Comment

The mother's low HAI antibody titres recorded in 1974 and 1977 may be interpreted either as spurious or as representing antibody concentrations inadequate to protect the fetus. An immune disorder in the mother seems unlikely since normal HAI antibody and specific IgM responses occurred after exposure early in her fourth pregnancy. Failure of rubella vaccination to confer effective immunity may be due to improper storage of the vaccine or to an inherent defect in any particular batch of vaccine. The chance of such a failure occurring twice seems remote.

A small but definite number of persons receiving rubella vaccine fail to show serological conversion to the immune state. Various trials report failure rates of 2% to 5%, depending chiefly on the type of vaccine used. As many as one-third of those vaccinated may respond with a low HAI titre.[1] Reinfection in both immunised and naturally immune subjects is well documented.[2 3] Such reinfection is more likely when HAI titres are low.[1 3] Immunisation with RA27/3 strains of vaccine, such as Almevax, is, however, associated with low failure rates, low reinfection rates, and a pattern of immune response closely resembling that following natural infection.[3] The evidence for reinfection causing fetal disease is scanty. In only three out of six reported cases of rubella reinfection during pregnancy is there documented evidence of fetal infection.[4] Grillner and Forssmann[5] have reported interference with rubella antibody formation when immunisation was given after blood transfusion. The amount of neutralising antibody likely to be present in a unit of donor blood may be sufficient to inactivate the vaccine. The immunisation failure in our patient may be explained in this way, since both her immunisations were immediately after a blood transfusion (table). We therefore suggest that when a blood transfusion has been given recently rubella immunisation should either be delayed or its effectiveness tested serologically.

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Frusemide-induced increases in serum isoamylases

Sporadic reports[1] have suggested that frusemide in some cases may be an aetiological agent in acute pancreatitis, but short-term studies have failed to show any effect of frusemide on the serum concentrations of amylases.[1] While treating patients with severe hypertension with frusemide we measured serum concentrations of pancreatic and salivary isoamylases and compared them with concentrations just before and two weeks after the end of the frusemide treatment.

Patients, methods, and results

We studied eight men and four women aged from 38 to 68 years (mean 56). All had essential hypertension. Frusemide 20 mg twice daily by mouth was added to the previous treatments, which included thiazides in all the patients, and the results were evaluated when the last patient admitted to the study had been treated for four weeks. This gave a mean treatment period of 12 weeks (range 4-27 weeks) and a mean frusemide dose of 75 mg/day (range 40-120 mg/day). Serum samples were taken just before frusemide was started, on the last day it was taken, and two weeks after the end of frusemide treatment. All samples were stored at −20°C until the study was completed, when all individual samples were assayed, blindly, in the same batch. Amylase isoenzymes were measured by cellulose-acetate electrophoresis.[2] Mean (±SD) concentrations measured in 26 healthy blood donors aged 37 to 60 years (mean 52) were: pancreatic isoamylase 98±35 U/l, salivary isoamylase 91±38 U/l, and total amylase 189±50 U/l. Since amylases are excreted by the kidneys and diuretics cause haemoconcentration, creatinine and albumin concentrations were measured in the same serum samples.

During treatment with frusemide pancreatic isoamylase and total amylase concentrations were significantly higher than those in blood donors ($p<0.05$ for both). Pancreatic isoamylase increased by 17% ($p<0.02$, table), salivary isoamylase by 7% (NS), and total amylase by 12% (NS). Individual increments in pancreatic isoamylase correlated positively with increments in salivary isoamylase ($r=0.76$, $p<0.001$). No dose correlations could be found. Serum creatinine concentrations were raised by 27% ($p<0.005$) and the increases in amylase isoenzymes correlated positively with the increases in creatinine ($r=0.75$ and 0.67 for pancreatic and salivary isoamylases respectively, $p<0.001$ for both). Albumin concentrations did not change. Individual pancreatic isoamylase:albumin ratios rose slightly higher by a mean 21% ($p<0.01$). Two weeks after withdrawal of frusemide none of the values differed significantly from prefrusemide levels.

Mean (±SD) serum concentrations of amylase isoenzymes, creatinine, and albumin in 12 hypertensive patients before, during, and two weeks after treatment with frusemide in a mean dose of 75 mg/day (range 40-120) for a mean period of 12 weeks (range 4-27)

	Before	During	After
Pancreatic isoamylases (U/l)	110±41*	129±56*†	114±45†
Salivary isoamylases (U/l)	107±50	114±45	100±48
Total amylases (U/l)	207±62	243±70‡	214±71‡
Creatinine (μmol/l)	97±27§	124±35§*	106±27*
Albumin (g/l)	45±2	45±2	44±2

*$p<0.02$. †$p<0.05$. ‡$p<0.01$. §$p<0.005$.
Conversion: SI to traditional units—Creatinine: 1 μmol/l ≈ 0·0113 mg/100 ml.

Comment

These results show that frusemide treatment is followed by small but significant increases in serum amylase isoenzyme concentrations. Frusemide stimulates pancreatic secretion,[3] but no postprandial increases in serum isoenzyme concentrations have been shown.[4] Therefore this does not seem a likely explanation for the rises in our patients, and the unchanged albumin concentrations in our study seem to eliminate the possibility of haemoconcentration as the cause. The rise in serum creatinine concentrations suggests that the increases in amylase isoenzymes may be explained by decreased renal excretion —especially in view of the highly significant correlation between the increases in the isoenzymes and those in the creatinine concentrations.

None of the patients complained of abdominal pain, but this does not exclude frusemide as causing acute pancreatitis in some cases. On the contrary, since the finding of low concentrations of pancreatic isoamylases is a diagnostic aid in pancreatic insufficiency, our findings suggest that false-normal values may be found in patients treated with diuretics.[5]

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