Lecture XI

Transplantation immunology

Cancer immunology

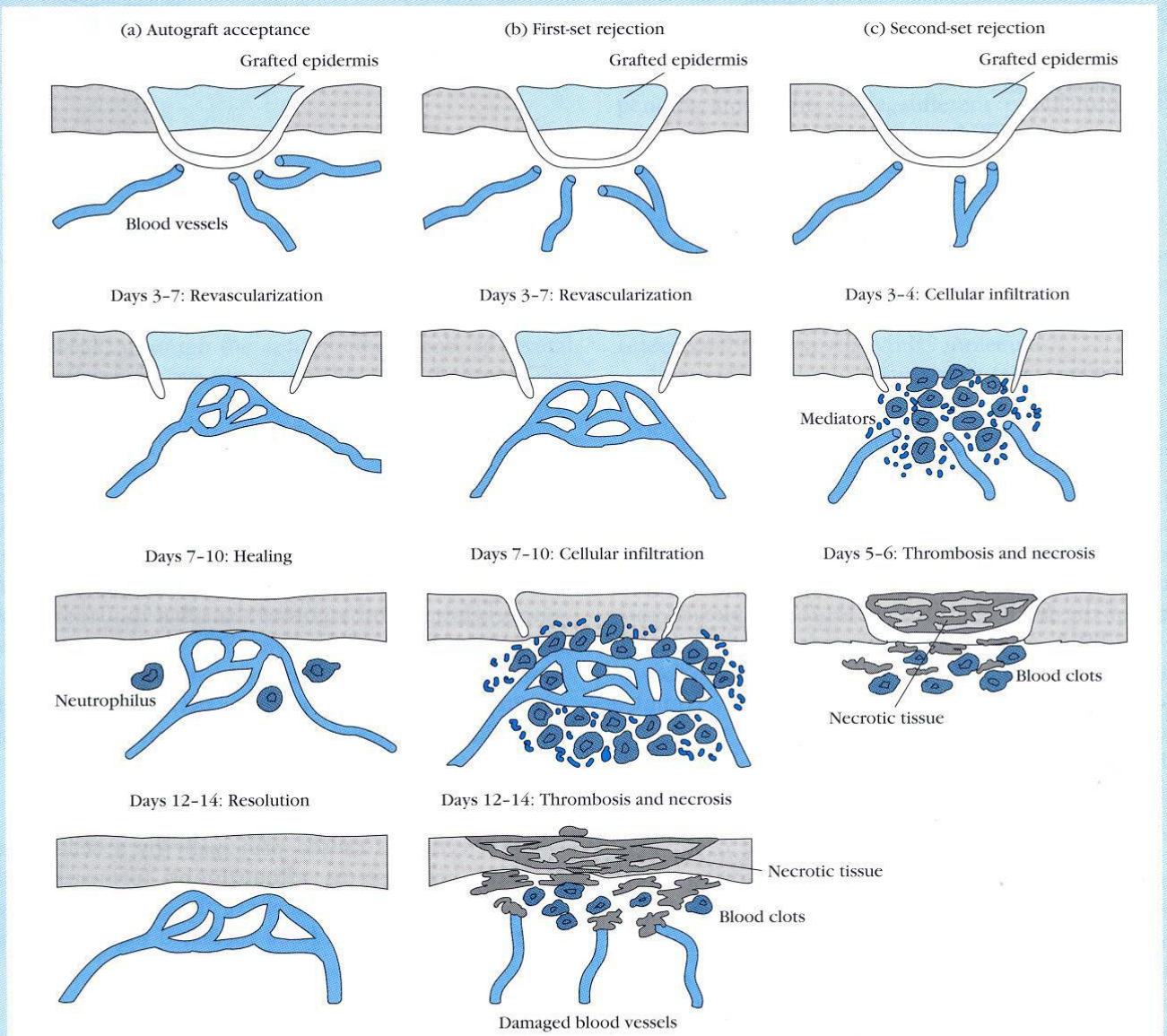


FIGURE 23-1

Schematic diagrams of the process of graft acceptance and rejection. (a) Acceptance of an autograft is completed within 12–14 days. (b) First-set rejection of an allograft begins 7–10 days after grafting, with full rejection occurring by 12–14 days. (c) Second-set rejection of an allograft begins within 3–4 days, with full rejection by 5–6 days. The cellular infiltrate that invades an allograft contains lymphocytes, phagocytes, and other inflammatory cells.

