and halts viral replication in infected cells. The authors showed that HCV E2 protein binds to PKR and inhibits its phosphorylation activity. As a result, PKR cannot inhibit eIF-2α; it loses its ability to mediate the activity of interferon to inhibit viral protein synthesis. Significantly, these effects can be seen only with E2 proteins of genotype 1 but not with other genotypes, the latter of which are more sensitive to interferon. This study thus unlocks the mystery of the clinical resistance of HCV to interferon and opens up the possibility of developing new strategies to improve interferon activity.

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(3) Science 1999; 285: 107-10

Mild aortic valve thickening is associated with adverse clinical outcomes
Degenerative aortic valve changes are seen in 21–25% of adults over the age of 65 years with a continuum of disease from mild leaflet thickening (aortic sclerosis) to severe obstruction to left ventricular outflow (aortic stenosis). In the past, aortic sclerosis has been considered to be a benign incidental finding on echocardiography. Our earlier study (J Am Coll Cardiol 1997; 29: 630-4) using the Cardiovascular Health Study population, demonstrated that older age, male gender, elevated LDL and Lp(a) levels, diabetes, hypertension and smoking, are associated with aortic sclerosis or stenosis, with a magnitude of risk similar to that seen with atherosclerosis.

Aortic stenosis (with blockage of blood flow out of the left ventricle) clearly is associated with adverse cardiovascular outcomes with symptomatic disease requiring valve replacement in about 30,000 adults per year in the U.S. However, it has been unclear whether milder degrees of leaflet thickening are associated with an increased risk of cardiovascular events. In the current study, we found about a 50% increase in cardiovascular mortality in subjects with aortic stenosis on echocardiography compared to those with normal valve leaflets. This increase in risk is seen even after adjustment for other clinical factors, including age, gender, cholesterol levels, hypertension, diabetes and smoking. Since this is a single study, validation of this finding in other populations is needed. In addition, studies defining the mechanism of the increased risk are needed. It may be likely that aortic sclerosis is simply a marker of subclinical coronary atherosclerosis rather than having a direct effect on clinical outcome. Further studies evaluating potential interventions to slow or reverse the disease process also are needed.

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Cloning of the prometastatic enzyme heparanase
In most cancer patients the primary tumour is not life-threatening and can be readily removed by surgery. It is the spread of the cancer to vital organs, a process termed metastasis, that usually causes death. In order for cancer cells to escape from the primary tumour mass, enter the circulation and pass through the walls of blood vessels in distant organs they need to degrade the extracellular matrix, a scaffolding surrounding cells, by using a battery of degradative enzymes. This paper describes the cloning and characterisation of an essential enzyme involved in cancer metastasis, an enzyme which has eluded researchers for 20 years. The enzyme, called heparanase, attacks heparan sulphate, a key sugar molecule which makes up the extracellular matrix. Exhaustive studies described in the paper revealed that only one type of heparanase exists in mammals. This makes the enzyme a particularly attractive target for the development of antimetastatic drugs as it is unlikely that metastasising tumour cells can bypass heparanase inhibitors by using alternative enzymes to perform the same function.

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Malaria modulates dendritic cell function
Malaria parasites cause repeated and prolonged infection, even in those constantly exposed to infected bites. Many mechanisms of immune evasion have been demonstrated for the parasite. We suspected other mechanisms existed and we therefore investigated the interaction between malaria and infected red blood cells and dendritic cells. These antigen-presenting cells are crucial to immune responses, whatever their nature, as they stimulate not only memory but also naïve T cells. We showed that malaria-infected erythrocytes adhere to the surface of dendritic cells and block subsequent maturation of the dendritic cell and