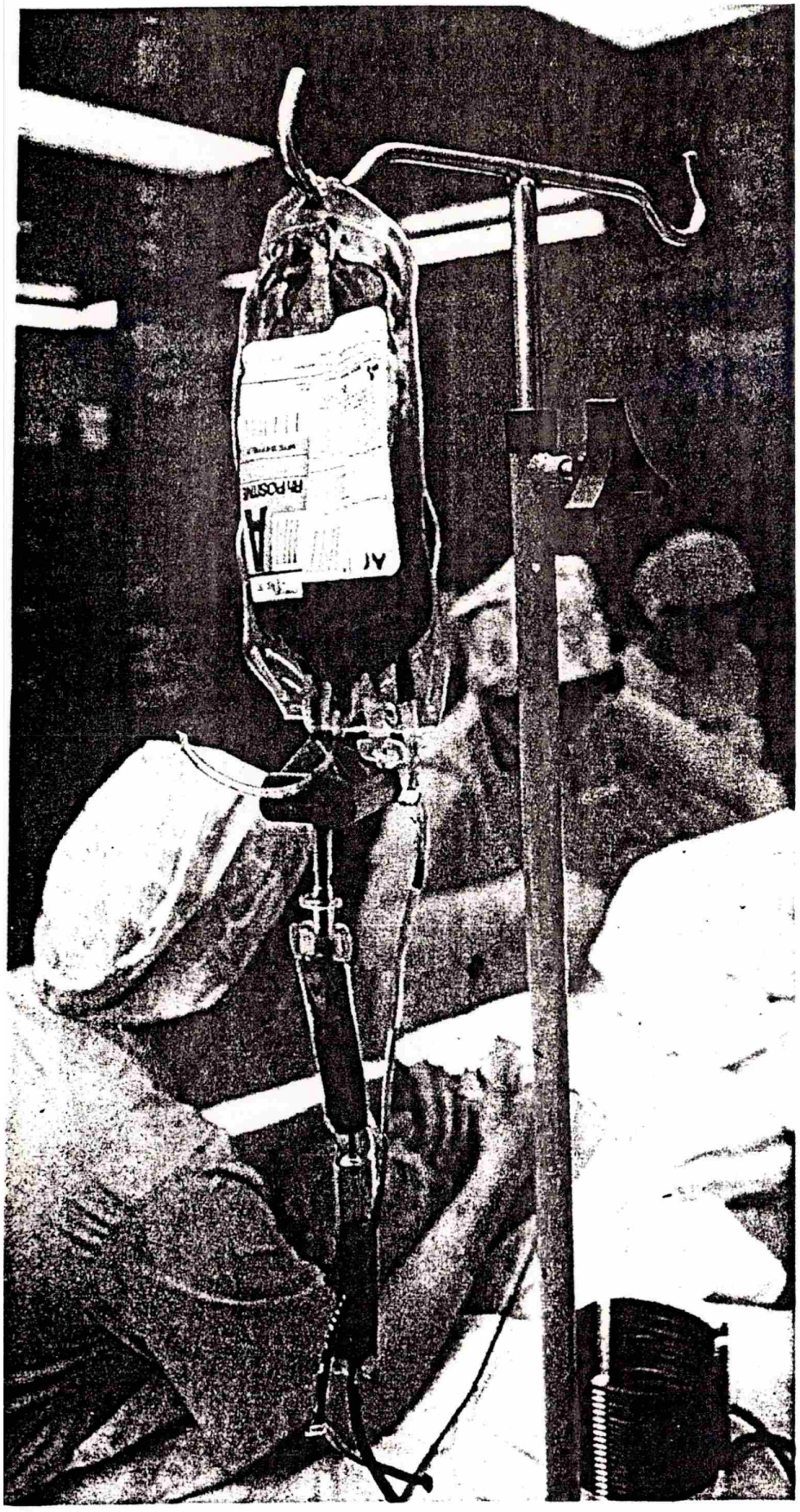


Pure but not simple

By Martin Stevenson

A brilliant British break through in bio-technology has led to the genetic engineering of the the blood clotting factor VIII and will soon come to the rescue of heamophiliacs — eliminating the threat of infection by hepatitis or the killer disease AIDS.

It was made possible by research carried out at Speywood Laboratories, a company founded by Nottingham pharmacist David Heath in 1973 to isolate and produce from pigs blood the factor VIII fraction which is missing or inactive in the blood of haemophiliacs.

Porcine factor VIII is needed to treat some heamophiliacs who have antibodies to human factor VIII.

The purification process developed by Speywood was then applied to human blood. In a joint project a research team at the Royal Free Hospital succeeded in isolating the pure protein for factor VIII.

It was the crucial break through and Genentech, the leading American genetic engineering company in California, then succeded in synthesising the protein. But it will probably be the 1990s before it becomes generally available.

Genentech set over 20 scientists to work, cloned the blood clotting gene — the final vital step before manufacture. But it will not be made in Britain. The British Technology Group, who were then the major Speywood shareholder, brought in new managment and renegotiated the mutual collaboration deal with Genentech.

Speywood gave up manufacturing rights in return for extended marketing rights in Europe and concentrated on its world beating process for making factor VIII from pigs blood which they now sell under the registered brand name of Hyate:C.

● *Blood transfusion at Nottingham City Hospital. Picture by hospital medical photographer Geoffrey Gilbert.*

There is every indication that the cloned factor VIII will eliminate the risk of heapatitis and the new killer disease AIDS which every haemophiliac dreads.

