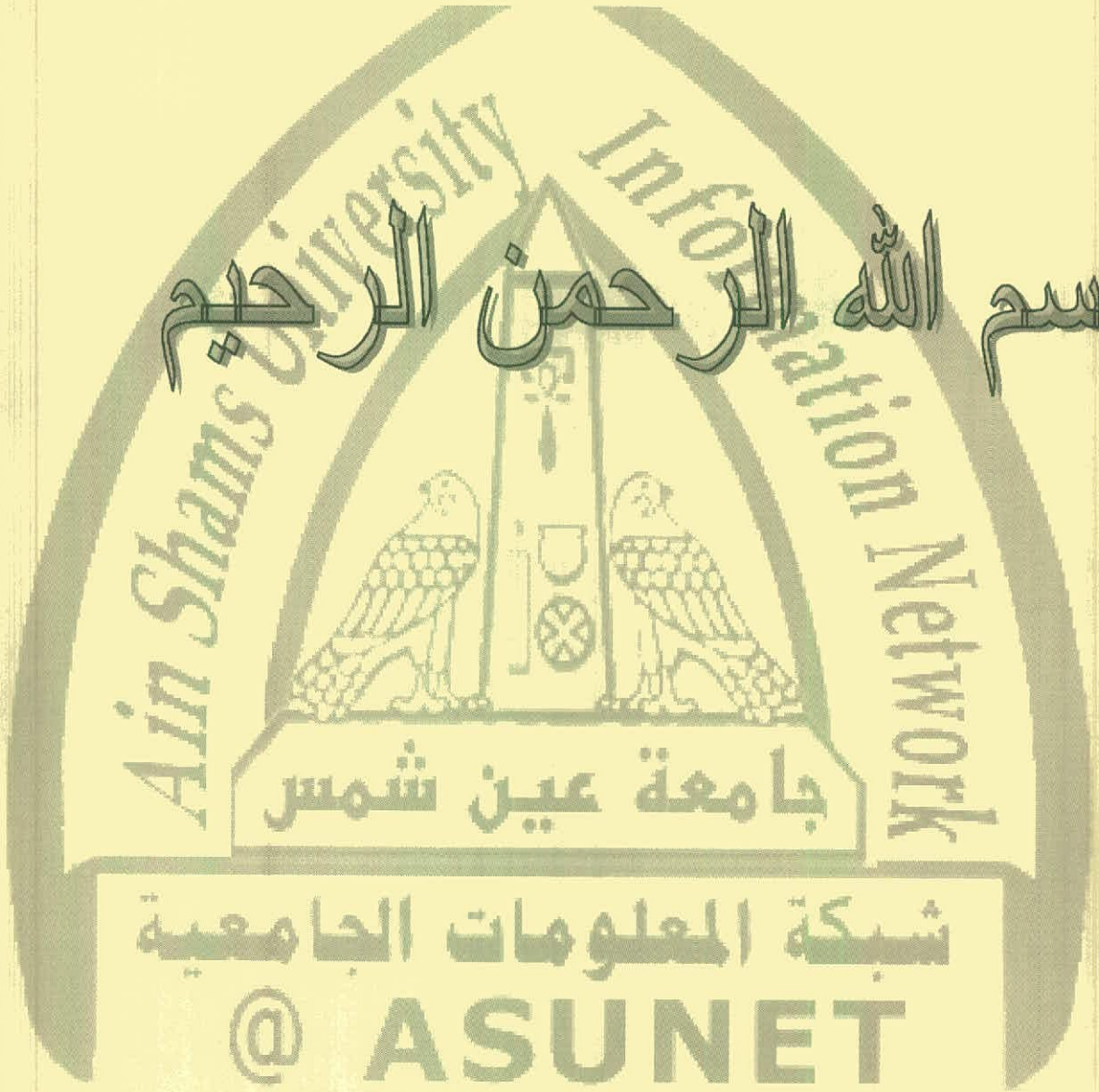
شبكة المعلومات الجامعية



بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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بعض الوثائـــــــق الاصليـــــة تالفـــة

بالرسالة صفحات لم ترد بالاصل

بسم الله الرحمن الرحيم

STUDY OF THE RELATION OF UPPER GASTROINTESTINAL ENDOSCOPY TO HEPATITIS C VIRUS INFECTION

Thesis
Submitted to the Faculty of Medicine
University of Alexandria
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Master of
Internal Medicine

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CONTENTS

CHAPTER I

INTRODUCTION

HEPATITIS C VIRUS

Identification of HCV:

Following the successful identification of hepatitis A and B viruses (HAV, HBV) in the 1970s, it rapidly became apparent that an agent or agents other than these 2 viruses were responsible for a significant proportion of hepatitis cases, especially following blood transfusion. Hepatitis in which neither HAV nor HBV could be incriminated became known as NANBH. In the following 2 decades, efforts to identify agents responsible for this syndrome using conventional virological methods were unsuccessful. In 1989 , Choo and associates [1] , applied creative molecular biological techniques that identified hepatitis C virus (HCV) , the agent now known to be responsible for most NANBH cases.