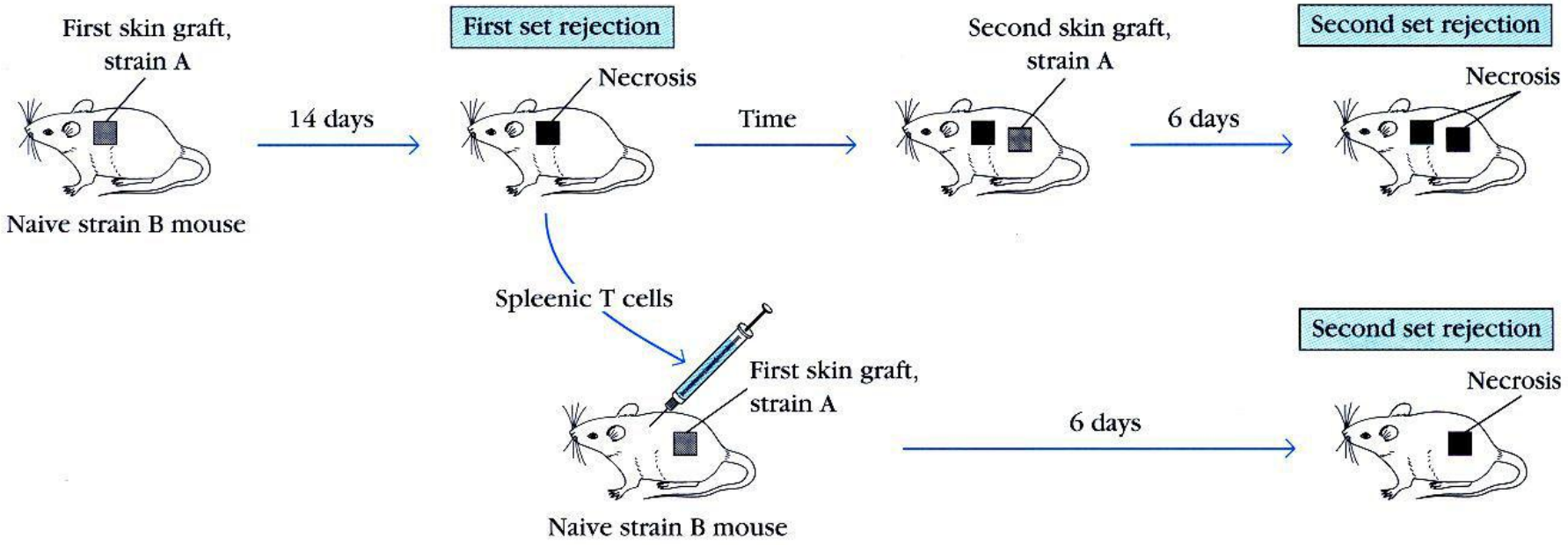


FIGURE 23-2

Experimental demonstration that T cells can transfer allograft rejection. When T cells derived from an allograft-primed mouse are transferred to an unprimed syngeneic mouse, the recipient mounts a second-set rejection to an initial allograft from the original allogeneic strain.

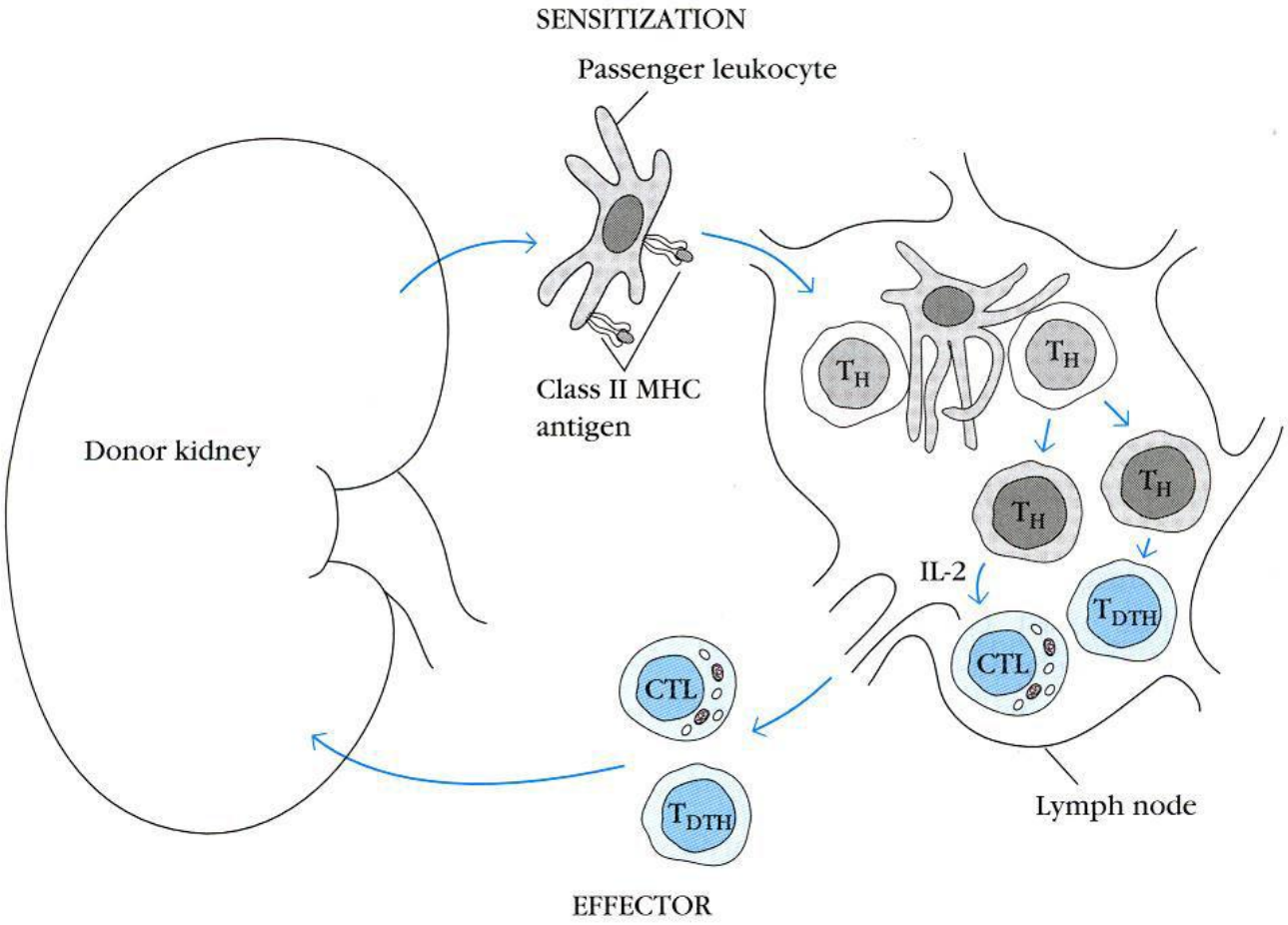


FIGURE 23-4

Migration of passenger leukocytes from a donor graft to regional lymph nodes of the recipient results in the activation of T_H cells in response to different class II MHC antigens expressed by the passenger leukocytes. These activated T_H cells (gray) then induce generation of T_{DTH} cells and/or CTLs (blue), both of which mediate graft rejection.

