explanation for the blocking activity observed in some patients. The cytotoxicity induced by normal effectors was not affected in our assay by the addition of several sera containing more than 200 mg of urea per 100 ml. There is experimental evidence that inhibition of ADCC can be produced by immune complexes (6, 12, 13) and by antibodies against lymphocyte surface antigens (9) via a common mechanism, namely competition for Fc receptors (19). Immune complexes that can inhibit ADCC are generated in mixtures of antibodies with lymphocytes (19). In kidney patients anti-HLA and anti-B cell antibodies, which are potent inhibitors of ADCC (10, 18, 20, 23), are often present. The autologous blocking found in some of our transplant and dialysis patients may be because of the formation of immune complexes between antibodies and soluble antigens from transusions or kidney grafts.

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LITERATURE CITED
3. Recipient of a Fellowship from the Belgian Fonds de la Recherche Scientifique et Medicale.

ELEVEN AND TWO-THIRDS YEARS' SURVIVAL AFTER CANINE ORTHOTOPIC LIVER TRANSPLANTATION

The first animal to survive chronically after orthotopic liver transplantation was a mongrel dog that received a hepatic homograft on March 23, 1964. The recipient was estimated to be 2 years old. The unrelated mongrel donor was of a different color and appearance. Immunosuppression was with azathioprine which was stopped after 120 days. Treatment was never resumed. The transplanted liver was biopsied on several occasions during the next 5 years and was always thought to be normal (2, 4).

After a brief illness, the dog died on the night of December 8, 1975, at the estimated age of 14 years and after a total survival post-transplantation of 11 years and appeared to be well close to death.

For most of the post-operative period, the dog had normal liver function. However, during the last few weeks before death, there was elevation of the serum bilirubin and azotemia. Treatment was always thought to be normal (2, 4).

Although the hepatic artery was patent and the homograft appeared to be well angiographically, the aorta was widely patent. On microscopic examination, the homograft showed atherosclerosis.

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Biliary reconstruction was with cholecysto-duodenostomy after ligation of the distal common duct. The gallbladder, the common duct, and all the intrahepatic ducts were filled with small or medium-sized stones closely with a soft, variably colored green to orange sludge. The stone analysis showed predominantly bilirubin with only trace amounts of cholesterol and bile salts.

Other significant findings at autopsy were pulmonary edema, coronary artery disease, and left ventricular hypertrophy. The immediate cause of death was congestive heart failure.

Histopathological evaluation of the homograft revealed portal fibrosis and linking of the enlarged portal tracts to one another by connective tissue septa (Fig. 2). There was concentric scarring around the interlobular and septal bile ducts and proliferation of ductules at the margins of the portal tracts. Many of the larger bile ducts were dilated and filled with inspissated bile. The epithelium of the affected ducts was ulcerated and there were aggregates of small lymphocytes, plasma cells, and macrophages.
around the ducts. A few bile "thrombi" were present in the centrilobular part of the bile canaliculi. Liver cell damage was slight. The arteries and arterioles were normal. These changes are typical of chronic large duct biliary obstruction. There was no evidence of rejection.

The thymus, mesenteric and mediastinal lymph nodes, and Peyer's patches appeared to be normal. The spleen had been removed at the time of transplantation.

Examination of the rest of the tissues confirmed the narrowing of the coronary arteries by atherosclerosis, the hypertrophied left ventricle, and the congestion and edema of the lungs. The atherosclerosis in the homograft aorta was severe, with large patches of calcification and bone formation with marrow. By contrast the recipient aorta was normal. The kidneys were normal.

Thus, although the dog died primarily of cardiovascular manifestations of old age, a potentially lethal biliary duct complication was present which would have independently caused death within a short time. A partial obstruction of the cystic duct was apparently the main cause of the extensive stone and sludge formation that had affected both the extrahepatic and intrahepatic ducts. The intrahepatic biliary plugging with ininspissated bile casts was similar to a syndrome that we (1, 3) and Waldram et al. (5) have noted in humans. Such findings in animals and man point again to the reconstructed biliary duct system as the Achilles' heel of liver transplantation.

