Haemophilia, new developments in patient treatment

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These are exciting times for those with an interest in haemophilia treatment. At least in the Western world, we have grown accustomed to safe and available clotting concentrates. To the clotting factors themselves, nothing major has changed for decades. This is now rapidly changing. First, longer acting products are becoming available in routine patient care. Both extended half-life factor VIII and IX concentrates are now licensed. For factor VIII, unfortunately, the different methods of extending half-life have not yet been able to overcome the limited half-life of the carrier Von Willebrand factor. For factor IX, longer acting products will permit prophylactic dosing once every week or two weeks. These products could be combined with regular half-life products, for a highly individualized treatment plan. This will ofcourse challenge our understanding of pharmacokinetics and individual haemostatic requirements.
For severe haemophilia, a number of gene therapy trials are underway, including also a number of Dutch patients. Results are good for haemophilia B, changing the fenotype to moderate in most cases. For haemophilia A, recently even better results were reported, also with AAV-mediated in vivo gene transfer to hepatocytes. Other options, such as stem cell based gene therapy, are also being explored. Some very exciting new approaches do not involve factor VIII or IX at all. They target other components of the clotting cascade, thus bypassing or compensating for the absence of factor VIII of IX. This would make them also effective in persons with inhibitors and, for some approaches, in patients with other hemostatic disorders. The bispecific antibody emicizumab targets FIXa and FX, exhibiting the cofactor activity that factor VIII normally has. A number of antibodies have been developed to block TFPI, and therefore stop the negative feedback loop through FXa. Lastly, a small interference RNA was developed that decreased the expression of antithrombin, ALN-AT3. For all these drugs, clinical trials are underway.