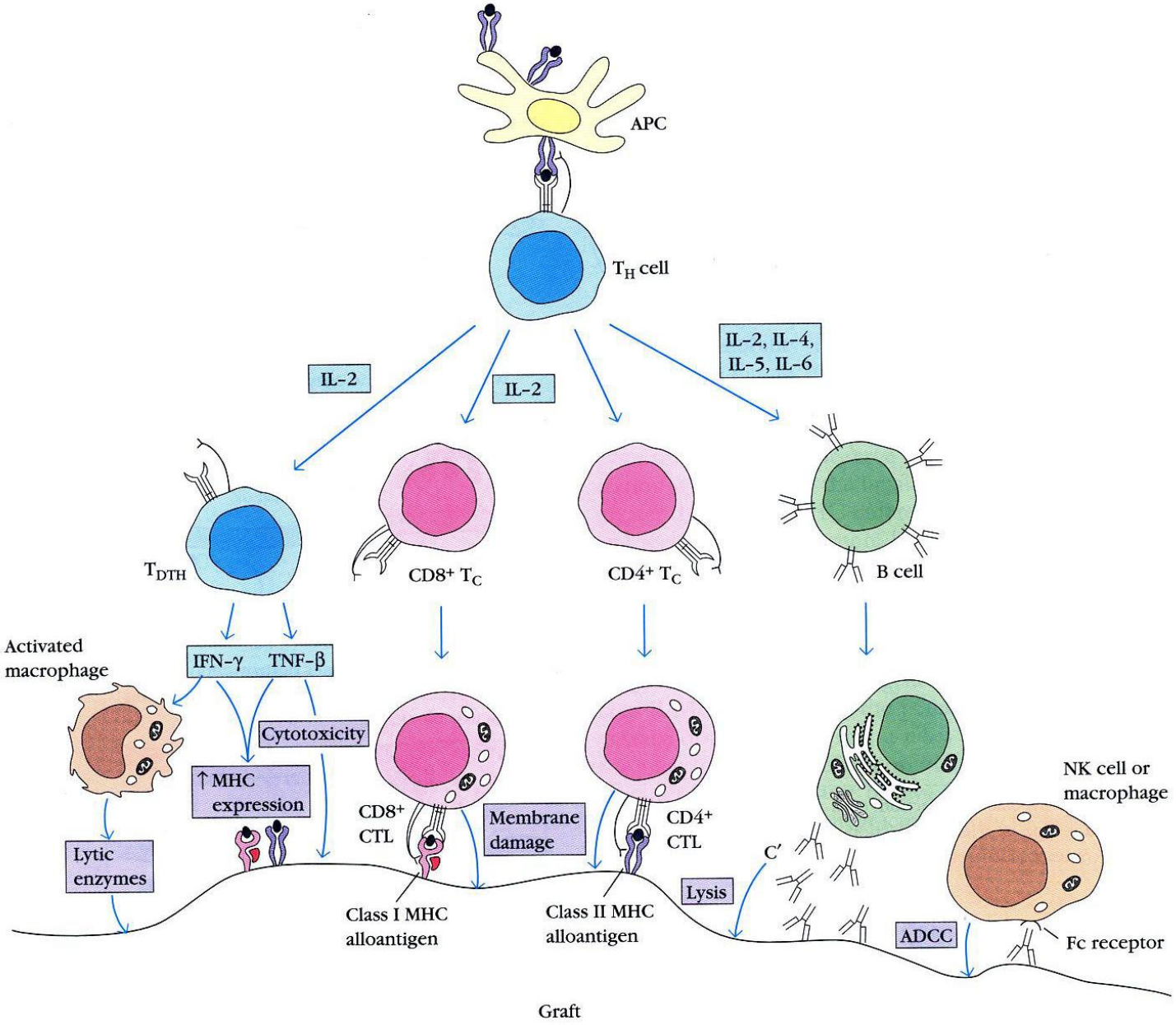


FIGURE 23-5

Effector mechanisms (purple blocks) involved in allograft rejection. The generation or activity of various effector cells depends directly or indirectly on cytokines (blue blocks) secreted by activated T_H cells. C′ = complement; ADCC = antibody-dependent cell-mediated cytotoxicity.

