

# Doctors debate safety of starch drips

Study fuels controversy over widely used intravenous fluids.

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Medical researchers are asking whether one of the fluids that doctors regularly administer to severely ill patients may actually be doing more harm than good.

The humble drip is one of the most common tools in medicine, used to put a variety of fluids into patients to treat a host of medical conditions. But a paper<sup>1</sup> published in the *New England Journal of Medicine (NEJM)* last month has fuelled smouldering doubts about one such type of fluid — hydroxyethyl starch. Scientists are now preparing for a US Food and Drug Administration (FDA) meeting next week in Bethesda, Maryland, where they will try to agree on whether the use of starches should be discontinued.

The NEJM study looked at people in intensive-care units (ICUs) with severe sepsis — whole-body inflammation caused by an infection, which results in a drop in blood pressure that must be corrected using fluid injections to expand the volume of their blood. Starches have been used in the belief that they are less likely to leach out of the circulatory system than saline. But the researchers found that after 90 days, 201 patients of 398 given starch had died, compared with 172 of 400 given a fluid called Ringer's acetate.

Exactly how often starch is used in hospitals around the world is unclear, with practice varying widely between countries and even between doctors in the same hospitals. But it is “highly used”, says Anders Perner, an intensive-care doctor at Copenhagen University Hospital and lead author of the study.

Perner says that starch is a standard option in doctors' toolkits — but it should not be. “We changed practice the day we saw the results. Many Scandinavian ICUs have done the same,” he says.

There are a number of different types of hydroxyethyl starch on the market, and some doctors question how well studies based on one kind will apply to others. It is also unclear how findings concerning people with sepsis will affect the use of starch to treat other conditions, especially outside ICUs — in operating theatres, for example. But the NEJM paper does indicate that the problems may be widespread: more patients receiving hydroxyethyl starch experienced kidney failure. Previous studies on different starches have also identified kidney problems<sup>2</sup>.

## Fluid situation

Leading ICU doctors and researchers are sharply divided on the safety and efficacy of starches. Some had stopped using starches even before the NEJM paper was published. Others insist that the latest developments are far from a death knell for the therapy.

Nigel Webster, president of the Critical Care Medicine Section of the UK Royal Society of Medicine, will not be changing his medical practice on the basis of Perner's paper. He says that trial participants who received starch were also given more blood products such as plasma than the people who received saline, which could affect outcomes.

Some doctors may be cautious about Perner's results owing to commotion in the community about a decade ago, when a meta-analysis<sup>3</sup> linked the use of the blood-plasma protein albumin as a replacement fluid to increased deaths, before a major study<sup>4</sup> in Australia showed that the result was probably not reliable. The scare has made people wary of changing their practices rapidly in response to similar claims, says Webster.

“The battle for finding the appropriate replacement fluid has been going on for decades,” says Clifford Deutschman, a critical-care doctor and researcher at the University of Pennsylvania in Philadelphia. Evidence that starches may be causing harm, he says, “is one



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The safety of hydroxyethyl starches used in IV drips is up for debate.

more step back in terms of finding it”.

Perner will travel to the United States for the FDA meeting on 6–7 September, where researchers will hear about his paper and another major study of starches. The Crystalloid Versus Hydroxy-Ethyl Starch Trials (CHEST) study headed by the George Institute for Global Health in Sydney, Australia, has studied 7,000 people in ICUs in Australia, comparing the effects of administering saline with those of a starch different from that used in Perner's study. The results are expected imminently.

Derek Angus, a critical-care doctor at the University of Pittsburgh School of Medicine in Pennsylvania, says that the results will be telling. “The biggest thing will be if the CHEST trial is in the same direction” as the NEJM paper, he adds.

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## References

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