Effect of GH replacement on cardiovascular risk factors

Risk factor in GH-deficient adults	Effects of GH replacement
Abdominal obesity	Decreased
Increased LDL-cholesterol	Decreased, unchanged
Decreased HDL-cholesterol	Increased, unchanged
Normal lipoprotein (a)	Increased
Increased triglycerides	Unchanged
Glucose intolerance, insulin sensitivity	Unchanged
Decreased plasma fibrinolytic activity	Increased, unchanged
Normal or increased diastolic blood pressure	Decreased, unchanged
Decreased nitric oxide formation	Increased

in response to the treatment could not account for the reduction in intima-media thickness. However, the simultaneous impact of GH-replacement therapy on several cardiovascular risk factors (panel) might explain the beneficial effects of this treatment on early atherosclerosis. Another possibility is that the influence of GH on the vascular wall is mediated through the direct action of GH/insulin-like growth factor (IGF)-I or through nitric oxide.[4] This proposal is supported by the inverse relation found between serum concentrations and IGF-I and intima-media thickness of the common carotid artery in Pfeifer and colleagues' study.

The reduction in intima-media thickness after only 6 months of GH treatment is surprising since it was much greater and occurred faster than in trials with lipid-lowering agents in patients with hyperlipidaemia.[10] Pfeifer and colleagues' study therefore indicates a profound impact of GH/IGF-I on the endothelial lining and on the evolution of early atherosclerosis. However, the study was small, the design was open, and the healthy control group was not followed up longitudinally. Moreover, the internal diameter of the common carotid artery was not measured. This point is important because GH therapy increases plasma volume and nitric oxide formation and can thereby increase the internal diameter of the artery, which in turn may reduce the intima-media thickness.[11]

Intima-media thickness is a surrogate variable for coronary and cerebral atherosclerosis and its consequences. Whether GH-replacement therapy will restore cardiovascular mortality rates to normal remains to be shown. Future studies are therefore warranted.

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Screening methods for congenital toxoplasma and risk of disease

If a woman acquires a primary *Toxoplasma gondii* infection during pregnancy, the fetus can become infected. Severe systemic and central-nervous-system signs of the infection may be apparent at birth, but most infected newborn babies do not have overt signs of the disease. Even so, infected infants are at substantial risk of developing long-term sequelae, including chorioretinal disease (up to 85% of infected children) and neurological abnormalities.[1–3] Significant reductions in the frequency and severity of disease at birth have been associated with in-utero treatment of infected fetuses.[4–7] Extended postnatal treatment regimens, started in the newborn period or early infancy,[8,9] or as a continuation of in-utero treatment,[5,6] have also been associated with a marked reduction in the expected long-term complications.

What are the risks of transmission of the infection to the fetus? Last week's *Lancet* contained two reports addressing this issue. David Dunn and colleagues,[10] using data from a cohort of about 600 women with primary infection during gestation, calculated the risks of transmission of infection to the fetus and the occurrence of early clinical findings of disease in infected infants in relation to gestational age at maternal seroconversion. Women were tested monthly for seroconversion, and almost all women with primary infection were given antiparasitic therapy. Infants found to be infected were put on an extended course of therapy. The overall transmission rate was 29%. Clinical findings in the infants, broadly defined as hydrocephalus,chorioretinal lesions, or isolated intracranial calcifications, were identified in 27% of the infected infants over a median follow-up period of 4·5 years. In 15 of the 41 liveborn children with clinical signs of disease, chorioretinal lesions were found after age 1 year. Risk of transmission of infection was low when women seroconverted at 13 weeks of gestation, but if fetal infection occurred, the babies were at high risk of having clinical signs of disease. With seroconversion at 36 weeks, the risk of transmission of infection was high, but the babies infected were unlikely to have clinical features of the disease. Seroconversion at 24–30 weeks was associated with intermediate risks of transmission of infection and clinical disease in infected infants but also with the highest overall risk (10%) of having an infant with "early" clinical signs of disease. Knowledge about risk is helpful in counselling of infected patients, but the study looked at the risk of having any clinical sign of disease in infected infants, and did not separate out the risk of severe complications. As noted by the the researchers,

some clinical signs (such as an isolated intracranial calcification) may not be associated with functional impairment, especially if the infant is put on extended therapy. Also, clinical features can develop years later, so a longer follow-up period is needed to ascertain whether late manifestations develop.