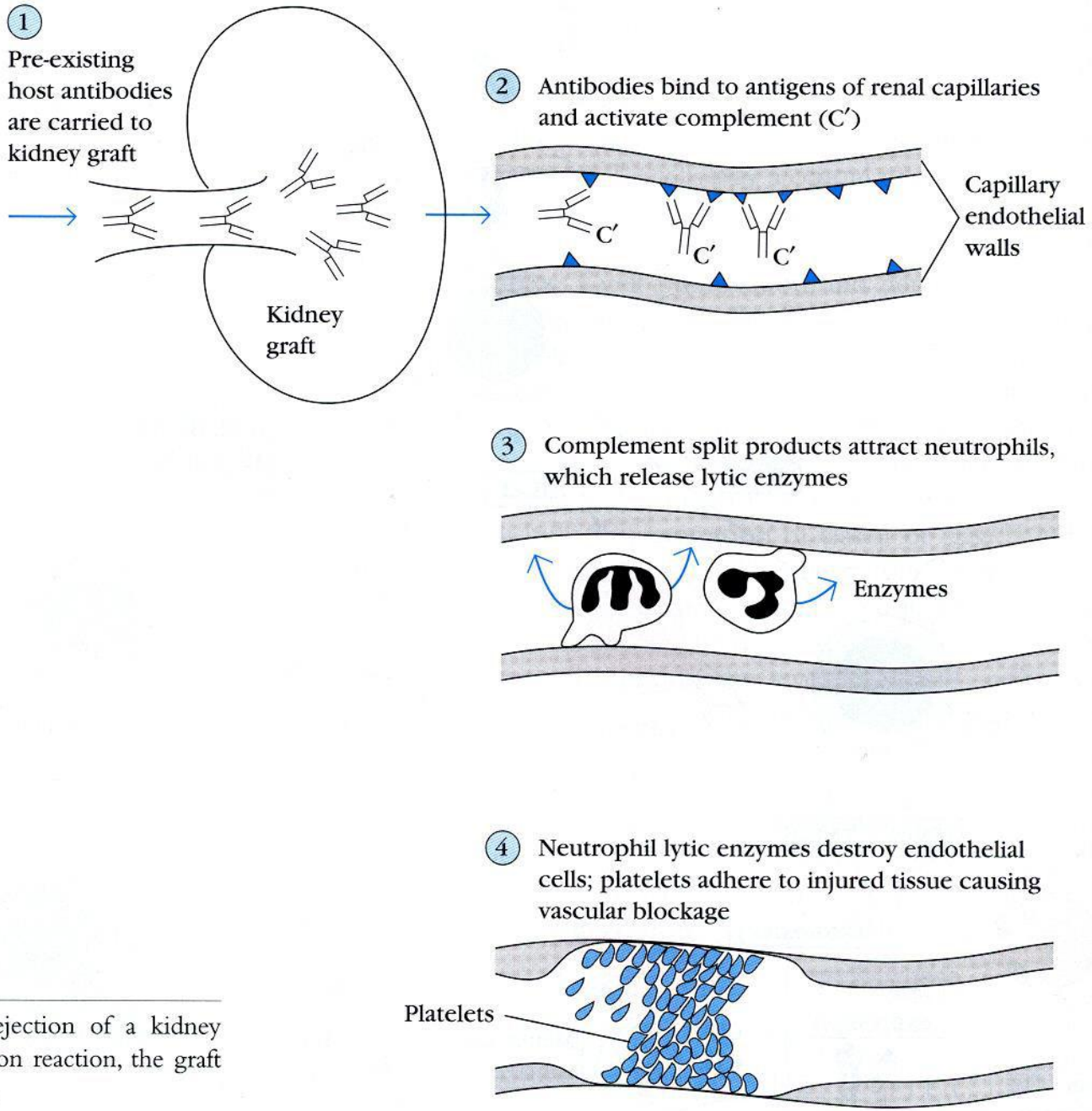
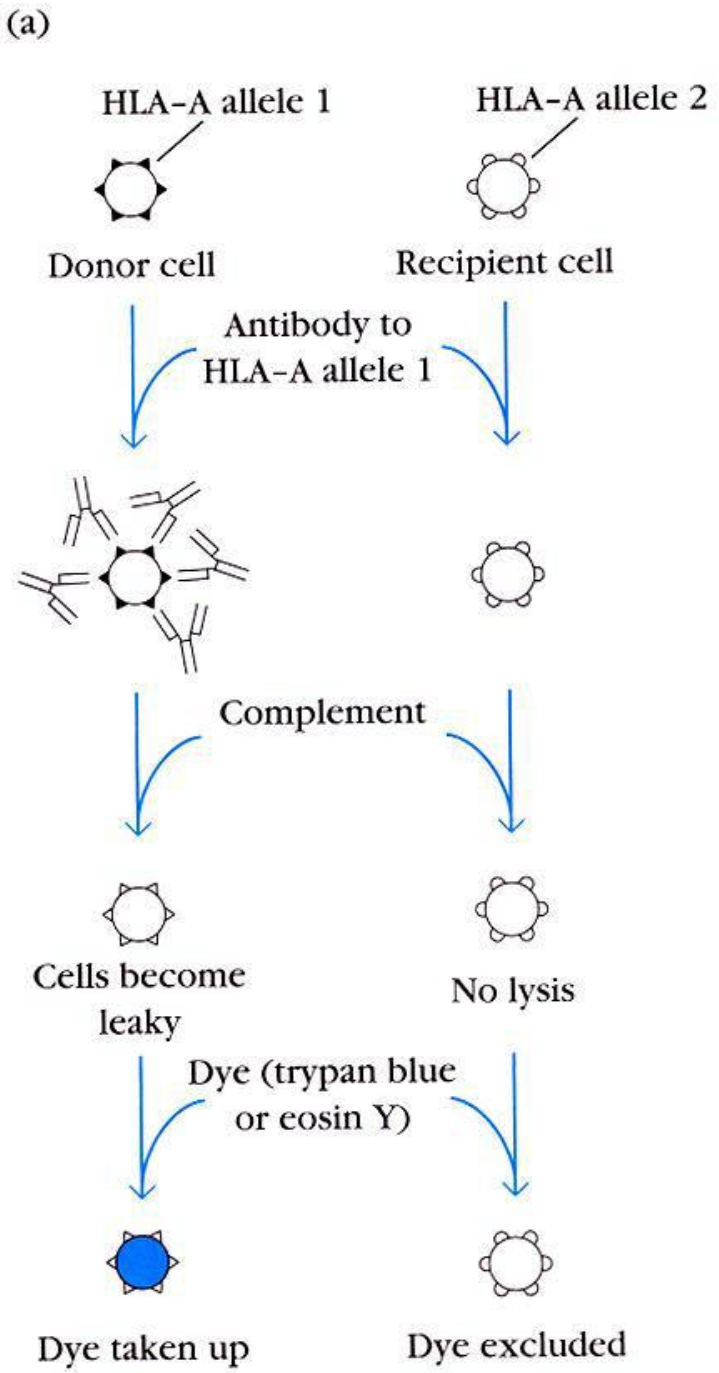


FIGURE 23-6

Steps in the hyperacute rejection of a kidney graft. In this type of rejection reaction, the graft never becomes vascularized.



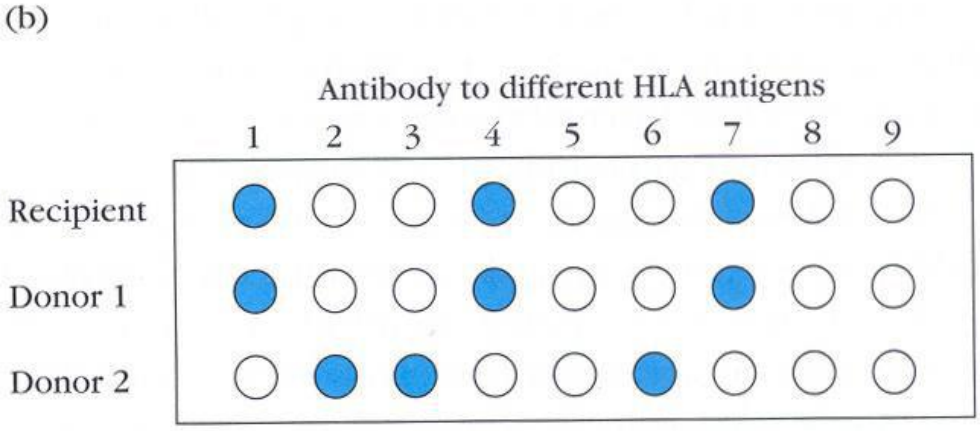


FIGURE 23-7

Microcytotoxicity HLA typing. (a) White blood cells from potential donors and the recipient are added to separate wells of a microtiter plate. The example depicts only one HLA antigen on donor and recipient cells and shows the reaction sequence on addition of antibody to one of these antigens. (b) Because cells express numerous HLA antigens, they are separately tested with a battery of monoclonal antibodies specific for various HLA antigens. Here, donor 1 shares antigens 1, 4, and 7 with the recipient, whereas donor 2 has no antigens in common with the recipient.

