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TITLE: Hepatitis C Virus Infection: Mechanism of Disease
Progression

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13. ABSTRACT (Maximum 200 Words) This proposal focuses on: (1) Effect of different HCV genotype infection in active duty military subjects. (2) Factors associated with progressive liver disease, (3) Liver histology progression of disease, (4) Laboratory evaluations on virologic and immunological markers of disease, (5) Detailed risk factor questionnaires, health survey and quality of life questionnaires. To date, 41 active duty subjects are enrolled in the study. It is premature to draw conclusions on this study. However, preliminary baseline data shows the following: The majority are Caucasians (58.5%), most are 40 years of age or older (63.4), most are men (85.4%) and 75.7% are enlisted service members. Liver biopsies showed fibrosis with portal expansion in 45%, bridging fibrosis (portal-portal or portal-central linkage) in 22.5%, cirrhosis in 17.5%, normal histology in 12.5% and 2.5% were inconclusive. The Child-Pugh's criteria showed that the majority of subjects were classified on grade A, two subjects were class C (one received a liver transplantation, one is waiting for one). One patient died recently of a brain tumor (hemagioblastoma) probably unrelated to HCV infection. Seventy six percent of these subjects received antiviral treatment.				
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INTRODUCTION

An estimated 170 million people are chronically infected with hepatitis C worldwide. Of these total, 4 million individuals in the USA are chronically infected with the hepatitis C virus. Annually 8,000 to 10,000 of these subjects die of liver related complications and approximately 5000 receive liver transplantation, placing hepatitis C infection as one of the major public health problem.

The United States military have rates of HCV infection similar to the general US population, that is an overall rate of 1.6%. However, it is a younger population and its natural history of HCV infection has not been studied. Therefore, the clinical outcome and impact of HCV infection in military subjects is largely unknown. Specific factors in military life have not been studied to observe their contribution to disease progression. Such knowledge is important for decisions regarding optimal management and prevention of this disease.

BODY:

This proposal focuses on (study objectives):

- Effect of different HCV genotype infection in active duty military subjects.
- Factors associated with progressive liver disease
- Liver histology progression of disease
- Laboratory evaluations on virologic and immunological markers of disease
- Detailed risk factor questionnaires, health survey and quality of life questionnaires.

HCV-infected subjects medical history is assessed retrospectively and subjects are followed prospectively for four years with clinic visits every six months during follow-up.

At the beginning of this proposal, we identified potential subjects to be enrolled in this study. Prospective volunteers were invited to participate.

A database was designed according to the parameters described in the original proposal in order to collect and analyze data. The database structure has been updated and optimized within the past few months and is compatible with SPSS for future statistical analysis.

To date, 46 active duty subjects with HCV infection were considered for enrollment in the study, 2 declined participation. Of the other 44 potential volunteers, 41 were enrolled. Two subjects did not fulfill eligibility criteria and one was withdrawn from the study. This group of subjects had a baseline visit where all the major study objectives (cited above) were assessed. This cohort is starting the six-months follow-up visits.

It is premature to draw conclusions on this study. However, preliminary baseline data shows the following:

- Ethnic distribution: 58.5% Caucasians, 29.3% African Americans, 4.9% Asians, 2.4% Latino/Non-Black, 4.9% Latino/Black.

- Age groups: younger than 40 years old (36.6%) and older than 40 years old (63.4%).
- Gender: Males 85.4% and females 14.6%.
- Military rank: 75.7% of enlisted and 26.4% officers.
- Sexual behavior was indicated as the most predominant mechanism of transmission for hepatitis C infection (per questionnaire). Other risk factors such as blood transfusion, tattoos/piercing and needle stick accounted for 17.1%, 14.6% and 9.8% respectively.
- Among laboratory abnormalities: alanine aminotransferase (ALT) abnormality was observed in 58.5%. HCV RNA was detected in 93% with a range from 600 IU/ml (viral particles/ml) to 1.3×10^7 IU/ml. The mean HCV RNA was 1.2×10^6 IU/ml. The most prevalent HCV genotype was genotype 1 (genotype 1a: 42.5% and genotype 1b: 25%), other genotypes in 30% and not determined in 2.5%.
- Liver biopsies assessed with the Knodell system showed fibrosis with portal expansion in 45%, bridging fibrosis (portal-portal or portal-central linkage) in 22.5%, cirrhosis in 17.5%, normal histology in 12.5% and 2.5% were inconclusive.
- The Child-Pugh's criteria showed that the majority of subjects were classified on grade A, two subjects were class C (one received a liver transplantation, one is waiting for one). One patient died recently of a brain tumor (hemangioblastoma) probably unrelated to HCV infection.
- Seventy six percent of these subjects received antiviral treatment (interferon and ribavirin) or have on-going treatment and 20% have not been treated.

KEY RESEARCH ACCOMPLISHMENTS

- Subject chart revisions for corroboration of hepatitis C infection;
- Review and summary of existing laboratory data;
- Identification of subject cohorts: prospective and retrospective;
- Enrollment of subjects into a prospective cohort consisting of the following: medical history, physical exam, questionnaires (Hepatitis C, Health Survey and Chronic Liver Disease Questionnaire); initial serum collection and laboratory parameters assessments;
- Liver biopsies: review of existing biopsies within the past 2 years and scheduling of new ones;
- Data Management: database design, data collection and entry.

REPORTABLE OUTCOMES

None to date

CONCLUSIONS

The ultimate significance of this work is the assessment of the impact of HCV infection in military populations. Evaluation of morbidity and mortality among servicemen and the risk factors that may contribute to infection with this virus are additional important

outcomes of this study. Response to antiviral treatment is also being assessed. The study is ongoing.

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