Table. Dose of Radiation Required to Inactivate 99.9 Percent of Foodborne Pathogens in Meat or Poultry with Electron, Gamma, or X-Ray Ionizing Radiation at 5°C.

Foodborne Pathogen	Dose of Radiation (kGy)
Campylobacter jejuni	0.48–0.60
Escherichia coli O157:H7	0.84–0.96
Listeria monocytogenes	1.26–1.44
Salmonella species	1.98–2.22
Staphylococcus aureus	1.32–1.44

product. Electrons with a maximal energy of 10 MeV penetrate to a depth of only 4.5 cm in water or equivalent, limiting their use to thin packages or to products with very low density; however, the required dose of radiation is delivered extremely quickly. The generation of x-rays is not very efficient, since only 6 to 12 percent of the electron energy is converted to x-rays; the remainder generates heat, which must be removed before the target melts.

The absorption of electrons or of photons produces the same effect, ionization. When a gamma or x-ray photon is absorbed, an electron is released, causing ionization. Water is the principal target for the radiation, because it is the largest component of most foods and microorganisms. Normally, approximately 70 percent of the radiation-induced ionization will occur in cellular water, and the target organisms will be inactivated because of secondary reactions, not because of a direct effect on the bacterial DNA. The same sequence occurs in frozen products, but the ice structure limits the migration of the free radicals that are generated by the ionization; therefore, a higher dose of radiation is required for frozen foods. There is much greater potential to produce adverse sensorial effects in fresh products than in frozen products.

The doses of radiation that are required to inactivate 99.9 percent of a contaminating population of a few important foodborne pathogens in meat and poultry are listed in the Table. The dose required to inactivate 99.9 percent of *Escherichia coli* O157:H7 in ground beef increases from approximately 0.90 kGy at 5°C to 1.35 kGy at −5°C. Food irradiation may offer the only reliable method of controlling foodborne pathogens in ground meat or poultry without cooking. Unfortunately, a high proportion of the poultry we bring into our homes or commercial kitchens remains contaminated with one or more of the pathogens listed in the Table. Cooking will kill most of these pathogens, but the problems associated with the cross-contamination of other foods remain. Some restaurants are now using irradiated poultry to prevent such contamination, and the public would benefit from greater implementation of this method of ensuring the safety of foods.

Dr. Thayer reports having received consulting or lecture fees from CFC Logistics, Master Foods, and Zero Mountain.

From Lower Gwynedd, Pa.

Exchanging Kidneys — Advances in Living-Donor Transplantation

Francis L. Delmonico, M.D.

This year marks the 50th anniversary of the first successful kidney transplantation from a living donor to his identical twin. Over the ensuing five decades, kidney transplantation has progressed from an experimental procedure to a widely accepted treatment for end-stage renal disease. The practice of kidney transplantation has also evolved remarkably, no longer depending on the unpredictable availability of a deceased organ donor; kidney transplantation from living donors has become the predominant approach. The superior outcomes of transplantation from living donors and the advent of laparoscopic nephrectomy (which carries minimal risk for healthy donors) have propelled this change in practice.

Furthermore, kidneys are now routinely transplanted from living donors who are unrelated to their recipients. As a result, spouses, friends, and even anonymous donors who are unknown to their

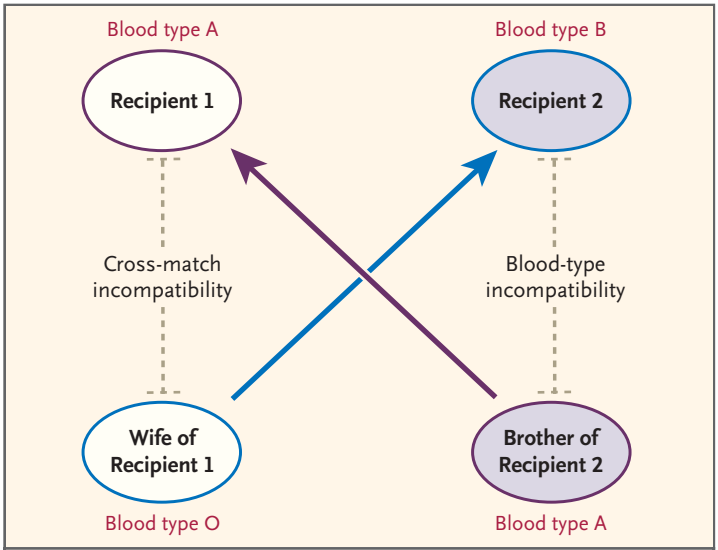

Figure. An Exchange Performed because of a Cross-Match Incompatibility in One Pair and a Blood-Type Incompatibility in the Other.

recipients currently provide nearly 25 percent of the kidneys that are transplanted from living donors.[1] This approach has had great success, with excellent long-term outcomes, irrespective of matching according to human lymphocyte antigen (HLA) type. Transplantations from haploidentical parents or siblings have outcomes similar to those from an HLA-mismatched spouse or friend. For example, the likelihood of five-year survival of a kidney allograft transplanted from a living donor with no DR mismatch is approximately 75 percent — no different from that of a transplant that represents a 1-DR or 2-DR mismatch between the donor and the recipient.[1] Virtually all transplants from unrelated living donors are HLA mismatched, so the degree of HLA disparity is no longer an obstacle to proceeding with transplantation.