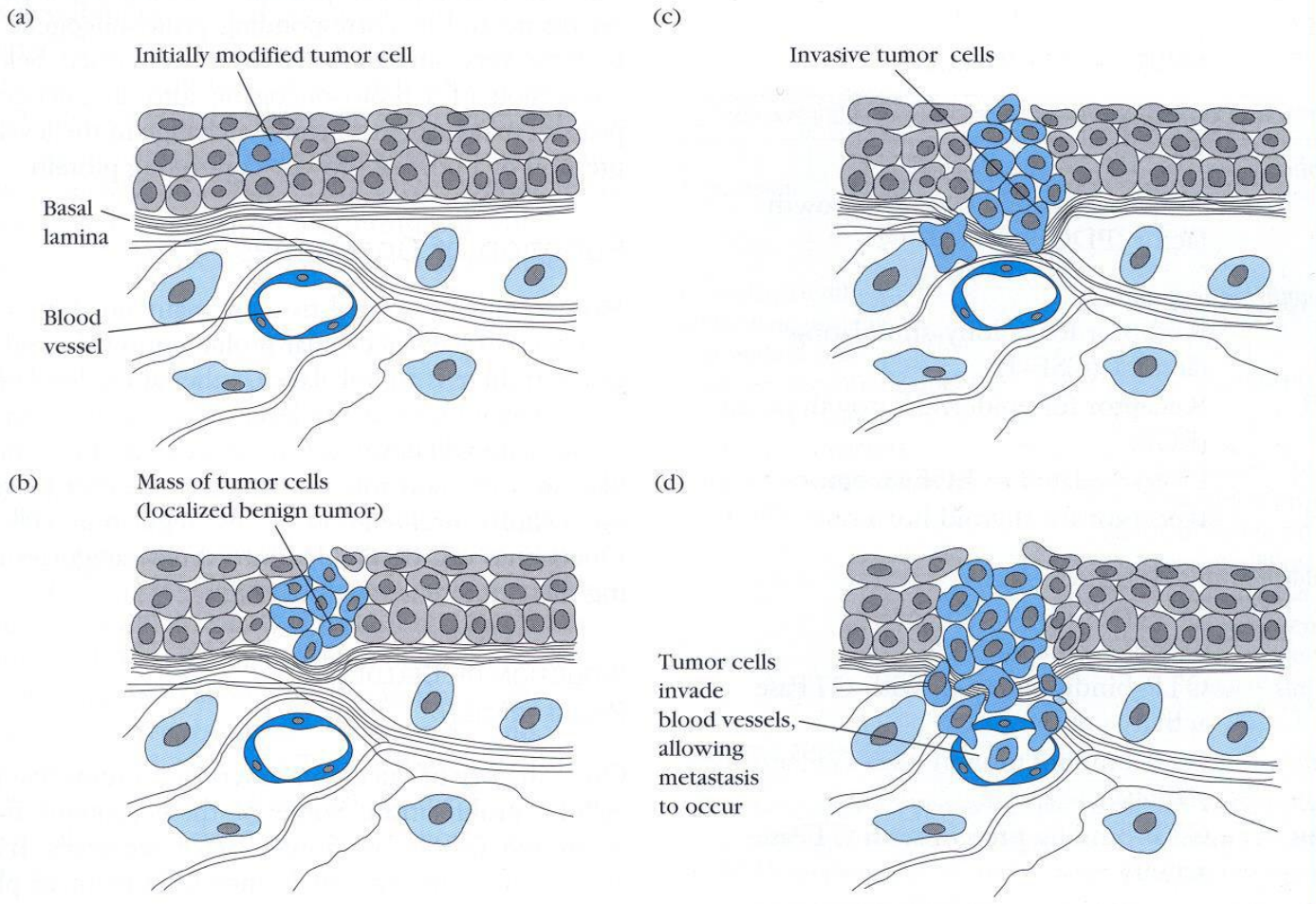


FIGURE 24-1

Tumor growth and metastasis. (a) A single cell develops altered growth properties at a tissue site. (b) The altered cell proliferates, forming a mass of localized tumor cells, or benign tumor. (c) The tumor cells become progressively more invasive, invading the underlying basal lamina. The tumor is now classified as malignant. (d) The malignant tumor metastasizes by generating small clusters of cancer cells that dislodge from the tumor and are carried by the blood or lymph to other sites in the body. [Adapted from J. Darnell et al., 1990, *Molecular Cell Biology,* 2d ed., Scientific American Books.]