In the second paper, Morten Lebech and colleagues[11] reported that screening of newborn babies in Denmark showed a 28% seroprevalence of toxoplasmosis among childbearing women. The investigators' main aim was to ascertain the feasibility of screening newborn babies for congenital toxoplasma infection in a low-prevalence region. A stored sample of maternal blood collected in the first-trimester was compared with that of a sample from the newborn baby for toxoplasma-specific IgG, to determine maternal seroconversion. This method captured most women who became infected during pregnancy in this cohort (the exclusions being those who had seroconverted before the collection of the 8–12-week blood sample and those who seroconverted postnatally). Postnatal serum samples were obtained from the women who seroconverted and from their babies, who were examined clinically for signs of congenital infection. In the last year of the study, IgG seroconversion was compared with the presence of toxoplasma-specific IgM in samples from the newborn babies. Of 64 884 women, 0·2% (139) seroconverted, and the rate of transmission of infection to the fetus was 19%.

Lebech and colleagues found that 15% (four) of congenitally infected babies had clinical signs of the disease at birth, whereas 40% of infected babies detected solely by newborn screening in the New England Regional Newborn Screening Program[8] had such signs. Some of the difference may be due to the methods used for clinical assessment. Alternatively, there may be geographical differences in the epidemiology of this infection. Another point about the report is that follow-up of the children was limited to 12 months. Finally, the sensitivity and specificity of postnatal serology in identifying congenital infection may be limited. Screening tests based on toxoplasma-specific IgM may miss some infected cases, since some congenitally infected infants (two of 11 in the Lebech study) do not have detectable toxoplasma-specific IgM at birth. Also, some newborn babies give a false-positive toxoplasma-IgM reaction (in this study 1·9/10 000), but will require serological and, in some cases, clinical follow-up to confirm that they were not infected.

Careful analysis of different approaches to prevention and treatment of this congenital infection is needed. Prenatal screening may be more expensive and cumbersome, especially in regions where the seroprevalence of toxoplasma is low. Also, prenatal tests to confirm fetal infection are invasive. However, several recent studies do report a lower incidence of severe disease when the disease is diagnosed and treated prenatally. Lebech and colleagues have shown that use of universally collected dried filter paper specimens for screening of babies for toxoplasma-specific IgM is a feasible alternative, but with screening at this stage the opportunity for prenatal therapy is lost. Each of these approaches must be compared with having no organised screening programme, as is presently the situation in most of the world outside of western Europe. Comparison of different studies and approaches is complicated since differences in prenatal and postnatal treatment regimens are common. In weighing the merits of the different approaches, outcome of the children is a critical component, as is duration of follow-up, especially in the case of neurodevelopmental and ocular complications. Fortunately, several centres are collaborating in long-term follow-up studies.

Prevention of toxoplasma infection in the mother as a means of limiting congenital toxoplasmosis should not be forgotten. The decreasing seroprevalence of toxoplasmosis in recent decades in some geographical regions may be due to a better and more widespread understanding of the risks of acquiring this infection. Although some women still become infected despite efforts at prevention, prenatal-care providers must include education about prevention of toxoplasma infection in the standard care of their patients.[12]

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Sexual dysfunction after surgery for rectal cancer

Sexual dysfunction is a common consequence of otherwise successful and potentially curative surgery for rectal cancer.[1] It used to be ascribed mainly to psychological overlay or to the negative effect of stoma formation.[2] Williams and Johnston,[3] in a 1983 study of 78 patients undergoing abdominoperineal excision or anterior resection, concluded that two-thirds of the former group had impaired sexual function compared with only 30% of the latter. Impotence may be partial and its incidence age related. Return of function is possible, at least in the early months after operation.

One alternative explanation for the sexual dysfunction is damage to the pelvic autonomic nerves (panel).[4] The inferior hypogastric plexus (IHP) is responsible in both men and women for erection, and the superior hypogastric plexus (SHP) for ejaculation mediated by the sympathetic system.[5] The SHP is a fenestrated network of fibres anterior