But not everybody is happy with the renegotiated deal. "It's a tragedy," says David Heath, the Nottingham pharmacist who founded Speywood Laboratories and initiated the research. "A disillusioning ten years of my life went into Speywood, wasted because the British didn't get the best out of it."

David Heath, resigned from Speywood in September 1983 and has formed Cavendish Technology Partnerships with Nottingham businessman Bob Pynegar to promote commercial development of university research.

When he set up Speywood, David Heath bought the rights for an American process which has been developed into a production process to make a porcine factor VIII that is purer than any product then available.

Previously porcine factor VIII was not ideal. It was used for some patients who were unable to tolerate the human blood derived product simply because there was nothing better on offer, but there were unwelcome side effects.

APPROVED

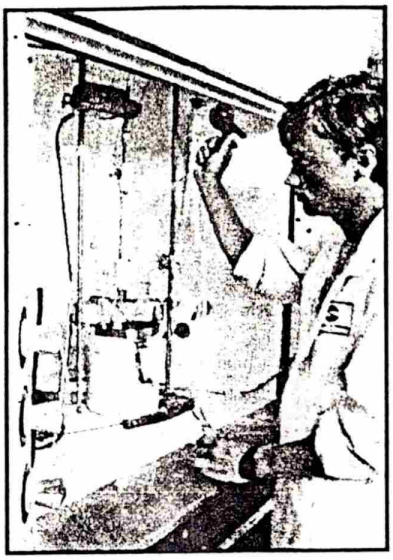
The new process was developed by Sarah Midddleton, former chief scientist to the company and now their Nottingham based technical consultant. She spent eight years with the Scottish blood transfusion service and two years in research at a haemophilia unit before joining Speywood in 1979.

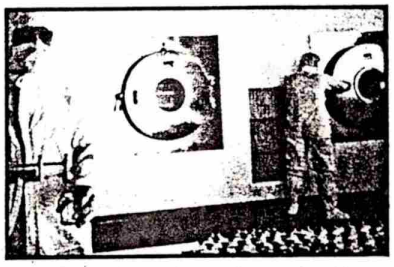
After two months in the United States picking up the new technology she came back to Wrexham where, working in two Portacabins with blood supplied by a nearby abbatoir, she headed a team refining the process. They produced a porcine factor VIII 30 times as pure as the previous product. "It proved to be superb in patients and since that time has been very effective," she says.

It has been approved for use in the UK, is undergoing clinical trials in America and is being used in many other countries.

Speywood, which was bought last June by the Porton International group of bio-technology companies, had set up a purpose built facility at Wrexham to make Hyate:C. Although intended for patients whose blood produces antibodies to human factor VIH the improved porcine product, which they market worldwide, could be used more widely.

Porton International have shown their total commitment to the staff and facility at Wrexham and have already invested heavily in establishing increased and improved production plant at the new factory.





● *Top: Research work at the Speywood Laboratory. Below: Freeze-drying Hyate:C.*

The poly electolyte technology used in the purification process was originally developed to clean virus out of sewage. As such it was a fairly rough and ready process.

Speywood improved the method to such an extent that when applied to blood fractionation it not only gave a product 30 times more pure than anything which had gone before, it also enabled them to isolate the pure factor VIII protein — something which because of its complex molecular structure had eluded other researchers.

WORLD SUPPLY

Factor VIII is present in the body in extremely small amounts, only about one milligram circulating in each adult. But it has a very high specific activity. Two kilograms of pure factor VIII — the weight of a couple of bags of sugar — is enough to supply the entire world for a year.

As it is in such minute amounts it requires a tremendous volume of blood to extract material in sufficient quantities. That made it very difficult to isolate the pure protein.

The process used for porcine factor VIII was then applied to human blood. Two more stages were added on in research carried out at the Royal Free Hospital School of Medicine in London in a joint project with Speywood and funded by them.

It was an amazing break through producing a protein more than four times the size of albumin, the largest then achieved by genetic engineering. Its complex structure has 2,300 amino acids — 40 times more than insulin and 15 times more than alpha interferon.

Speywood sent Genentech the pure protein which they then succeeded in cloning. At last the way was open to produce purely artificial blood. But there is still a very long way to go.

It will probably be the early 1990s before the artificial factor VIII is generally available, says Sarah Middleton.

When the engineered factor VIII is readily available it will be unethical for anyone to risk using the naturally based human product with the inherent risks of AIDS or other virus infections.

The way is opening up to genetically engineer or synthesise other blood fractions, including one which can be used to treat emphysema, which are difficult to extract by present methods.

RESEARCH PROJECTS

At Cavendish Technology Partnerships, David Heath has picked up some of the research dropped by Speywood. "We've got some more genes and other things which will make other blood proteins because when factor VIII goes, all the other bits will become very expensive if they're going to be made at all," he says.

There are plenty of people working on replacing them with synthetic components — but there are some very difficult ones.

"So many medicines can be made in this way — quickly and more efficiently than the old hit or miss methods of finding medicines. You can actually design your medicine with bio-technology."

Cavendish Technology Partnerships is in the business of technology transfer — finding good research projects in universities which fall flat because there is no company to pick up the expensive research, test it and assess it in man and animals.

He tries first to find British sponsors. If that fails (and it often does) he goes to America. He helps raise the funding and organise the science if that is required.

British companies are very slow in making up their minds if you can't show that in two years time you'll make big profits. They always want returns too quickly "whereas Americans are prepared to go for long term and take a punt at it," he says.

"The British are very shy in investing in these very high risk things — a lot will fall by the wayside. But those that don't will be very, very profitable and lead in technology. Once you've captured the technology that's it."