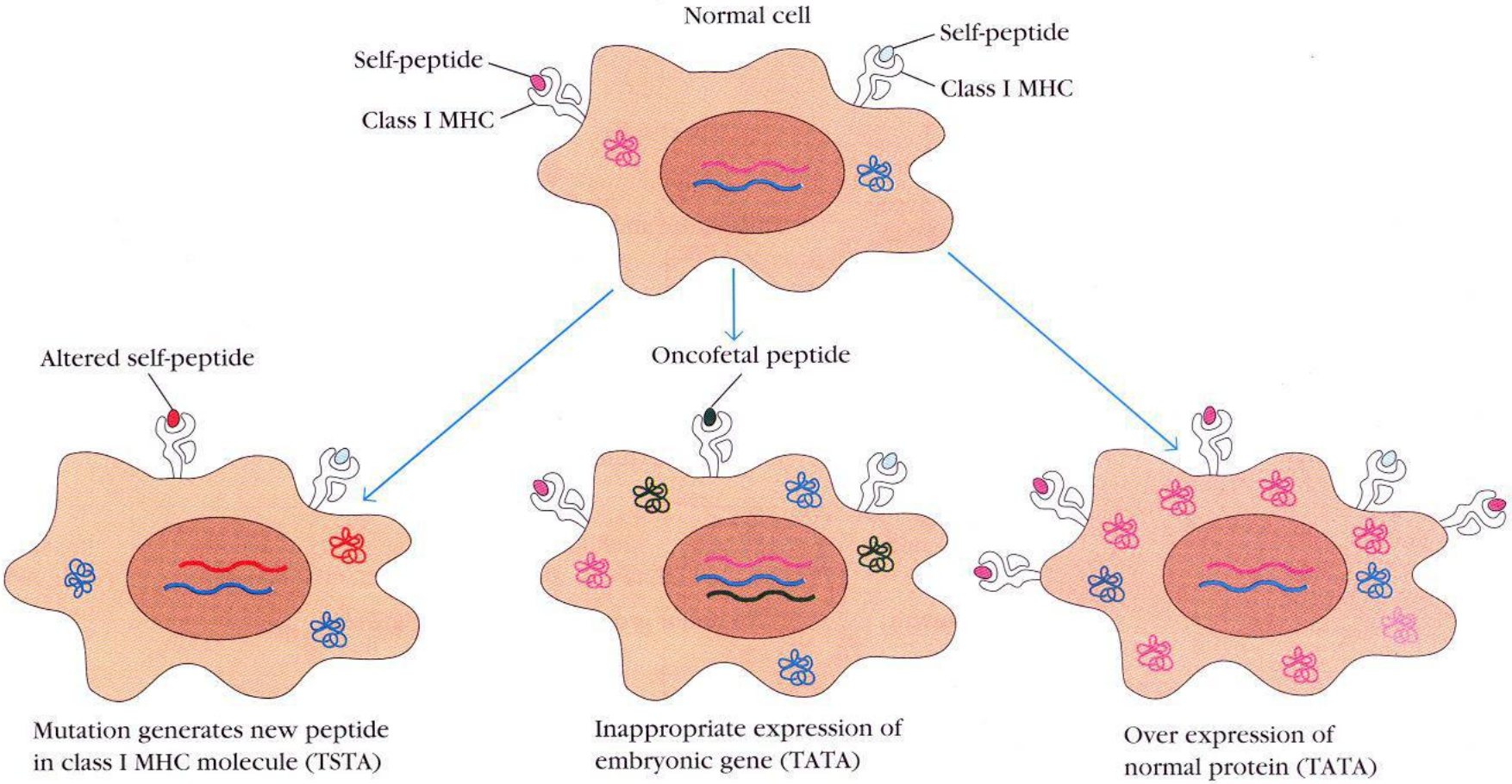


FIGURE 24-6

Different mechanisms generate tumor-specific transplantation antigens (TSTAs) and tumor-associated transplantation antigens (TATAs). The latter are more common.

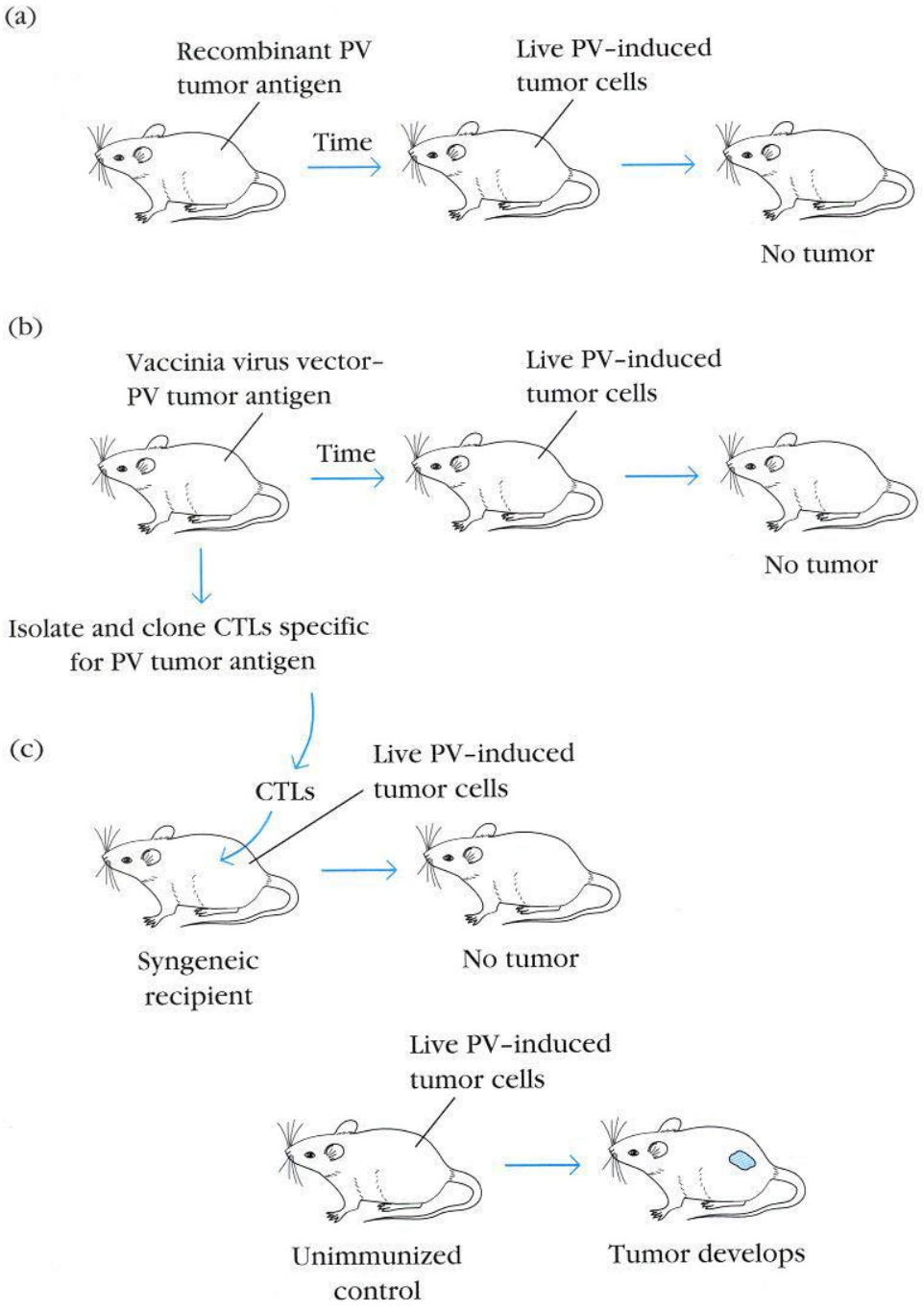


FIGURE 24-9

Experimental induction of immunity against tumor cells induced by polyoma virus (PV) has been achieved by immunizing mice with recombinant polyoma tumor antigen (a), with a vaccinia vector vaccine containing the gene encoding the PV tumor antigen (b), or with CTLs specific for the PV tumor antigen (c). Unimmunized mice (*bottom*) develop tumors when injected with live polyoma-induced tumor cells, whereas the immunized mice do not

