THE ECONOMIST FEBRUARY 24TH 2001

SCIENCE AND TECHNOLOGY

Autoimmune disease

Mother's ruin

SCLERODERMA, which hardens the skin and then goes on to immobilise many of the body's internal organs, looks very different from multiple sclerosis, which cripples its victims by stripping away the protective sheaths of their nerve cells. Systemic lupus erythematosus, which can fatally damage the kidneys, looks different again.

Yet they have something in common. They and more than 70 other diseases—including such familiar ailments as psoriasis and rheumatoid arthritis—are all the result of the immune system mistaking one or another of the proteins that the body makes as being "foreign" rather than "self". This misidentification means that the immune system attacks cells containing that protein as if they were invading bacteria or viruses.

Many researchers view such autoimmune disorders as members of a family, with the same underlying mechanism and varying only in the details of what has gone wrong and where. According to the researchers who addressed the AAAS session on autoimmune diseases, that familial relationship helps to explain why these illnesses do not obey the usual rules of inheritance.

Noel Rose, an immunologist at Johns Hopkins University in Baltimore, pointed out that if these diseases were entirely genetic then if one identical twin had such a disease the other might be expected to come down with it, too. In fact, no autoimmune disease has more than a 50% chance of appearing in one twin if the other is affected, and with some diseases, such as early-onset or "type 1" diabetes, that figure is only about 5%. In Dr Rose's view, what is often being inherited is not a genetic predisposition to a particular autoimmune disease, but rather a generalised predisposition to the whole class of them. Which disorder actually develops is more or less accidental.

This generalised predisposition has been demonstrated by another of the session's speakers, Denise Faustman, of the Massachusetts General Hospital in Boston. She has been studying a strain of laboratory mice which has been bred so that its members are genetically identical. These mice tend to develop a form of type 1 diabetes that closely mimics its human counterpart. Despite their genetic identity, however, about 20% of them are healthy.

This led Dr Faustman to wonder what would happen if she mated healthy males and females. The offspring of these unions did not become diabetic either, but some of the females in the resulting litters developed rheumatoid arthritis when they reached reproductive age. This suggests that the same set of "autoimmunity" genes can result in different outcomes.

Such findings also highlight a second curious feature of autoimmune diseases—that in all species studied so far, they affect females more than males. Women are three times as likely to be afflicted as men. The reason seems to be that besides genetic inheritance, autoimmunity is subject to a second, and very odd, form of "heredity": you can get it from your children.

This reverse inheritance happens during pregnancy and is caused by cells from the fetus making their way into the mother's bloodstream and staying there for years, a condition known as "microchimerism". J. Lee Nelson, at the Fred Hutchinson Cancer Centre in Seattle, has found that women with scleroderma have at least ten times more fetal cells in their blood after the birth of a baby than mothers who are free of the dreadful disease.

Dr Nelson speculates that such microchimerism is disrupting normal interactions in the mother's immune system. This interference might cause scleroderma, which resembles graft-versus-host disease, another nasty immune reaction caused by a mixing of cells which occurs when a mismatched tissue transplant attacks the body of its new owner. Much more work needs to be done to understand exactly how fetal cells might wreak such havoc in the mother. Sharper than a serpent's tooth, indeed.