However, since the early days of living-donor transplants, incompatibility with respect to ABO blood type or cross-match reactivity has precluded successful kidney transplantation. A cross-match performed between the prospective donor and recipient may reveal antibodies that would result in the accelerated rejection of the allograft. Natural antibodies to the A or B blood type can also cause immediate allograft loss. Until recently, these biologic realities have thwarted the intention of willing kidney donors to provide organs for patients in need of transplantation. Protocols have now been developed to overcome these barriers by using plasma exchange to remove either the isoagglutinin or HLA antibodies.[2] Nevertheless, these conditioning regimens are expensive and are still associated with an unpredictable rate of graft loss that could be averted through other innovative methods of living-donor transplantation. One such approach is living-donor exchange — that is an, exchange involving two donors who are incompatible with their intended recipients so that each donates to a compatible recipient. With donor exchange, the hazards associated with blood-type or cross-match incompatibility can be avoided, while both recipients derive the benefit of kidney transplantation from a living donor.

In several locations around the world, programs of living-donor exchange have been initiated and have proved to be models of altruism, ethical propriety, and good medical care.[3] In Washington, D.C., two women have received kidneys exchanged by their husbands, and in New England, two men have received kidneys exchanged by their wives. A living-donor exchange has even defied political and social constraints. In the Middle East, members of Palestinian and Israeli families participated in a kidney exchange in two regional hospitals. In this exchange, a 45-year-old Arab truck driver received a kidney from a 38-year-old Jewish donor, and the Jewish donor's 10-year-old son received a kidney from the truck driver's wife.

The logistic issues involved in accomplishing a living-donor exchange can be formidable but are clearly surmountable. It has been helpful in a region such as New England to have a system of notification that enlarges the network of participating transplantation centers and patients. The donor and the recipient enter the system as a pair to be considered for living-donor exchange. The patients must give consent to have their identity revealed to an oversight panel of transplantation physicians (the panel in the New England region operates under the auspices of the local organ-procurement organizations — the New England Organ Bank and Life Choice Donor Services). Before information on blood type, age, relationship, cause of renal failure, and geographic location is submitted to the medical directors of the relevant organ-procurement organizations, the donor and recipient must be found to be medically suitable for a transplantation procedure (to which there are no contraindications other than blood-type or cross-match incompatibility). The date when the donor–recipient pair is submitted for consideration is also recorded.

The medical directors of the organ-procurement organizations can determine the ABO compatibility of the exchange pairs and the proximity of their centers and note the date of the listings. Equipoise should be achieved in terms of the medical characteristics of the donors and recipients; therefore, donors and recipients should be aware of the medical characteristics of their exchange partners, even if anonymity is preserved. This revelation should allay any understandable apprehension about whether the two kidney transplantations have similar prospects of success. Nevertheless, each transplantation center should reevaluate the medical information of the other donor and recipient in keeping with its own standards. As with any kidney transplantation from a living donor, both the donor and the recipient must realize that there is no guarantee that the exchange will yield a successful outcome. Finally, these exchange procedures must comply with the National Organ Transplant Act of 1984, which prohibits monetary transfers or transfers of valuable property among donors, recipients, and brokers in sales transactions.

In New England, the two transplantation procedures take place simultaneously by design, even when they are performed in different centers that may be at distant locations. Each donor travels to the recipient's center. When these elements of the procedure are maintained, the risk that one donor will withdraw his or her commitment after the other donor has undergone nephrectomy can be avoided.

Exchange transplants in instances in which there was cross-match incompatibility between recipients and their intended donors have been particularly gratifying. For example, a brother with blood type A who was incompatible with his sibling because of an A-to-B blood-type disparity donated his kidney to a man with blood type A who was sensitized to the HLA antigens of his wife, who had blood type O. The wife simultaneously donated her kidney to the exchange donor's brother (see Figure). A father with blood type A who could not donate his kidney to his daughter, who had blood type B, gave his kidney to a teenager with blood type A, and the teenager's sister provided a kidney for the exchange donor's daughter.

Clearly, we have come a long way since the first living-donor transplantation between twins, which was performed after skin grafts had been exchanged between the prospective donor and the recipient in order to verify their genetic identity. Half a century later, irrespective of genetic relationships, we are no longer impeded by either blood-type or cross-match incompatibility if we transplant kidneys from living donors as part of donor-exchange programs.

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1. Ojo A. The Scientific Registry of Transplant Recipients. (Accessed April 8, 2004, at http://www.ustransplant.org.)
2. Zachary AA, Montgomery RA, Ratner LE, et al. Specific and durable elimination of antibody to donor HLA antigens in renal-transplant patients. Transplantation 2003;76:1519-25.
3. Park K, Moon JI, Kim SI, Kim YS. Exchange donor program in kidney transplantation. Transplantation 1999;67:336-8.

Translating Cancer Genomics into Clinical Oncology

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Clinical medicine is in the midst of a revolution that is being driven by an increasing understanding of the human genome and advances in molecular biotechnology. This revolution promises to transform clinical practice from population-based risk assessment and empirical treatment to a predictive, individualized model based on the molecular classification of disease and targeted therapy. The expectation is, of course, that personalized approaches to clinical care will increase the efficacy of treatment while decreasing its toxicity and cost.

Nowhere is this transformation more apparent than in oncology. Cancer is a complex disease. Our current taxonomy of cancers, which is based mostly on histopathology, includes more than 200 distinct entities arising from diverse types of cells. In addi-