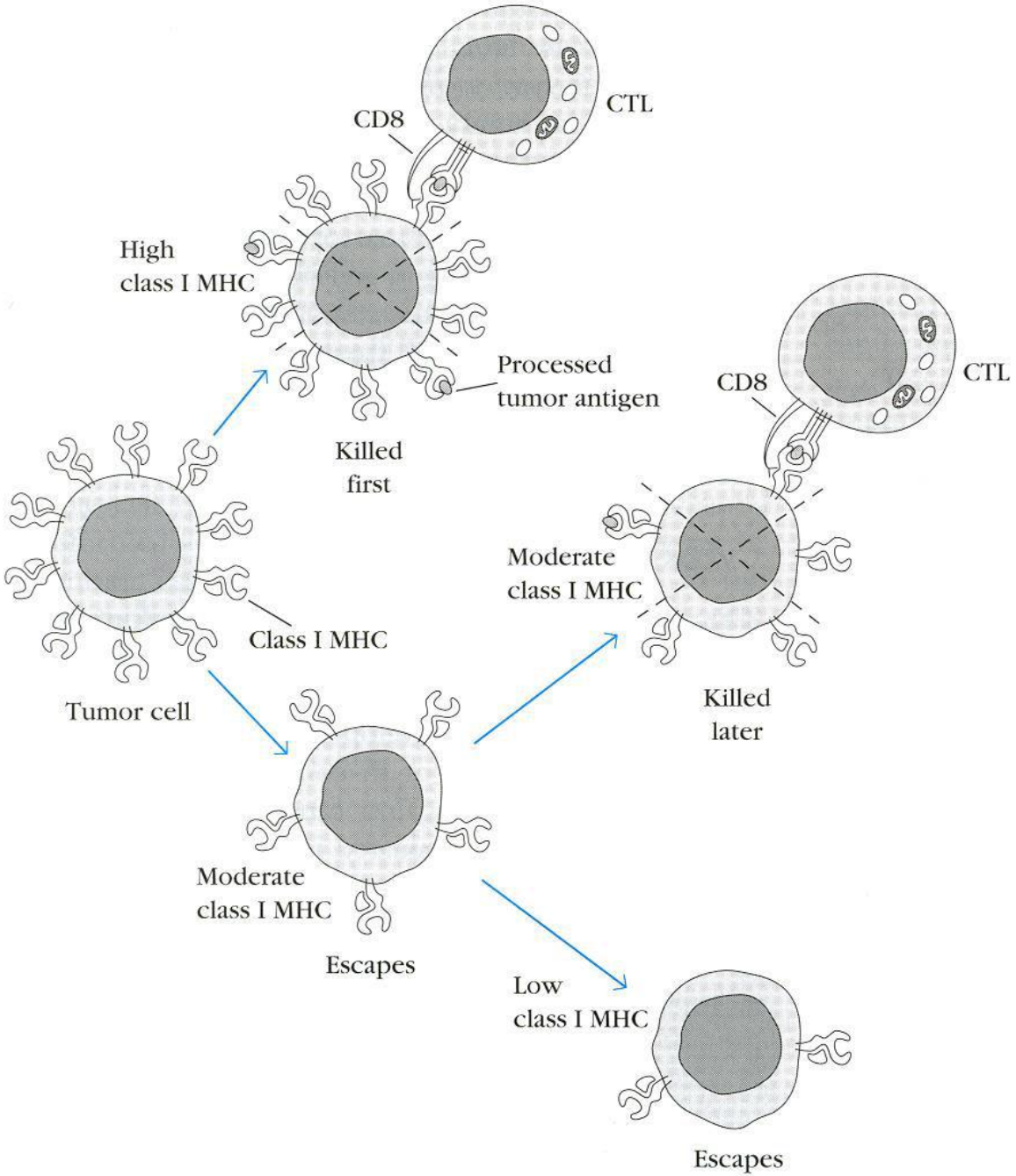


FIGURE 24-10

Down-regulation of class I MHC expression on tumor cells may allow a tumor to escape CTL-mediated recognition. The immune response may play a role in selecting for tumor cells expressing lower levels of class I MHC molecules by preferentially eliminating those cells expressing high levels of class I molecules. With time, malignant tumor cells may express progressively fewer MHC molecules and thus escape CTL-mediated destruction.

