Blood cleansing gets report card

Plasmapheresis is one of those medical procedures that seem to make inherent sense: Where a blood-borne agent such as an antibody is responsible for a disease, treat the illness by essentially washing the culprit out of the blood. Clinical experience doesn't always go along with what seems to make sense, though. Last week, a panel of experts concluded that plasmapheresis is useful in treating certain neurological diseases in which antibodies are suspected of causing the problem, but not in others.

After reviewing sometimes-conflicting data from clinical trials, the panel, which was convened by the National Institutes of Health in Bethesda, Md., declared that plasmapheresis is helpful in treating Guillain-Barré syndrome and acute myasthenia gravis but is not useful in amyotrophic lateral sclerosis (ALS). According to the panel, more data are needed to determine its value in multiple sclerosis and other neurological diseases.

In the procedure, which costs about $1,000, blood is removed from the patient and centrifuged to separate the plasma from the blood cells. The cells are put back into the patient, along with a reconstituted plasma component from donated blood. Each year about 15,000 people with neurological diseases in the United States undergo plasmapheresis; another 15,000 undergo it for other conditions such as metabolic disorders.

In myasthenia gravis, a condition marked by muscle weakness and fatigue, plasmapheresis removes an antibody against a receptor on muscle cells that normally responds to a nerve signal. While researchers have yet to conduct a trial comparing plasmapheresis to sham treatment, uncontrolled trials suggest it helps during acute stages of the disease when respiratory function is seriously impaired, the panel found.

The panel also concluded that plasmapheresis is useful in managing Guillain-Barré syndrome, characterized by loss of muscle strength, reflexes and sensation. As with myasthenia gravis, no controlled trials have been done, but the panel recommends the procedure for patients with severe weakness. Since the cause of the syndrome is unknown, the efficacy of plasmapheresis "challenges us to figure out what it is in the patient that is being removed," says Barry G. Arnason of the University of Chicago, who headed the panel.

But plasmapheresis isn't of help in ALS, a disease marked by unrelenting deterioration of the nerves that stimulate voluntary muscles. "The fact that [plasmapheresis] isn't helpful makes the possibility that ALS is an autoimmune disease less likely," says Arnason. — *J. Silberner*

Hormone conversion key to long life?

Death may have it all over taxes these days in terms of predictability, but the way we get there is still a mystery to scientists. Though there is a growing consensus that aging is a multilevel, multicause phenomenon, one researcher's hypothesis suggests that a hormone system may underlie some of the oddities of the human aging process.

Humans took a leap into longevity when they split off from other primates. Not all the excess years can be chalked up to the protection afforded by civilization; humans also have a better "innate ability" to maintain biological functions, says Richard Cutler of the Francis Scott Key Medical Center in Baltimore. Yet this improvement came by grace of very few changes in design, since humans are quite chimpanzeelike at the genetic level.

A number of species-specific characteristics of the human life span may provide clues to the aging process, Solomon Katz of the University of Pennsylvania reported recently in Philadelphia at the annual meeting of the American Association for the Advancement of Science. Humans are the slow starters of the animal kingdom, with an unusually long period of dependency on parents. They are also unusual in the length of their postreproductive life span, which gives them plenty of time to raise laggardly children to self-sufficiency.

The key to these patterns in humans, according to Katz, may lie in a more efficient conversion of one hormone to another. Dehydroepiandrosterone sulfate (DHEAS) is the most plentiful adrenal steroid in human circulation, but scientists know very little about its function. However, the timing of DHEAS secretion may be "a major biological clock," Katz says, and may be responsible in part for signaling the end of childhood.

In humans, an enzyme that removes the sulfate from DHEAS converts it to dehydroepiandrosterone (DHEA), which in various ways, Katz suggests, may help to prolong life. By inhibiting fat synthesis (by blocking a step in the glucose metabolic pathway), he says, DHEA may protect against the life-threatening problems associated with obesity. The hormone also inhibits DNA and RNA synthesis; researchers have speculated that DHEA may block the runaway growth of tumors.

While the effects of DHEA in general seem to be ones that would increase life span, Katz speculates that DHEAS may be involved in some of the health risks associated with obesity. In heavy youngsters, for instance, Katz says, DHEAS "pushes them along, making them more mature" in terms of skeletal growth and sexual development. That's not good: DHEAS, early sexual maturation and high levels of body fat are associated with hypertension, adult-onset diabetes and some forms of cancer.

Perhaps, Katz speculates, humans live longer because other primates are not as well equipped to convert DHEAS to DHEA. The gene for the enzyme responsible for the conversion has been found on the short arm of the X chromosome. According to Katz, it is on a portion that evolved right around the time that human stock diverged from the other primates.

The location of the gene may also explain why human females tend to live longer than males, Katz says. While females have two X chromosomes to males' one, each cell in a female generally "turns off" one or the other of its X chromosomes so that females produce the same amount of X-linked factors as males. But the portion of the X chromosome containing the enzyme-coding gene is not turned off, Katz says, so females get a double dose of the enzyme.

Cautions Vincent Cristofalo, of the University of Pennsylvania in Philadelphia, the important question is whether scarcity of DHEA limits biological reactions in males; after all, half as much of the hormone might be quite adequate. He adds, "The major apparent differences in longevity between men and women are grossly overrated, because many causes of death [in males] are not age-related — they're behavior-related, or violence-related."

An X-linked factor for increased longevity may explain the social organization of many human cultures, Katz says, in which lineage is determined by the father, and daughters move out of the family after marriage. "If you're a grandmother and you have this potential selective advantage, which grandchild should you favor?" Katz says. Your daughter's daughters may have none of your X chromosomes, Katz says, if your daughter passed on the X chromosome she got from her father instead of the one she got from you. But your son's daughters will have one of your X chromosomes, since the only X your son has came from you. This "shifts the selective advantage to certain kinship patterns," Katz says. It is in patrilineal, patrilocal societies that a grandmother with an X-linked advantage could best nurture the grandchildren carrying on that advantage.

"This is more of a testable hypothesis than a conclusion at this point," Katz says. But "the model fits with the idea of small but significant evolutionary changes which account for the increase in human longevity." — *L. Davis*