Doctors advised to take special care with human albumin

Richard Woodman, *London*

The Committee on Safety of Medicines has advised doctors to restrict the use of, and take special care when using, human albumin after concerns that far from saving life the preparation may actually increase mortality.

A systematic review by the Cochrane Group published last year (*BMJ* 1998;317:253-40) of 23 randomised controlled trials, including 1419 critically ill patients with hypovolaemia, burns, and hypoalbuminaemia, found that the risk of death in the group treated with albumin was significantly higher than in patients who received either crystalloids or no treatment.

The relative risk of death was 1.46 (confidence interval 0.97 to 2.22) for hypovolaemia, 2.40 (1.11 to 5.19) for burns, and 1.69 (1.07 to 2.67) for hypoalbuminaemia. The pooled difference in the risk of death with albumin was 6% (3% to 9%).

Ian Roberts of the Institute of Child Health, London, who carried out the review, which attracted numerous protests, emphasised at the time that the results must be interpreted with caution because the trials were relatively small and involved only a limited number of deaths. But he also pointed out that 100 000 patients receive human albumin in the United Kingdom each year and warned: "The really worrying thing is that if these results apply to just 10% of these patients, six deaths per 100 would work out at 600 deaths a year. This could be one of the biggest medical disasters in a long time."

An expert working group set up by the Committee on Safety of Medicines to examine the findings has now concluded, however, that there is "insufficient evidence of harm to warrant withdrawal of albumin products from the market" and that the effect of albumin on mortality can "only be answered by conducting large, purpose designed, randomised, controlled clinical trials."

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Albumin: possible association with increased mortality

Nevertheless, it has recommended that the indication for human albumin solutions should focus on the use of albumin to replace lost fluids rather than the underlying illness resulting in hypovolaemia and that hypoalbuminaemia in itself is not an appropriate indication.

The working group's recommendations—published on 11 June in *Current Problems in Pharmacovigilance*—add that product information should contain warnings about the risks of hypervolaemia and cardiovascular overload and emphasise that monitoring in patients receiving albumin should be undertaken.□

New research demolishes link between MMR vaccine and autism

Hilary Bower, *London*

A leading virologist is calling on the scientific community to spend no more time investigating alleged links between the MMR (measles, mumps, and rubella) vaccine, inflammatory bowel disease, and autism after the publication last week of two further studies, which seemed to demolish the theory that vaccination increased the risk of the conditions.

The studies—one published in the *Lancet* by a team from the Royal Free Hospital Medical School, London, the second in *Current Problems in Pharmacovigilance* from a specially convened working party of the Committee on Safety of Medicines—both found no evidence that the vaccine causes either autism or inflammatory bowel disease, which has been suggested as the link mechanism.

In the Royal Free's study, Brent Taylor, professor of community child health, and colleagues investigated 498 children with autism born since 1979 in the North Thames region. They found that the age at which autism was diagnosed was the same regardless of whether they had received the MMR vaccine before or after 18 months old or had never been vaccinated.

There was no clustering of developmental regression after vaccination, and no more children in the group with autism had been immunised than in the general population of the region. The team said that, although the number of cases of autism had increased steadily since 1979, there was no sign of any steep rise coinciding with the introduction of the MMR vaccine in 1988.

The Committee on the Safety of Medicines' study examined medical records of 92 children with autism and 15 with Crohn's disease; the records had been passed to the committee by a firm of solicitors. Evidence of autism before vaccination was found in 36 cases, and another 28 showed family history of the condition. Eight autistic children and four with Crohn's disease seemed to have developed symptoms after MMR vaccination, but, the authors said, the small numbers and the fact that onset of autism frequently occurs around age 18 months meant that this is not enough to prove causation.

Add these findings to those of last year's Medical Research Council's team of 37 experts who examined the issue and also concluded that no link existed, and, said Norman Begg, head of the Communicable Disease Surveillance Centre's immunisation division, it is clear this issue must now be laid to rest. "These are important papers. They are further evidence that this vaccine causes neither autism nor inflammatory bowel disease," he stated. □