

# This Week's Citation Classic

Kissmeyer-Nielsen F, Olsen S, Posborg Petersen V & Fjeldborg O. Hyperacute rejection of kidney allografts, associated with pre-existing humoral antibodies against donor cells. *Lancet* 2:662-5, 1966. [Blood Bank and Blood Grouping Lab. and Dept. Surg., Aarhus Kommunehospital, and Depts. Pathol. and Intern. Med., Univ. Aarhus, Aarhus, Denmark]

**The paper presents very clearly the association between presence of circulating antibodies active against leukocytes, platelets, and kidney extract, and resulting in hyperacute rejection of two cadaver kidney grafts. When the grafts were removed total cortical necrosis was found caused by microthrombi in the glomeruli. Both recipients were females, and the presensitization obviously caused by previous pregnancies and blood transfusions. The antibodies were active against donor specific antigen. [The SCI® indicates that this paper has been cited over 280 times since 1966.]**

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'Kidney transplantation was started early in 1964 in our centre, and we have by now performed ~600 transplants —mostly from cadavers. The two classical cases were seen in relation to our kidney transplants, Numbers 14 and 17, performed November 4, 1965, and January 1, 1966, respectively. They were remarkably similar in their cause, and we felt absolutely certain that the circulating antibodies were of crucial importance for the 'disaster.'

"It should here be mentioned that allograft rejection at that time was thought mainly to be caused by an attack of immunocompetent cells (i.e., lymphocytes). In mice it had been impossible to transfer the rejection phenomenon by injection of serum from presensitized animals from inbred strains. (Retrospectively, it can be stated that this most probably is caused by too small doses of antibody being transferred by this passive immunization.)

"We were convinced about the importance of our observations —later resulting in the compulsory use of a direct crossmatch between recipient serum and lymphocytes from the donor. However, being untraditional, we experienced great difficulties in getting our data published. First, a lecture at the International Congress for Nephrology in Washington, DC

(1966) was rejected During the first International Congress of Transplantation in Paris (1967), I was allowed to speak for three minutes, and to show one slide and I am quoting now: 'One slide only!'

"We feel that we submitted a very well-documented article to *Lancet* in 1966, but to our surprise it was rejected without any explanation. This was obviously caused by a referee who did not believe in 'serology,' but only a cellular (lymphocyte-mediated) cause for rejection.

"I became slightly desperate, and returned the article to the very nice editor for *Lancet*, and stated shortly that we really felt that our observations were indeed important —and we asked for a second thought by a different reviewer —without changing a comma in the article. Then the article was finally accepted.

"It should here be added that our article resulted in a letter to the editor in *Lancet* from one of the transplant pioneers, W.J. Dempster.<sup>1</sup> He stated that what we described could be 'the same complications (as seen) when newcomers start work in this laboratory' —and he ended his letter with the following sentence: 'To ascribe these two early anurias to preexisting antibodies (as have Hamburger et al. in their first two cases) is to be fashionable at the expense of accuracy. A more humble but less impressive diagnosis would be "unknown."'

"After the publication we became aware that Hamburger<sup>2</sup> had seen similar pathological findings (very similar to the Schwartzmann phenomenon), but they did not correlate with serological findings. Almost simultaneously, Terasaki et al.<sup>3</sup> during a congress in the US, made very similar observations.

"This publication has been highly cited for the following reason. Our findings were controversial, but, as gradually accepted, they were found to be of great practical importance in relation to kidney transplantation —the direct crossmatch problem in particular. For a recent survey the reader can refer to P.J. Morris.<sup>4</sup>

"I do believe that the publication cited here is one of the major reasons for my receiving the following honourable presentations and awards: (1) the Emily Cooly lecture, 1970 (American Association of Blood Banks); (2) Hoist Knudsen honorary prize, 1968, from the University of Aarhus; and (3) very recently (February 14, 1981) the Danish Novo prize."

1. Dempster W J. Rejection of kidney allografts. (Letter to the editor.) *Lancet* 2:972-3, 1966.
2. Hamburger J, Vaysse J, Crosnier J, Auvert J, LaLanne C M & Dormont J. Six attempted renal homotransplantations in humans after irradiation of the recipient. *Rev. Fr. Étud. Clin. Biol.* 7:20-39, 1962.
3. Terasaki P I, Thrasher D L & Hauber T H. Serotyping for homotransplantation. XIII. Immediate kidney transplant rejection and associated preformed antibodies. (Dausset J, Hamburger J & Mathe G, eds.) *Advances in transplantation*. Baltimore: Williams and Wilkins, 1967. p. 225-9.
4. Morris P J, ed. *Kidney transplantation: principles and practice*. London: Academic Press, 1979. 408 p.