Morphology and Structure:

HCV belongs to the family ***Flaviviridae***. It is classified in a separate genus called ***Hepacivirus***.[2] It is a spherical enveloped virus of approximately 50 nm in Diameter.[3] Its genome is a single –stranded linear RNA of positive (protein coding) sense.[4] It is approximately 9.5 kb in size.[5] It consists of 5' non coding (NC) region of approximately 340 nucleotides, large open reading frame (ORF) of approximately 9,000 nucleotides and 3'NC region of approximately 50 nucleotides. The (ORF) encodes a large polyprotein precursor of approximately 3,000 amino acids that is cleaved into separate proteins by a combination of host and viral proteases. A capsid protein (C) ,at least two envelope proteins (E1 and E1)and a small putative protein of

unknown function (P7) are encoded in the 5' portion of the (ORF). At least six nonstructural proteins (NS2, NS3, NS4a, NS4b, NS5a, NS5b) including protease, helicase, and RNA polymerase enzymes and regulatory peptides are arrayed in the 3' portion of the (ORF).[6,7]

Physicochemical Properties:

HCV is inactivated by exposure to chloroform, ether and other organic solvents and by detergents.[8] The effect of heat and other inactivating procedures have been discovered by studies of the infectivity of products manufactured from plasma such as the factor VIII and IX concentrates used to treat clotting disorders. For example, dry heat treatment at 80°C or wet-heat at 60°C, organic solvents (n-heptane) and detergents efficiently remove infectivity for HCV in recipients.[8]

Types, Subtypes and Quasispecies:

Perhaps the most important characteristic of the HCV genome is its sequence heterogeneity.[9] The genetic heterogeneity of HCV is not uniform across the genome: the most highly conserved regions of the genome are parts of the 5'NC region and the terminal 3'NC region. The most highly conserved region of the (ORF) is the capsid gene. In contrast, the most heterogeneous portions of the genome are the genes encoding the envelope proteins. The 5' end of the E2 gene is the most heterogeneous region of all and has been named the first hypervariable region (HVR1).[10,11] It is believed to be a major neutralization epitope of HCV.[12-15]A few strains have a second HVR just 3' of HVR1; HVR2 appears to be limited to strains of genotype 1b.[11]

Based on their genetic heterogeneity, HCV strains can be divided into six major groups called types or genotypes. These have been

designated types 1 through 6. More than 50 subtypes have been described. They have been given letter designations e.g.(1a,1b,...) .[12]

The major genotypes of HCV differ in their distributions worldwide. Genotypes 1, 2, and 3 and their subtypes are distributed worldwide. In contrast, genotype 4 appears to be a Pan-African type (the principal genotype in Zaire and Egypt), and genotype 5 has been found to be the principal genotype in South Africa. Genotype 6 and its many variants have been found principally in Asia.[16]

The complex of genetic variants found within an individual isolate is termed the quasispecies. The quasispecies composition of HCV results from the accumulation of mutations during viral replication in the host. [17] The degree of diversity is related to the progression of liver disease.[18] The quasispecies show different sensitivities to interferon.[19,20] Lower heterogeneity increases the response to antiviral treatment as there are fewer variants to evade immune surveillance and survive after antiviral treatment.[19]

Immunity and Resistance to Infection:

There is lack of immunity to re-infection in repeatedly exposed individuals.[21] Data supporting this conclusion come from children with thalassemia major undergoing repeated blood transfusions in Sardinia were found to be re-infected and to experience a second case of clinical hepatitis C following re-exposure, even when the re-exposure was with a virus very closely related to the original infecting virus.[21]

Excretion of HCV RNA in Body Fluids:

The prevalence of HCV RNA in the body fluids of patients with

chronic liver disease who are positive for anti-HCV and serum HCV RNA is 100% in ascites , 48% in saliva , 24% in seminal fluid , and 7% in urine.[22] Hence sexual and household contact are likely modes of nonparentral transmission of type C hepatitis. Furthermore , the high prevalence of HCV RNA in ascites and saliva may have important implications in medical and dental practice.[22]

Epidemiology:

Hepatitis C Virus (HCV) infection appears to be endemic in most parts of the world, with an estimated overall prevalence of 3%.[23] However, there is considerable geographic and temporal variation in the incidence and prevalence of HCV infection. Using age-specific prevalence data, at least three distinct transmission patterns can be identified. In countries with the first pattern (e.g., United States, Australia), most infections are found among persons 30-49years old, indicating that the risk for HCV infection was greatest in the relatively recent past (10-30 years ago) and primarily affected young adults.[23] In countries with the second pattern (e.g., Japan, Italy), most infections are found among older persons, consistent with the risk for HCV infection having been greatest in the distant past.[23] In countries with the third pattern (e.g., Egypt), high rates of infection are observed in all age groups, indicating an ongoing high risk for acquiring HCV infection.[23] In countries with the first pattern, injecting drugs has been the predominant risk factor for HCV infection, whereas in those with the second or third patterns, unsafe injections and contaminated equipment used in healthcare-related procedures appear to have played a predominant role in transmission.[23]