system symptoms appears to be lower with trientine than d-penicillamine. Researchers are still studying the side effects; however, some health care providers prefer to prescribe trientine as the first treatment of choice because it appears to be safer. A health care provider should consider future screening on any newborn whose parent has Wilson disease. A health care provider will prescribe zinc for patients who do not have symptoms, or after a person has completed successful treatment using a chelating agent and symptoms begin to improve. Although most people taking zinc usually do not experience side effects, some people may experience stomach upset. A health care provider may prescribe zinc for children with Wilson disease who show no symptoms. Women may take the full dosage of zinc safely during pregnancy. Maintenance, or long term, treatment begins when symptoms improve and tests show that copper is at a safe level. Maintenance treatment typically includes taking zinc or a lower dose of a chelating agent. A health care provider closely monitors the person and reviews regular blood and urine tests to ensure maintenance treatment controls the copper level in the body. Treatment for people with Wilson disease who have no symptoms may include a chelating agent or zinc in order to prevent symptoms from developing and stop or slow disease progression. People with Wilson disease will take medications for the rest of their lives. Changes in Eating, Diet, and Nutrition People with Wilson disease should reduce their dietary copper intake by avoiding foods that are high in copper, such as shellfish.

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7: Immunology - Wikipedia

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8: The liver: Structure, function, and disease

Autoimmune hepatitis (AIH) is a unique form of immune-mediated disease that attacks the liver through a variety of immune mechanisms. The outcomes of AIH are either acute liver disease, which can be fatal, or, more commonly, chronic progressive liver disease, which can lead to decompensated liver cirrhosis if left untreated.

9: Liver Disease and Diabetes Mellitus

The mission of the Laboratory of Liver Diseases is to investigate the immunological aspects and molecular pathogenesis of alcoholic and nonalcoholic fatty liver diseases, and to explore novel therapeutic targets for the treatment of these disorders.

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