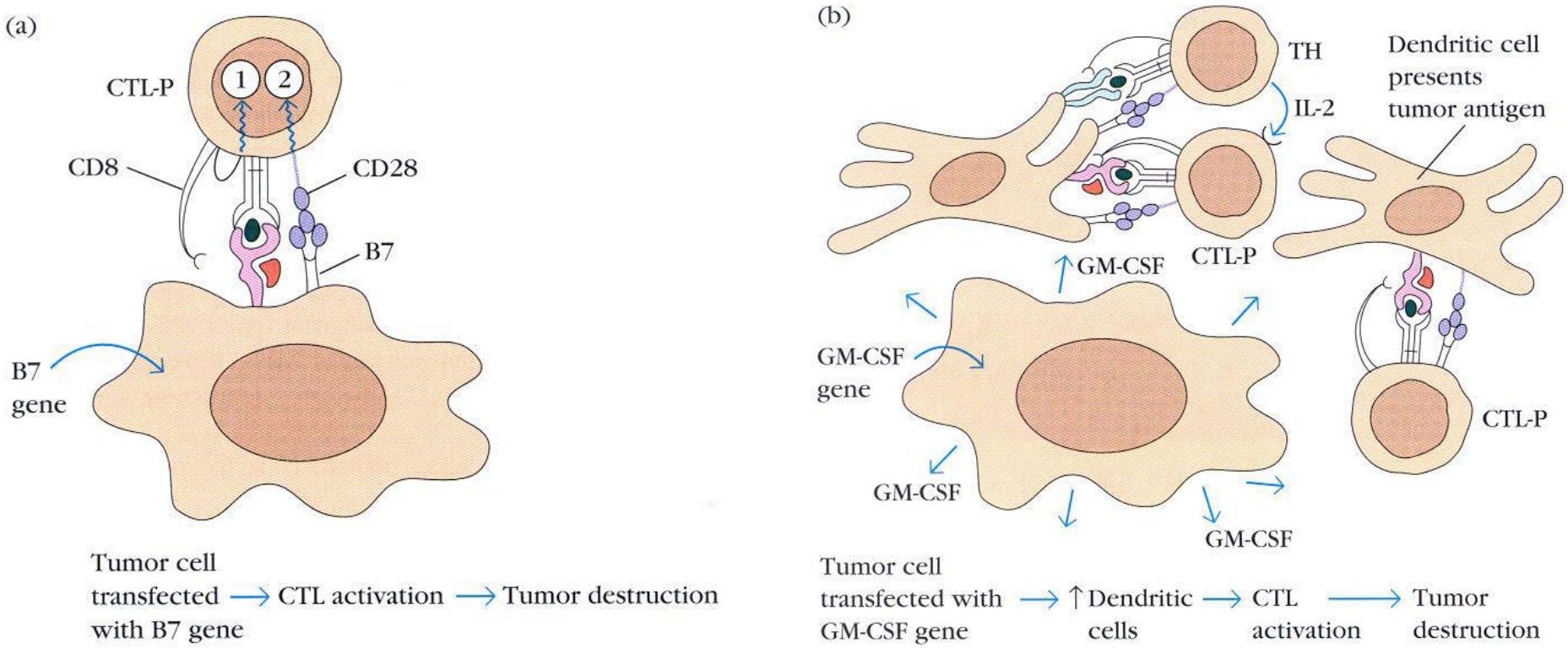


FIGURE 24-11

Use of transfected tumor cells for cancer immunotherapy. (a) Tumor cells transfected with the B7 gene express the co-stimulatory B7 molecule, enabling the tumor cells to provide both activating signal 1 and co-stimulatory signal 2 to CTL-Ps. As a result of the combined signals, the CTL-Ps differentiate into effector CTLs, which can mediate tumor destruction. In effect, the transfected tumor cell acts as an antigen-presenting cell. (b) Transfection of tumor cells with the gene encoding GM-CSF allows the tumor cells to secrete high levels of GM-CSF. This cytokine will activate dendritic cells in the vicinity of the tumor, enabling the dendritic cells to present tumor antigens to both T_H cells and CTL-Ps.

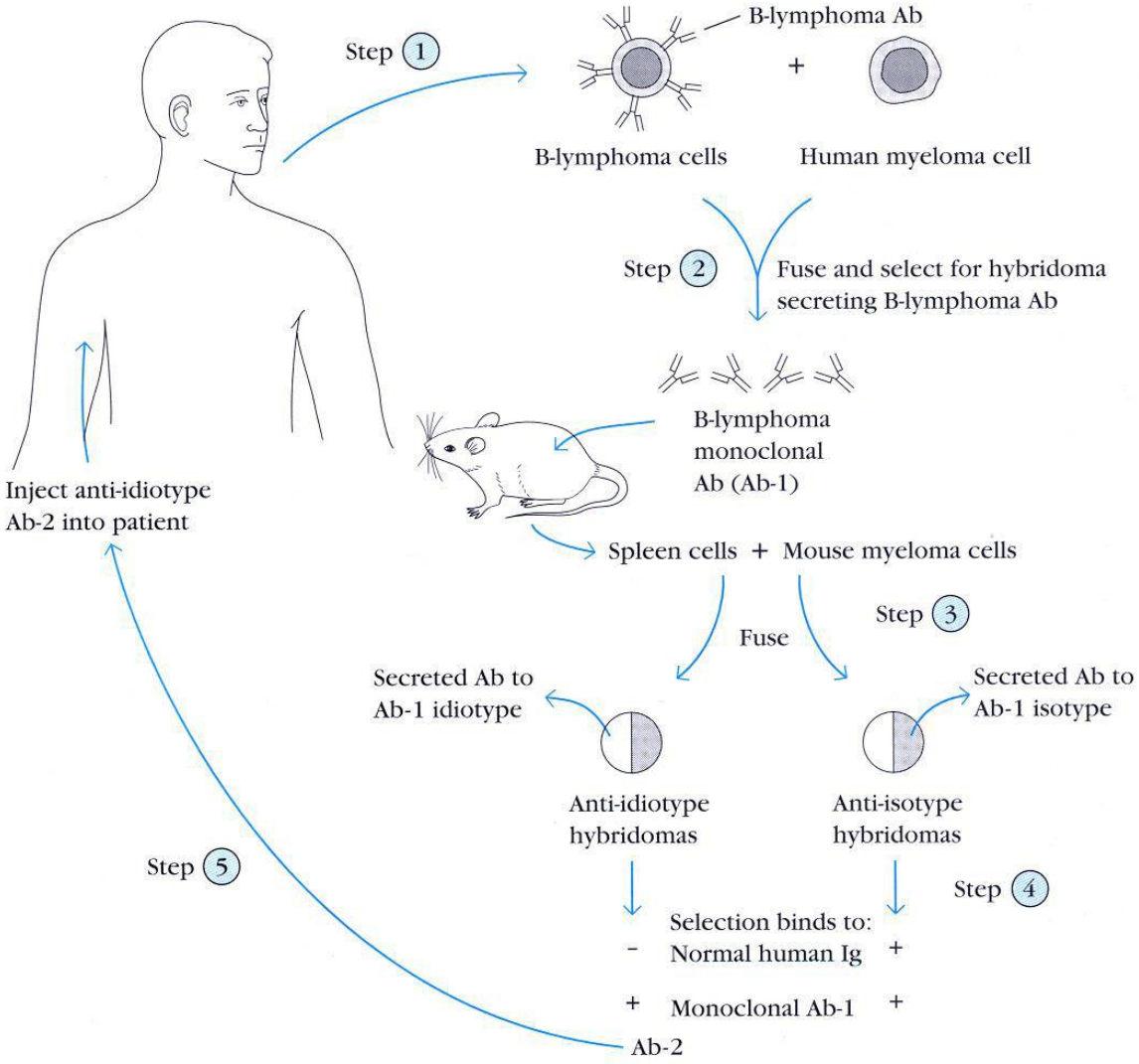


FIGURE 24-14

Treatment of B-cell lymphoma with monoclonal antibody specific for idiotypic determinants on the cancer cells. Because all the lymphoma cells are derived from a single transformed B cell, they all express membrane-bound antibody (Ab-1) with the same idiotype (i.e., the same antigenic specificity). In the procedure illustrated, monoclonal anti-idiotype antibody (Ab-2) against the B-lymphoma membrane-bound antibody was produced (steps 1–4). When this anti-idiotype antibody was injected into the patient (step 5), it bound selectively to B-lymphoma cells, which then were susceptible to complement-plus-antibody lysis.