



## Research Update

### Doing more with less: red-cell transfusions in critical care

A major cross-Canada study shows that giving critically ill patients less blood is equally effective as and possibly superior to transfusing more liberally (*N Engl J Med* 1999;340:409-17). Patients with acute myocardial infarction and unstable angina may constitute an exception to this finding.

Red-cell transfusion to provide oxygen to tissues has been a mainstay of critical care. However, the threshold for transfusion and the target hemoglobin concentration vary widely in practice, according to principal author Dr. Paul Hébert of the Ottawa Hospital and the

University of Ottawa. "The only data available show considerable variability in 6 major centres in Canada," he explains. "Until now, there were no clinical studies indicating what is a superior approach. Practice was based on data from laboratory studies and some observational studies."

In addition to concern about practice variation, there are fears that transfusion may pose immediate risks, as well as the long-term risks from blood-borne disease.

The study involved 838 critically ill patients admitted to 25 intensive care

units across Canada between November 1994 and November 1997. Patients were randomly assigned to either a restrictive transfusion strategy, in which transfusion was started if the hemoglobin concentration fell below 7 g/dL and concentrations were maintained at 7 to 9 g/dL, or a liberal strategy, with a threshold concentration of 10 g/dL and a maintenance level of 10 to 12 g/dL.

Patients treated with the restrictive strategy tended to have a lower mortality rate. While the difference in the 30-day mortality rate did not achieve statistical significance between the 2 groups, mortality rates were significantly lower in the restrictive-strategy group among patients who were less acutely ill and among those younger than 55 years. The in-hospital mortality rate was also significantly lower for those given less blood.

An understanding of why greater blood transfusion results in a higher risk of death remains elusive. "At this time we can only speculate as to the mechanisms explaining the study's results," says Hébert. Since blood is an immunosuppressant, it may have immune effects in ill patients. Transfusion can also lead to microcirculatory complications. The blood storage process itself may be harmful. Since blood is stored for as long as 42 days, older blood may not deliver red cells for a variety of reasons. Hébert and his colleagues plan to investigate these theories in future studies.

This study was conducted by the Canadian Critical Care Trials Group, a volunteer group of Canadian critical care physicians who meet twice a year to plan, implement and vet clinical trials in this important area of medicine. It is one of the few such groups in existence, making Canada "the envy of the world" in regard to large-scale critical-care trials like this one, according to Hébert. The trial was managed and supported by the Clinical Epidemiology Unit at the University of Ottawa. — C.J. Brown

#### Research news . . .

##### **Screening fetuses for heart defects**

Major heart defects in fetuses can often be seen on an ultrasonographic examination at 10 to 14 weeks' gestation, a huge population-based study has found (*BMJ* 1999;318:81-5). Most congenital abnormalities of the heart and great arteries are associated with edema in the nape of the neck, which appears as increased translucency thickness on sonograms. In the study, 28 out of 50 cases of major heart and artery defects appeared as increased translucency thickness on sonograms. Ultrasonographic determination of translucency thickness in the nape of the neck is therefore considered a sensitive method of screening for such defects.

##### **The pill and mortality**

A major British study that followed 46 000 women for 25 years has found that the use of oral contraceptives does not increase the risk of death from all causes (*BMJ* 1999;318:96-100). In confirmation of many previous reports, the study

found that women currently or recently (within the last 10 years) taking oral contraceptives had a much lower risk of death from ovarian cancer but a much higher risk of death from cervical cancer and cerebrovascular disease than women not taking the pill. However, these effects disappeared within 10 years of discontinuing oral contraceptives.

##### **Birth complications linked to genetic mutations**

Birth complications such as severe pre-eclampsia, abruptio placentae, fetal growth retardation and stillbirth are associated with the genetic mutations that can lead to thrombosis, an Israeli study has found (*N Engl J Med* 1999;340:9-13). More than half of mothers with obstetrical complications — and only 17% of control mothers without complications — had mutations affecting the factor V Leiden gene, the gene encoding methylenetetrahydrofolate reductase or the prothrombin gene. These genetic mutations increase the risk of thrombosis and other forms of thrombophilia.