radiation biology on biomedical research: basic and applied investigations in molecular biology, cellular biology, genetics, and the mechanisms involved in the development of cancer.

The continuity and diversity of life forms depend upon the replication (duplication of genetic material), the recombination (the exchange of genetic material to yield genetic diversity), and the repair (the removal of damage resulting from environmental agents or from mistakes in replication) of DNA. When DNA repair mechanisms are functioning normally, cell survival increases while the mutation rate and the probability of cancer or other abnormal changes in tissues resulting from exposure to radiation or a toxic chemical decreases. The discovery of DNA repair, a landmark achievement, was a direct outcome of OHER-supported investigations in radiation biology—in this case, research on the genetic effects of ultraviolet light.

Cell cycle studies using agents such as radioactive thymidine (^{3}H-thymidine) and radioactive iodine (iodine-125) have led to increased understanding of DNA replication, DNA repair, and the genetics and biochemistry of specific phases of the cell life cycle. In addition, many effects of endogenous and exogenous environmental agents on these cellular functions have been determined. Drawing on this research, more rational and scientific uses of chemotherapy for the management of cancer and other proliferative diseases have been formulated and adopted.

The ability to perform many of the procedures in molecular biology now common in laboratories throughout the world clearly resulted from earlier work on radioactive precursors of DNA, as well as from the development of techniques for manipulating, isolating, and analyzing radiation-damaged DNA. Today, these techniques are being put into practical use in genetic engineering for the production of insulin, growth hormones, and other biological materials of great utility to mankind. Another consequence of the early studies of DNA synthesis is the current interest in human genetic diseases associated with defects in the DNA repair mechanism or in the proteins that, along with DNA, form the genetic material of living cells, known as chromatin. Diseases of this type include xeroderma pigmentosa, ataxia telangiectasia, Bloom's syndrome, and Fanconi's anemia.

Knowledge of DNA repair and other cell cycle phenomena arose from attempts to understand radiobiological phenomena. The concepts and methodologies of DNA repair research have now been extended to two other important areas of biological research—the study of the chemical causes of cancer and aging. The connection between the chemical and radiological causes of cancer arises from the important discovery that the modes of repair of chemical damage in DNA of human cells mimic either ultraviolet damage and repair or radiation damage and repair. Hence, DNA repair is a general phenomenon, not one peculiar to radiation. Active repair of DNA in bacterial or mammalian cells treated with potential mutation or cancer-causing substances, mutagens or carcinogens, respectively, is taken as evidence of DNA damage and is the basis for several rapid tests for agents that cause harm or destroy genes. The use of bacteria that lack the ability to repair damage to DNA in such tests, for example, the Ames test, enhances by orders of magnitude their sensitivity for detecting cancer-causing chemicals.

In 1974 researchers at the Brookhaven National Laboratory (BNL) made the intriguing finding that the ability of cultured cells from different mammalian species to carry out the repair of ultraviolet-induced DNA damage increased as the life span of the species increased. Human cells are very good at excision repair; mouse cells are poor. The notion that there is a correlation between aging and DNA repair ability was derived from early experiments at Oak Ridge National Laboratory (ORNL) on the accumulation of single-strand breaks in the DNA of tissues of old mice. This area of new and fruitful research was opened up by OHER support for radiation biology and DNA repair.

Radiation biology has had massive impacts on human medicine since the late 1940's, as discussed in the section entitled "Nuclear Medicine." We can get a glimpse of its significance in another important area of medicine from two summaries on the use of bone marrow transplantation in contemporary medical treatment. Bone marrow transplants were first used as a treatment for radiation-induced damage to blood-forming cells in bone marrow. R. A. Good writing in *The New England Journal of Medicine* in 1982 said, "Indeed more than 20 previously fatal diseases can now be successfully treated with bone marrow transplantation. These disorders range from genetically determined severe combined immunodeficiency diseases to acute leukemias." Similarly, E. Beutler of *The Journal of the American Medical Association* in 1981 pointed out, "Until recently, our mind-set was that leukemia was not curable." In selected leukemia patients and under appropriate circumstances,

> *the vast majority (well over 90%) survive the transplantation procedure, and the extent of morbidity does not differ greatly from that associated with ordinary induction chemotherapy. Despite the occurrence of graft-vs-host disease and occasional relapses, the overall cure rate of this selected group of patients seems to be between 70% and 80%.*

Epidemiology of Radiation Exposure Quantitative data have been produced from epidemiologic studies of the genetic (on the germ or reproductive cells) and somatic (on the body as a whole or on cells other than germ or reproductive cells) effects observed in humans exposed to radiation. These data allow the establishment of upper-bound estimates of the genetic risk and numerical estimates of the somatic risk of such exposures.