Hepatitis B infection: current concepts and future challenges

The above comprehensive review by Nebbia and colleagues is the second in the current mini-series on viral infections and relevant immunological responses in infected individuals. The review follows the style of the previous paper in this series which considered hepatitis C infection. It begins with an overview of the epidemiology of hepatitis B and then moves on to summarise aspects of human immunological responses to the virus which could enable the development of future therapeutic options. Hepatitis B is indeed a common virus of some considerable clinical significance with over 350 million people considered to be chronic carriers of the infection, some of whom develop cirrhosis or hepatocellular carcinoma. In order to understand current and future strategies for the management of hepatitis B infection in infected individuals, it is important to acknowledge two key events in its natural infection history. The first of which, known as covalently closed circular DNA, results from the development of replicative intermediates in the nucleus of the hepatocyte which form the basis for persistence of viral infection. Reverse transcription step is the second event which enables the emergence of highly heterogeneous viral populations. There are four phases in the natural history of infection with this virus: these relate to immune tolerance, immune clearance, inactivity and reactivation. The current major therapeutic goal is one of prevention of disease progression. Commonly used anti-viral agents have limitations in efficacy and possess significant side-effects. The ideal therapeutic approach will be one of boosting of the host immune system along with clearance of the virus. Current research is currently directed towards more precise harnessing of the host immune response while blocking potential pathways for liver damage.

Management of acute exacerbation of chronic obstructive pulmonary disease

The second review in this month’s issue from Messer and colleagues considers current evidence regarding the appropriateness of current management strategies for patients who present with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) with particular reference to admission to the intensive care unit (ICU). This represents a therapeutic dilemma in that while the short to medium prognosis for this group of patients following ICU admission is relatively encouraging; the longer term outlook is disappointingly poor. The aim of the review was to evaluate the prognostic significance of a number of clinical variables including pre-morbid factors and laboratory/physical parameters for patients with AECOPD. The task was admittedly challenging, as previous work in this area has unhelpfully resulted in conflicting opinion and varying recommendations. A five step integrative review process was undertaken that included precise identification of the problem and synthesis of relevant literature. Several prognostic variables (prior to ICU admission) were found to be associated with adverse intermediate term outcome. The relevant variables were those which represented acute physiological disturbance and severity of acute disease, particularly: adverse Glasgow Coma Scale, cardio-respiratory arrest, prolonged length of stay and cardiac dysrhythmia. Interestingly, it was found that pre-morbid variables such as age, functional capacity, body mass index and use of long-term oxygen therapy were not found to be associated with intermediate term mortality. While this information is useful, the next step should be the...
development of a scoring system based upon the findings from this review.

The safety profile of statins

We publish yet another paper which considers the efficacy and safety profile of statins. At least 10 papers have been published in QJM on this broad theme over the last three years so what additional information or perspective does the meta-analysis by Alberton et al. contribute to this debate? This subject is one which is capable of provoking strongly held and divisive viewpoints. As statins are reputed to be one of most prescribed drugs in the world, the authors justify a meta-analysis that employed indirect comparisons in order to identify risk associated with statins as a drug class and with individual statins. The analysis focussed on overall mortality, cancers, rhabdomylosis, diabetes, and abnormalities in AST, ALT, and CK as this type of data is more consistently reported. The overall finding was there was an increased risk of diabetes and of raised AST associated with the use of statins when compared to controls. Indirect comparisons demonstrated somewhat different risks between individual statins such as the observation that simvastatin significantly increased CK levels when compared to rosuvastatin. However, the meta-analysis also showed that the use of statin therapy significantly decreased the risk of all-cause mortality and acknowledged that the use of statin therapy for cardiovascular disease is associated with a relatively low risk of adverse events.

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