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The 'Baby Fae' baboon heart transplant – potential cause of rejection

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Dear Sir,

In their very thoughtful commentary discussing our paper on the possibility of achieving immunological tolerance to pig heart xenografts in neonates,¹ Jeffrey Platt and his coauthors² discuss the well-known transplant of a baboon heart into the patient known as Baby Fae in 1984 by Loma Linda surgeon, Leonard Bailey.³ Despite ABO-incompatibility between patient and graft, the baboon heart functioned well for two weeks, but then underwent rejection, the baby sadly dying on day 20.

In the light of extensive more recent experience by Lori West and her colleagues,^{4,5} Platt et al do not believe that blood group incompatibility was a major factor in failure of the graft, a conclusion with which we agree. Many years ago, studies of heart transplantation between closely-related nonhuman primate species demonstrated that, although ABO-incompatibility had some detrimental effect, the species discrepancy appeared to be more important.^{6,7}

However, Platt et al. go on to state that “none of the saccharide antigens thought to impair transplantation of hearts from pigs into humans should have been pertinent to the fate of the transplant in Baby Fae.” With this point, we respectfully disagree.

We suggest that a major factor might have been the fact that baboon organs express N-glycolylneuraminic acid (Neu5Gc) (as do all Old World nonhuman primates, including chimpanzees and gorillas), but human organs do not.^{8,9} Humans therefore make anti-Neu5Gc antibodies, which can be detected in almost all human sera,¹⁰ and can increase in activity after exposure to the carbohydrate. Indeed, after galactose- α 1,3-galactose (Gal), Neu5Gc appears to be the next most important target for human anti-pig antibodies (though in Old World monkeys Sd^a would appear more important).¹¹ The blood transfusions that Baby Fae received might have increased the anti-Neu5Gc antibody titers.

It is very likely that antibodies directed against Neu5Gc also played a role in the outcome of the clinical chimpanzee kidney transplants carried out by Keith Reemtsma in 1964¹² and of the other transplants in which nonhuman primate organs were transplanted into patients¹³.

We suggest that the presence of antibodies to Neu5Gc in Baby Fae's blood might well account for rejection of the baboon heart graft.

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