Scientists find a new way around blood clotting disorders

Abi Berger *BMJ*

People with clotting disorders are usually lacking factor VIII or IX from the intrinsic clotting pathway. Conventional treatment for these conditions involves regular injections of plasma products containing the missing factors, or injections of recombinant products.

The injected products are associated with two problems: they lack stability, and so the injections need to be repeated frequently; and the recipient may raise an immune response to the foreign products, which causes inactivation of the injected products.

Professor Harvey Pollard from the Uniformed Services University, Bethesda, Maryland, and his team have now come up with a new approach that bypasses both of these problems and could lead to an entirely new way of treating clotting disorders (*Nature Biotechnology* 2000;18:289-95).

Scientists have known for about 20 years that activated factor VII (VIIa) also plays an important part in the clotting cascade, and this has encouraged the development of alternative "bypass strategies" for people who have developed inhibitors to factors VIII and IX.

Factor VIIa directly activates

factor X (promoting normal coagulation), effectively bypassing the need for factor VIII or IX. But factor VIIa has a short half life, so intravenous injections of factor VIIa have to be given every two hours.

An alternative way to produce factor VIIa would be to inject factor Xa or XIIa because both of these activate plasma factor VII. This method would have the serious disadvantage, however, of converting the body's supply of soluble fibrinogen into insoluble fibrin, and this could lead to disseminated intravascular coagulopathy—a condition that is often fatal.

To get around this problem, Professor Pollard and his colleagues have designed an implantable capsule that allows a continuous production of factor VIIa, using factor XIIa, without allowing it to convert soluble fibrinogen into insoluble fibrin.

"We have devised a way of encapsulating factor XIIa without letting it loose in the body," explained Professor Pollard. The capsule is an enclosed membrane with tiny holes in it, like a saltcellar, which can be surgically implanted in the peritoneum.

Factor XIIa is immobilised on solid supports inside the membrane, and plasma factor VII can diffuse into the capsule. On interacting with the immobilised factor XIIa, the plasma factor VII is activated, and this newly generated factor VIIa diffuses back out again through the porous membrane into the plasma to circulate.

This in turn activates plasma factor X, bypassing the need for factors VIII and IX, allowing the

Blood coagulation sequence showing the role that factor VIIa could have in treatment of blood clotting disorders

normal clotting cascade to continue.

Professor Pollard's team has successfully tried its device in guinea pigs and in two rhesus monkeys. One of the monkeys was given an active device, and

the second had a capsule inserted with no factor XIIa inside it.

The monkey with the active device achieved coagulation levels of 20% of normal and was therefore considered "therapeutically fixed." □

Romanian national insurance cannot cover GPs' prescriptions

Tudor Toma *Bucharest*

The Romanian national health insurance organisation (Casa Nationala de Asigurari de Sanatate) has informed general practitioners that it cannot cover the cost of all the drugs that they prescribe. GPs may thus have to pay for some of the prescriptions themselves.

The national insurance system is meant to pay for up to 80% of the cost of a prescription for a generic drug; the rest

of the cost is supposed to be met by the patient. But the organisation has set the budget for prescriptions for each GP at an exceptionally low level. Each GP has been given a budget of 4 million lei (£133, \$213) a month for drugs, a sum which is meant to cover the drugs for all of the patients seen by the doctor; each doctor has about 1500 patients on his or her list.

General practitioners will be monitored to determine what they prescribe that exceeds this limit. If GPs exhaust their budgets but continue to write subsidised prescriptions the excess cost will be automatically deducted from their salaries.

In the last month alone, most GPs wrote prescriptions worth 30 million lei, about seven times more than they are meant to. Under the new budget a GP who has 1500 people on his or her list and who sees 300 patients a month will be able to prescribe the equivalent of one aspirin per patient. Patients will have to pay in full for everything else. Many people with chronic diseases will

not be able to afford to pay.

The new insurance system was launched in July 1999. It initially had enough money to pay for all medical services, including prescriptions, but it now has a cash flow crisis. Ionel Adrian, a regional chairman of the insurance organisation, said: "In our region [Iasi] we cannot collect insurance from everybody, and we pay for expenses which should be the responsibility of the state. This is a temporary rationing that does not apply everywhere in the country."

Dan Pletea, a GP in Iasi said: "It is impossible to practise medicine if doctors are punished for giving correct treatment." □