to be associated with approximately a 85–90% chance of SVR. There have also been concerns that RVR may differ depending on which assay is used. In other words, will using a very sensitive PCR assay with lower limit of detectability to approximately 10 IU/mL show the same predictability as the older assays with a detection limit of 50 IU/mL or those who use an assay with a limit of 500 IU/mL? Current evidence seems to suggest that no matter which assay is used, RVR holds its strong predictive value.

While 24wk in genotype 1 RVR is now accepted and even recommended in some consensus guidelines, shortening treatment to 16 in those with RVR and genotypes 2 and 3 remains controversial. The largest study with nearly 1500 patients of genotypes 2 and 3 showed that even those who achieve RVR would benefit (slightly but significantly) from the full 24wk of treatment compared to only 16 wk. Further study is needed to better define those subgroups with genotype 2 and 3 who may be able to shorten duration of treatment without compromising the chance of achieving viral clearance. We also need to study increasing duration or intensifying treatment in those genotype 2 and 3 patients who do not achieve RVR (about 1/3 of genotype 2 and 3 patients do not achieve RVR), as their sustained virological response (SVR) rates are only approximately 50% with 24 wk of treatment. Finally, we should probably start considering genotypes 2 and 3 separately rather than lumping together as a single homogeneous entity. It is clear that they behave slightly differently in response to treatment.

I-55 Management of chronic hepatitis B and C in HIV-co-infected patients

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Due to sharing the same route of transmission, co-infection of HIV-HBV or HIV-HCV can occur in some patients. Co-infection with HBV or HCV accelerates liver disease progression and increases the risk of liver-related mortality in HIV-infected patients.

Due to low baseline ALT, high baseline HBV DNA and decreased HBV-specific T-cell response in HBV-HIV co-infected patients, treatment with IFN has low efficacy with HBeAg loss in 0–20% and less tolerability. IFN treatment should be considered only in patients with ALT more than 2 times ULN, HBV DNA less than 7 logs copies/ml and CD_4 count greater than 500 cells/mm^3. Anti HBV agents without effect on HIV such as adefovir dipivoxil or telbivudine is the treatment of choice for patients who not require HAART. Lamivudine and tenofovir plus other anti HIV agent are recommended in patients with CD_4 more than 200 cells/mm^3 whom HAART is indicated. In order to prevent immune reconstitution induced-hepatitis flare, patients with advanced liver disease and low CD_4 count should be initially treated with lamivudine plus tenofovir until HBV DNA become undetectable before adding the third agent of HAART.

Peg-IFN plus ribavirin treatment is the standard treatment for both HCV mono-infection and HCV-HIV co-infection. As in mono-infected patients, HCV genotype 2, 3 have better sustained virological (SVR) than genotype 1 (44–69% vs 11–38% in HIV-coinfected patients treated with Peg/IFN plus ribavirin). Drug interaction and mitochondrial toxicity must be carefully monitored through out treatment period in patient receiving HAART. Didanosine should be avoided in patients receiving ribavirin. On treatment virological response have a good predictive of response and may be used to guide treatment decision.

Concurrent Session 11 – Emerging Infectious Diseases: Pathogen in Animal and Human

I-56 Death and severity of meningococcal disease – influence of microbial phenotype, host genotype and environment

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Across Europe the incidence of meningococcal disease varies from between 1 per 100,000 up to 14.3 per 100,000 population per annum. The case fatality rate overall is approximately 8%, but amongst survivors there is a relatively high frequency of severe sequelae including hearing impairment, neuro-cognitive abnormalities, severe skin and soft tissue abnormalities including loss of limbs, and renal failure. Physicians and paediatricians who treat meningococcal disease observe a range of severity from relatively benign disease to severe physiological disruption leading to death. In general terms, those who present with meningitis tend to have a better prognosis, whilst those who present with severe sepsis syndrome have the worst prognosis. Study of factors associated with the severity of meningococcal disease is difficult and confounded by factors such as the sporadic nature of the disease and marked differences in access to health systems between individuals. Many studies have shown that the outcome of meningococcal disease is associated with the phenotype of the infecting organism. The odds of death from disease are highest for certain sequence types, for example ST-11/ET-37 complex and ST-32/ET-5 complex. The precise phenotypes responsible for the enhanced virulence of these sequence types has not been precisely defined. The major virulence determinants of *Neisseria meningitidis* include the polysialic capsule, LPS immunotypes, sialylation, and outer membrane proteins including Opa and Opc. Whilst there is no consistent segregation of virulence determinants in clonal groups associated with the most severe disease, organisms expressing serogroup C have been associated with fatal outcome.

A number of host factors have been identified as important in determining severity of disease. Chief amongst these is age at presentation, with the worst prognosis being associated with adults. Some of this may be explained by the increasing sophistication of paediatric intensive care. Twin studies have indicated that death from severe infectious disease has a familial component and in the case of meningococcal disease a large number of studies have been conducted to investigate the role of genes encoding components of the immune system, the inflammatory response and coagulation pathways. The difficulty faced by geneticists is that death is the most easily verifiable end point for the purpose of studying genetic modifiers of severity of disease. Because of the death rate of only 8% this means that very small cohorts are available for study. However, association studies have revealed a relationship between a number of genes and the likelihood of death in meningococcal disease. These include Fc receptors, polymorphisms of plasminogen activator inhibitor type 1, properdin deficiencies, and polymorphisms within interleukin 1 and the interleukin 1 receptor antagonist.

In several countries, there have been increasing reporting of isolates of *Neisseria meningitidis* with reduced sensitivity to penicillin. Treatment failure has been reported extremely rarely and studies have failed to demonstrate any association between reduced penicillin susceptibility and fatal outcome. Most doctors consider that emergency treatment of newly-presenting cases with penicillin in the community is mandatory. Controversially, a recent study has suggested that treatment in the home with injected penicillin may be associated with increased severity of disease. This will be discussed.