

Research Update

In the news . . .

Worked to death

Sudden cardiac death due to overwork is so common in Japan that it has a name, *karoshi*. However, evidence of *karoshi*'s existence has been mainly anecdotal. A recent Japanese case–control study of men who had heart attacks and their healthy counterparts shows a U-shaped relation between working hours and the risk of heart attack (*BMJ* 1998;317:775-80). Men who worked 7 to 9 hours a day had the lowest risk, whereas men who worked more than 11 hours a day had 2 1/2 times the risk of a heart attack. Finally, men who worked less than

7 hours a day had 3 times the risk, even after other risk factors were taken into account.



Herbal treatment for prostate cancer high in estrogen

A popular herbal mixture used to treat prostate cancer, PC-SPES, has high levels of estrogenic activity, yeast assays and experiments involving mice and humans have indicated (*N Engl J Med* 1998;339:785-91). Men taking the alternative therapy experienced breast tenderness, loss of libido and, in 1 case, venous thrombosis. This study, and an accompanying editorial, point out the dangers of allowing substances with strong pharmacologic activity on the market without the rigorous testing and regulation required for prescription drugs. In this case, the herbal product may offer some benefit for men with prostate cancer, but may also have serious side effects and may not be taken into consideration when physicians are formulating a therapeutic plan.

Immune system problem causes fetal loss

Recurring fetal loss with no other explanation may be due to an immunologic abnormality, according to a new study (*Nature Med* 1998;4:1020-4). Researchers found that women with unexplained recurring fetal loss had decreased production of leukemia inhibitory factor, interleukin-4 and interleukin-10 in T cells, compared with women with normal gestation. Leukemia inhibitory factor is believed to be essential for embryo implantation.

Overcoming another barrier to xenotransplantation

One of the main barriers to transplanting animal organs into humans is the humoral immune response, which leads to rejection of organs from other species. In a mouse model, researchers have surmounted this barrier by introducing an engineered gene into bone marrow to "turn off" the enzyme causing rejection (*Science* 1998;281:1845-7). Similar results in humans could remove this barrier to xenotransplantation.

Dead end for proposed ALS therapy

It has recently been discovered that genes involved in amyotrophic lateral sclerosis (ALS) encode a mutant form of the enzyme superoxide dismutase (SOD). This finding had led to the idea of replacing SOD activity to treat ALS. However, a new study shows that ALS has the same course in mice, regardless of whether SOD activity was eliminated or elevated (*Science* 1998;281:1851-4). Hence, therapy to mimic SOD activity appears to be of no value in ALS.

Key to fever

Research is progressing into the mechanism that produces fever. Since anti-inflammatory drugs such as ASA inhibit the synthesis of prostaglandins and mitigate fever, it is thought that prostaglandins plays a role in causing fever. New experiments in mice that lack the receptors for prostaglandins show that only 1 receptor — EP_3 — is necessary for prostaglandins E_2 to produce fever (*Nature* 1998; 395:281).