Renal Fibrosis

Editor’s choice

I draw your attention to the second review in the commissioned series on fibrosis. The paper by Hughes and colleagues from Edinburgh focuses on renal fibrosis. As is the case with disease processes involving other organs, renal fibrosis represents a final common endpoint of a wide variety of disease entities. Unfortunately, the development of renal fibrosis is invariably associated with an adverse prognostic outcome. A complex process is associated with the development of renal fibrosis involving cellular and molecular mediators – hence the use of the term ‘cellular orchestrators’ in the title of the review is particularly apt. The review considers the key players and events in the development of renal fibrosis including the myofibroblast, infiltration of renal tissue by monocyte macrophages and the role of various molecular mediators. The key clinical question is whether renal fibrosis may be reversible. The answer appears to be yes but at present only to a point. Unfortunately for severe cases of renal fibrosis, the therapeutic options are currently rather limited. Future developments in this area might include strategies for the targeted depletion of macrophages and the administration of serum amyloid P.

Amyloidosis and the heart

The second review paper this month is by Dubrey and represents a comprehensive consideration of amyloid cardiomyopathy. Human amyloid disease may be caused by many different precursor proteins and it is now thought that there are three main types of cardiac amyloidosis: light chain, senile systemic and hereditary amyloidosis (most often due to a mutant form of transthyretin). The aetiology may vary across the world with infection and inflammation representing the main cause of cardiac amyloidosis in developing countries. A restrictive cardiomyopathy develops which is associated with reduced cardiac output. There are two main treatment objectives. In the first instance, diuretics and restriction of dietary salt broadly represent the main current supportive therapeutic options. The second objective is to limit the amyloid process itself by means of reduction of the individual precursor protein. Cardiac arrhythmia is not uncommon in this group of patients and unfortunately the use of standard anti-arrhythmic drugs may be less than fully effective. A number of new but promising therapeutic modalities are outlined which include high dose mephalan and thalidomide. Heart transplantation has been undertaken in a number of patients with cardiac amyloidosis. The outcome has not always been successful as a result of progression of the underlying systemic disorder. Other approaches have included a combination of chemotherapy, heart transplantation and dexamethasone. Sadly, the current situation for patients with this disorder is that disease progression seems inevitable unless more effective drugs that reduce the amount of amyloid-forming below the threshold for fibril deposition are developed. Novel therapeutic avenues are being explored which include amyloid constituent inhibitors.

Another role for Vitamin D?

Numerous papers on the many roles that vitamin D may play in the prevention of disease processes have been published in QJM over the years. Recently, the journal has published research that demonstrated an association between vitamin D, statins and muscle function. A paper in 2002 looked at effects of vitamin D deficiency on post-menopausal women. This month researchers from Israel claim to provide evidence that vitamin D plays an important role in the immune system. 130 patients who were admitted to an intensive care unit and who required mechanical ventilation were included in the study. Patients who had taken Vitamin D supplementation prior to admission were excluded. Vitamin D concentration was estimated on admission and as a result, over 100 patients were found to have Vitamin D deficiency. There were two major findings: patients with adequate Vitamin D concentration survived longer and,
furthermore, their white blood count was found to be more responsive to infection than those patients with low levels of Vitamin D. Vitamin D deficiency is associated with a wide variety of disease especially tuberculosis, myocardial infarction, cardiac failure and diabetes. The question however is whether this paper provides sufficient evidence for active Vitamin D supplementation of critically ill intensive care patients.

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