The completely normal findings in this dog's lymphoid system were of interest, since no immunosuppression whatever had been given for 111/2 years.

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There have been rejection and the phenomenon (9, 15) manifestation of known to be the their transplant chemically active has also been demonstrated to skin allografts that the high but these cells could (18).

It was original antibody response much delayed, rejection of the graft. evidence that be significant role ever, antibodies soon after grafting and have been so titer at about the tigation is complete. Algire and his and his can moral antibodies important role despite the fact high titers of sim patients that, although allografts is primally competent role play an ancillary humoral factor destruction of some unsatisfactory, as far as the majority of the patients are concerned by a cellular response. Since the initiation of...
THE CELLULAR INFILTRATE IN CARDIAC ALLOGRAFT REJECTION IN MICE

There have been many studies of allograft rejection and the cellular response to this phenomenon (9, 15, 16). The main cytological manifestation of the allograft response is known to be the activation of lymphocytes and their transformation into blasts (4, 20). A histochemically active population of macrophages has also been demonstrated in the cellular infiltrate that occurs as an immunological response to skin allografts in mice and it was thought that the high build-up of lysosomal activity in these cells could be responsible for rejection (18).

It was originally thought that the humoral antibody response to an allograft was very much delayed, reaching its peak after destruction of the graft. This was cited as part of the evidence that humoral factors do not play a significant role in the rejection process. However, antibodies are demonstrable in the serum soon after grafting from the 4th day onward and have been shown to reach their maximum titer at about the same time the graft destruction is complete (2). The classic experiments of Algire and his colleagues (1) indicate that humoral antibodies alone probably do not play an important role in solid allograft destruction, despite the fact that such hosts produce fairly high titers of specific H-2 antibodies. It would seem that, although destruction of solid tissue allografts is primarily mediated by immunologically competent cells, humoral factors may play an ancillary role. The evidence incriminating humoral factors as major contributors to the destruction of solid tissue allografts remains unsatisfactory, and the current view is that, as far as the majority of types of solid tissue allografts are concerned, destruction is mediated by a cellular rather than a humoral immunity.

Since the initial observations that the thymus-dependent (T) line of lymphocytes was necessary for graft rejection (17), several T cell as well as non-T cell candidates for effector cells in cell-mediated immunity have been proposed. Antibody-dependent cell-mediated lysis of target cells in vitro may be carried out by a subset of B cells and/or surface adherent cells belonging to the monocyte-macrophage-erythroblast cell line (5, 6, 7, 19, 22). In terms of in vivo graft rejection, however, it is likely that the effector cell population must come into contact with graft tissue and therefore be represented in the immune cellular infiltrate. Since it is now possible to identify lymphocytes in frozen tissue sections which bear surface antigens characteristic of the T cell and B cell (Ig bearing) lines (6, 10-13), we initiated a series of experiments to identify the cells involved in the immune cell infiltrates to cardiac allografts in mice.

The purpose of this study is 3-fold: to attempt to establish the type of cells present in the graft-host rejection site, the time relationships of the appearance of these cells, and finally to find out whether the type of cell changes as the graft becomes established.

Mice

Three groups of mice were used.

A. Allogeneic group. Donor hearts were from newborn (12 to 24 hr) BALB/cJ mice. The recipients were healthy adult C57BL/6J mice.

B. Preimmunized group. This group was similar to group A except that adult C57BL/6J recipients were preimmunized with 1 x 10^7 washed BALB/cJ spleen cells injected i. p. 10 days prior to transplant.

C. Syngeneic group. Both the newly born donor hearts and the recipient adult mice were of the BALB/cJ strain.

Antisera

A. Anti-T. Rabbit anti-BALB thymus serum was prepared as previously described (12). This